Package ‘CNORode’

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R topics documented:
cnolistCNORodeExample ............................................. 2
CNORode .................................................................. 2
createLBodeContPars ................................................. 3
defaultParametersGA ............................................... 4
defaultParametersSSm ............................................... 5
getLBodeContObjFunction ......................................... 6
getLBodeDataSim ................................................... 7
getLBodeMINLPObjFunction ....................................... 9
getLBodeModelSim .................................................. 10
getLBodeSimFunction ............................................... 12
getStates ............................................................. 13
incidence2Adjacency ................................................. 13
indices ............................................................... 14
minlpLBodeSSm ..................................................... 14
model ................................................................. 16
parEstimationLBode ............................................... 16
parEstimationLBodeGA ............................................ 18
parEstimationLBodeSSm .......................................... 20
plotLBodeFitness ................................................... 22
plotLBodeModelSim .......................................................... 24
simdata2cnolist .............................................................. 25
simulate ................................................................. 26

Index 28

A cnolist from CellNoptR to use with provided CNORode examples.

Description

This package is used for the simulation and fitting of logic based ODE models based on the Odefy approach.

Details

| Package: | CNORode |
| Type: | Package |
| Version: | 1.2.0 |
| Date: | 2012-03-14 |
| License: | GPL-3 |
| LazyLoad: | yes |

Author(s)

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References


createLBodeContPars


See Also


createLBodeContPars  Create a list with ODE parameter information needed to perform parameter estimation

Description

Creates a list with the continuous parameters to simulate the model, upper and lower bounds for the parameter estimation, parameters names, indices of the parameters and other information.

Usage

createLBodeContPars(model, LB_n = 1, LB_k = 0.1, LB_tau = 0.01, UB_n = 5, UB_k = 0.9, UB_tau = 10, default_n = 3, default_k = 0.5, default_tau = 1, LB_in = c(), UB_in = c(), opt_n = TRUE, opt_k = TRUE, opt_tau = TRUE, random = FALSE)

Arguments

model The logic model to be simulated.
LB_n A numeric value to be used as lower bound for all parameters of type n.
LB_k A numeric value to be used as lower bound for all parameters of type k.
LB_tau A numeric value to be used as lower bound for all parameters of type tau.
UB_n A numeric value to be used as upper bound for all parameters of type n.
UB_k A numeric value to be used as upper bound for all parameters of type k.
UB_tau A numeric value to be used as upper bound for all parameters of type tau.
default_n The default parameter to be used for every parameter of type n.
default_k The default parameter to be used for every parameter of type k.
default_tau The default parameter to be used for every parameter of type tau.
LB_in An array with the the same length as ode_parameters$parValues with lower bounds for each specific parameter.
UB_in An array with the the same length as ode_parameters$parValues with upper bounds for each specific parameter.
opt_n Add all parameter n to the index of parameters to be fitted.
opt_k Add all parameter k to the index of parameters to be fitted.
opt_tau Add all parameter tau to the index of parameters to be fitted.
random logical value that determines that a random solution is for the parameters to be optimized.
**Value**

- **parNames**: An array containing the names of the parameters.
- **parValues**: An array containing the values of the parameters, in the same order as the names.
- **index_opt_pars**: An array containing the indexes for the parameters to be fitted.
- **index_n**: An array containing the indexes of the parameters of type n.
- **index_k**: An array containing the indexes of the parameters of type k.
- **index_tau**: An array containing the indexes of the parameters of type tau.
- **LB**: An array containing the lower bound for each parameter.
- **UB**: An array containing the upper bound for each parameter.

**Author(s)**

David Henriques, Thomas Cokelaer

**Examples**

```r
library(CNORode)
data("ToyCNOlist", package="CNORode");
data("ToyModel", package="CNORode");
data("ToyIndices", package="CNORode");
ode_parameters=createLBodeContPars(model, opt_n=FALSE, default_n=2,
random=TRUE, LB_k=0.25, UB_k=0.8, LB_tau=0.01, UB_tau=10);
```

**Description**

This function returns a list with several arguments for performing parameter estimation with the genetic algorithm from the package genalg.

**Usage**

```r
defaultParametersGA()
```

**Value**

- **mutationChance**: NA
- **popSize**: 200
- **iters**: 100
- **elitism**: NA
- **time**: 1
- **monitor**: TRUE
- **verbose**: 0
- **transfer_function**: 3

*Create default options to perform parameter estimation with a genetic algorithm.*
defaultParametersSSm

reltol 1e-04
atol 0.001
maxStepSize Inf
maxNumSteps 1e+05
maxErrTestsFails 50
nan_fac = 1 0

Author(s)
David Henriques, Thomas Cokelaer

See Also
CellNOptR parEstimationLBode parEstimationLBodeGA

defaultParametersSSm
Create default options to perform parameter estimation with scatter search meta-heuristic.

Description
This function returns a list with several arguments for performing parameter estimation with scatter search meta-heuristic algorithm from the package essR.

Usage
defaultParametersSSm()

Value
maxeval Inf
maxtime 100
ndiverse NULL
dim_refset NULL
local_solver NULL
verbose 0
transfer_function 3
reltol 1e-04
atol 0.001
maxStepSize Inf
maxNumSteps 1e+05
maxErrTestsFails 50
nan_fac 1
getLBodeContObjFunction

Author(s)
David Henriques, Thomas Cokelaer

See Also
CellNOptR parEstimationLBode parEstimationLBodeSSm

getLBodeContObjFunction

*Returns the objective function to perform parameter estimation.*

Description
This function configures returns the objective function that can be used to evaluate the fitness of a logic based ODE model using a particular set of parameters. This function can be particularly useful if you are planning to couple a nonlinear optimization solver. The returned value of the objective function corresponds to the mean squared value normalized by the number of data points.

Usage

```r
getLBodeContObjFunction(cnolist, model, ode_parameters, indices=NULL, time = 1, verbose = 0, transfer_function = 3, reltol = 1e-04, atol = 0.001, maxStepSize = Inf, maxNumSteps = 1e+05, maxErrTestsFails = 50, nan_fac = 1, useVariances = F, initial_state=0.1)
```

Arguments

- **cnolist**: A list containing the experimental design and data.
- **model**: The logic model to be simulated.
- **ode_parameters**: A list with the ODEs parameter information. Obtained with `createLBodeContPars`.
- **indices**: Indices to map data in the model. Obtained with `indexFinder` function from `CellNOptR`.
- **time**: An integer with the index of the time point to start the simulation. Default is 1.
- **verbose**: A logical value that triggers a set of comments.
- **transfer_function**: The type of used transfer. Use 1 for no transfer function, 2 for Hill function and 3 for normalized Hill function.
- **reltol**: Relative Tolerance for numerical integration.
- **atol**: Absolute tolerance for numerical integration.
- **maxStepSize**: The maximum step size allowed to ODE solver.
- **maxNumSteps**: The maximum number of internal steps between two points being sampled before the solver fails.
- **maxErrTestsFails**: Specifies the maximum number of error test failures permitted in attempting one step.
- **nan_fac**: A penalty for each data point the model is not able to simulate. We recommend higher than 0 and smaller that 1.
- **useVariances**: if `True`, use the variance in the fitness
- **initial_state**: initial state of the dynamic nodes (non-measured) (Defaults to 0.1)
**Details**

Check CellNOptR for details about the cnolist and the model format. For more details in the configuration of the ODE solver check the CVODES manual.

**Value**

Returns a function to evaluate the model fitness. This function receives a vector containing both continuous parameters and integer values representing which reactions should be kept in the model.

**Author(s)**

David Henriques, Thomas Cokelaer

**See Also**

CellNOptR createLBodeContPars

**Examples**

```r
library(CNORode)
data("ToyCNOlist", package="CNORode");
data("ToyModel", package="CNORode");
data("ToyIndices", package="CNORode");

ode_parameters=createLBodeContPars(model, random=TRUE);
minlp_obj_function=getLBodeContObjFunction(cnolistCNORodeExample, model, ode_parameters, indices);
x=ode_parameters$parValues;
f=minlp_obj_function(x);
```

---

**getLBodeDataSim**  
*Simulate value signals a CNO list With Logic-Based ODEs.*

**Description**

This function receives a set of inputs, namely the cnolist and the model and returns a list with the same size of the cnolist$valueSignals.

**Usage**

```r
getLBodeDataSim(cnolist, model, ode_parameters = NULL, indices = NULL, timeSignals=NULL, time = 1, verbose = 0, transfer_function = 3, reltol = 1e-04, atol = 0.001, maxStepSize = Inf, maxNumSteps = 1e+05, maxErrTestsFails = 50, initial_state=0.1)
```
Arguments

cnolist A list containing the experimental design and data.
model A list with the ODEs parameter information. Obtained with `createLBodeContPars`
ode_parameters A list with the ODEs parameter information. Obtained with `makeParameterList` function.
indices Indices to map data in the model. Obtained with `indexFinder` function from `CellNOptR`.
timeSignals An array containing a different timeSignals. If you use this argument, it will also modify the dimensions from valueSignals.
time An integer with the index of the time point to start the simulation. Default is 1.
verbose A logical value that triggers a set of comments.
transfer_function The type of used transfer. Use 1 for no transfer function, 2 for Hill function and 3 for normalized Hill function.
reltol Relative Tolerance for numerical integration.
atol Absolute tolerance for numerical integration.
maxStepSize The maximum step size allowed to ODE solver.
maxNumSteps The maximum number of internal steps between two points being sampled before the solver fails.
maxErrTestsFails Specifies the maximum number of error test failures permitted in attempting one step.
initial_state initial state of the dynamic nodes (non-measured) (Defaults to 0.1)

Details
Check `CellNOptR` for details about the cnolist and the model format. For more details in the configuration of the ODE solver check the CVODES manual.

Value

Returns a list with simulated data that has the same structure as the cnolist$valueSignals. One matrix for each time-point.

Author(s)
David Henriques, Thomas Cokelaer

See Also

`CellNOptR parEstimationLBode parEstimationLBodeSSm`

Examples

```r
library(CNORode)
data("ToyCNOList", package="CNORode");
data("ToyModel", package="CNORode");
data("ToyIndices", package="CNORode");
dataSimulation=getLBodeDataSim(cnolistCNORodeExample, model, indices=indices);
```
getLBodeMINLPObjFunction

Get the objective function to evaluate the fitness of a given model structure and set of parameters.

Description

This function configures returns the objective function that can be used to evaluate the fitness of a logic based ODE model using a particular set of parameters and model structure. This function can be particular useful if you are planing to couple a mixed integer nonlinear programming optimization solver. The returned value of the objective function corresponds to the mean squared value.

Usage

getLBodeMINLPObjFunction(cnolist, model, ode_parameters, indices=NULL, time = 1, verbose = 0, transfer_function = 3, reltol = 1e-04, atol = 0.001, maxStepSize = Inf, maxNumSteps = 1e+05, maxErrTestsFails = 50, nan_fac = 1)

Arguments

cnolist A list containing the experimental design and data.
model The logic model to be simulated.
ode_parameters A list with the ODEs parameter information. Obtained with createLBodeContPars.
indices Indices to map data in the model. Obtained with indexFinder function from CellNOptR.
time An integer with the index of the time point to start the simulation. Default is 1.
verbose A logical value that triggers a set of comments.
transfer_function The type of used transfer. Use 1 for no transfer function, 2 for Hill function and 3 for normalized Hill function.
reltol Relative Tolerance for numerical integration.
atol Absolute tolerance for numerical integration.
maxStepSize The maximum step size allowed to ODE solver.
maxNumSteps The maximum number of internal steps between two points being sampled before the solver fails.
maxErrTestsFails Specifies the maximum number of error test failures permitted in attempting one step.
nan_fac A penalty for each data point the model is not able to simulate. We recommend higher than 0 and smaller that 1.

Details

Check CellNOptR for details about the cnolist and the model format. For more details in the configuration of the ODE solver check the CVODES manual.
getLBodeModelSim

Value

Returns a function to evaluate the model fitness. This function receives a continuous parameter vector.

Author(s)

David Henriques, Thomas Cokelaer

See Also

CellNOptR createLBodeContPars

Examples

library(CNORode)
data("ToyCNOlist",package="CNORode");
data("ToyModel",package="CNORode");
data("ToyIndices",package="CNORode");

ode_parameters=createLBodeContPars(model,random=TRUE);
minlp_obj_function=getLBodeMINLPObjFunction(cnolistCNORodeExample, model,ode_parameters,indices);

n_int_vars=dim(model$interMat)[2];
x_int=round(runif(n_int_vars))
x_cont=ode_parameters$parValues;
x=c(x_cont,x_int);
f=minlp_obj_function(x);

getLBodeModelSim  Simulate the logic-based ODE model

Description

This function simulates a logic-based ODE model and return a list with one matrix for each time point. The input species in the model are filled with NA values. If the simulation of a particular set of initial conditions fails the solver will fill the experience row with NA values.

Usage

getLBodeModelSim(cnolist, model, ode_parameters = NULL, indices = NULL, timeSignals=NULL, time = 1,verbose = 0, transfer_function = 3, reltol = 1e-04, atol = 0.001, maxStepSize = Inf, maxNumSteps = 1e+05, maxErrTestsFails = 50)

Arguments

cnolist  A list containing the experimental design and data.
model    The logic model to be simulated.
ode_parameters  A list with the ODEs parameter information. Obtained with createLBodeContPars.
indices   Indices to map data in the model. Obtained with indexFinder function from CellNOptR.
getLBodeModelSim

timeSignals An array containing a different timeSignals. If you use this argument, it will
also modify the dimensions from valueSignals.
time An integer with the index of the time point to start the simulation. Default is 1.
verbose A logical value that triggers a set of comments.
transfer_function The type of used transfer. Use 1 for no transfer function, 2 for Hill function and
3 for normalized Hill function.
reltol Relative Tolerance for numerical integration.
atol Absolute tolerance for numerical integration.
maxStepSize The maximum number of internal steps between two points being sampled be-
fore the solver fails.
maxNumSteps The maximum number of internal steps between two points being sampled be-
fore the solver fails.
maxErrTestsFails Specifies the maximum number of error test failures permitted in attempting one
step.

Details

Check CellNOptR for details about the cnolist and the model format. For more details in the con-
figuration of the ODE solver check the CVODES manual.

Value

Returns a list with simulated data with similar structure to cnolist$valueSignals. Contains one
matrix for each time-point. Each matrix contains one row per experiment and one columns per
model species.

Author(s)

David Henriques, Thomas Cokelaer

See Also

CellNOptR createLBodeContPars

Examples

library(CNORode)
data('ToyCNOList', package='CNORode');
data('ToyModel', package='CNORode');
data('ToyIndices', package='CNORode');
modelSimulation=getLBodeModelSim(cnolistCNORodeExample, model, indices=indices);
getLBodeSimFunction  

Get a function to simulate a logic based ODE model.

Description

This function is internally used by CNORode to configure the simulation function with default arguments.

Usage

getLBodeSimFunction(cnolist1, model1, adjMatrix1, indices1, odeParameters1, time1 = 1, verbose1 = 0, transfer_function1 = 3, reltol1 = 1e-04, atol1 = 0.001, maxStepSize1 = Inf, maxNumSteps1 = 1e+05, maxErrTestsFails1 = 50, initial_state1=0.1)

Arguments

- cnolist1: A list containing the experimental design and data.
- model1: The logic model to be simulated.
- adjMatrix1: An adjacency matrix from the model.
- indices1: Indices to map data in the model. Obtained with indexFinder function from CellNOptR.
- odeParameters1: A list with the ODEs parameter information. Obtained with createLBodeContPars.
- time1: An integer with the index of the time point to start the simulation. Default is 1.
- verbose1: A logical value that triggers a set of comments.
- transfer_function1: The type of used transfer. Use 1 for no transfer function, 2 for Hill function and 3 for normalized Hill function.
- reltol1: Relative Tolerance for numerical integration.
- atol1: Absolute tolerance for numerical integration.
- maxStepSize1: The maximum step size allowed to ODE solver.
- maxNumSteps1: The maximum number of internal steps between two points being sampled before the solver fails.
- maxErrTestsFails1: Specifies the maximum number of error test failures permitted in attempting one step.
- initial_state1: initial state of the dynamic nodes (non-measured) (Defaults to 0.1)

Value

A function that returns a simulated model.

Note

This function is for CNORode internal use.

Author(s)

David Henriques, Thomas Cokelaer
**getStates**

See Also

- CellNoptR
- CNORode

---

### Description

Find which species in the model are states.

### Usage

```r
getStates(adjacency)
```

### Arguments

- `adjacency`: An adjacency matrix from the model.

### Value

A numeric vector with 0’s for positions which are states and 1’s for positions which are.

### Note

For internal use of CNORode.

### Author(s)

David Henriques, Thomas Cokelaer

### See Also

- incidence2Adjacency

---

**incidence2Adjacency**

Convert an incidence matrix into an adjacency matrix.

---

### Description

Convert the incidence matrix (model representation of CellNoptR) into an adjacency matrix. Denotes the inputs/output relationships.

### Usage

```r
incidence2Adjacency(model)
```

### Arguments

- `model`: Model from CellNoptR.
minlpLBodeSSm

Value

Directed Adjacency matrix of size \( n_{\text{species}} \) by \( n_{\text{species}} \).

Note

For internal use of CNORode.

Author(s)

David Henriques, Thomas Cokelaer

See Also

CellNOptR

indices

Indices that relate cnolist to model

Description

A list with indices that relate the cnolist with the model from CellNOptR

minlpLBodeSSm

Search for the best combination of continuous parameters and logic gates.

Description

This function uses essR to search for the best set of continuous parameters and model structure. The objective function is the same as the one provided by getLBodeMINLPObjFunction.

Usage

\[
\text{minlpLBodeSSm}(\text{cnolist}, \text{model}, \text{ode}\_\text{parameters} = \text{NULL}, \text{int}_x0=\text{NULL}, \text{indices} = \text{NULL}, \text{maxeval} = \text{Inf}, \text{maxtime} = 100, \text{ndiverse} = \text{NULL}, \text{dim}\_\text{refset} = \text{NULL}, \text{local}_\text{solver} = \text{NULL}, \text{time} = 1, \text{verbose} = 0, \text{transfer}\_\text{function} = 3, \text{reltol} = 1e-04, \text{atol} = 0.001, \text{maxStepSize} = \text{Inf}, \text{maxNumSteps} = 1e+05, \text{maxErrTestsFails} = 50, \text{nan}_\text{fac} = 1)
\]

Arguments

cnolist A list containing the experimental design and data.
model The logic model to be simulated.
ode\_parameters A list with the ODEs parameter information. Obtained with createLBodeContPars.
int\_x0 Vector with initial solution for integer parameters.
indices Indices to map data in the model. Obtained with indexFinder function from CellNOptR.
maxeval Maximum number of evaluation in the optimization procedure.
maxtime Maximum number of evaluation spent in optimization procedure.
ndiverse Duration of the optimisation procedure.
dim_refset Number of diverse initial solutions.
local_solver Local solver to be used in SSm.
time An integer with the index of the time point to start the simulation. Default is 1.
verbose A logical value that triggers a set of comments.
transfer_function The type of used transfer. Use 1 for no transfer function, 2 for Hill function and for normalized Hill function.
reltol Relative Tolerance for numerical integration.
atol Absolute tolerance for numerical integration.
maxStepSize The maximum step size allowed to ODE solver.
maxNumSteps The maximum number of internal steps between two points being sampled before the solver fails.
maxErrTestsFails Specifies the maximum number of error test failures permitted in attempting one step.
nan_fac A penalty for each data point the model is not able to simulate. We recommend higher than 0 and smaller that 1.

Details

Check CellNOptR for details about the cnolist and the model format. For more details in the configuration of the ODE solver check the CVODES manual.

Value

LB_n A numeric value to be used as lower bound for all parameters of type n.
LB_k A numeric value to be used as lower bound for all parameters of type k.
LB_tau A numeric value to be used as lower bound for all parameters of type tau.
UB_n A numeric value to be used as upper bound for all parameters of type n.
UB_k A numeric value to be used as upper bound for all parameters of type k.
UB_tau A numeric value to be used as upper bound for all parameters of type tau.
default_n The default parameter to be used for every parameter of type n.
default_k The default parameter to be used for every parameter of type k.
default_tau The default parameter to be used for every parameter of type tau.
LB_in An array with the the same length as ode_parameters$parValues with lower bounds for each specific parameter.
UB_in An array with the the same length as ode_parameters$parValues with upper bounds for each specific parameter.
opn_n Add all parameter n to the index of parameters to be fitted.
opn_k Add all parameter k to the index of parameters to be fitted.
opn_tau Add all parameter tau to the index of parameters to be fitted.
random A logical value that determines that a random solution is for the parameters to be optimised.
model The best fitting found model structure.
smm_results A list containing the information provided by the nonlinear optimization solver.
Author(s)

David Henriques, Thomas Cokelaer

See Also

CellNOptR createLBodeContPars essR

Examples

## Not run:
data("ToyCNolist", package="CNORode");
data("ToyModel", package="CNORode");
data("ToyIndices", package="CNORode");
ode_parameters=createLBodeContPars(model, random=TRUE);

# Visualize initial solution
simulatedData=plotLBodeFitness(cnolistCNORodeExample, model, ode_parameters, indices=indices)
ode_parameters=minlpLBodeSSm(cnolistCNORodeExample, model, ode_parameters);
model=ode_parameters$model;

# Visualize fitted solution
simulatedData=plotLBodeFitness(cnolistCNORodeExample, model, indices=indices);

## End(Not run)

model  
A model from CellNOptR

Description

A model from CellNOptR to use with provided examples

parEstimationLBode  
Perform parameter estimation using a genetic algorithm (package genalg) or ssm (if package essm available).

Description

This function is an alias to the parEstimationLBode variants (parEstimationLBodeGA and parEstimationLBodeSSm)

Usage

parEstimationLBode(cnolist, model, method="ga", ode_parameters = NULL, indices = NULL, paramsGA=NULL, paramsSSm=NULL)
Arguments

- **cnolist**: A list containing the experimental design and data.
- **model**: The logic model to be simulated.
- **method**: Only "ga" or "essm" arguments are accepted.
- **ode_parameters**: A list with the ODEs parameter information. Obtained with `createLBodeContPars`.
- **indices**: Indices to map data in the model. Obtained with `indexFinder` function from `CellNOptR`.
- **paramsGA**: A list of GA parameters. Default is the list returned by `defaultParametersGA`.
- **paramsSSm**: A list of SSm parameters. Default is the list returned by `defaultParametersSSm`.

Value

- **LB_n**: A numeric value to be used as lower bound for all parameters of type n.
- **LB_k**: A numeric value to be used as lower bound for all parameters of type k.
- **LB_tau**: A numeric value to be used as lower bound for all parameters of type tau.
- **UB_n**: A numeric value to be used as upper bound for all parameters of type n.
- **UB_k**: A numeric value to be used as upper bound for all parameters of type k.
- **UB_tau**: A numeric value to be used as upper bound for all parameters of type tau.
- **default_n**: The default parameter to be used for every parameter of type n.
- **default_k**: The default parameter to be used for every parameter of type k.
- **default_tau**: The default parameter to be used for every parameter of type tau.
- **LB_in**: An array with the the same length as `ode_parameters$parValues` with lower bounds for each specific parameter.
- **UB_in**: An array with the the same length as `ode_parameters$parValues` with upper bounds for each specific parameter.
- **opt_n**: Add all parameter n to the index of parameters to be fitted.
- **opt_k**: Add all parameter k to the index of parameters to be fitted.
- **opt_tau**: Add all parameter tau to the index of parameters to be fitted.
- **random**: A logical value that determines that a random solution is for the parameters to be optimized.
- **res**: A list containing the information provided by the solver.

Author(s)

David Henriques, Thomas Cokelaer

See Also

`CellNOptR` `createLBodeContPars` `rbga`
Examples

data("ToyCNOlist", package="CNORode");
data("ToyModel", package="CNORode");
data("ToyIndices", package="CNORode");

ode_parameters=createLBodeContPars(model, random=TRUE);

# Visualize initial solution
simulatedData=plotLBodeFitness(cnolistCNORodeExample, model, ode_parameters, indices=indices)
paramsGA = defaultParametersGA()
paramsGA$maxStepSize = 1
paramsGA$popSize = 10
paramsGA$iter = 10
paramsGA$transfer_function = 2

ode_parameters=parEstimationLBode(cnolistCNORodeExample, model, ode_parameters=ode_parameters, paramsGA=paramsGA)

# Visualize fitted solution
simulatedData=plotLBodeFitness(cnolistCNORodeExample, model, ode_parameters, indices=indices)


Description

This function uses a genetic algorithm (package genalg) to perform parameter estimation. The objective function is the same as the one provided by getLBodeContObjFunction.

Usage

parEstimationLBodeGA(cnolist, model, ode_parameters = NULL, indices = NULL, mutationChance = NA, popSize = 200, iters = 100, elitism = NA, time = 1, monitor = TRUE, verbose = 0, transfer_function = 3, reltol = 1e-04, atol = 0.001, maxStepSize = Inf, maxNumSteps = 1e+05, maxErrTestsFails = 50, nan_fac = 1, initial_state=0.1)

Arguments

cnolist  A list containing the experimental design and data.
model  The logic model to be simulated.
ode_parameters  A list with the ODEs parameter information. Obtained with createLBodeContPars.
indices  Indices to map data in the model. Obtained with indexFinder function from CellNOptR.
mutationChance  the chance that a gene in the chromosome mutates. By default 1/(size+1). It affects the convergence rate and the probing of search space: a low chance results in quicker convergence, while a high chance increases the span of the search space.
popSize  the population size.
iters  the number of iterations.
elitism  the number of chromosomes that are kept into the next generation. By default is about 20% of the population size.
time
An integer with the index of the time point to start the simulation. Default is 1.

monitor
If TRUE a plot will be generated to monitor the objective function

verbose
A logical value that triggers a set of comments.

transfer_function
The type of used transfer. Use 1 for no transfer function, 2 for Hill function and 3 for normalized Hill function.

reltol
Relative Tolerance for numerical integration.

atol
Absolute tolerance for numerical integration.

maxStepSize
The maximum step size allowed to ODE solver.

maxNumSteps
The maximum number of internal steps between two points being sampled before the solver fails.

maxErrTestsFails
Specifies the maximum number of error test failures permitted in attempting one step.

nan_fac
A penalty for each data point the model is not able to simulate. We recommend higher than 0 and smaller that 1.

initial_state
initial state of the dynamic nodes (non-measured) (Defaults to 0.1)

Value

LB_n
A numeric value to be used as lower bound for all parameters of type n.

LB_k
A numeric value to be used as lower bound for all parameters of type k.

LB_tau
A numeric value to be used as lower bound for all parameters of type tau.

UB_n
A numeric value to be used as upper bound for all parameters of type n.

UB_k
A numeric value to be used as upper bound for all parameters of type k.

UB_tau
A numeric value to be used as upper bound for all parameters of type tau.

default_n
The default parameter to be used for every parameter of type n.

default_k
The default parameter to be used for every parameter of type k.

default_tau
The default parameter to be used for every parameter of type tau.

LB_in
An array with the the same length as ode_parameters$parValues with lower bounds for each specific parameter.

UB_in
An array with the the same length as ode_parameters$parValues with upper bounds for each specific parameter.

opt_n
Add all parameter n to the index of parameters to be fitted.

opt_k
Add all parameter k to the index of parameters to be fitted.

opt_tau
Add all parameter tau to the index of parameters to be fitted.

random
A logical value that determines that a random solution is for the parameters to be optimized.

res
A list containing the information provided by the nonlinear optimization solver (genalg).

Author(s)

David Henriques, Thomas Cokelaer
parEstimationLBodeSSm

Perform parameter estimation using essR.

Description

This function uses essR to perform parameter estimation. The objective function is the same as the one provided by `getLBodeContObjFunction`.

Usage

```r
parEstimationLBodeSSm(cnolist, model, ode_parameters = NULL, indices = NULL,
maxeval = Inf, maxtime = 100, ndiverse = NULL, dim_refset = NULL, local_solver = NULL,
time = 1, verbose = 0, transfer_function = 3, reltol = 1e-04, atol = 0.001,
maxStepSize = Inf, maxNumSteps = 1e+05, maxErrTestsFails = 50, nan_fac = 1,
useVariances = FALSE, initial_state = 0.1)
```

Arguments

- **cnolist**: A list containing the experimental design and data.
- **model**: The logic model to be simulated.
- **ode_parameters**: A list with the ODEs parameter information. Obtained with `createLBodeContPars`.
- **indices**: Indices to map data in the model. Obtained with indexFinder function from `CellNOptR`.
- **maxeval**: Maximum number of evaluation in the optimization procedure.
- **maxtime**: Duration of the optimization procedure.
- **ndiverse**: Number of diverse initial solutions.
- **dim_refset**: Size of the reference set.
- **local_solver**: Local solver to be used in SSm.
- **time**: An integer with the index of the time point to start the simulation. Default is 1.
- **verbose**: A logical value that triggers a set of comments.
transfer_function

The type of used transfer. Use 1 for no transfer function, 2 for Hill function and 3 for normalized Hill function.

reltol
Relative Tolerance for numerical integration.

atol
Absolute tolerance for numerical integration.

maxStepSize
The maximum step size allowed to ODE solver.

maxNumSteps
The maximum number of internal steps between two points being sampled before the solver fails.

maxErrTestsFails
Specifies the maximum number of error test failures permitted in attempting one step.

nan_fac
A penalty for each data point the model is not able to simulate. We recommend higher than 0 and smaller that 1.

useVariances
Uses variance if any

initial_state
initial state of the dynamic nodes (non-measured) (Defaults to 0.1)

Details
Check CellNOptR for details about the cnolist and the model format. For more details in the configuration of the ODE solver check the CVODES manual.

Value

LB_n
A numeric value to be used as lower bound for all parameters of type n.

LB_k
A numeric value to be used as lower bound for all parameters of type k.

LB_tau
A numeric value to be used as lower bound for all parameters of type tau.

UB_n
A numeric value to be used as upper bound for all parameters of type n.

UB_k
A numeric value to be used as upper bound for all parameters of type k.

UB_tau
A numeric value to be used as upper bound for all parameters of type tau.

default_n
The default parameter to be used for every parameter of type n.

default_k
The default parameter to be used for every parameter of type k.

default_tau
The default parameter to be used for every parameter of type tau.

LB_in
An array with the the same length as ode_parameters$parValues with lower bounds for each specific parameter.

UB_in
An array with the the same length as ode_parameters$parValues with upper bounds for each specific parameter.

opt_n
Add all parameter n to the index of parameters to be fitted.

opt_k
Add all parameter k to the index of parameters to be fitted.

opt_tau
Add all parameter tau to the index of parameters to be fitted.

random
A logical value that determines that a random solution is for the parameters to be optimized.

smm_results
A list containing the information provided by the nonlinear optimization solver.

Author(s)

David Henriques, Thomas Cokelaer
plotLBodeFitness

Plot data against simulated values.

Description

Plots the simulated values with the logic-based ODE against the the data contained in the cnolist. The data values are represented with a black line and the simulated values with a blue line. Additionally this function returns the simulated values.

Usage

plotLBodeFitness(cnolist, model, ode_parameters = NULL, indices = NULL, adjMatrix = NULL, time = 1, verbose = 0, transfer_function = 3, reltol = 1e-04, atol = 0.001, maxStepSize = Inf, maxNumSteps = 1e+05, maxErrTestsFails = 50, plot_index_signals = NULL, plot_index_experiments = NULL, plot_index_cues = NULL, colormap="heat", plotParams=list(margin=0.1, width=15, height=12, cmap_scale=1, cex=1.6, ymin=NULL), initial_state=0.1 )

Arguments

cnolist  A list containing the experimental design and data.
model  The logic model to be simulated.
ode_parameters  A list with the ODEs parameter information. Obtained with createLBodeContPars.
indices  Indices to map data in the model. Obtained with indexFinder function from CellNOptR.
adjMatrix  Model representation in the form of an adjacency matrix. When not provided will be automatically computed based in the model.
time  An integer with the index of the time point to start the simulation. Default is 1.
plotLBodeFitness

Verbose

A logical value that triggers a set of comments.

Transfer function

The type of used transfer. Use 1 for no transfer function, 2 for Hill function and 3 for normalized Hill function.

RelTol

Relative Tolerance for numerical integration.

Atol

Absolute tolerance for numerical integration.

MaxStepSize

The maximum step size allowed to ODE solver.

MaxNumSteps

The maximum number of internal steps between two points being sampled before the solver fails.

MaxErrTestsFails

Specifies the maximum number of error test failures permitted in attempting one step.

Plot_index_signals

In case you only want to plot some signals, provide an integer vector with the indexes.

Plot_index_experiments

In case you only want to plot some experiments, provide an integer vector with the indexes.

Plot_index_cues

In case you only want to plot some cues, provide an integer vector with the indexes.

Colormap

Uses the same colormap as in CellNOptR by default. If set to "green", it uses the deprecated colormap.

PlotParams

Additional parameters to refine the plogging. See plotOptimResultsPan function in CellNOptR for more details.

Initial_state

Initial state of the dynamic nodes (non-measured) (Defaults to 0.1)

Details

Check CellNOptR for details about the cnolist and the model format. For more details in the configuration of the ODE solver check the CVODES manual.

Value

Returns a list with simulated data that has the same structure as the cnolist$valueSignals. One matrix for each time-point.

Author(s)

David Henriques, Thomas Cokelaer

See Also

CellNOptR createLBodeContPars

Examples

library(CNORode)
data("ToyCNOlist", package="CNORode");
data("ToyModel", package="CNORode");
data("ToyIndices", package="CNORode");
ode_parameters=createLBodeContPars(model, random=TRUE);
dataSimulation=plotLBodeFitness(cnolistCNORodeExample, model, indices=indices);
plotLBodeModelSim

Simulate the model and plot the obtained with the different experimental conditions.

Description

Plots the simulated values of the logic based ODE model. Only dynamic states are plotted, i.e. those that are not inputs. A blue line. Additionally this function returns the the simulated values.

Usage

plotLBodeModelSim(cnolist, model, ode_parameters = NULL, indices = NULL, adjMatrix = NULL, timeSignals=NULL, time = 1, verbose = 0, transfer_function = 3, reltol = 1e-04, atol = 0.001, maxStepSize = Inf, maxNumSteps = 1e+05, maxErrTestsFails = 50, large = FALSE, nsplit = 4, show=T)

Arguments

cnolist A list containing the experimental design and data.
model The logic model to be simulated.
ode_parameters A list with the ODEs parameter information. Obtained with createLBodeContPars.
indices Indices to map data in the model. Obtained with indexFinder function from CellNOptR.
adjMatrix Model representation in the form of an adjacency matrix. When not provided will be automatically computed based in the model.
timeSignals An array containing a different time Signals. If you use this argument, it will also modify the dimensions from valueSignals.
time An integer with the index of the time point to start the simulation. Default is 1.
verbose A logical value that triggers a set of comments.
transfer_function The type of used transfer. Use 1 for no transfer function, 2 for Hill function and 3 for normalized Hill function.
reltol Relative Tolerance for numerical integration.
atol Absolute tolerance for numerical integration.
maxStepSize The maximum step size allowed to ODE solver.
maxNumSteps The maximum number of internal steps between two points being sampled before the solver fails.
maxErrTestsFails Specifies the maximum number of error test failures permitted in attempting one step.
large Boolean variable defining if the plot should split into several subplots.
nsplit In case the large plot options is selected define how many subplots will exist. Default is 4.
show show the error (defaults to TRUE)
Value
Returns a list with simulated Model values. One matrix of size number of species by number of experimental conditions for each time-point.

Author(s)
David Henriques, Thomas Cokelaer

See Also
CellNOptR createLBodeContPars

Examples

```r
library(CNORode)
data("ToyCNOlist",package="CNORode");
data("ToyModel",package="CNORode");
data("ToyIndices",package="CNORode");
modelSimulation=plotLBodeModelSim(cnolistCNORodeExample, model,indices=indices);
```

---

simdata2cnolist  \hspace{2em}  \textit{converts output of getLBodeModelSim to cnolist}

Description
This function converts the simulated data returned by getLBodeModelSim into a valid CNOlist data structure.

Usage

```r
simdata2cnolist(sim_data, cnolist, model)
```

Arguments

- `sim_data`: structure returned by getLBodeModelSim
- `cnolist`: A list containing the experimental design and data.
- `model`: The logic model to be simulated.

Value

- a CNOlist

Author(s)
Thomas Cokelaer

See Also

CellNOptR createLBodeContPars
Examples

data('ToyCNolist',package='CNORode');
data('ToyModel',package='CNORode');
data('ToyIndices',package='CNORode');
simdata = getLBodeModelSim(cnolistCNORodeExample, model, indices=indices)
cnolist = simdata2cnolist(simdata, cnolistCNORodeExample, model)

cnolist = simdata2cnolist(simdata, cnolistCNORodeExample, model)

simulate

Simulate value signals a CNO list With Logic-Based ODEs.

Description

This function receives a set of inputs, namely the cnolist and the model and returns a list with the same size of the cnolist$valueSignals.

Usage

simulate(cnolist, model, ode_parameters=NULL, indices=NULL, adjMatrix=NULL, time=1, verbose=0, transfer_function=3, reltol=1e-04, atol=0.001, maxStepSize=Inf, maxNumSteps=1e+05, maxErrTestsFails=50)

Arguments

cnolist: A list containing the experimental design and data.
model: A list with the ODEs parameter information. Obtained with createLBodeContPars.
ode_parameters: A list with the ODEs parameter information. Obtained with makeParameterList function.
indices: Indices to map data in the model. Obtained with indexFinder function from CellNOptR.
adjMatrix: The adjacency matrix. Recomputed if not provided
time: An integer with the index of the time point to start the simulation. Default is 1.
verbose: A logical value that triggers a set of comments.
transfer_function: The type of used transfer. Use 1 for no transfer function, 2 for Hill function and 3 for normalized Hill function.
reltol: Relative Tolerance for numerical integration.
atol: Absolute tolerance for numerical integration.
maxStepSize: The maximum step size allowed to ODE solver.
maxNumSteps: The maximum number of internal steps between two points being sampled before the solver fails.
maxErrTestsFails: Specifies the maximum number of error test failures permitted in attempting one step.
simulate

Details

Check CellNOptR for details about the cnolist and the model format. For more details in the configuration of the ODE solver check the CVODES manual.

Value

Returns a list with simulated data that has the same structure as the cnolist$valueSignals. One matrix for each time-point.

Author(s)

David Henriques, Thomas Cokelaer

See Also

CellNOptR parEstimationLBode parEstimationLBodeSSm

Examples

library(CNORode)
data("ToyCNOList",package="CNORode");
data("ToyModel",package="CNORode");
data("ToyIndices",package="CNORode");
dataSimulation = simulate(cnolistCNORodeExample, model,indices=indices);
Index

*Topic CNORode
  CNORode, 2
*Topic CVODES
  getLBodeSimFunction, 12
*Topic CellNOptR
  parEstimationLBode, 16
  parEstimationLBodeGA, 18
*Topic SSm
  defaultParametersSSm, 5
*Topic adjacency
  getStates, 13
  incidence2Adjacency, 13
*Topic algorithm
  defaultParametersGA, 4
  parEstimationLBode, 16
  parEstimationLBodeGA, 18
*Topic default
  defaultParametersGA, 4
  defaultParametersSSm, 5
*Topic essR
  defaultParametersSSm, 5
*Topic genetic
  defaultParametersGA, 4
  parEstimationLBode, 16
  parEstimationLBodeGA, 18
*Topic incidence
  incidence2Adjacency, 13
*Topic logic
  parEstimationLBode, 16
  parEstimationLBodeGA, 18
*Topic matrix
  incidence2Adjacency, 13
*Topic model
  parEstimationLBode, 16
  parEstimationLBodeGA, 18
*Topic parameters
  defaultParametersGA, 4
*Topic states
  getStates, 13

cnolistCNORodeExample, 2
CNORode, 2, 13

createLBodeContPars, 3, 6–12, 14, 16–18, 20, 22–26
defaultParametersGA, 4
defaultParametersSSm, 5
getLBodeContObjFunction, 6, 18, 20
getLBodeDataSim, 7
getLBodeMINLPObjFunction, 9, 14
getLBodeModelSim, 3, 10
getLBodeSimFunction, 3, 12
getStates, 13
incidence2Adjacency, 13, 13
indices, 14
minlpLBodeSSm, 14
model, 16
parEstimationLBode, 3, 5, 6, 8, 16, 27
parEstimationLBodeGA, 5, 16, 18
parEstimationLBodeSSm, 6, 8, 16, 20, 27
plotLBodeFitness, 3, 22
plotLBodeModelSim, 24
rbga, 17, 20
simdata2cnolist, 25
simulate, 26