

# Package ‘CellNOptR’

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**Type** Package

**Title** Training of boolean logic models of signalling networks using prior knowledge networks and perturbation data.

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**Author** T.Cokelaer, F.Eduati, A.MacNamara, S.Schrier, C.Terfve

**Maintainer** T.Cokelaer <cokelaer@ebi.ac.uk>

**Depends** R (>= 2.15.0), RBGL, graph, methods

**Suggests** Rgraphviz,RUnit, BiocGenerics

**Enhances** Rgraphviz

**biocViews** CellBasedAssays, CellBiology, Proteomics, Bioinformatics,TimeCourse

## Description

This package does optimisation of boolean logic networks of signalling pathways based on a previous knowledge network and a set of data upon perturbation of the nodes in the network.

**License** GPL-2

**LazyLoad** yes

**SystemRequirements** Graphviz version >= 2.2

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CellNOptR-package	<i>R version of CellNOptR, boolean features</i>
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## Description

This package does optimisation of boolean logic networks of signalling pathways based on a previous knowledge network and a set of data collected upon perturbation of some of the nodes in the network.

## Details

Package:	CellNOptR
Type:	Package
Version:	1.3.33
Date:	2012-09-20
License:	GPLv2
LazyLoad:	yes

## Author(s)

T. Cokelaer, A. MacNamara, F. Eduati, S. Schrier, C. Terfve  
Maintainer: T. Cokelaer <cokelaer@ebi.ac.uk>

## References

J. Saez-Rodriguez, L. G. Alexopoulos, J. Epperlein, R. Samaga, D. A. Lauffenburger, S. Klamt and P. K. Sorger. Discrete logic modeling as a means to link protein signaling networks with functional analysis of mammalian signal transduction, *Molecular Systems Biology*, 5:331, 2009.

## Examples

```
library(CellNOptR)

# quick 1 time point optimisation of a Prior Knowledge Network to MIDAS data.
data(CNOlistToy,package="CellNOptR")
data(ToyModel,package="CellNOptR")
model = preprocessing(CNOlistToy, ToyModel)
results = gaBinaryT1(CNOlistToy, model, verbose=FALSE)
plotFit(results)
cutAndPlot(CNOlistToy, model, list(results$bString))

# Same as above and HTML report
CNORwrap(name="Toy",
  namesData=list(CNOlist="ToyData",model="ToyModel"),
  data=CNOlistToy, model=ToyModel)
```

---

`checkSignals`*Check the CNOList and model matching*

---

### Description

This function checks that all the signals in a CNOList match to species in the model. It also checks that the CNOList and Model lists have the right format and contain the right fields. It is called by the [preprocessing](#) function so there is no need to call it directly anymore if you use the [preprocessing](#) function.

In version 1.3.20, check of inhibitors and stimuli is also performed.

### Usage

```
checkSignals(CNOList, model)
```

### Arguments

CNOList	A CNOList structure, as created by <a href="#">makeCNOList</a> .
model	A model structure, as created by <a href="#">readSIF</a> .

### Details

If the formats are wrong, this function produces an error. If the signals/inhibitors/stimuli do not match the species, this function produces a warning that explains which signals does no match any species.

### Author(s)

C. Terfve, T. Cokelaer

### See Also

[makeCNOList](#), [readSIF](#), [preprocessing](#)

### Examples

```
data(CNOListToy, package="CellNOptR")
data(ToyModel, package="CellNOptR")
checkSignals(CNOListToy, ToyModel)
```

---

CNOList-class	Class "CNOList"
---------------	-----------------

---

### Description

This function takes as input the filename of a MIDAS file (or the list returned by [makeCNOList](#)) and returns an instance of CNOList class. It provides an object oriented approach to manipulate CNOList. This function calls [readMIDAS](#) and [makeCNOList](#).

### Objects from the Class

Objects can be created by calls of the form `new("CNOList", ...)`.

### Slots

**cues:** Object of class "matrix"

**inhibitors:** Object of class "matrix"

**stimuli:** Object of class "matrix"

**signals:** Object of class "list"

**timepoints:** Object of class "vector" timepoints contained in the signals matrix.

### Methods

**show** signature(object="CNOList"): ...

**plot** signature(x="CNOList"): Please see the help page for the `plot.CNOList` method in the CellNOptR package

### Author(s)

T.Cokelaer

### See Also

[readMIDAS](#), [makeCNOList](#)

### Examples

```
showClass("CNOList")
```

```
files<-dir(system.file("ToyModel",package="CellNOptR"),full=TRUE)
```

```
cnolist = CNOList(files[[1]])
```

```
# accessors:
```

```
cnolist@cues
```

```
cnolist@inhibitors
```

```
cnolist@signals
```

```
cnolist@timepoints
```

```
cnolist@stimuli
```

```
# In version 1.3.30 and above, use the plot method instead of former plotCNOList function.
```

```
plot(cnolist)
```

CNOListDREAM

*Data used for the DREAM3 challenge*

---

**Description**

This data object contains the DREAM data used in the package vignette, already loaded and formatted as a CNOList object. This is to be used with the model "DreamModel". This is a data collected on HepG2 cells cultivated with or without stimulation of tgfa, ilk, mek12, pi3k and p38, in combination with inhibition of igf1 and/or il1a. Seven phosphoproteins are measured using Luminex xMAP assays: akt, erk12, ikb, jnk12, p38, hsp27 and mek12.

**Usage**

CNOListDREAM

**Format**

CNOListDREAM is a list with the fields "namesCues" (character vector), "namesStimuli" (character vector), "namesInhibitors" (character vector), "namesSignals" (character vector), "timeSignals" (numerical vector), "valueCues" (numerical matrix), "valueInhibitors" (numerical matrix), "valueStimuli" (numerical matrix), "valueSignals" (numerical matrix).

**Source**

This data and model is extracted from the Matlab version of CellNOpt1.0 (<http://www.ebi.ac.uk/saezrodriguez/software.html#CellNetOptimizer>).

**References**

1. J. Saez-Rodriguez, L. G. Alexopoulos, J. Epperlein, R. Samaga, D. A. Lauffenburger, S. Klamt and P. K. Sorger. Discrete logic modeling as a means to link protein signaling networks with functional analysis of mammalian signal transduction, *Molecular Systems Biology*, 5:331, 2009.
2. Prill RJ, Marbach D, Saez-Rodriguez J, Sorger PK, Alexopoulos LG, Xue X, Clarke ND, Altan-Bonnet G, and Stolovitzky G. Towards a rigorous assessment of systems biology models: the DREAM3 challenges. *PLoS One*, 5(2):e9202, 2010.

---

CNOListToy*Toy data*

---

**Description**

This data object contains the data associated with the Toy Model example from the package vignette, already loaded and formatted as a CNOList object.

**Usage**

CNOListToy

**Format**

CNOListToy is a list with the fields "namesCues" (character vector), "namesStimuli" (character vector), "namesInhibitors" (character vector), "namesSignals" (character vector), "timeSignals" (numerical vector), "valueCues" (numerical matrix), "valueInhibitors" (numerical matrix), "valueStimuli"(numerical matrix), "valueSignals"(numerical matrix).

**Source**

This data and model is extracted from the Matlab version of CellNOpt1.0 (<http://www.ebi.ac.uk/saezrodriguez/software.html#CellNetOptimizer>).

**References**

J. Saez-Rodriguez, L. G. Alexopoulos, J. Epperlein, R. Samaga, D. A. Lauffenburger, S. Klamt and P. K. Sorger. Discrete logic modeling as a means to link protein signaling networks with functional analysis of mammalian signal transduction, *Molecular Systems Biology*, 5:331, 2009.

---

CNOListToy2

*Toy data with 2 time points*

---

**Description**

This data object contains the data associated with the Toy Model example from the package vignette, already loaded and formatted as a CNOList object, and modified to contain 2 time points. The second time point is such a way that all of the signals stay as in time 1, except for cJun and Jnk which go to zero.

**Usage**

CNOListToy

**Format**

CNOListToy is a list with the fields "namesCues" (character vector), "namesStimuli" (character vector), "namesInhibitors" (character vector), "namesSignals" (character vector), "timeSignals" (numerical vector), "valueCues" (numerical matrix), "valueInhibitors" (numerical matrix), "valueStimuli"(numerical matrix), "valueSignals"(numerical matrix).

**Source**

This data and model is extracted from the Matlab version of CellNOpt1.0 (<http://www.ebi.ac.uk/saezrodriguez/software.html#CellNetOptimizer>).

**References**

J. Saez-Rodriguez, L. G. Alexopoulos, J. Epperlein, R. Samaga, D. A. Lauffenburger, S. Klamt and P. K. Sorger. Discrete logic modeling as a means to link protein signaling networks with functional analysis of mammalian signal transduction, *Molecular Systems Biology*, 5:331, 2009.

---

CNORbool

*Simple Boolean analysis standalone*

---

### Description

This function performs the optimisation of a PKN model to a CNOList data set. It optimises each time point found in the data and returns the processed model as well as a list of optimised bitstring corresponding to each time points that has been optimised.

This function does not create any plots or reports.

### Usage

```
CNORbool(CNOList, model, paramsList=defaultParameters(),
         compression=TRUE, expansion=TRUE, cutNONC=TRUE, verbose=FALSE)
```

### Arguments

CNOList	a CNOList structure, as created by <a href="#">makeCNOList</a> or a MIDAS filename
model	a model structure, as created by <a href="#">readSIF</a> or a SIF filename.
paramsList	Parameters of the genetic algorithm. If not provided, it is populated with the <a href="#">defaultParameters</a> function.
compression	compress the model (default TRUE)
expansion	expand the gates (default TRUE)
cutNONC	cut the NONC nodes off the model by (default TRUE)
verbose	FALSE

### Value

This function returns 2 components. The first one is the processed model used in the optimisation. The second is a list of optimised bitstrings found for each time points available in the MIDAS data set.

### Author(s)

T.Cokelaer, S.Schrier

### Examples

```
data(CNOListToy,package="CellNOptR")
data(ToyModel,package="CellNOptR")
res = CNORbool(CNOList=CNOListToy, model=ToyModel)
```



**Description**

This function is a wrapper around the whole CNOR analysis, it performs the following steps:

1. Plot the CNOlist;
2. Checks data to model compatibility;
3. Call the preprocessing function (Cut the nonc off the model, compress the model and expand the gates);
4. Compute the residual error;
5. Prepare for simulation;
6. Optimisation T1 and T2 (optional);
7. Plot simulated and experimental results;
8. Plot the evolution of fit;
9. Write the scaffold and PKN;
10. Write the report

**Usage**

CNORwrap(paramsList=NA, data=NA, model=NA, name, namesData=NA, time=1, compression=TRUE, expansion=TRUE, cutNONC=TRUE)

**Arguments**

paramsList      A list of parameters related to the Genetic Algorithm parameters:

1. sizeFac: default to 1e-04;
2. NAFac: default to 1;popSize: default to 50;
3. pMutation: default to 0.5;
4. maxTime: default to 60;
5. maxGens: default to 500;
6. stallGenMax: default to 100;
7. selPress: default to 1.2;
8. elitism: default to 5;
9. relTol: default to 0.1;
10. verbose: default to FALSE (default to true in the functions used by CNOR-wrap but CNORwrap sets them to false by default).

and the Data and Model structure.

If paramsList is not provided (NA), it is filled internally with the [defaultParameters](#) function.

If Data and Model are not provided in paramList, the function looks for Data and Model arguments.

If Data and Model are provided, the function overwrites the field data and model in paramsList.

data	a CNOList structure, as created by <a href="#">makeCNOList</a>
model	a model structure, as created by <a href="#">readSIF</a> .
name	a string that will be used to name the project and all graphs produced
namesData	a list with two elements:CNOList and Model, each containing a string that is a reference for the user to know which model/data set was used (it will be included in the report). If not provided, the list is built automatically using the name arguments.
time	either 1 or 2: Do you want to perform a one time point steady state optimisation or a 2 time points pseudo steady state optimisation. By default this is set to 1.
compression	compress the model (default TRUE)
expansion	expand the gates (default TRUE)
cutNONC	cut the NONC nodes off the model by (default TRUE)

### Details

If you do not provide a parameters list, you can provide only essential elements, and all other parameters will be set to their default values. In this case, you should set `paramsList=NA`, and provide the following fields: `data`, `model`, `name`, `time`.

### Value

This function does not return anything, it does the analysis, produces all the plots and puts them in a folder that is in your working directory, and is called "Name".

### Author(s)

C. Terfve

### Examples

```
#version with paramslist

tmpdir<-tempdir()
setwd(tmpdir)

data(CNOListToy,package="CellNOptR")
data(ToyModel,package="CellNOptR")

pList = defaultParameters(CNOListToy, ToyModel)
pList$maxGens = 5
pList$popSize = 5

CNORwrap(paramsList=pList, name="Toy",
          namesData=list(CNOList="ToyData", model="ToyModel"))

## Not run:
#version with default parameters

data(CNOListToy,package="CellNOptR")
data(ToyModel,package="CellNOptR")

CNORwrap(name="Toy",
          namesData=list(CNOList="ToyData",model="ToyModel"),
```

```
data=CNOListToy, model=ToyModel)
## End(Not run)
```

---

compressModel	<i>Compress a model</i>
---------------	-------------------------

---

### Description

This function compresses a model by compressing species that are not signals/inhibited/stimulated and that are not dead ends/in complex logic (i.e. only species with either one input or one output are compressed)/in self loops.

You can also use [preprocessing](#) function instead that calls [compressModel](#) and other preprocessing functions.

### Usage

```
compressModel(model, indexes)
```

### Arguments

model	a model structure as produced by <a href="#">readSIF</a> .
indexes	list of indexes of the species stimulated/inhibited/measured in the model, as created by <a href="#">indexFinder</a> .

### Details

Be aware that in the multiple inputs/one output case, if one of the outputs is an '&' gate this function handles it fine as long as it is an '&' with 2 inputs and no more.

### Value

a compressed model list, with an additional field called 'speciesCompressed' that contains the names of the species that have been compressed

### Note

No need to call this function directly since version 0.99.24. Use [preprocessing](#) instead.

### Author(s)

C. Terfve

### See Also

[indexFinder](#), [readSIF](#), [preprocessing](#)

**Examples**

```
#load data

data(CNolistToy,package="CellNOptR")
data(ToyModel,package="CellNOptR")

indicesToy<-indexFinder(CNolistToy,ToyModel,verbose=FALSE)
toyComp<-compressModel(ToyModel,indicesToy)
```

---

computeScoreT1	<i>Compute the score of a model/data set using a bitString to cut the model.</i>
----------------	--

---

**Description**

The bitString made of 0 and 1 allows to select a submodel from the model provided. Then, the simulator function are called to compute the objective function. The sizeFac and NAFac are penalties added to the final score as described in gaBinaryT1. The indexList and simList arguments can be provided to speed up the code otherwise, they are recomputed from the CNolist and model.

**Usage**

```
computeScoreT1(CNolist, model, bString, simList=NULL, indexList=NULL, sizeFac=0.0001, NAFac=1)
```

**Arguments**

CNolist	a CNolist structure, as created by makeCNolist.
model	a model structure, as created by codereadSIF, normally pre-processed but that is not a requirement of this function.
bString	a bitstring of the same size as the number of reactions in the model above
simList	If provided, simList should be created by prep4sim, that has also already been cut to contain only the reactions to be evaluated.
indexList	If provided, indexList should contain a list of indexes of the species stimulated/inhibited/measured in the model, as created by indexFinder.
sizeFac	the scaling factor for the size term in the objective function, default to 0.0001
NAFac	the scaling factor for the NA term in the objective function, default to 1

**Value**

score	See gaBinaryT1 for details
-------	----------------------------

**Author(s)**

T. Cokelaer

**Examples**

```
data(CNolistToy,package="CellNOptR")
data(ToyModel,package="CellNOptR")
model <- preprocessing(CNolistToy,ToyModel)
score = computeScoreT1(CNolistToy, model, bString=rep(1,16))
```

---

computeScoreTN	<i>Compute the score at TN of a model/data set using a bitString to cut the model.</i>
----------------	--

---

### Description

The bitString made of 0 and 1 allows to select a submodel from the model provided. Then, the simulator function are called to compute the objective function. The sizeFac and NAFac are penalties added to the final score as described in gaBinaryTN.

### Usage

```
computeScoreTN(CNolist, model, simList=NULL, indexList=NULL, simResPrev=NULL,
  bStringPrev=NULL, bStringNext=NULL, timeIndex=NULL, sizeFac=0.0001, NAFac=1, bStrings=NULL)
```

### Arguments

CNolist	a CNolist structure, as created by makeCNolist.
model	a model structure, as created by codereadSIF, normally pre-processed but that is not a requirement of this function.
simList	a simList as created by prep4sim, that has also already been cut to contain only the reactions to be evaluated. If not provided, it is recomputed automatically.
indexList	a list of indexes of the species stimulated/inhibited/measured in the model, as created by indexFinder. If not provided ,it is recomputed automatically.
simResPrev	Results of Previous simulation at time TN-1 step.
bStringPrev	the best bitString at time TN-1
bStringNext	the bitString to use to compute the score at time TN
timeIndex	Future feature will allows timeIndex to provide the exact list of indices to cut and plot. For now, it is based on the bitStrings provided.
sizeFac	the scaling factor for the size term in the objective function, default to 0.0001
NAFac	the scaling factor for the NA term in the objective function, default to 1
bStrings	list of optimised bitstrings found at the previous time points

### Value

score	See gaBinaryTN for details
-------	----------------------------

### Author(s)

T. Cokelaer, S.Schrier

### Examples

```
data(CNolistToy2,package="CellNOptR")
data(ToyModel2,package="CellNOptR")
model <- preprocessing(CNolistToy2, ToyModel2)
bStringT1 = c(0,0,1,1,1,1,1,1,0,0,1,1,1,1,1)
simT1<-simulateTN(CNolist=CNolistToy2, model=model, bStrings=list(bStringT1))

score1 = computeScoreTN(CNolistToy2, model, bStrings=list(bStringT1,c(1,0,1,0)))
```

---

cSimulator

*C-implementation of simulatorT1.*


---

### Description

This is the simulator, inspired from BoolSimEngMKM in the Matlab CellNOpt, to be used on one time point simulations. Use the R interface provided by [simulatorT1](#).

### Usage

```
cSimulator(CNOList, model, simList, indexList)
```

### Arguments

CNOList	a CNOList
model	a model that only contains the reactions to be evaluated
simList	a simList as created by prep4sim, that has also already been cut to contain only the reactions to be evaluated
indexList	an indexList as created by indexFinder

### Details

Differences from the BoolSimEngMKM simulator include: the valueInhibitors has not been previously flipped; the function outputs the values across all conditions for all species in the model, instead of only for the signal species. This is because then the output of this function can be used as initial values for the version of the simulator that works on time point 2 (not implemented in this version).

If you would like to compute the output of a model that contains some of the gates in the model but not all, we suggest that you use the function SimulateT1 and specify in the bStringT1 argument which gates you want to be included. Indeed, SimulateT1 is a wrapper around simulatorT1 that takes care of cutting the model for you before simulating it.

### Value

This function outputs a single matrix of format similar to valueSignals in the CNOList but that contains an output for each species in the model. This matrix is the simulated equivalent of valueSignals at time 1, if you consider only the columns given by indexSignals.

### Author(s)

A. MacNamara based on former simulatorT1 version from C.Terfve.

### References

1. J. Saez-Rodriguez, L. G. Alexopoulos, J. Epperlein, R. Samaga, D. A. Lauffenburger, S. Klamt and P. K. Sorger. Discrete logic modeling as a means to link protein signaling networks with functional analysis of mammalian signal transduction, *Molecular Systems Biology*, 5:331, 2009.
2. M. K. Morris, J. Saez-Rodriguez, D. Clarke, P. K. Sorger, D. A. Lauffenburger. Training Signaling Pathway Maps to Biochemical Data with Constrained Fuzzy Logic: Quantitative Analysis of Liver Cell Responses to Inflammatory Stimuli, *PLoS Comp. Biol.*, 7(3): e1001099, 2011.

**See Also**

[simulatorT1](#).

---

cutAndPlot

*Interface to cutAndPlotResults functions.*

---

**Description**

This function takes a model and cnolist as well as a list of optimised bitstring at different time points. It calls the appropriate cutAndPlotResultsTX function.

**Usage**

```
cutAndPlot(CNolist, model, bStrings, plotPDF=FALSE, tag=NULL,
plotParams = list(maxrow = 10))
```

**Arguments**

CNolist	a CNolist, corresponding to the optimisation one
model	a model (the full one that was used for optimisation)
bStrings	a bitstring for T1 as output by gaBinaryT1 (i.e. a vector of 1s and 0s)
plotPDF	TRUE or FALSE; tells whether you want a pdf to be produced or not
tag	NULL or string; tells whether you want to prefix filenames with a tag (replaces the default behaviour).
plotParams	a list of option related to the PDF and plotting outputs. (1) maxrow is the maximum number of row used to plot the results. See <a href="#">plotOptimResultsPan</a> for other fields.

**Value**

This function returns nothing. It plots a graph in your graphic window and save it in a file if asked

**Author(s)**

T. Cokelaer

**See Also**

[cutAndPlotResultsT1](#)

**Examples**

```
#load data

data(CNolistToy,package="CellNOptR")
data(ToyModel,package="CellNOptR")

#pre-process model
model = preprocessing(CNolistToy, ToyModel)

cutAndPlot(CNolistToy, model,
bStrings=list(rep(1,length(model$reacID))),plotPDF=FALSE)
```

---

cutAndPlotResultsT1 *Plot the results of an optimisation at t1*

---

### Description

This function takes a model and an optimised bitstring, it cuts the model according to the bitstring and plots the results of the simulation along with the experimental data.

### Usage

```
cutAndPlotResultsT1(model, bString, simList=NULL, CNOList, indexList=NULL, plotPDF = FALSE, tag = NULL, tPt=CNOList@timepoints[2], plotParams = list(maxrow=10))
```

### Arguments

model	a model (the full one that was used for optimisation)
bString	a bitstring for T1 as output by gaBinaryT1 (i.e. a vector of 1s and 0s)
simList	deprecated argument kept for back compatibility. a simlist corresponding to the model, as output by prep4sim
CNOList	a CNOList, corresponding to the optimisation one
indexList	deprecated argument kept for back compatibility. an indexList, produced by indexFinder ran on the model and the CNOList above
plotPDF	TRUE or FALSE; tells whether you want a pdf to be produced or not
tag	NULL or string; tells whether you want to prefix filenames with a tag (replaces the default behaviour).
tPt	The number of time points in the data.
plotParams	a list of option related to the PDF and plotting outputs. (1) maxrow is the maximum number of row used to plot the results. See <a href="#">plotOptimResultsPan</a> for other fields.

### Value

This function returns a list of filenames that have been created.

### Author(s)

C.Terfve, T. Cokelaer, A. MacNamara

### See Also

[gaBinaryT1](#)



**Examples**

```

#load data

data(CNolistToy,package="CellNOptR")
data(ToyModel,package="CellNOptR")

#pre-process model
model = preprocessing(CNolistToy, ToyModel)

#optimise
ToyT1opt<-gaBinaryT1(
CNolist=CNolistToy,
model=model,
maxGens=2,
popSize = 5,
verbose=FALSE)

#plotting
cutAndPlotResultsT1(
model=model,
CNolist=CNolistToy,
bString=ToyT1opt$bString,
plotPDF=FALSE)

```

---

cutAndPlotResultsT2 *Plot the results of an optimisation at t2 (deprecated since v1.3.28; use [cutAndPlotResultsTN](#) instead)*

---

**Description**

This function takes a model and an optimised bitstring, it cuts the model according to the bitstring and plots the results of the simulation along with the experimental data. This function is designed to work on results of a 2 step optimisation.

**Usage**

```

cutAndPlotResultsT2(model, bStringT1, bStringT2, CNolist, simList=NULL, indexList=NULL,
plotPDF = FALSE, tag=NULL, tPt=CNolist@timepoints[2:3],
plotParams = list(maxrow = 10))

```

**Arguments**

model	a model (the full one that was used for optimisation)
bStringT1	a bitstring for T1 as output by gaBinaryT1
bStringT2	a bitstring for T2 as output by gaBinaryT2
CNolist	a CNolist, corresponding to the optimisation one
simList	deprecated argument kept for back compatibility. a simlist corresponding to the model, as output by prep4sim

indexList	deprecated argument kept for back compatibility. an indexList, produced by indexFinder ran on the model and the CNOList above
plotPDF	TRUE or FALSE, tells whether you want a pdf to be produced or not
tag	NULL or string; tells whether you want to prefix filenames with a tag (replaces the default behaviour).
tPt	The number of time points in the data.
plotParams	a list of option related to the PDF and plotting outputs. (1) maxrow is the maximum number of row used to plot the results. See <a href="#">plotOptimResultsPan</a> for other fields.

### Value

This function doesn't return anything, it only plots the graph in your graphic window, and in a pdf file if asked

### Author(s)

C. Terfve, T. Cokelaer, A. MacNamara

### See Also

[gaBinaryT1](#), [cutAndPlotResultsT1](#)

### Examples

```
#load data

data(CNOListToy2,package="CellNOptR")
data(ToyModel2,package="CellNOptR")

#pre-process model
model = preprocessing(CNOListToy2, ToyModel2)

#optimise t1
ToyT1<-gaBinaryT1(
  CNOList=CNOListToy2,
  model=model,
  maxGens=2,
  popSize = 5,
  verbose=FALSE)

#Optimise T2

ToyT2<-gaBinaryT2(
  CNOList=CNOListToy2,
  model=model,
  bStringT1=ToyT1$bString,
  maxGens=2,
  popSize = 5,
  verbose=FALSE)

cutAndPlotResultsT2(
  CNOList=CNOListToy2,
  model=model,
  bStringT1=ToyT1$bString,
```

```
bStringT2=ToyT2$bString,
plotPDF=FALSE)
```

---

cutAndPlotResultsTN *Plot the results of an optimisation at tN*

---

### Description

This function takes a model and an optimised bitstring, it cuts the model according to the bitstring and plots the results of the simulation along with the experimental data. This function is designed to work on results of a 2 step optimisation.

### Usage

```
cutAndPlotResultsTN(CNolist, model, bStrings, plotPDF = FALSE, tag=NULL,
plotParams = list(maxrow = 10))
```

### Arguments

CNolist	a CNolist, corresponding to the optimisation one
model	a model (the full one that was used for optimisation)
bStrings	a list of bitstring at different time points
plotPDF	TRUE or FALSE, tells whether you want a pdf to be produced or not
tag	NULL or string; tells whether you want to prefix filenames with a tag (replaces the default behaviour).
maxrow	maximum number of row in the plot.
plotParams	a list of option related to the PDF and plotting outputs. (1) maxrow is the maximum number of row used to plot the results. See <a href="#">plotOptimResultsPan</a> for other fields.

### Value

This function doesn't return anything, it only plots the graph in your graphic window, and in a pdf file if asked

### Note

New in version 1.3.28

### Author(s)

T. Cokelaer, A. MacNamara, Sarah Schrier, C. Terfve based on [cutAndPlotResultsT1](#)

### See Also

[gaBinaryT1](#), [prep4sim](#), [cutAndPlotResultsT1](#)

**Examples**

```

#load data

data(CNolistToy2,package="CellNOptR")
data(ToyModel2,package="CellNOptR")

#pre-process model
model = preprocessing(CNolistToy2, ToyModel2)

#optimise t1
ToyT1<-gaBinaryT1(
CNolist=CNolistToy2,
model=model,
maxGens=2,
popSize = 5,
verbose=FALSE)

#Optimise T2
ToyT2<-gaBinaryTN(
CNolist=CNolistToy2,
model=model,
bString=list(ToyT1$bString),
maxGens=2,
popSize = 5,
verbose=FALSE)

cutAndPlotResultsTN(
CNolist=CNolistToy2,
model=model,
bStrings=list(ToyT1$bString, bStringT2=ToyT2$bString),
plotPDF=FALSE)

```

---

cutModel

*Cut a model structure according to a bitstring*


---

**Description**

This function is for developers only.

**Usage**

```
cutModel(model, bString)
```

**Arguments**

model	the model object to cut.
bString	the bitString to be used to cut the model object.

**Value**

cutModel	the new model object
----------	----------------------

**Note**

added in version 1.3.16

**Author(s)**

T. Cokelaer

---

cutNONC

*Cuts the non-observable/non-controllable species from the model*

---

**Description**

This function cuts the non-observable and/or non-controllable species from the model, and returns a cut model.

**Usage**

```
cutNONC(model, NONCindexes)
```

**Arguments**

model	a model structure, as produced by readSIF
NONCindexes	a vector of indices of species to remove in that model, as produced for example by findNONC

**Details**

This function takes in a model and a vector of indices of species to remove in that model and it removes those species and any reaction involving them (be aware, if you have  $x+y=z$  and  $x$  is to be removed, then the function produces  $y=z$ , because it works by removing entire rows of the model matrices and then removes the columns that do not have either an input or an output). This function could actually be used to cut any species, not only NONC species.

**Value**

a model

**Note**

No need to call this function directly since version 0.99.24. Use [preprocessing](#) instead.

**Author(s)**

C.Terfve

**See Also**

[findNONC](#), [readSIF](#)

**Examples**

```
data(CNolistToy,package="CellNOptR")
data(ToyModel,package="CellNOptR")
indicesToy<-indexFinder(CNolistToy,ToyModel,verbose=FALSE)
ToyNCNOindices<-findNONC(ToyModel,indicesToy,verbose=FALSE)
ToyNCNOcut<-cutNONC(ToyModel,ToyNCNOindices)
```

---

cutSimList	<i>Cut a simList structure according to a bitstring</i>
------------	---

---

**Description**

This function is for developers only.

**Usage**

```
cutSimList(simList, bString)
```

**Arguments**

simList	the simList object to cut.
bString	the bitString to be used to cut the simList object.

**Value**

cutSimList	the new simList object
------------	------------------------

**Author(s)**

T. Cokelaer

---

defaultParameters	<i>Create a list of default parameters</i>
-------------------	--

---

**Description**

This function provides a list of default parameters including the Genetic Algorithm parameters.

**Usage**

```
defaultParameters(data=NA, model=NA)
```

**Arguments**

data	a CNolist structure, as created by makeCNolist
model	a model structure, as created by readSIF, normally pre-processed but that is not a requirement of this function

**Details**

The list contains the Genetic Algorithm parameter, a verbose option and can be used to store the Data and Model.

**Value**

params            a list with the fields: data, model, verbose and all default parameters of [gaBinaryT1](#)

**Author(s)**

T. Cokelaer

**Examples**

```
data(ToyModel, package="CellNOptR")
data(CNolistToy, package="CellNOptR")
params = defaultParameters(CNolistToy, ToyModel)
```

---

expandGates	<i>Expand the gates of a model</i>
-------------	------------------------------------

---

**Description**

This function takes in a model and splits all AND gates into ORs. In addition, wherever there are more than one, it creates all possible ANDs combinations of them, but considering only ANDs with 2, 3 or 4 inputs according to the user argument (default is 2)

**Usage**

```
expandGates(model, ignoreList=NA, maxInputsPerGate=2)
```

**Arguments**

model	a model structure
ignoreList	a list of reactions indices to ignore
maxInputsPerGate	maximum number of input per gates (Default is 2; up to 4)

**Details**

This function returns a model with additional fields that help keep track of the processing done on the network. I would advice not to overwrite on the initial model but rather to assign the result of this function to a variable with a different name.

**Value**

returns a model, with additional fields:

SplitANDs	list that contains a named element for each AND reac that has been split, and each element contains a vector with the names of the of the reactions that result from the split if nothing was split, this element has the default value \$initialReac [1] "split1" "split2"
newANDs	list that contains an element for each new '&' gate, named by the name of this new and reac, and containing a vector of the names of the reactions from which it was created (contains all the reacts in that pool, not the particular ones, this could be improved)

**Note**

No need to call this function directly since version 0.99.24. Use [preprocessing](#) instead.

**Author(s)**

C.Terfve, T. Cokelaer, A.MacNamara

**Examples**

```
#load data

data(CNolistToy,package="CellNOptR")
data(ToyModel,package="CellNOptR")

#pre-process the model

indicesToy<-indexFinder(CNolistToy,ToyModel,verbose=TRUE)
ToyNCNOindices<-findNONC(ToyModel,indicesToy,verbose=TRUE)
ToyNCNOcut<-cutNONC(ToyModel,ToyNCNOindices)
indicesToyNCNOcut<-indexFinder(CNolistToy,ToyNCNOcut)
ToyNCNOcutComp<-compressModel(ToyNCNOcut,indicesToyNCNOcut)
indicesToyNCNOcutComp<-indexFinder(CNolistToy,ToyNCNOcutComp)
ToyNCNOcutCompExp<-expandGates(ToyNCNOcutComp, maxInputsPerGate=4)
```

---

findNONC

*Find the indexes of the non-observable and non controllable species*

---

**Description**

This function finds the indexes of the non-observable and non controllable species and returns the indices, in the model, of the species to remove

**Usage**

```
findNONC(model, indexes, verbose=FALSE)
```



**Arguments**

model	a model structure, as created by <a href="#">readSIF</a>
indexes	a list of indexes of the species stimulated/inhibited/measured, as created by <a href="#">indexFinder</a> from a model.
verbose	verbose option (default to FALSE)

**Details**

This function uses the function `floyd.warshall.all.pairs.sp` from the package `RBGL`. Non observable nodes are those that do not have a path to any measured species in the model, whereas non controllable nodes are those that do not receive any information from a species that is perturbed in the data.

**Value**

a vector of indices of species to remove

**Note**

No need to call this function directly since version 0.99.24. Use [preprocessing](#) instead.

**Author(s)**

C. Terfve

**See Also**

[cutNONC](#), [indexFinder](#), [readSIF](#)

**Examples**

```
data(CNolistToy, package="CellNOptR")
data(ToyModel, package="CellNOptR")
checkSignals(CNolistToy, ToyModel)
indicesToy <- indexFinder(CNolistToy, ToyModel)
ToyNCNOindices <- findNONC(ToyModel, indicesToy)
```

---

gaBinaryT1

*Genetic algorithm used to optimise a model*

---

**Description**

This function is the genetic algorithm to be used to optimise a model by fitting to data containing one time point.

**Usage**

```
gaBinaryT1(CNolist, model, initBstring=NULL, sizeFac = 1e-04,
  NAFac = 1, popSize = 50, pMutation = 0.5, maxTime = 60, maxGens = 500,
  stallGenMax = 100, selPress = 1.2, elitism = 5, relTol = 0.1, verbose=TRUE,
  priorBitString=NULL, maxSizeHashTable=5000)
```

**Arguments**

CNOlist	a CNOlist on which the score is based (based on valueSignals[[2]], i.e. data at time 1)
model	a model structure, as created by readSIF, normally pre-processed but that is not a requirement of this function
initBstring	an initial bitstring to be tested, should be of the same size as the number of reactions in the model above (model\$reacID). Default is all ones.
sizeFac	the scaling factor for the size term in the objective function, default to 0.0001
NAFac	the scaling factor for the NA term in the objective function, default to 1
popSize	the population size for the genetic algorithm, default set to 50
pMutation	the mutation probability for the genetic algorithm, default set to 0.5
maxTime	the maximum optimisation time in seconds, default set to 60
maxGens	the maximum number of generations in the genetic algorithm, default set to 500
stallGenMax	the maximum number of stall generations in the genetic algorithm, default to 100
selPress	the selective pressure in the genetic algorithm, default set to 1.2
elitism	the number of best individuals that are propagated to the next generation in the genetic algorithm, default set to 5
relTol	the relative tolerance for the best bitstring reported by the genetic algorithm, i.e., how different from the best solution, default set to 0.1
verbose	logical (default to TRUE) do you want the statistics of each generation to be printed on the screen?
priorBitString	At each generation, the GA algorithm creates a population of bitstrings that will be used to perform the optimisation. If the user knows the values of some bits, they can be used to overwrite bit values proposed by the GA algorithm. If provided, the priorBitString must have the same length as the initial bitstring and be made of 0, 1 or NA (by default, this bitstring is set to NULL, which is equivalent to setting all bits to NA). Bits that are set to 0 or 1 are used to replace the bits created by the GA itself (see example).
maxSizeHashTable	a hash table is use to store bitstring and related score. This allows the GA to be very efficient is the case of small models. The size of the hash table is 5000 by default, which may be too large for large models.

**Details**

The whole procedure is described in details in Saez-Rodriguez et al. (2009). The basic principle is that at each generation, the algorithm evaluates a population of models based on excluding or including some gates in the initial pre-processed model (this is encoded in a bitstring with contains 0/1 entries for each gate). The population is then evolved based on the results of the evaluation of these networks, where the evaluation is obtained by simulating the model (to steady state) under the various conditions present in the data, and then computing the squared deviation from the data, to which a penalty is added for size of the model and for species in the model that do not reach steady state.

**Value**

This function returns a list with elements:

bString	the best bitstring
results	a matrix with columns "Generation", "Best_score", "Best_bitString", "Stall_Generation", "Avg_Score_C"
stringsTol	the bitstrings whose scores are within the tolerance
stringsTolScores	the scores of the above-mentioned strings

**Author(s)**

C. Terfve. T. Cokelaer

**References**

J. Saez-Rodriguez, L. G. Alexopoulos, J. Epperlein, R. Samaga, D. A. Lauffenburger, S. Klamt and P. K. Sorger. Discrete logic modeling as a means to link protein signaling networks with functional analysis of mammalian signal transduction, *Molecular Systems Biology*, 5:331, 2009.

**See Also**

[gaBinaryTN](#), [simulatorT1](#)

**Examples**

```
data(CNolistToy,package="CellNOptR")
data(ToyModel,package="CellNOptR")

#pre-process model
model = preprocessing(CNolistToy, ToyModel)

#optimise

initBstring<-rep(1,length(model$reacID))
ToyT1opt<-gaBinaryT1(
  CNolist=CNolistToy,
  model=model,
  initBstring=initBstring,
  maxGens=10, popSize=10, verbose=FALSE)

# During the optimisation, some bits can be overwritten by your prior knowledge
# First, you need to create a priorBitString made of NA where known bit values
# are replaced by 0 or 1
priorBitString = rep(NA, length(model$reacID))
priorBitString[1] = 0
priorBitString[2] = 1

# Second, you call the gaBinaryT1 function by providing the priorBitString
# argument:
ToyT1opt<-gaBinaryT1(CNolist=CNolistToy, model=model,
  initBstring=initBstring,maxGens=10, popSize=10, verbose=FALSE,
  priorBitString=priorBitString)
```

gaBinaryT2

*Genetic algorithm for time point 2***Description**

This is the genetic algorithm for time point 2, that should follow optimisation based on time point 1.

Deprecated in version 1.3.28. Use [gaBinaryTN](#) instead.

**Usage**

```
gaBinaryT2(CNOList, model, bStringT1, sizeFac = 1e-04, NAFac = 1,
popSize = 50, pMutation = 0.5, maxTime = 60, maxGens = 500,
stallGenMax = 100, selPress = 1.2, elitism = 5, relTol = 0.1, verbose=TRUE,
priorBitString=NULL, maxSizeHashTable=5000)
```

**Arguments**

CNOList	a CNOList on which the score is based (based on valueSignals[[3]], i.e. data at t2)
model	a model structure, as created by readSIF, normally pre-processed but that is not a requirement of this function
bStringT1	the optimal bitstring from optimisation at time 1 (i.e. a vector of 0s and 1s)
sizeFac	the scaling factor for the size term in the objective function, default to 0.0001
NAFac	the scaling factor for the NA term in the objective function, default to 1
popSize	the population size for the genetic algorithm, default set to 50
pMutation	the mutation probability for the genetic algorithm, default set to 0.5
maxTime	the maximum optimisation time in seconds, default set to 60
maxGens	the maximum number of generations in the genetic algorithm, default set to 500
stallGenMax	the maximum number of stall generations in the genetic algorithm, default to 100
selPress	the selective pressure in the genetic algorithm, default set to 1.2
elitism	the number of best individuals that are propagated to the next generation in the gen. al. default set to 5
relTol	the relative tolerance for the best bitstring reported by the genetic algorithm, i.e. how different from the best solution can solutions be to be reported as well, default set to 0.1
verbose	logical (default to TRUE) do you want the statistics of each generation to be printed on the screen
priorBitString	A bitString of same length at the initial bitstring made of 0, 1 or NA. By default, this bitstring is set to NULL (equivalent to setting all bits to NA). If provided, all bitstring in a population will be changed to be in agreement with the prior-BitString list.
maxSizeHashTable	a hash table is use to store bitstring and related score. This allows the GA to be very efficient is the case of small models. The size of the hash table is 5000 by default, which may be too large for large models.

**Details**

This function takes in the same input as the T1 ga, but in addition it takes in the bitstring optimised for T1, and does not take an initial bitstring. Be aware that the bitString that this function returns is one that only includes the bits that it actually looks at, i.e. the bits that were 0 in the bStringT1

**Value**

This function returns a list with elements:

bString	the best bitstring
results	a matrix with columns "Generation", "Best_score", "Best_bitString", "Stall_Generation", "Avg_Score_C"
stringsTol	the bitstrings whose scores are within the tolerance
stringsTolScores	the scores of the above-mentioned strings

**Author(s)**

C.Terfve, T. Cokelaer

**See Also**

[getFit](#), [prep4sim](#), [indexFinder](#), [simulatorT1](#), [simulatorT2](#), [gaBinaryT2](#)

**Examples**

```
#load data

data(CNolistToy2,package="CellNOptR")
data(ToyModel2,package="CellNOptR")

#pre-process model

checkSignals(CNolistToy2,ToyModel2)
model = preprocessing(CNolistToy2, ToyModel2)

#optimise t1
ToyT1<-gaBinaryT1(
  CNolist=CNolistToy2,
  model=model,
  maxGens=10,
  popSize = 10,
  verbose=FALSE)

#Optimise T2

ToyT2<-gaBinaryT2(
  CNolist=CNolistToy2,
  model=model,
  bStringT1=ToyT1$bString,
  maxGens=10,
  popSize = 10,
  verbose=FALSE)
```

gaBinaryTN

*Genetic algorithm for time point N***Description**

This is the genetic algorithm for time point N, that should follow optimisation based on time point 1.

Replaces [gaBinaryT2](#) since version 1.3.28

**Usage**

```
gaBinaryTN(CNOlist, model, bStrings, sizeFac = 1e-04, NAFac = 1,
popSize = 50, pMutation = 0.5, maxTime = 60, maxGens = 500,
stallGenMax = 100, selPress = 1.2, elitism = 5, relTol = 0.1, verbose=TRUE,
priorBitString=NULL, maxSizeHashTable=5000)
```

**Arguments**

CNOlist	a CNOlist on which the score is based (based on valueSignals[[3]], i.e. data at t2)
model	a model structure, as created by readSIF, normally pre-processed but that is not a requirement of this function
bStrings	the optimal bitstring from optimisation at time 1 (i.e. a vector of 0s and 1s)
sizeFac	the scaling factor for the size term in the objective function, default to 0.0001
NAFac	the scaling factor for the NA term in the objective function, default to 1
popSize	the population size for the genetic algorithm, default set to 50
pMutation	the mutation probability for the genetic algorithm, default set to 0.5
maxTime	the maximum optimisation time in seconds, default set to 60
maxGens	the maximum number of generations in the genetic algorithm, default set to 500
stallGenMax	the maximum number of stall generations in the genetic algorithm, default to 100
selPress	the selective pressure in the genetic algorithm, default set to 1.2
elitism	the number of best individuals that are propagated to the next generation in the gen. al. default set to 5
relTol	the relative tolerance for the best bitstring reported by the genetic algorithm, i.e. how different from the best solution can solutions be to be reported as well, default set to 0.1
verbose	logical (default to TRUE) do you want the statistics of each generation to be printed on the screen
priorBitString	A bitString of same length at the initial bitstring made of 0, 1 or NA. By default, this bitstring is set to NULL (equivalent to setting all bits to NA). If provided, all bitstring in a population will be changed to be in agreement with the prior-BitString list.
maxSizeHashTable	a hash table is use to store bitstring and related score. This allows the GA to be very efficient is the case of small models. The size of the hash table is 5000 by default, which may be too large for large models.

**Details**

This function takes in the same input as the T1 ga, but in addition it takes in the bitstring optimised for T1, and does not take an initial bitstring. Be aware that the bitString that this function returns is one that only includes the bits that it actually looks at, i.e. the bits that were 0 in the bStringT1

**Value**

This function returns a list with elements:

bString	the best bitstring
results	a matrix with columns "Generation", "Best_score", "Best_bitString", "Stall_Generation", "Avg_Score_C"
stringsTol	the bitstrings whose scores are within the tolerance
stringsTolScores	the scores of the above-mentioned strings

**Author(s)**

C.Terfve, T. Cokelaer

**See Also**

[getFit](#), [simulatorT1](#), [simulatorT2](#), [gaBinaryT2](#)

**Examples**

```
#load data

data(CNolistToy2,package="CellNOptR")
data(ToyModel2,package="CellNOptR")

#pre-process model

checkSignals(CNolistToy2,ToyModel2)
model = preprocessing(CNolistToy2, ToyModel2)

#optimise t1
ToyT1<-gaBinaryT1(
  CNolist=CNolistToy2,
  model=model,
  maxGens=10,
  popSize = 10,
  verbose=FALSE)

#Optimise T2

ToyT2<-gaBinaryTN(
  CNolist=CNolistToy2,
  model=model,
  bStrings=list(ToyT1$bString),
  maxGens=10,
  popSize = 10,
  verbose=FALSE)
```

---

getFit

---

*Compute the score of a model*


---

### Description

This function computes the value of the objective function for a model and an associated data set, as a sum of a term that computes the fit of model to data, a term that penalises the NA values produced by the model, and a term that penalises increasing size of the model.

### Usage

```
getFit(simResults, CNOList, model, indexList, timePoint=c("t1", "t2"),
sizeFac=1e-04, NAFac=1, nInTot, simResultsT0=NA)
```

### Arguments

simResults	matrix of simulated results (the full one as output by the simulator)
CNOList	a CNOList to compare the simulated results with
model	a model that has already been cut to contain only the reactions in the optimal bitstring
indexList	list of indexes as produced by indexFinder
timePoint	"t1" or "t2" tells which time point we are looking at. If timePoint=t1 then we will compare the simResults to the results stored in CNOList\$valueSignals[[2]]. If timePoint=t2 then we will compare the simResults to the results stored in CNOList\$valueSignals[[1]]
sizeFac	weights the penalty for the size of the model, default=0.0001
NAFac	weights the penalty for the number of NAs
nInTot	the number of inputs in the model prior to cutting, used to normalised the size penalty
simResultsT0	Results of the time 0 simulator (internal usage of gaBinaryT1)

### Details

BE AWARE: contrary to what is done in the Matlab version of CellNOpt, here the simulation results are computed beforehand and the model that is input into this function is a model that has already been cut i.e. that only contains the reactions present in the optimised model (i.e. should be the same model as the one that you input into the simulator). Also, the simResults matrix is the full one as output by the simulator, i.e. it contains results for all species in the model, not only the signals

### Value

This function returns a single number, the value of the objective function.

### Author(s)

C. Terfve



## References

J. Saez-Rodriguez, L. G. Alexopoulos, J. Epperlein, R. Samaga, D. A. Lauffenburger, S. Klamt and P. K. Sorger. Discrete logic modeling as a means to link protein signaling networks with functional analysis of mammalian signal transduction, *Molecular Systems Biology*, 5:331, 2009.

## See Also

[gaBinaryT1](#), [simulatorT1](#)

## Examples

```
#Here we will evaluate the fit of the full initial model,
#without pre-processing or any optimisation

data(CNolistToy,package="CellNOptR")
data(ToyModel,package="CellNOptR")

indicesToy<-indexFinder(CNolistToy,ToyModel,verbose=FALSE)
ToyFields4Sim<-prep4sim(ToyModel)
simResults<-simulatorT1(
  CNolist=CNolistToy,
  model=ToyModel,
  simList=ToyFields4Sim,
  indexList=indicesToy)
Score<-getFit(
  simResults=simResults,
  CNolist=CNolistToy,
  model=ToyModel,
  indexList=indicesToy,
  timePoint="t1",
  nInTot=length(which(ToyModel$sinterMat == -1))
)
```

---

graph2sif

*Convert graph to SIF*

---

## Description

This function converts a network from graph format to SIF format. The resulting table can also be saved in a SIF file.

## Usage

```
graph2sif(graph, writeSif=FALSE, filename="Graph")
```

## Arguments

graph	a graph, as generated using <a href="#">sif2graph</a>
writeSif	if writeSif=FALSE (default) the SIF file is not saved. If writeSif=TRUE it is saved.
filename	the name of the SIF file saved if writeSif=TRUE. Default is Model.sif.

**Details**

The sign of link is supposed to be encoded in the graph as the weight of the edge (-1 negative regulation, +1 positive regulation).

**Value**

sifFile            a table with all the links in the model in the format sourceNode-tab-sign-tab-targetNode

**Author(s)**

F. Eduati

**See Also**

[model2sif](#), [sif2graph](#), [readSIF](#),

---

indexFinder	<i>Finds the indices, in the model fields, of the species that are measured/inhibited/stimulated</i>
-------------	--

---

**Description**

This function finds the indices, in the model fields, of the species that are measured/inhibited/stimulated. It looks for their position in model\$namesSpecies which has the same order as the rows of interMat and notMat, and therefore these indexes can be used there as well.

**Usage**

```
indexFinder(CNOlist, model, verbose=FALSE)
```

**Arguments**

CNOlist	a CNOlist structure, as produced by makeCNOlist
model	a model structure, as produced by readSIF
verbose	do you want information about the cues and signals identities printed on the screen? Default if false but we would advise to set it to true when the function is called for the first time.

**Value**

a list with fields:

signals	vector of indices of the measured species
stimulated	vector of indices of the stimulated species
inhibited	vector of indices of the inhibited species

**Note**

For internal usage since version 1.3.28

**Author(s)**

C. Terfve

**See Also**

[makeCNOList](#), [readSIF](#)

**Examples**

```
data(CNOListToy,package="CellNOptR")
data(ToyModel,package="CellNOptR")
indicesToy<-indexFinder(CNOListToy,ToyModel,verbose=TRUE)
```

---

LiverDREAM

*Model used for the DREAM3 challenge*

---

**Description**

This data object contains the model used in the package vignette, already loaded and formatted as a Model object. This is to be used with the data in "CNOListDREAM"

**Usage**

DreamModel

**Format**

DreamModel is a list with fields "reacID" (character vector), "namesSpecies" (character vector), "interMat" (numerical matrix), "notMat"(numerical matrix).

**Source**

This data and model is extracted from the Matlab version of CellNOpt1.0 (<http://www.ebi.ac.uk/saezrodriguez/software.html#CellNetOptimizer>).

**References**

1. J. Saez-Rodriguez, L. G. Alexopoulos, J. Epperlein, R. Samaga, D. A. Lauffenburger, S. Klamt and P. K. Sorger. Discrete logic modeling as a means to link protein signaling networks with functional analysis of mammalian signal transduction, *Molecular Systems Biology*, 5:331, 2009.
2. Prill RJ, Marbach D, Saez-Rodriguez J, Sorger PK, Alexopoulos LG, Xue X, Clarke ND, Altan-Bonnet G, and Stolovitzky G. Towards a rigorous assessment of systems biology models: the DREAM3 challenges. *PLoS One*, 5(2):e9202, 2010.

---

makeCNOList	<i>Make a CNOList structure</i>
-------------	---------------------------------

---

### Description

This function takes as input the output of readMIDAS and extracts the elements that are needed in a CNO project

### Usage

```
makeCNOList(dataset, subfield, verbose=TRUE)
```

### Arguments

dataset	output of readMIDAS
subfield	TRUE or FALSE, specifies if the column headers contain subfields or not i.e. if I should look for TR:sthg:sthg or just TR:sthg
verbose	logical (default to TRUE) print information on the screen.

### Details

Be aware that most of the functions in this package, including this one, expect the data to contain measurements at time 0, but these should all be equal to zero according to the normalisation procedure that should be used. Therefore, if you have one time point, the files valueSignals contains two matrices, one for t0 and one for t1.

If there are replicate rows in the MIDAS file (i.e., identical cues and identical time), this function averages the values of the measurements for these replicates.

Columns with the following tags are ignored: NOINHIB, NO-INHIB, NO-LIG, NOCYTO.

### Value

a CNOList with fields

namesCues	a vector of names of cues
namesStimuli	a vector of names of stimuli
namesInhibitors	a vector of names of inhibitors
namesSignals	a vector of names of signals
timeSignals	a vector of times
valueCues	a matrix of dimensions nConditions x nCues, with 0 or 1 if the cue is present or absent in the particular condition
valueInhibitors	a matrix of dimensions nConditions x nInhibitors, with 0 or 1 if the inhibitor is present or absent in the particular condition
valueStimuli	of dimensions nConditions x nStimuli, with 0 or 1 if the stimuli is present or absent in the particular condition
valueSignals	a list of the same length as timeSignals, each element containing a matrix of dimensions nConditions x nsignals, with the measurements.

**Author(s)**

C. Terfve

**References**

J. Saez-Rodriguez, L. G. Alexopoulos, J. Epperlein, R. Samaga, D. A. Lauffenburger, S. Klamt and P. K. Sorger. Discrete logic modeling as a means to link protein signaling networks with functional analysis of mammalian signal transduction, *Molecular Systems Biology*, 5:331, 2009.

**See Also**

[readMIDAS](#), [CNOList-class](#)

**Examples**

```
tmpdir<-tempdir()
setwd(tmpdir)
cpfile<-dir(system.file("ToyModel",package="CellNOptR"),full=TRUE)
file.copy(from=cpfile,to=getwd(),overwrite=TRUE)
dataToy<-readMIDAS(MIDASfile='ToyDataMMB.csv')
CNOListToy<-makeCNOList(dataset=dataToy,subfield=FALSE)
```

---

mapBack

*Map an optimised model back onto the PKN model.*

---

**Description**

Map an optimised model back onto the PKN model.

**Usage**

```
mapBack(model, PKN, bString)
```

**Arguments**

model	the optimised model
PKN	the Prior Knowledge network
bString	the optimised bitString

**Value**

bStringPKN the corresponding bitstring corresponding to the original PKN.

**Author(s)**

F.Eduati

**See Also**

[graph2sif](#), [sif2graph](#), [readSIF](#),

---

model2sif	<i>Convert a model object in sif format</i>
-----------	---

---

### Description

This function receives as input a model object and converts it to the cytoscape sif format. It can be used to convert either the whole model (before or after pre-processing) or the optimized one (if the corresponding bitString is provided). The resulting table can also be saved in a sif file.

### Usage

```
model2sif(model,optimRes=NA,writeSif=FALSE, filename="Model")
```

### Arguments

model	the model as generated using <a href="#">readSIF</a>
optimRes	the output of the optimisation (as obtained using <a href="#">gaBinaryT1</a> ), default set to NA the whole model in converted
writeSif	if writeSif=FALSE (default) the sif file is not saved. If writeSif=TRUE it is saved.
filename	the name of the sif file saved if writeSif=TRUE. Default is Model.sif.

### Details

All links in the model are converted in sif format that is sourceNode-tab-sign-tab-targetNode. If there are ANDs, they are converted using dummy nodes called and# (e.g. A+B=C will be A-tab-1-tab-and1; B-tab-1-tab-and1; and1-tab-1-tab-C).

### Value

sifFile	a table with all the links in the model in the format sourceNode-tab-sign-tab-targetNode
---------	--

### Author(s)

F.Eduati

### See Also

[graph2sif](#), [sif2graph](#), [readSIF](#),

---

normaliseCNOList      *Normalisation for boolean modelling.*

---

### Description

This function takes in a CNOList and does the normalisation of the data between 0 and 1, according to two different procedures (see details).

### Usage

```
normaliseCNOList(CNOList, EC50Data=0.5, HillCoef=2, EC50Noise=0.1, detection=0,
  saturation=Inf, changeTh=0, norm2TorCtrl="time")
```

### Arguments

CNOList	a CNOList
EC50Data	parameter for the scaling of the data between 0 and 1, default=0.5
HillCoef	Hill coefficient for the scaling of the data, default to 2
EC50Noise	parameter for the computation of a penalty for data comparatively smaller than other time points or conditions.
detection	minimum detection level of the instrument, everything smaller will be treated as noise (NA), default to 0
saturation	saturation level of the instrument, everything over this will be treated as NA, default to Inf.
changeTh	threshold for relative change considered significant, default to 0
norm2TorCtrl	"time" or "ctrl": choice of a normalisation method: compute the relative change compared to the control at the same time, or to the same condition and measurement at time 0.

### Details

The normalisation procedure works as follows:

1. every value that is out of the dynamic range of the equipment (as specified by the parameters detection and saturation are set to NA,
2. values are transformed to fold changes relative to the same condition at t0 (if norm2TorCtrl="time") or the control condition (i.e. same inhibitors, no stimuli) at the same time (if norm2TorCtrl="ctrl"),
3. the fold changes are transformed with a Hill function  $\frac{x^{HillCoef}}{((EC50Data^{HillCoef})+(x^{HillCoef}))}$
4. a penalty for "noisiness" is computed for each measurement as the value divided by the maximum value for that readout across all conditions and times (excluding values out of the dynamic range)
5. the noise penalty is transformed by a saturation function (for each measurement  $\frac{x}{(EC50Noise+x)}$  where  $x = \frac{x}{\max x}$ ),
6. the noise penalty and Hilled fold changes are multiplied,

7. if the fold change is negative and bigger than `ChangeTh`, the resulting product is multiplied by -1, if the fold change is smaller than `ChangeTh` (either positive or negative), it is set to 0. The normalisation procedure applied here is explained in details in saez-Rodriguez et al. (2009).

As the normalisation procedure works by computing a fold change relative to the same condition at time 0 or the control condition, if the aforementioned conditions have a value of zero (which is not expected with any common biochemical technique), then the fold change calculation will return a "NaN" value. If this is a problem for your particular case then we would suggest putting a dummy, very low value, instead of the zero, or setting that measurement to "NA" in the MIDAS file.

### Value

a normalised CNOList

### Author(s)

C. Terfve

### References

J. Saez-Rodriguez, L. G. Alexopoulos, J. Epperlein, R. Samaga, D. A. Lauffenburger, S. Klamt and P. K. Sorger. Discrete logic modeling as a means to link protein signaling networks with functional analysis of mammalian signal transduction, *Molecular Systems Biology*, 5:331, 2009.

### See Also

[makeCNOList](#)

### Examples

```
#Load a CNOList

data(CNOListToy,package="CellNOptR")

#Replace the values in the list by random values
#(for demonstration purposes, when actually using this function you would simply load a non-normalised CNOList)

CNOListToy$valueSignals$t0<-matrix(
data=runif(n=(dim(CNOListToy$valueSignals$t0)[1]*dim(CNOListToy$valueSignals$t0)[2]),min=0,max=400),
nrow=dim(CNOListToy$valueSignals$t0)[1],
ncol=dim(CNOListToy$valueSignals$t0)[2])
CNOListToy$valueSignals[[2]]<-CNOListToy$valueSignals[[1]]+matrix(
data=runif(n=(dim(CNOListToy$valueSignals$t0)[1]*dim(CNOListToy$valueSignals$t0)[2]),min=0,max=100),
nrow=dim(CNOListToy$valueSignals$t0)[1],
ncol=dim(CNOListToy$valueSignals$t0)[2])

CNOListToyN<-normaliseCNOList(
CNOListToy,
EC50Data = 0.5,
HillCoef = 2,
EC50Noise = 0.1,
detection = 0,
saturation = Inf,
changeTh = 0,
norm2TorCtrl = "time")
```



---

plot-method

*plot a "CNOList" object - methods*

---

### Description

A plot method for CNOList.

### Usage

signature(x="CNOList"): Please see the help page for the plot.CNOList method in the CellNOptR package

### arguments

**x** The CNOList object to plot

### Author(s)

T.Cokelaer

### See Also

[readMIDAS](#), [makeCNOList](#)

### Examples

```
showClass("CNOList")

files<-dir(system.file("ToyModel",package="CellNOptR"),full=TRUE)
cnolist = CNOList(files[[1]])
# accessors:
cnolist@cues
cnolist@inhibitors
cnolist@signals
cnolist@timepoints
cnolist@stimuli
# In version 1.3.30 and above, use the plot method instead of former plotCNOList function.
plot(cnolist)
```

---

plotCNOList

*Plot the data in a CNOList*

---

### Description

This function plots the data in a CNOList as a matrix of plots with a row for each condition and a column for each signal, and an extra plot for each row that specifies which cues are present..

### Usage

```
plotCNOList(CNOList)
```

**Arguments**

CNOList            a CNOList

**Details**

This function can plot the normalised values or the un-normalised ones, it just needs a CNOList.

**Value**

This function just produces a plot on your graphics window

**Author(s)**

C. Terfve

**See Also**

plotCNOListPDF, plotCNOListLarge, plotCNOListLargePDF

**Examples**

```
data(CNOListToy,package="CellNOptR")
plotCNOList(CNOListToy)
```

---

plotCNOListLarge

*Plot the data in a CNOList, for lists with many conditions.*

---

**Description**

This function plots the data in a CNOList as a matrix of plots with a row for each condition and a column for each signal, and an extra plot for each row that specifies which cues are present.

**Usage**

```
plotCNOListLarge(CNOList,nsplit=4, newDevice=FALSE)
```

**Arguments**

CNOList            a CNOList

nsplit             the number of splits in the condition dimension (one new plot window will be produced for each split, i.e. if you have 80 conditions and specify 4 splits you will get 4 plots with 20 conditions each).

newDevice         nsplit plots are created within the same device. In principle, most of the R Graphical User Interface will allow the user to navigate between the different plots. However, if scripting only the last plot will be seen. If you want to create new device for each different plot, then set this option to TRUE.

**Details**

This function can plot normalised values or the un-normalised ones, it just needs a CNOList. This function makes plots of CNOLists that are more readable when many conditions are present in the data. In addition to plotting the conditions divided into multiple plots, this function also plots the cues divided in two columns, one for inhibitors and one for stimuli.

**Value**

This function just produces plots on your graphics window.

**Author(s)**

C. Terfve

**See Also**

[plotCNOList](#), [plotCNOListPDF](#), [plotCNOListLargePDF](#)

**Examples**

```
data(CNOListDREAM,package="CellNOptR")
plotCNOListLarge(CNOListDREAM, nsplit=2)
```

---

`plotCNOListLargePDF` *Plots a CNOList into a pdf file, for lists with many conditions.*

---

**Description**

This function is a wrapper for `plotCNOListLarge`, that plots the output directly in a pdf file.

**Usage**

```
plotCNOListLargePDF(CNOList, filename, nsplit, width=14, height=7)
```

**Arguments**

CNOList	a CNOList
filename	a name for your pdf file, eg. "plot.pdf"
nsplit	the number of splits along the condition dimension (see <code>plotCNOListLarge</code> )
width	set the width of the PDF document.
height	set the height of the PDF document.

**Details**

This function makes plots of CNOLists that are more readable when many conditions are present in the data. In addition to plotting the conditions divided into multiple plots, this function also plots the cues divided in two columns, one for inhibitors and one for stimuli.

**Value**

This function doesn't return anything, it just produces a pdf file with your plots, in your current working directory.

**Author(s)**

C. Terfve

**See Also**

[plotCNOListLarge](#), [plotCNOList](#), [plotCNOListPDF](#)

**Examples**

```
tmpdir<-tempdir()
setwd(tmpdir)
data(CNOListDREAM,package="CellNOptR")
plotCNOListLargePDF(CNOListDREAM, filename="dreamData.pdf",nsplit=2)
```

---

plotCNOListPDF	<i>Plots a CNOList into a pdf file.</i>
----------------	---

---

**Description**

This function is a wrapper for `plotCNOList`, that plots the output directly in a pdf file.

**Usage**

```
plotCNOListPDF(CNOList, filename)
```

**Arguments**

CNOList	a CNOList
filename	a name for your pdf file, eg. "plot.pdf"

**Value**

This function doesn't return anything, it just produces a pdf file containing your plot, in your working directory.

**Author(s)**

C. Terfve

**See Also**

[plotCNOList](#), [plotCNOListLarge](#), [plotCNOListLargePDF](#)

**Examples**

```
tmpdir<-tempdir()
setwd(tmpdir)
data(CNOListToy,package="CellNOptR")
plotCNOListPDF(CNOList=CNOListToy,filename="ToyModelGraph.pdf")
```

---

`plotFit`*Plot the evolution of an optimisation*

---

**Description**

This function takes in the results of an optimisation by `gaBinaryT1` and plots the evolution of best fit and average fit against generations.

**Usage**

```
plotFit(optRes, filename = NULL)
```

**Arguments**

<code>optRes</code>	an object created by the optimisation engine ( <code>gabinaryT1</code> )
<code>filename</code>	NULL or string: if provided, the plot is save in PDF format in the filename.

**Value**

This function doesn't return anything, it just produces a plot in your graphics window.

**Author(s)**

C. Terfve

**See Also**

[gaBinaryT1](#)

**Examples**

```
data(CNolistToy,package="CellNOptR")
data(ToyModel,package="CellNOptR")

#process the model
model = preprocessing(CNolistToy,ToyModel)

#optimise

ToyT1opt<-gaBinaryT1(
  CNolist=CNolistToy,
  model=model,
  maxGens=10,
  popSize=10,
  verbose=FALSE)

plotFit(optRes=ToyT1opt)
```

---

 plotModel

*Plot a model*


---

### Description

This function can be used to plot a prior model network before any pre-processing step. However, additional information can be provided such as a CNOList (see makeCNOList and readMIDAS) or information related to the pre-processing steps (compression, NONC nodes, expansion gates). It can also be used to plot optimised model given the optimisation bitstring.

### Usage

```
plotModel(model, CNOList=NULL, bString=NULL, indexIntegr=NULL, signals=NULL, stimuli=NULL,
inhibitors=NULL, NCNO=NULL, compressed=NULL, output="STDOUT",filename=NULL,
graphvizParams=list(), remove_dot=TRUE)
```

### Arguments

model	a model as returned by readSIF. Alternatively, the filename can also be provided.
CNOList	output of makeCNOList
bString	a sequence made of numbers between 0 and 1 of same length as the one returned by the Genetic Algorithm (GA). This is a generalisation of the bitString returned by the GA function: several bit strings can be averaged and used
indexIntegr	additional indices to highlight some edge (optional).
signals	a list of nodes belonging to the signals class
stimuli	a list of nodes belonging to the stimuli class
inhibitors	a list of nodes belonging to the inhibitors class
NCNO	a list of NCNO nodes.
compressed	a list of compressed nodes
filename	the filename (without extension) used to write the dot file
output	the type of output (PNG, PDF, SVG accepted)
graphvizParams	a list of optional arguments dedicated to Rgraphviz. Accepted arguments are: arrowsize (default is 2); size (a string for the dot output default is "15,15");fontsize (default is 22);edgecolor (default is "black").
remove_dot	remove the dot file that has been created .default if False)

### Details

This function plots the model and also saves it in a dot file that can be processed later on. However, you can also save the plot in PNG or PDF or SVG format (one at a time).

The CNOList argument contains the signals/stimuli/inhibitors so if you provide a CNOList there is no need to use these arguments. If you decide to use them they will overwrite the contents of the CNOList argument.

optimRes is the output of gaBinary. One of its field is called bString and contains a list of 0 and 1 (the optimisation is performed with a binary procedure). This list of 0 and 1 is then used to plot or

not the edges of the model. However, you can provide a bitString made of floats (e.g., average of several bitStrings). In such case, edges will appear in gray light or dark according to the bistring value (between 0 and 1).

### Value

a graph representation of the model

graph\$g	A graph representation of the model
graph\$attrs	graph attributes
graph\$nodeAttrs	nodes attributes
graph\$edgeAttrs	edges attributes
graph\$clusters	clusters of nodes

### Note

This function depends on the Rgraphviz package.

### Author(s)

T. Cokelaer

### See Also

[readMIDAS](#), [readSIF](#), [makeCNOList](#), [writeNetwork](#), [writeDot](#), [gaBinaryT1](#)

### Examples

```
## Not run: library(CellNOptR)
data(CNOListToy,package="CellNOptR")
data(ToyModel,package="CellNOptR")
res<-plotModel(ToyModel, CNOList=CNOListToy, compressed=c("TRAF6", "p38"))

## End(Not run)
```

---

plotOptimResults

*Plot the data and simulated values*

---

### Description

This function is the equivalent of CNOPlotFits, it plots the data and the simulated values, along with an image plot that tells which cues were present. The plots are coloured according to the fit between data and simulated data.

### Usage

```
plotOptimResults(simResults, expResults, times, namesCues, namesSignals,
valueCues, formalism="new")
```

**Arguments**

simResults	a list with a field for each time point, each containing a matrix of dimensions (number of conditions) * (number of signals), with the first field being t0. Typically produced by simulating a model and then extracting the columns that correspond to signals
expResults	same as above, but contains the experimental results, ie this is CNOList\$valueSignals
times	a vector of times, its length should be the same as the number of fields in simResults and ExpResults
namesCues	a vector of names, typically CNOList\$namesCues
namesSignals	a vector of names, typically CNOList\$namesSignals
valueCues	a matrix of dimensions (number of conditions) * (number of cues), typically CNOList\$valueCues
formalism	New convention is to take the time=0 data set into account to compute the MSE. you can use the previous convection by setting this argument to something different from the default value.

**Details**

The colouring of the background is done as follows: the mean absolute difference between observed and simulated values are computed, and colours are chosen based on this value: red (above 0.9), indianred1 (between 0.8 and 0.9), lightpink2 (between 0.7 and 0.8), lightpink (between 0.6 and 0.7), mistyrose (between 0.5 and 0.6), palegoldenrod (between 0.4 and 0.5), palegreen (between 0.3 and 0.4), darkolivegreen3 (between 0.2 and 0.3), chartreuse3 (between 0.1 and 0.2), forestgreen (between 0 and 0.1). This function is used inside cutAndPlotResultsT1.

**Value**

This function doesn't return anything, it just produces a plot in your graphics window.

**Author(s)**

C. Terfve

**References**

J. Saez-Rodriguez, L. G. Alexopoulos, J. Epperlein, R. Samaga, D. A. Lauffenburger, S. Klamt and P. K. Sorger. Discrete logic modeling as a means to link protein signaling networks with functional analysis of mammalian signal transduction, *Molecular Systems Biology*, 5:331, 2009.

**See Also**

cutAndPlotResultsT1

**Examples**

```
tmpdir<-tempdir()
setwd(tmpdir)
```

```
#We will plot the fit of the full initial model compared to the data, without any optimisation
```

```
#This is normally not done on a stand alone basis, but if you have a model and would like to visualise its output compared
```

```
#load and prepare data
```



```

data(CNolistToy,package="CellNOptR")
data(ToyModel,package="CellNOptR")
indicesToy<-indexFinder(CNolistToy,ToyModel,verbose=TRUE)
ToyFields4Sim<-prep4sim(ToyModel)

#simulate model

Sim<-simulatorT1(CNolist=CNolistToy,model=ToyModel,simList=ToyFields4Sim,indexList=indicesToy)

#format data and results

simRes<-Sim[,indicesToy$signals]
simResults<-list(t0=matrix(data=0,nrow=dim(simRes)[1],ncol=dim(simRes)[2]),t1=simRes)
expResults<-list(t0=CNolistToy$valueSignals[[1]],t1=CNolistToy$valueSignals[[2]])

#plot

plotOptimResults(
simResults=simResults,
expResults=expResults,
times=CNolistToy$timeSignals[1:2],
namesCues=CNolistToy$namesCues,
namesSignals=CNolistToy$namesSignals,
valueCues=CNolistToy$valueCues)

```

---

plotOptimResultsPan     *Plots the data and simulated values from any CellNOptR formalism*

---

## Description

This function plots the data and simulated values according to each experiment in CNolist. The data is shown as black triangles and the simulation by a blue dashed line. The combination of cues is given by a panel where black denotes the presence and white the absence of the cue. The goodness-of-fit between model and data is color-coded on a continuous scale from white to red.

## Usage

```

plotOptimResultsPan(simResults, yInterpol=NULL, xCoords=NULL,
CNolist=CNolist, formalism=c("ss1", "ss2", "ssN", "dt", "ode"), pdf=FALSE,
pdfFileName="", tPt=NULL,
plotParams = list(margin = 0.1, width=15, height=12, cmap_scale=1, cex=1.6))

```

## Arguments

simResults	A list with a field for each time point, each containing a matrix of dimensions (number of conditions) * (number of signals), with the first field being t0. Typically produced by simulating a model and then extracting the columns that correspond to signals.
yInterpol	If using CNORdt, these are the interpolated experimental results from getFit-TimeScale() that are needed to compare against the Boolean simulation.

xCoords	These are the x-coordinates obtained from the optimized scaling factor in CNORdt that allow for comparison between time course experimental data and a Boolean model.
CNOlist	A CNOlist.
formalism	An abbreviation of the CellNOptR formalism being used.
pdf	A Boolean argument denoting whether to print the figure produced by this function to file.
pdfFileName	If printing to file, the filename to be used.
tPt	The number of time points in the data.
plotParams	a list of option related to the PDF and plotting outputs. Currently, the following attributes are used: (1) margin of the boxes, (2) width and height used while creating the PDF, (3) cmap_scale a value that scales the colors towards small errors (<1) or large errors (>1); default is 1 (linear colormap) (4) cex is the fontsize used in the header.

### Details

Depending on the logic formalism, this function is generally called from `cutAndPlotResults*()`. As shown in the example below however, it can plot the fit of any data and corresponding compatible model. The color denotes the goodness-of-fit, where white shows no difference between simulation and data and red is the maximum error from all conditions and readouts.

### Value

This function does not return a value.

### Author(s)

A. MacNamara

### References

J. Saez-Rodriguez, L. G. Alexopoulos, J. Epperlein, R. Samaga, D. A. Lauffenburger, S. Klamt and P. K. Sorger. Discrete logic modeling as a means to link protein signaling networks with functional analysis of mammalian signal transduction, *Molecular Systems Biology*, 5:331, 2009.

### See Also

`cutAndPlotResultsT1`

### Examples

```
data(CNOlistToy,package="CellNOptR")
data(ToyModel,package="CellNOptR")
indicesToy <- indexFinder(CNOlistToy, ToyModel, verbose=TRUE)
ToyFields4Sim <- prep4sim(ToyModel)

# simulate model
Sim <- simulatorT1(CNOlist=CNOlistToy, model=ToyModel, simList=ToyFields4Sim, indexList=indicesToy)

# format data and results
```

```

simRes <- Sim[,indicesToy$signals]
simResults <- list(t0=matrix(data=0, nrow=dim(simRes)[1], ncol=dim(simRes)[2]), t1=simRes)

# plot
plotOptimResultsPan(simResults,
  CNOList=CNOListToy,
  formalism="ss1",
  pdf=FALSE,
  tPt=10
)

```

---

plotOptimResultsPDF *Plot the data and simulated values in a pdf file*

---

### Description

This is a wrapper for plotOptimResults

### Usage

```

plotOptimResultsPDF(simResults, expResults, times, namesCues, namesSignals,
  valueCues, filename, formalism="new")

```

### Arguments

simResults	a list with a field for each time point, each containing a matrix of dimensions number of conditions * number of signals, with the first field being t0. Typically produced by simulating a model and then extracting the columns that correspond to signals
expResults	same as above, but contains the experimental results, ie this is CNOList\$valueSignals
times	a vector of times, its length should be the same as the number of fields in simResults and ExpResults
namesCues	a vector of names, typically CNOList\$namesCues
namesSignals	a vector of names, typically CNOList\$namesSignals
valueCues	a matrix of dimensions (number of conditions) * (number of cues), typically CNOList\$valueCues
filename	a name for your file, eg. "plot.pdf"
formalism	New convention is to take the time=0 data set into account to compute the MSE. you can use the previous convection by setting this argument to something different from the default value.

### Details

The coloring of the background is done as follows: the mean absolute difference between observed and simulated values are computed, and colours are chosen based on this value: red (above 0.9), indianred1 (between 0.8 and 0.9), lightpink2 (between 0.7 and 0.8), lightpink (between 0.6 and 0.7), mistyrose (between 0.5 and 0.6), palegoldenrod (between 0.4 and 0.5), palegreen (between 0.3 and 0.4), darkolivegreen3 (between 0.2 and 0.3), chartreuse3 (between 0.1 and 0.2), forestgreen (between 0 and 0.1). This function is used inside cutAndPlotResultsT1.

**Value**

This function doesn't return anything, it just produces a plot in a pdf document in your working directory.

**Author(s)**

C. Terfve

**See Also**

plotOptimResults, cutAndPlotResultsT1

**Examples**

```
tmpdir<-tempdir()
setwd(tmpdir)

#We will plot the fit of the full initial model compared to the data, without any optimisation
#This is normally not done on a stand alone basis, but if you have a model and would like to visualise
#its output compared to your data, then this is what you should do

#load and prepare data

data(CNolistToy,package="CellNOptR")
data(ToyModel,package="CellNOptR")
indicesToy<-indexFinder(CNolistToy,ToyModel,verbose=TRUE)
ToyFields4Sim<-prep4sim(ToyModel)

#simulate the model

Sim<-simulatorT1(CNolist=CNolistToy,model=ToyModel,simList=ToyFields4Sim,indexList=indicesToy)

#format the results and data as expected by plotOptimResults

simRes<-Sim[,indicesToy$signals]
simResults<-list(t0=matrix(data=0,nrow=dim(simRes)[1],ncol=dim(simRes)[2]),t1=simRes)
expResults<-list(t0=CNolistToy$valueSignals[[1]],t1=CNolistToy$valueSignals[[2]])

#plot

plotOptimResultsPDF(
simResults=simResults,
expResults=expResults,
times=CNolistToy$timeSignals[1:2],
namesCues=CNolistToy$namesCues,
namesSignals=CNolistToy$namesSignals,
valueCues=CNolistToy$valueCues,
filename="Toyfull.pdf")
```

**Description**

Adds to the model some fields that are used by the simulation engine

**Usage**

```
prep4sim(model)
```

**Arguments**

model	a model list, as output by readSIF, normally pre-processed but that is not a requirement of this function
-------	---

**Details**

This adds fields that are necessary for the simulation engine in a version that is extensible for constrained Fuzzy logic extension of the methods applied here (in development).

**Value**

this function returns a list with fields:

finalCube	stores, for each reac(row) the location of its inputs (col)
ixNeg	stores, for each reac(row) and each input (col) whether it is a negative input
ignoreCube	logical matrix of the same size as the 2 above, that tells whether the particular cell is filled or not
maxIx	row vector that stores, for each reac, the location of its output
modelName	stores the name of the model from which these fields were derived
maxInput	stores the max number of inputs observed in the model for a single reaction

**Note**

For internal usage since version 1.3.28

**Author(s)**

C. Terfve, T. Cokelaer

**See Also**

[simulatorT1](#)

**Examples**

```
data(ToyModel,package="CellNOptR")
ToyFields4Sim<-prep4sim(ToyModel)
```

---

```
preprocessing           Performs the pre-processing steps
```

---

### Description

This function performs any of the following preprocessing steps:

1. removes Non-Controllable and Non-Observables nodes
2. compress the model
3. and-gates expansion

### Usage

```
preprocessing(data, model, cutNONC=TRUE, compression=TRUE,
              expansion=TRUE, ignoreList=NA, maxInputsPerGate=2, verbose=TRUE)
```

### Arguments

data	the CNOList that contains the data that you will use
model	the model object as returned by <a href="#">readSIF</a>
cutNONC	Removes the NONC nodes using <a href="#">cutNONC</a> and <a href="#">findNONC</a> (Default is TRUE).
compression	Compress the model using <a href="#">compressModel</a> (Default is TRUE).
expansion	Add and gates using <a href="#">expandGates</a> (Default is TRUE).
ignoreList	list of reactions indices to ignore in the expansion step.
maxInputsPerGate	used by the <a href="#">expandGates</a> function to set maximum inputs per and gates.
verbose	verbose option (Default is TRUE).

### Details

The function can apply any or none of the pre-processing steps. It returns the new model and the indices returned by [indexFinder](#).

### Value

the new model

### Author(s)

T. Cokelaer

### See Also

[readSIF](#), [readMIDAS](#), [cutNONC](#), [findNONC](#), [compressModel](#), [expandGates](#).

### Examples

```
data(ToyModel,package="CellNOptR")
data(CNOListToy,package="CellNOptR")
model = preprocessing(CNOListToy, ToyModel, cutNONC=FALSE)
```

---

readMIDAS	<i>Reads in a CSV MIDAS file</i>
-----------	----------------------------------

---

### Description

This function takes in a single argument, the name of a CSV MIDAS file containing the data, and returns a list that contains all the elements to build a CNOList. The output of this function should be used as input for [makeCNOList](#).

### Usage

```
readMIDAS(MIDASfile, verbose=TRUE)
```

### Arguments

MIDASfile	a CSV MIDAS file (see details)
verbose	logical (default to TRUE).

### Details

This function does not return a CNOList, but the output of this function can be used directly into [makeCNOList](#) to create one. The MIDAS file format is described in Saez-Rodriguez et al. (2008).

If you have all of the readouts measured at the same series of time points, you can specify a unique DA: column which must have the format "DA:ALL".

### Value

this function returns a list with fields:

dataMatrix	matrix containing the data in the MIDAS file
TRcol	indexes of the columns that contain the treatments (excluding cell line)
DAcol	indexes of the columns that contain the data time points
DVcol	indexes of the columns that contain the actual values (measurements)

### Author(s)

C.Terfve

### References

J. Saez-Rodriguez, A. Goldsipe, J. Muhlich, L. Alexopoulos, B. Millard, D. A. Lauffenburger, P. K. Sorger *Flexible Informatics for Linking Experimental Data to Mathematical Models via DataRail*. *Bioinformatics*, 24:6, 840-847 (2008).

### See Also

[makeCNOList](#)

**Examples**

```
tmpdir<-tempdir()
setwd(tmpdir)
cpfile<-dir(system.file("ToyModel",package="CellNOptR"),full=TRUE)
file.copy(from=cpfile,to=getwd(),overwrite=TRUE)
dataToy<-readMIDAS(MIDASfile='ToyDataMMB.csv')
CNolistToy<-makeCNolist(dataset=dataToy,subfield=FALSE)
```

---

readSIF

*Read a SIF file and create a model object*


---

**Description**

This function reads in a cityscape SIF file and creates a model object that can be used in the CellNOptR procedure.

**Usage**

```
readSIF(sifFile)
```

**Arguments**

sifFile            the name of a SIF file

**Details**

This function takes in a single argument, sifFile, that points to a previous knowledge network in SIF format i.e. sourceNode-tab-sign-tab-targetNode. If there are ANDs they should be introduced as dummy nodes called and# (don't forget the number after "and" otherwise this won't be recognised). Please be aware that "and" nodes are not expected to be negated, i.e. there are not supposed to be !and1=xyz because that amounts to inverting the sign of all inputs of and1, which is more simply done at the inputs level.

**Value**

a model list with fields:

interMat	contains a matrix with column for each reaction and a row for each species, with a -1 where the species is the source node and a +1 where the species is a target node, and 0 otherwise
notMat	has the same format as interMat but just contains a 1 if the source node enters the reac with a negative effect, and 0 otherwise
namesSpecies	vector that contains the names of the species in the same order as the rows of the interMat and notMat matrices
reacID	vector that holds character strings specifying the reaction in full letters, in the same order as the columns of interMat and notMat

**Author(s)**

C. Terfve



## References

Shannon P, Markiel A, Ozier O, Baliga NS, Wang JT, Ramage D, Amin N, Schwikowski B, Ideker T. Cytoscape: a software environment for integrated models of biomolecular interaction networks. *Genome Research* 2003 Nov; 13(11):2498-504.

## Examples

```
tmpdir<-tempdir()
setwd(tmpdir)
cpfile<-dir(system.file("ToyModel",package="CellNOptR"),full=TRUE)
file.copy(from=cpfile,to=getwd(),overwrite=TRUE)
ToyModel<-readSIF(sifFile="ToyPKNMMB.sif")
```

---

residualError

*Compute the residual error for a dataset*

---

## Description

This function takes in a CNOList and computes the residual error, which is the minimum error between the scaled continuous data and a binary boolean approximation of this data.

## Usage

```
residualError(CNOList)
```

## Arguments

CNOList            a CNOList

## Details

Be aware that it is expected that \$valueSignals[[1]] holds t0 (all signals=0) and \$valueSignals[[2]] holds t1, \$valueSignals[[3]] holds t2 and so on. The output is a list of residual errors at each time greater than 2. In addition, the total error is stored. For back compatibility, an additional field called t1andt2 is stored (NA is only t1 provided).

## Value

a vector with named entries t1, t2, ...tn, t1andt2 and total. If only t1 is provided, t1andt2 is set to NA. The field t1andt2 may be removed in the future. Use the field called total instead.

## Author(s)

C. Terfve, T. Cokelaer

## See Also

[makeCNOList](#), [normaliseCNOList](#), [getFit](#)

## Examples

```
data(CNOListToy,package="CellNOptR")
resECNOListToy<-residualError(CNOListToy)
```

---

sif2graph	<i>Convert sif to graph</i>
-----------	-----------------------------

---

**Description**

This function receives as input a network in form sif format and converts it to graph format.

**Usage**

```
sif2graph(sif)
```

**Arguments**

sif                    the name of a sif file or the equivalent table

**Details**

This function takes a network in sif format (table or file), i.e. sourceNode-tab-sign-tab-targetNode. If there are ANDs they should be introduced as dummy nodes called and# (don't forget the number after "and" otherwise this won't be recognised). Please be aware that "and" nodes are not expected to be negated, i.e. there are not supposed to be !and1=xyz because that amounts to inverting the sign of all inputs of and1, which is more simply done at the inputs level.

In the resulting graph, the sign of each link is encoded as the weight of the edge (-1 negative regulation, +1 positive regulation).

**Value**

g                    the corresponding graph

**Author(s)**

F.Eduati

**See Also**

[graph2sif](#), [model2sif](#), [readSIF](#),

---

simulateT1	<i>deprecated since version 1.3.28. Cut and simulation of a boolean model at t1</i>
------------	---

---

**Description**

This function cuts a model according to a bitstring optimised at T1, and simulates the model accordingly.

**Usage**

```
simulateT1(CNOlist, model, bStringT1, simList, indexList)
```

**Arguments**

CNOList	a CNOList object
model	a full model
bStringT1	a bitstring to cut the model, as output by gaBinaryT1 (i.e. a vector of 1s and 0s, of length equal to the number of reactions in the model)
simList	a list of additional fields for simulation as created by prep4sim, corresponding to the full model
indexList	a list of indexes as created by indexFinder

**Details**

This function is a wrapper for simulatorT1, that cuts the model before simulating it

**Value**

a matrix of simulated values, including all species in the model, i.e. to be used as input of gaBinaryT2 (not implemented here) but not to be used directly in plotOptimResults.

**Author(s)**

C.Terfve

**See Also**

cutAndPlotOptimResultsT1, simulatorT1

**Examples**

```
# This will compute the output of a random model obtained by randomly selecting
# which gates of the initial models are included.
```

```
data(CNOListToy,package="CellNOptR")
data(ToyModel,package="CellNOptR")
```

```
indicesToy<-indexFinder(CNOListToy,ToyModel,verbose=FALSE)
ToyFields4Sim<-prep4sim(ToyModel)
```

```
simRes<-simulateT1(
  CNOList=CNOListToy,
  model=ToyModel,
  bStringT1=round(runif(length(ToyModel$reacID))),
  simList=ToyFields4Sim,
  indexList=indicesToy)
```

---

 simulateTN

*Cut and simulation of a boolean model at t1*


---

**Description**

This function cuts a model according to a bitstring optimised at T1, and simulates the model accordingly.

**Usage**

```
simulateTN(CNOList, model, bStrings)
```

**Arguments**

CNOList	a CNOList object
model	a full model
bStrings	a bitstring to cut the model, as output by gaBinaryT1 (i.e. a vector of 1s and 0s, of length equal to the number of reactions in the model)

**Details**

This function is a wrapper around the family of functions called simulatorT1 , T2 and TN.

**Value**

a matrix of simulated values, including all species in the model, i.e. to be used as input of gaBinaryTN.

**Author(s)**

T.Cokelaer, S.Schrier based on simulatorT1 (C.Terfve)

**See Also**

[cutAndPlotResultsT1](#), [simulatorT1](#)

**Examples**

```
# This will compute the output of a random model obtained by randomly selecting
# which gates of the initial models are included.
```

```
data(CNOListToy,package="CellNOptR")
data(ToyModel,package="CellNOptR")
```

```
simRes<-simulateTN(
  CNOList=CNOListToy,
  model=ToyModel,
  bStrings=list(round(runif(length(ToyModel$reacID))))))
```

---

simulatorT0	<i>Simulation of a boolean model</i>
-------------	--------------------------------------

---

**Description**

This is the simulator, inspired from BoolSimEngMKM in the Matlab CellNOpt, to be used on one time point simulations

**Usage**

```
simulatorT0(CNOList, model, simList, indexList)
```

**Arguments**

CNOList	a CNOList
model	a model that only contains the reactions to be evaluated
simList	a simList as created by prep4sim, that has also already been cut to contain only the reactions to be evaluated
indexList	an indexList as created by indexFinder

**Details**

Differences from the BoolSimEngMKM simulator include: the valueInhibitors has not been previously flipped; the function outputs the values across all conditions for all species in the model, instead of only for the signal species. This is because then the output of this function can be used as initial values for the version of the simulator that works on time point 2 (not implemented in this version).

If you would like to compute the output of a model that contains some of the gates in the model but not all, we suggest that you use the function SimulateT1 and specify in the bStringT1 argument which gates you want to be included. Indeed, SimulateT1 is a wrapper around simulatorT1 that takes care of cutting the model for you before simulating it.

**Value**

This function outputs a single matrix of format similar to valueSignals in the CNOList but that contains an output for each species in the model. This matrix is the simulated equivalent of valueSignals at time 1, if you consider only the columns given by indexSignals.

**Author(s)**

T. Cokelaer

**References**

1. J. Saez-Rodriguez, L. G. Alexopoulos, J. Epperlein, R. Samaga, D. A. Lauffenburger, S. Klamt and P. K. Sorger. Discrete logic modeling as a means to link protein signaling networks with functional analysis of mammalian signal transduction, *Molecular Systems Biology*, 5:331, 2009.
2. M. K. Morris, J. Saez-Rodriguez, D. Clarke, P. K. Sorger, D. A. Lauffenburger. Training Signaling Pathway Maps to Biochemical Data with Constrained Fuzzy Logic: Quantitative Analysis of Liver Cell Responses to Inflammatory Stimuli, *PLoS Comp. Biol.*, 7(3): e1001099, 2011.

**See Also**

[simulateTN](#), [cutAndPlotResultsT1](#)

**Examples**

#This computes the output of the full model, which is normally not done on a stand alone basis, but if you have a model and

```
data(CNolistToy,package="CellNOptR")
data(ToyModel,package="CellNOptR")
```

```
indicesToy<-indexFinder(CNolistToy,ToyModel,verbose=TRUE)
ToyFields4Sim<-prep4sim(ToyModel)
```

```
Sim<-simulatorT0(
  CNolist=CNolistToy,
  model=ToyModel,
  simList=ToyFields4Sim,
  indexList=indicesToy)
```

---

simulatorT1

*Simulation of a boolean model*

---

**Description**

This is the simulator, inspired from BoolSimEngMKM in the Matlab CellNOpt, to be used on one time point simulations

**Usage**

```
simulatorT1(CNolist, model, simList, indexList)
```

**Arguments**

CNolist	a CNolist
model	a model that only contains the reactions to be evaluated
simList	a simList as created by prep4sim, that has also already been cut to contain only the reactions to be evaluated
indexList	an indexList as created by indexFinder

**Details**

Differences from the BoolSimEngMKM simulator include: the valueInhibitors has not been previously flipped; the function outputs the values across all conditions for all species in the model, instead of only for the signal species. This is because then the output of this function can be used as initial values for the version of the simulator that works on time point 2 (not implemented in this version).

If you would like to compute the output of a model that contains some of the gates in the model but not all, we suggest that you use the function SimulateT1 and specify in the bStringT1 argument which gates you want to be included. Indeed, SimulateT1 is a wrapper around simulatorT1 that takes care of cutting the model for you before simulating it.

**Value**

This function outputs a single matrix of format similar to valueSignals in the CNOList but that contains an output for each species in the model. This matrix is the simulated equivalent of valueSignals at time 1, if you consider only the columns given by indexSignals.

**Author(s)**

C. Terfve

**References**

1. J. Saez-Rodriguez, L. G. Alexopoulos, J. Epperlein, R. Samaga, D. A. Lauffenburger, S. Klamt and P. K. Sorger. Discrete logic modeling as a means to link protein signaling networks with functional analysis of mammalian signal transduction, *Molecular Systems Biology*, 5:331, 2009.
2. M. K. Morris, J. Saez-Rodriguez, D. Clarke, P. K. Sorger, D. A. Lauffenburger. Training Signaling Pathway Maps to Biochemical Data with Constrained Fuzzy Logic: Quantitative Analysis of Liver Cell Responses to Inflammatory Stimuli, *PLoS Comp. Biol.*, 7(3): e1001099, 2011.

**See Also**

[simulateTN](#), [cutAndPlotResultsT1](#)

**Examples**

#This computes the output of the full model, which is normally not done on a stand alone basis, but if you have a model and

```
data(CNOListToy,package="CellNOptR")
data(ToyModel,package="CellNOptR")

indicesToy<-indexFinder(CNOListToy,ToyModel,verbose=TRUE)
ToyFields4Sim<-prep4sim(ToyModel)

Sim<-simulatorT1(
  CNOList=CNOListToy,
  model=ToyModel,
  simList=ToyFields4Sim,
  indexList=indicesToy)
```

---

simulatorT2

*Deprecated since 1.3.28. Use [simulateTN](#) function instead. Simulation of a boolean model for time 2*

---

**Description**

This function simulates a boolean model at time 2 where time 2 is assume to be a pseudo-steady states at a time scale slower than the pseudo-steady state evaluated at time 1

**Usage**

```
simulatorT2(simResultsT1, CNOList, model, simList, indexList, timeIndex=3)
```

**Arguments**

simResultsT1	a matrix that is the output of simulatorT1 (i.e. one row per condition and one column per species IN THE MODEL)
CNOlist	a CNOlist
model	a Model that only contains the reactions to be evaluated, and the additional field model\$times that should have been created inside the gabinaryT2 optimisation engine.
simList	a simList as created by prep4sim, that has also already been cut to contain only the reactions to be evaluated
indexList	an indexList as created by indexFinder
timeIndex	argument requiter only for steady states T3 and above to specify the Time indices.

**Details**

This is the simulator for time T2, it is very similar to simulatorT1 but here we assume that we start from the simulated results at t1 (i.e. we start from a pseudo-steady state) then it does a first iteration, and whatever branch is set to be active at t2 has an effect that cannot be changed after the first iteration, i.e. the output node of a t2 iteration is fixed. We assume here that the model has already been cut, and that the cutting is based on keeping all the edges that are set to either 1 or 2, and there is an additional field \$times in the model that keeps the info of the t1/t2 (it is a vector of 1s and 2s of length=number of reaches present). Structurally the function is almost identical to simulatorT1 but it does a first iteration where all the gates that lead to a node that also receives a T2 gates are set to the same value as the t2 gate in the ANDs calculation. In the main loop, the nodes that are targets of t2 interactions are constantly reset to their value at the first iteration, at the end of each iteration (similarly to what is done with stimulated and inhibited species)

The model\$times field is a vector of 1s and 2s that tells the simulator which interactions are expected to be active at t1 and which are at t2.

**Value**

This function outputs a single matrix of format similar to valueSignals in the CNOlist but that contains an output for each species in the model. This matrix is the simulated equivalent of valueSignals at time 2 if you consider only the columns given by indexSignals

**Author(s)**

C. Terfve

**See Also**

[simulateTN](#), [cutAndPlotResultsT1](#), [simulatorT1](#)

**Examples**

```
# This computes the output of the full model, which is normally not done on a
# stand alone basis, but if you have a model and would like to visualise its
# output compared to your data, then this is what you should do
```

```
data(CNOlistToy2,package="CellNOptR")
data(ToyModel2,package="CellNOptR")
```



```

#Sim<-simulatorTN(
#  CNOList=CNOListToy2,
#  model=ToyModel2)

#Sim2<-simulatorTN(
#  simResultsT1=Sim,
#  CNOList=CNOListToy2,
#  model=ToyModel2,
#  simList=ToyFields4Sim,
#  indexList=indicesToy, timeIndex=3)

```

---

simulatorTN	<i>Simulation of a boolean model at any time points dependent on a previous one.</i>
-------------	--

---

### Description

This is the simulator at TN using a C implementation. The computation relies on the time TN-1. T1 is a special case that is solved by using [simulatorT2](#).

### Usage

```
simulatorTN(simResultsPrev, CNOList, model, simList, indexList, timeIndex=3)
```

### Arguments

simResultsPrev	a matrix that is the output of simulatorTN (i.e. one row per condition and one column per species IN THE MODEL)
CNOList	a CNOList
model	a model that only contains the reactions to be evaluated
simList	a simList as created by prep4sim, that has also already been cut to contain only the reactions to be evaluated
indexList	an indexList as created by indexFinder
timeIndex	3 by default to behave like deprecated function simulatorT2. This is the timeIndex at which the simulation is requested.

### Details

Differences from the BoolSimEngMKM simulator include: the valueInhibitors has not been previously flipped; the function outputs the values across all conditions for all species in the model, instead of only for the signal species. This is because then the output of this function can be used as initial values for the version of the simulator that works on time point 2 (not implemented in this version).

If you would like to compute the output of a model that contains some of the gates in the model but not all, we suggest that you use the function SimulateT1 and specify in the bStringT1 argument which gates you want to be included. Indeed, SimulateT1 is a wrapper around simulatorT1 that takes care of cutting the model for you before simulating it.

**Value**

This function outputs a single matrix of format similar to valueSignals in the CNOList but that contains an output for each species in the model. This matrix is the simulated equivalent of valueSignals at time 1, if you consider only the columns given by indexSignals.

**Author(s)**

T. Cokelaer, based on [cSimulator](#) (A. MacNamara)

**References**

1. J. Saez-Rodriguez, L. G. Alexopoulos, J. Epperlein, R. Samaga, D. A. Lauffenburger, S. Klamt and P. K. Sorger. Discrete logic modeling as a means to link protein signaling networks with functional analysis of mammalian signal transduction, *Molecular Systems Biology*, 5:331, 2009.
2. M. K. Morris, J. Saez-Rodriguez, D. Clarke, P. K. Sorger, D. A. Lauffenburger. Training Signaling Pathway Maps to Biochemical Data with Constrained Fuzzy Logic: Quantitative Analysis of Liver Cell Responses to Inflammatory Stimuli, *PLoS Comp. Biol.*, 7(3): e1001099, 2011.

**See Also**

[simulateTN](#), [cutAndPlotResultsT1](#)

**Examples**

#This computes the output of the full model, which is normally not done on a stand alone basis, but if you have a model ar

```
data(CNOListToy,package="CellNOptR")
data(ToyModel,package="CellNOptR")

indicesToy<-indexFinder(CNOListToy,ToyModel,verbose=TRUE)
ToyFields4Sim<-prep4sim(ToyModel)

#Sim<-simulatorTN(
# CNOList=CNOListToy,
# model=ToyModel,
# simList=ToyFields4Sim,
# indexList=indicesToy)
```

---

ToyModel

*Toy model*

---

**Description**

This data object contains the Toy model from the package vignette, already loaded and formatted as a Model object.

**Usage**

ToyModel

**Format**

ToyModel is a list with fields "reacID" (character vector), "namesSpecies" (character vector), "interMat" (numerical matrix), "notMat"(numerical matrix).

**Source**

This data and model is extracted from the Matlab version of CellNOpt1.0 (<http://www.ebi.ac.uk/saezrodriguez/software.html#CellNetOptimizer>).

**References**

J. Saez-Rodriguez, L. G. Alexopoulos, J. Epperlein, R. Samaga, D. A. Lauffenburger, S. Klamt and P. K. Sorger. Discrete logic modeling as a means to link protein signaling networks with functional analysis of mammalian signal transduction, *Molecular Systems Biology*, 5:331, 2009.

---

ToyModel2

*Toy model*

---

**Description**

This data object contains the Toy model from the package vignette, already loaded and formatted as a Model object, and modified for the 2 time points version (a negative feedback between cJun and Jnk (!cJun=Jnk) is added).

**Usage**

ToyModel

**Format**

ToyModel is a list with fields "reacID" (character vector), "namesSpecies" (character vector), "interMat" (numerical matrix), "notMat"(numerical matrix).

**Source**

This data and model is extracted from the Matlab version of CellNOpt1.0 (<http://www.ebi.ac.uk/saezrodriguez/software.html#CellNetOptimizer>).

**References**

J. Saez-Rodriguez, L. G. Alexopoulos, J. Epperlein, R. Samaga, D. A. Lauffenburger, S. Klamt and P. K. Sorger. Discrete logic modeling as a means to link protein signaling networks with functional analysis of mammalian signal transduction, *Molecular Systems Biology*, 5:331, 2009.

---

 writeDot

*Write a model, and attached features, to a dot file*


---

### Description

This function writes a model to a Graphviz dot file with encoded features such as edge weight and nodes status (see details).

### Usage

```
writeDot(dotNodes,dotMatrix,model,filename)
```

### Arguments

dotNodes	internal variables created by writeNetwork or writeScaffold; dotNodes is a matrix with 2 columns: the first has the node names, and the second the attributes (signal, stimulated, inhibited, compressed, nano). A node can appear twice in this matrix if it belongs to more of one of the above categories; a node could also not appear here if it is none of these categories
dotMatrix	internal variables created by writeNetwork or writeScaffold; dotMatrix is a matrix with 4 or 5 columns, and a row for each reaction: the first column holds the name of the input node, the second column holds the sign of the reaction (-1 if negative, 1 if positive), the third column holds the name of the output node, the fourth column holds the time stamp (0,1,2), an optional 5th column holds the weights of the edges
model	A model to be plotted, if used inside writeNetwork then this should be the previous knowledge network (modelOriginal), if inside writeScaffold then this should be the scaffold (modelComprExpanded)
filename	a name for the file

### Details

This function is not to be used on its own, it should be used internally to writeNetwork or writeScaffold. For the colouring of the nodes, nodes that are both stimulated and inhibited or any other combination, only one colour per category is used, and the following order of priority for the colours is used: signals prime over inhibited nodes which primes over stimulated nodes which primes over non-controllable/non-observable nodes, which primes over compressed. Nodes that are neither of those have a black contour, stimulated nodes are green, inhibited are red, measure are blue, compressed and non-controllable/non-observable nodes are black and dashed. Edges are coloured according to time stamp in the optimal model (green=t1, blue=t1 and/or t2, grey=neither); on the scaffold, the strokes of the edges reflects the weights in the models within reltol (i.e. for each edge, the weight is the frequency with which it appeared among the models within the relative tolerance boundaries around the best solution).

### Value

This function does not have any output, it just writes a dot file in your working directory.

### Author(s)

C. Terfve

## References

Emden R. Gansner , Stephen C. North. An Open Graph Visualization System and Its Applications to Software Engineering. Software - Practice and Experience (1999)

## See Also

[writeNetwork](#), [writeScaffold](#)

## Examples

```
tmpdir<-tempdir()
setwd(tmpdir)

#load data

data(CNolistToy,package="CellNOptR")
data(ToyModel,package="CellNOptR")

#pre-process model

indicesToy<-indexFinder(CNolistToy,ToyModel,verbose=TRUE)
ToyNCNOindices<-findNONC(ToyModel,indicesToy,verbose=TRUE)
ToyNCNOcut<-cutNONC(ToyModel,ToyNCNOindices)
indicesToyNCNOcut<-indexFinder(CNolistToy,ToyNCNOcut)
ToyNCNOcutComp<-compressModel(ToyNCNOcut,indicesToyNCNOcut)
indicesToyNCNOcutComp<-indexFinder(CNolistToy,ToyNCNOcutComp)
ToyNCNOcutCompExp<-expandGates(ToyNCNOcutComp)

#optimise

ToyFields4Sim<-prep4sim(ToyNCNOcutCompExp)
initBstring<-rep(1,length(ToyNCNOcutCompExp$reacID))
ToyT1opt<-gaBinaryT1(
  CNolist=CNolistToy,
  model=ToyNCNOcutCompExp,
  initBstring=initBstring,
  maxGens=2,
  popSize=5,
  verbose=TRUE)

#write network

writeNetwork(
  modelOriginal=ToyModel,
  modelComprExpanded=ToyNCNOcutCompExp,
  optimResT1=ToyT1opt,
  optimResT2=NA,
  CNolist=CNolistToy)
```

**Description**

This function takes a CNOList structure (output of makeCNOList and readMIDAS) and save it a MIDAS format.

**Usage**

```
writeMIDAS(CNOList, filename)
```

**Arguments**

CNOList	a CNOList structure
filename	a filename. Not overwritten if it exists already

**Author(s)**

T. Cokelaer

**See Also**

[makeCNOList](#), [readMIDAS](#), [CNOList](#)

**Examples**

```
tmpdir<-tempdir()
setwd(tmpdir)
data(CNOListToy)
writeMIDAS(CNOListToy, 'test.csv')
readMIDAS('test.csv')
```

---

writeNetwork

*Write a previous knowledge network model to a sif file (with attribute files), as well as a dot file*

---

**Description**

This function writes the original previous knowledge network (the model that you loaded in the beginning of your analysis) in a sif file, with a nodes attribute file that specifies if each node was stimulated/inhibited/signal/compressed/non-controllable-non-observable and an edge attribute file that specifies if the edge was absent in the optimal model (0) present in the optimal model at t1 (1) or present in the optimal model at t2 (2).

This function also writes a Graphviz dot file that contains the same information (see writeDot for more information about the dot file conventions).

**Usage**

```
writeNetwork(modelOriginal, modelComprExpanded, optimResT1, optimResT2, CNOList,
tag = NULL,verbose=FALSE)
```

**Arguments**

modelOriginal	The PKN model
modelComprExpanded	The scaffold model (i.e. compressed and expanded)
optimResT1	The results of the optimisation process at t1
optimResT2	The results of the optimisation process at t2 (set this to NA if you have performed a one time point optimisation).
CNOList	The CNOList on which the optimisation is based
tag	NULL or string; tells whether you want to prefix filenames with a tag (replaces the default behaviour).
verbose	If verbose=TRUE, the function prints a message every time an edge in the scaffold network couldn't be mapped back to the PKN

**Details**

The weights of the edges are computed as the mean across models within the relative tolerance limits, as output in the results from the optimisation `$stringsTol`. Strings that are in `$stringsTol` are the ones that are within the relative tolerance limits around the best solution in the population across all generations of the optimisation.

!If there is no time 2, then the argument `optimResT2` should be = NA

This function maps back the edges weights from the optimised (expanded and compressed) model to the original model. The mapping back only works if the path has length 2 at most (i.e. you have `node1-comp1-comp2-node2`, where `comp` refer to nodes that have been compressed).

**Value**

This function does not have any output, it just writes a `sif` file, an edge attribute file, and a node attribute file

**Note**

The mapback of this function is still an open question, even in the Matlab version. Future developments will include more robust versions of the mapping back algorithm, probably as a separate mapback function.

**Author(s)**

C. Terfve

**See Also**

`writeScaffold`, `writeDot`

**Examples**

```
tmpdir<-tempdir()
setwd(tmpdir)

#load data

data(CNOListToy,package="CellNOptR")
```

```

data(ToyModel,package="CellNOptR")

#pre-process model

indicesToy<-indexFinder(CNOlistToy,ToyModel,verbose=TRUE)
ToyNCNOindices<-findNONC(ToyModel,indicesToy,verbose=TRUE)
ToyNCNOcut<-cutNONC(ToyModel,ToyNCNOindices)
indicesToyNCNOcut<-indexFinder(CNOlistToy,ToyNCNOcut)
ToyNCNOcutComp<-compressModel(ToyNCNOcut,indicesToyNCNOcut)
indicesToyNCNOcutComp<-indexFinder(CNOlistToy,ToyNCNOcutComp)
ToyNCNOcutCompExp<-expandGates(ToyNCNOcutComp)

#optimise

ToyFields4Sim<-prep4sim(ToyNCNOcutCompExp)
initBstring<-rep(1,length(ToyNCNOcutCompExp$reacID))
ToyT1opt<-gaBinaryT1(
  CNOlist=CNOlistToy,
  model=ToyNCNOcutCompExp,
  initBstring=initBstring,
  verbose=TRUE,
  maxGens=2,
  popSize=5)

#write network

writeNetwork(
  modelOriginal=ToyModel,
  modelComprExpanded=ToyNCNOcutCompExp,
  optimResT1=ToyT1opt,
  optimResT2=NA,
  CNOlist=CNOlistToy)

```

---

writeReport

---

*Write a report of a CellNOptR analysis*


---

## Description

This function writes a short report of a CellNOptR analysis in an html page, that is linked to the various graphs produced

## Usage

```

writeReport(modelOriginal, modelOpt, optimResT1, optimResT2, CNOlist, directory,
  namesFiles = list(dataPlot = NA, evolFitT1=NA, evolFitT2=NA, simResultsT1=NA,
  simResultsT2=NA, scaffold=NA, scaffoldDot=NA, tscaffold=NA, wscaffold=NA,
  PKN=NA, PKNdot=NA, wPKN=NA,nPKN=NA), namesData = list(CNOlist=NA, model=NA),
  resE=NULL)

```

## Arguments

**modelOriginal**    the original previous knowledge network (i.e. model that you loaded) in a model list format



modelOpt	the model that was actually used for optimisation (i.e. the scaffold network, after compression and expansion) in a model list format
optimResT1	the results of the optimisation at t1, as output by gabinaryT1
optimResT2	the results of the optimisation at t2, as output by gabinaryT2. Set this to NA if you have performed a one time point optimisation.
CNOlist	a CNOlist
directory	the name of a new directory that will be created, where your results will be moved
namesFiles	a list of the names of the files that should have been created. Depending on whether a t2 optimisation was performed or not, all or some of the following fields are expected: dataPlot, evolFitT1, evolFitT2, simResultsT1, simResultsT2, scaffoldDot, scaffold, tscaffold, wscaffold, PKN, PKNdot, wPKN, nPKN.
namesData	a list with fields \$CNOlist and \$model that contain strings that are meaningful identifiers of your data and previous knowledge network (for your own record).
resE	a vector with named entries t1, t2 t1andt2, as produced by the function ResidualError, that contains the residual error associated with the discretisation of the data. Since version 1.3.29, there is no need to provide this argument. Kept for back compatibility.

### Details

Future versions of this function might directly write and compile a tex file.

### Value

This function produces a directory and moves all the files of namesFiles to it, then it creates an html report that contains infos about the optimisation process.

### Author(s)

C. Terfve

### See Also

[writeNetwork](#), [writeScaffold](#)

### Examples

```
tmpdir<-tempdir()
setwd(tmpdir)

#load data

data(CNOlistToy,package="CellNOptR")
data(ToyModel,package="CellNOptR")

#pre-process model (partial)

indicesToy<-indexFinder(CNOlistToy,ToyModel,verbose=TRUE)
ToyNCNOcutComp<-compressModel(ToyModel,indicesToy)
indicesToyNCNOcutComp<-indexFinder(CNOlistToy,ToyNCNOcutComp)
ToyNCNOcutCompExp<-expandGates(ToyNCNOcutComp)
```

```

#optimise

ToyFields4Sim<-prep4sim(ToyNCNOcutCompExp)
initBstring<-rep(1,length(ToyNCNOcutCompExp$reacID))
ToyT1opt<-gaBinaryT1(
  CNOList=CNOListToy,
  model=ToyNCNOcutCompExp,
  initBstring=initBstring,
  maxGens=2,
  popSize=5,
  verbose=TRUE)

#write report

namesFilesToy<-list(
  dataPlot=NA,
  evolFitT1=NA,
  evolFitT2=NA,
  simResultsT1=NA,
  simResultsT2=NA,
  scaffold=NA,
  scaffoldDot=NA,
  tscaffold=NA,
  wscaffold=NA,
  PKN=NA,
  PKNdot=NA,
  wPKN=NA,
  nPKN=NA)

writeReport(
  modelOriginal=ToyModel,
  modelOpt=ToyNCNOcutCompExp,
  optimResT1=ToyT1opt,
  optimResT2=NA,
  CNOList=CNOListToy,
  directory="testToy",
  namesFiles=namesFilesToy,
  namesData=list(CNOList="Toy",model="ToyModel"),
  resE=NA)

```

---

writeScaffold	<i>Writes the scaffold network to a sif file (with attributes) and to a dot file</i>
---------------	--

---

## Description

This function writes a cytoscape SIF file for the scaffold network, with an associated edge attribute file that holds whether the edge is present at t1,t2 or not present at all and another associated edge attribute file that holds the weights of the edges. This function also writes a dot file that contains the same information (see writeDot for more information about the dot file conventions).

## Usage

```
writeScaffold(modelComprExpanded, optimResT1, optimResT2, modelOriginal,
  CNOList, tag=NULL)
```

**Arguments**

modelComprExpanded	The scaffold model (i.e. compressed and expanded)
optimResT1	The results of the optimisation process at t1
optimResT2	The results of the optimisation process at t2 (set this to NA if you have performed a one time point optimisation).
modelOriginal	The PKN model
CNOlist	The CNOlist on which the optimisation is based
tag	NULL or string; tells whether you want to prefix filenames with a tag (replaces the default behaviour).

**Details**

By scaffold network we mean the network that is used as a basis for optimisation (i.e. a compressed and expanded network), therefore no map back of the weights is necessary here.

The weights of the edges are computed as the mean across models within the relative tolerance limits, as output in the results from the optimisation `$stringsTol`. Strings that are in `$stringsTol` are the ones that are within the relative tolerance limits around the best solution in the population across all generations of the optimisation.

!If there is no time 2, then the argument `optimResT2` should be = NA.

**Value**

This function does not return anything, it writes a `sif` file and 2 edge attributes files, and a dot file, in your working directory.

**Author(s)**

C.Terfve

**See Also**

`writeNetwork`, `writeDot`

**Examples**

```
tmpdir<-tempdir()
setwd(tmpdir)

#load the data

data(CNOlistToy,package="CellNOptR")
data(ToyModel,package="CellNOptR")

#pre-process the model (partial)

indicesToy<-indexFinder(CNOlistToy,ToyModel,verbose=TRUE)
ToyNCNOcutComp<-compressModel(ToyModel,indicesToy)
indicesToyNCNOcutComp<-indexFinder(CNOlistToy,ToyNCNOcutComp)
ToyNCNOcutCompExp<-expandGates(ToyNCNOcutComp)

#optimise
```

```

ToyFields4Sim<-prep4sim(ToyNCNOcutCompExp)
initBstring<-rep(1,length(ToyNCNOcutCompExp$reacID))
ToyT1opt<-gaBinaryT1(
CNOList=CNOListToy,
model=ToyNCNOcutCompExp,
initBstring=initBstring,
maxGens=3,
popSize=5,
verbose=TRUE)

#write the network

writeScaffold(
modelOriginal=ToyModel,
modelComprExpanded=ToyNCNOcutCompExp,
optimResT1=ToyT1opt,
optimResT2=NA,
CNOList=CNOListToy)

```

---

writeSIF

---

*Convert a model into a SIF format and save the result in a file.*


---

### Description

This function takes as input a model (as created by e.g., read from a SIF data set with readSIF function) and save it into a file.

### Usage

```
writeSIF(model, filename)
```

### Arguments

model	the model
filename	the filename

### Author(s)

T Cokelaer

### Examples

```

tmpdir<-tempdir()
setwd(tmpdir)
cpfile<-dir(system.file("ToyModel",package="CellNOptR"),full=TRUE)
file.copy(from=cpfile,to=getwd(),overwrite=TRUE)
ToyModel<-readSIF(sifFile="ToyPKNMMB.sif")
writeSIF(ToyModel, "ToyPKNMMB_copy.sif")

```

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