

Package ‘ternarynet’

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Title Ternary Network Estimation

Description A computational Bayesian approach to ternary gene regulatory network estimation from gene perturbation experiments.

Author Matthew N. McCall <mccallm@gmail.com>, Anthony Almudevar <Anthony_Almudevar@urmc.rochester.edu>

Maintainer Matthew N. McCall <mccallm@gmail.com>

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R topics documented:

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attractorSummary *Summarize Attractors*

Description

This function summarizes the posterior probability of possible attractors.

Usage

```
attractorSummary(tpost, post.prob.limit = 0.01, wildtype = TRUE)
```

Arguments

tpost	a ternaryPost object
post.prob.limit	the minimum posterior probability for an attractor to be listed
wildtype	if TRUE, the wildtype attractors are summarized; if FALSE, the perturbed attractors are summarized.

Value

The function returns a matrix of attractors and posterior probabilities for each perturbation.

Author(s)

Matthew N. McCall and Anthony Almudevar

See Also

Almudevar A, McCall MN, McMurray H, Land H (2011). Fitting Boolean Networks from Steady State Perturbation Data, *Statistical Applications in Genetics and Molecular Biology*, 10(1): Article 47.

Examples

```
ssObj <- matrix(c(1,1,1,0,1,1,0,0,1),nrow=3)
pObj <- matrix(c(1,0,0,0,1,0,0,0,1),nrow=3)
rownames(ssObj) <- rownames(pObj) <- colnames(ssObj) <- colnames(pObj) <- c("Gene1", "Gene2", "Gene3")
tnfitObj <- tnetfit(ssObj, pObj)
tnpostObj <- tnetpost(tnfitObj, mdelta=10, msample=10)
attractorSummary(tnpostObj)
```

graphPosterior	<i>Network Topology</i>
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Description

This function summarizes the topology of the ternary network using marginal edge probabilities.

Usage

```
graphPosterior(tpost)
```

Arguments

tpost a ternaryPost object

Value

The function returns a matrix of marginal posterior probabilities of each possible network edge – rows are children and columns are parents. The first column represents no parents.

Author(s)

Matthew N. McCall and Anthony Almudevar

See Also

Almudevar A, McCall MN, McMurray H, Land H (2011). Fitting Boolean Networks from Steady State Perturbation Data, *Statistical Applications in Genetics and Molecular Biology*, 10(1): Article 47.

Examples

```
ssObj <- matrix(c(1,1,1,0,1,1,0,0,1),nrow=3)
pObj <- matrix(c(1,0,0,0,1,0,0,0,1),nrow=3)
rownames(ssObj) <- rownames(pObj) <- colnames(ssObj) <- colnames(pObj) <- c("Gene1", "Gene2", "Gene3")
tnfitObj <- tnetfit(ssObj, pObj)
tnpostObj <- tnetpost(tnfitObj, mdelta=10, msample=10)
graphPosterior(tnpostObj)
```

`plotFit`*Network Fit Plot*

Description

This function plots the graph corresponding to the minimum scoring network.

Usage

```
plotFit(ternaryFit, type="interactive", ...)
```

Arguments

<code>ternaryFit</code>	a ternaryFit object
<code>type</code>	the type of plot to produce. "interactive" produces a plot that can be altered in the plotting window using the <code>tkplot</code> function from the <code>igraph</code> package. "static" produces a standard plot in any R graphics device.
<code>...</code>	additional parameters passed to the plotting function

Value

A plot of the network corresponding to the minimum score (stored in the `graphObjMin` slot) is plotted.

Author(s)

Matthew N. McCall and Anthony Almudevar

See Also

Almudevar A, McCall MN, McMurray H, Land H (2011). Fitting Boolean Networks from Steady State Perturbation Data, *Statistical Applications in Genetics and Molecular Biology*, 10(1): Article 47.

Examples

```
ssObj <- matrix(c(1,1,1,0,1,1,0,0,1),nrow=3)
pObj <- matrix(c(1,0,0,0,1,0,0,0,1),nrow=3)
tnfitObj <- tnetfit(ssObj, pObj)
plotFit(tnfitObj, type="static")
```

plotPost	<i>Network Posterior Plot</i>
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Description

This function plots the graph consisting of all edges with a marginal posterior probability greater than the selected threshold.

Usage

```
plotPost(ternaryPost, threshold=0.5, type="interactive", ...)
```

Arguments

ternaryPost	a ternaryPost object
type	the type of plot to produce. "interactive" produces a plot that can be altered in the plotting window using the tkplot function from the igraph package. "static" produces a standard plot in any R graphics device.
threshold	the marginal posterior probability required for an edge to be included in the plot.
...	additional parameters passed to the plotting function

Value

A plot of the network consisting of all edges with a marginal posterior probability greater than the selected threshold.

Author(s)

Matthew N. McCall and Anthony Almudevar

See Also

Almudevar A, McCall MN, McMurray H, Land H (2011). Fitting Boolean Networks from Steady State Perturbation Data, *Statistical Applications in Genetics and Molecular Biology*, 10(1): Article 47.

Examples

```
ssObj <- matrix(c(1,1,1,0,1,1,0,0,1),nrow=3)
pObj <- matrix(c(1,0,0,0,1,0,0,0,1),nrow=3)
tnfitObj <- tnetfit(ssObj, pObj)
tnpostObj <- tnetpost(tnfitObj, mdelta=10, msample=10)
plotPost(tnpostObj, type="static")
```

plotTraces *Network Fit Traces*

Description

This function plots the trace of four model parameters.

Usage

```
plotTraces(tfit)
```

Arguments

tfit a ternaryFit object

Value

The function creates a 2x2 grid of the four trace plots.

Author(s)

Matthew N. McCall and Anthony Almudevar

See Also

Almudevar A, McCall MN, McMurray H, Land H (2011). Fitting Boolean Networks from Steady State Perturbation Data, *Statistical Applications in Genetics and Molecular Biology*, 10(1): Article 47.

Examples

```
ssObj <- matrix(c(1,1,1,0,1,1,0,0,1),nrow=3)
pObj <- matrix(c(1,0,0,0,1,0,0,0,1),nrow=3)
tnfitObj <- tnetfit(ssObj, pObj)
plotTraces(tnfitObj)
```

predictAttractor *Predict the attractor(s) resulting from a given perturbation*

Description

This function computes the posterior probabilities of attractors reached for a given perturbation using the networks from a ternaryPost object.

Usage

```
predictAttractor(tpost, perturbations, wildtype = TRUE, verbose = FALSE)
```

Arguments

tpost	a ternaryPost object
perturbations	a list with two elements: perturbed.genes and forced.states
wildtype	if TRUE, the wildtype attractors are summarized; if FALSE, the perturbed attractors are summarized.
verbose	if TRUE, periodic reports on progress are printed.

Value

The function returns a list with two elements: \ post.prob: the posterior probability of each attractor
 \ attractor.summary: a single vector of steady states based on the resulting attractor

Author(s)

Matthew N. McCall and Anthony Almudevar

See Also

Almudevar A, McCall MN, McMurray H, Land H (2011). Fitting Boolean Networks from Steady State Perturbation Data, *Statistical Applications in Genetics and Molecular Biology*, 10(1): Article 47.

Examples

```
ssObj <- matrix(c(1,1,1,0,1,1,0,0,1),nrow=3)
pObj <- matrix(c(1,0,0,0,1,0,0,0,1),nrow=3)
rownames(ssObj) <- rownames(pObj) <- colnames(ssObj) <- colnames(pObj) <- c("Gene1","Gene2","Gene3")
tnfitObj <- tnetfit(ssObj, pObj)
tnpostObj <- tnetpost(tnfitObj, mdelta=10, msample=10)
predictAttractor(tnpostObj, list(perturbed.genes=c(1,2),forced.states=c(1,1)))
```

simulateSteadyState *Simulate Steady State Data*

Description

This function generates simulated steady state data from a given network.

Usage

```
simulateSteadyState(perturbationObj, tableObj, graphObj, degreeObj, wildtype=FALSE)
```

Arguments

perturbationObj	a matrix of perturbation experiments. Rows are genes and columns are experiments.
tableObj	a matrix containing the transition function tables
graphObj	a matrix containing the parents of each node
degreeObj	a vector containing the in-degree of each node
wildtype	if TRUE, the perturbations are assumed to be transient; if FALSE, the perturbations are assumed to be persistent.

Value

The function creates a steadyStateObj.

Author(s)

Matthew N. McCall and Anthony Almudevar

See Also

Almudevar A, McCall MN, McMurray H, Land H (2011). Fitting Boolean Networks from Steady State Perturbation Data, *Statistical Applications in Genetics and Molecular Biology*, 10(1): Article 47.

Examples

```
pObj <- matrix(c(1,0,0,0,1,0,0,0,1),nrow=3)
degreeObj <- c(0,1,1)
graphObj <- matrix(nrow=1,ncol=3)
graphObj[1,1] <- 0
graphObj[1,2] <- 1
graphObj[1,3] <- 2
tableObj <- matrix(nrow=3,ncol=3)
tableObj[,1] <- rep(0,3)
tableObj[,2] <- c(-1,0,1)
tableObj[,3] <- c(-1,0,1)
ssObj <- simulateSteadyState(pObj, tableObj, graphObj, degreeObj)
```

ternaryFit-class

Ternary Network Fit

Description

This is a class representation of the output of the ternary network fitting algorithm implemented in the function tnetfit.

Creating Objects

While one can create their own objects using the function `ternaryFit()`, this is highly discouraged. Typically this class is created by running the `tnetfit` function.

Slots

`perturbationObj`: a matrix of perturbation experiments. Rows are genes and columns are experiments.

`steadyStateObj`: a matrix of steady gene expression observations from a perturbation experiment. Rows are genes and columns are experiments.

`geneNames`: a vector of gene names corresponding to the rows of the `perturbationObj` and `steadyStateObj`.

`experimentNames`: a vector of experiment names corresponding to the columns of the `perturbationObj` and `steadyStateObj`.

`degreeObjMin`: a vector containing the in-degree of each node in the fit achieving the minimum score

`graphObjMin`: a matrix containing the parents of each node in the fit achieving the minimum score

`tableObjMin`: a matrix containing the table in the fit achieving the minimum score

`newScore`: the most recent score

`minScore`: the minimum score

`finalTemperature`: the final value of the temperature parameter

`traces`: a dataframe contain the traces for 4 parameters

`stageCount`: the number of stages

`xSeed`: the random seed.

`inputParams`: the `ternaryFitParameters` object used.

Methods

All named elements can be accessed and set in the standard way (e.g. `xSeed(object)` and `xSeed(object)<-`).

Author(s)

Matthew N. McCall and Anthony Almudevar

See Also

`tnetpost`, `ternaryFitParameters-class`, `ternaryPost-class`. Almudevar A, McCall MN, McMurray H, Land H (2011). Fitting Boolean Networks from Steady State Perturbation Data, *Statistical Applications in Genetics and Molecular Biology*, 10(1): Article 47.

Examples

```
ssObj <- matrix(c(1,1,1,0,1,1,0,0,1),nrow=3)
pObj <- matrix(c(1,0,0,0,1,0,0,0,1),nrow=3)
tnfitObj <- tnetfit(ssObj, pObj)
class(tnfitObj)
```

 ternaryFitParameters-class

Ternary Network Fitting Parameters

Description

This is a class representation of the input parameters for the ternary network fitting algorithm implemented in the function `tnetfit`.

Creating Objects

```
ternaryFitParameters()
```

This creates a `ternaryFitParameters` object with the default fitting parameters.

Slots

perturbationType: this parameter currently can only be set to 1

scoreType: the method to score networks. Can be set to either 1 or 2, corresponding the the score types in Almudevar et al. (2011).

backupStage: current fit is output periodically according to this parameter

maxStage: the maximum number of stages permitted. Ideally, the actual number of stages required until convergence should be much less than this value.

maxTransition: This parameter provides an adaptive truncation of the stage sample size. The stage terminates before the specified fixed sample size if the number of transitions resulting in a strict increase of the score reaches this value. If the sampler is in steady state, then this count should be approximately half the number of transitions in which the score changes value.

epsilon: Convergence tolerance.

beta0: Algorithm terminates when this number of consecutive convergence events have occurred.

chi0: The target initial acceptance rate. This should be close to 1, although setting it too close will increase computation time.

delta: The increment change in steady state distribution between stages (as variational distance). Larger values tend to decrease computation time, but too large a value will result in spurious convergence.

ne: The fixed sample size (number of MCMC transitions) per stage.

m0: The sample size (number of transitions) used to determine the initial temperature.

maxDegree: Maximum number of parents per node permitted in model topology.

pAddParent: This is the probability of adding a parent to a randomly selected node in the proposal function.

pExchangeParent: This parameter gives the probability of a parent exchange in the proposal function. The `AddParent` operation takes precedence, so this probability should be interpreted as being conditional on the rejection of the `AddParent` operation.

neighborDegree: Number of applications of the proposal function.

pNeighborhood: Vector of probabilities denoted, which generates the random number of proposal function iterations. The length is one less than neighborDegree. If neighborDegree equals 1 then no iteration is performed, and this vector is ignored.

rho: Weight parameter for the exponential smoothing of the variance estimate. For no smoothing set to 1.

edgePenalty: This parameter provides a complexity penalty. This number times the number of edges is added to the score. To apply no penalty set this parameter to 0.

Methods

All named elements can be accessed and set in the standard way (e.g. `scoreType(object)` and `scoreType(object)<-`).

Author(s)

Matthew N. McCall and Anthony Almudevar

See Also

`tnetfit`, `ternaryFit-class`, `ternaryPost-class`. Almudevar A, McCall MN, McMurray H, Land H (2011). Fitting Boolean Networks from Steady State Perturbation Data, *Statistical Applications in Genetics and Molecular Biology*, 10(1): Article 47.

Examples

```
# create an instance
ternaryFitParameters()
```

`ternaryPost-class` *Ternary Network Posterior*

Description

This is a class representation of the output of the ternary network posterior sampling algorithm implemented in the function `tnetpost`.

Creating Objects

While one can create their own objects using the function `ternaryPost()`, this is highly discouraged. Typically this class is created by running the `tnetpost` function.

Slots

perturbationObj: a matrix of perturbation experiments. Rows are genes and columns are experiments.

steadyStateObj: a matrix of steady gene expression observations from a perturbation experiment. Rows are genes and columns are experiments.

geneNames: a vector of gene names corresponding to the rows of the perturbationObj and steadyStateObj.

experimentNames: a vector of experiment names corresponding to the columns of the perturbationObj and steadyStateObj.

scores: the score of each sample

degreeObjs: the in-degree vector for each sample

graphObjs: the graph matrix for each sample

tableObjs: the table matrix for each sample

inputParams: the ternaryFitParameters object used

Methods

All named elements can be accessed and set in the standard way (e.g. `scores(object)` and `scores(object)<-`).

Author(s)

Matthew N. McCall and Anthony Almudevar

See Also

`tnetfit`, `ternaryFitParameters-class`, `ternaryFit-class`. Almudevar A, McCall MN, McMurray H, Land H (2011). Fitting Boolean Networks from Steady State Perturbation Data, *Statistical Applications in Genetics and Molecular Biology*, 10(1): Article 47.

Examples

```
ssObj <- matrix(c(1,1,1,0,1,1,0,0,1),nrow=3)
pObj <- matrix(c(1,0,0,0,1,0,0,0,1),nrow=3)
tnfitObj <- tnetfit(ssObj, pObj)
tnpostObj <- tnetpost(tnfitObj, mdelta=10, msample=10)
class(tnpostObj)
```

tnetfit	<i>Ternary Network Fitting</i>
---------	--------------------------------

Description

This function fits a ternary network based on perturbation experiments.

Usage

```
tnetfit(steadyStateObj, perturbationObj, params=ternaryFitParameters(),  
xSeed=NA)
```

Arguments

`steadyStateObj` a matrix of steady gene expression observations from a perturbation experiment. Rows are genes and columns are experiments.

`perturbationObj` a matrix of perturbation experiments. Rows are genes and columns are experiments.

`params` a `ternaryFitParameters` object

`xSeed` an integer random seed. If NA, a random seed is generated.

Value

The function returns a `ternaryFit` object.

Author(s)

Matthew N. McCall and Anthony Almudevar

See Also

Almudevar A, McCall MN, McMurray H, Land H (2011). Fitting Boolean Networks from Steady State Perturbation Data, *Statistical Applications in Genetics and Molecular Biology*, 10(1): Article 47.

Examples

```
ssObj <- matrix(c(1,1,1,0,1,1,0,0,1),nrow=3)  
pObj <- matrix(c(1,0,0,0,1,0,0,0,1),nrow=3)  
rownames(ssObj) <- rownames(pObj) <- colnames(ssObj) <- colnames(pObj) <- c("Gene1", "Gene2", "Gene3")  
tnfitObj <- tnetfit(ssObj, pObj)
```

`tnetpost`*Ternary Network Posterior Sampling*

Description

This function samples from the posterior density of a ternary network based on perturbation experiments.

Usage

```
tnetpost(tfit, mdelta=as.integer(10000), msample=as.integer(2000), temperatureScale=1.0, xSeed=NA)
```

Arguments

<code>tfit</code>	a ternaryFit object
<code>mdelta</code>	number of transitions between samples
<code>msample</code>	number of samples
<code>temperatureScale</code>	the final temperature is multiplied by this value for sampling
<code>xSeed</code>	an integer random seed. If NA, a random seed is generated.

Value

The function returns a ternaryPost object.

Author(s)

Matthew N. McCall and Anthony Almudevar

See Also

Almudevar A, McCall MN, McMurray H, Land H (2011). Fitting Boolean Networks from Steady State Perturbation Data, *Statistical Applications in Genetics and Molecular Biology*, 10(1): Article 47.

Examples

```
ssObj <- matrix(c(1,1,1,0,1,1,0,0,1),nrow=3)
pObj <- matrix(c(1,0,0,0,1,0,0,0,1),nrow=3)
rownames(ssObj) <- rownames(pObj) <- colnames(ssObj) <- colnames(pObj) <- c("Gene1", "Gene2", "Gene3")
tnfitObj <- tnetfit(ssObj, pObj)
tnpostObj <- tnetpost(tnfitObj, mdelta=10, msample=10)
```

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