Package ‘CNORode’

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CNORode

**CNORode**

Logic based ODE extension for CellNOptR

**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)**

David Henriques, Thomas Cokelaer
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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.
defaultParametersGA

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

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

defaultParametersGA()

Value

mutationChance  NA
popSize  200
iters  100
elitism  NA
time  1
monitor  TRUE
verbose  0
transfer_function  3
defaultParametersSSm

reutol  1e-04
atol   0.001
maxStepSize Inf
maxNumSteps Inf
maxErrTestsFails 3
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
reutol 1e-04
atol 0.001
maxStepSize Inf
maxNumSteps Inf
maxErrTestsFails 3
nan_fac 1
getLBodeContObjFunction

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

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)
getLBodeDataSim

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

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

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)
getLBodeDataSim

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("ToyCNORlist", 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**

```r
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 before the solver fails.

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.

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 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('ToyCNOnlist',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

getStates

Find which species in the model are states.

Description
Receives an adjacency matrix (model$interMat from CellNOptR) and finds which species are states (i.e. not inputs).

Usage
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
incidence2Adjacency(model)

Arguments
model Model from CellNOptR.
Value
Directed Adjacency matrix of size n_species by n_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
minlpLBodeSSm(cnolist, model, ode_parameters = NULL, int_x0 = 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)

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 creatLBodeContPars.
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.

**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 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**

```r
## 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

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**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**

```r
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

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 = F, initial_state = 0.1)

Arguments

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

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 simulation
# simulatedData=plotLBodeFitness(cnolistCNORodeExample, model, ode_parameters, indices=indices)

ode_parameters=parEstimationLBodeGA(cnolistCNORodeExample, model, ode_parameters=ode_parameters, indices=indices, maxStepSize=1, atol=1e-3, reltol=1e-5, transfer_function=2, popSize=10, iter=40);
# Visual solution after optimization
simulatedData=plotLBodeFitness(cnolistCNORodeExample, model, indices=indices, ode_parameters=ode_parameters);
The type of used transfer. Use 1 for no transfer function, 2 for Hill function and 3 for normalized Hill function.

Relative Tolerance for numerical integration.

Absolute tolerance for numerical integration.

The maximum step size allowed to ODE solver.

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

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

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

Uses variance if any

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

Check `CellN0ptR` for details about the cnolist and the model format. For more details in the configuration of the ODE solver check the CVODES manual.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

David Henriques, Thomas Cokelaer
plotLBodeFitness

Plot data against simulated values.

Description

Plots the simulated values with the logic-based ODE against 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 on the model.
time     An integer with the index of the time point to start the simulation. Default is 1.

See Also

CellNOptR createLBodeContPars

Examples

## Not run:
data("ToyCNOlist",package="CNORode");
data("ToyModel",package="CNORode");
data("ToyIndices",package="CNORode");

ode_parameters=createLBodeContPars(model,random=TRUE);

#Visualize initial simulation
simulatedData=plotLBodeFitness(cnolistCNORodeExample, model,ode_parameters,indices=indices)

ode_parameters=parEstimationLBodeSSm(cnolistCNORodeExample,model,ode_parameters,indices=indices,maxtime=20,ndiverse=50,dim_refset=6);

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

## End(Not run)
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 ploggin. 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);
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 functions 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 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.
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)
**simdata2cnolist**

**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** 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

```r
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

```r
simulate(cnolist, model, ode_parameters=NULL, indices=NULL,
adjMatrix=NULL, time=1, verbose=0, transfer_function=3,
reitol=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.
- `reitol` 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);
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