# Package 'networkBMA'

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<b>Title</b> Regression-based network inference using Bayesian Model Averaging
<b>Description</b> An extension of Bayesian Model Averaging (BMA) for network construction using time series gene expression data.  Includes assessment functions and sample test data.
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contabs
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## Description

Contingency table values relative to known truth for probabilistic networks given thresholds on edge probabilies.

## Usage

```
contabs(network, reference, size, thresholds = NULL)
```

## Arguments

_	
network	A network represented as a data frame in which each row corresponds to an edge with nonzero estimated probability. The first column gives the name of the regulator, the second column gives the name of the regulated gene, and the third column gives the estimated probability for the regulator-gene pair. If the third column is omitted it is assumed that all edges are assigned probability 1.
reference	A reference network represented as a two-column data frame in which each row corresponds to an edge, and the columns give the regulator and target genes, respectively. This is the true underlying network for determining the contingency table values.
size	The size of the network if all possible edges were included.
thresholds	Threshold values on the probability of edges being in the network for which contingency tables are desired. The default is all distinct nonzero probabilities in the network. Thresholds should be specified as probabilities rather than percentages.

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#### **Details**

Pairs for which edges do not exist in reference are not enumerated, because their numbers could be very large. Instead, the size parameter is used to account for pairs that are not edges. However, the assumption is that all edges that are in the network but not in the reference are accounted for in size.

Care must be taken in specifying size. For example, if the reference does not contain self-edges while the network does, and size does not count self-edges, then contabs will not give the correct number of false negatives.

#### Value

Outputs a data frame giving the contingency table values for the specified thresholds, with row names being the threshold values. The variables (columns) are of the data frame are as follows:

TP	true positives, or regulator-gene pairs correctly identified as being linked in the reference network,
FN	false negatives, or gene pairs that are linked in the reference network but not in the proposed network,
FP	false positives, or gene pairs that are linked in the proposed network but not in the reference network,
TN	true negatives, or gene pairs that are not linked both networks.

#### See Also

```
networkBMA, contabs.netwBMA
```

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contabs.netwBMA

Network assessment with incomplete context.

#### **Description**

Contingency table values for the intersection of a probabilistic network of regulator-target gene edges with a reference network with incomplete knowledge.

## Usage

```
contabs.netwBMA(network, reference, known = NULL, thresholds = NULL)
```

#### **Arguments**

network

A network represented as a data frame in which each row corresponds to a directed edge (regulator-gene pair) with nonzero estimated probability. The first column gives the name of the regulator, the second column gives the name of the regulated gene, and the third column gives the estimated probability for the regulator-gene pair. If the third column is omitted it is assumed that all edges are assigned probability 1.

are assign

reference

A reference network represented as a two-column data frame in which each row corresponds to a regulator-gene pair (or network edge), and the columns give the corresponding regulator and target gene names, respectively. This reference network is used as the standard for determining contingency table entries.

known

A 2-column matrix of regulatory relationships that were known (hard-coded) in the modeling process that produced network. Each row corresponds to a known regulator-gene pair (edge in the network), and the columns give the corresponding regulator and target gene names, respectively. These known regulatory relationships should all be included in network (this is checked), and they may also have regulator-gene pairs in common with reference.

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thresholds

Threshold values on the probability of edges being in the network for which contingency tables are desired. The default is all distinct nonzero probabilities in the network. Nonzero thresholds are treated as inclusive. Thresholds should be specified as probabilities rather than percentages.

#### **Details**

For real gene networks, complete information on the true underlying network is not available. contabs.netwBMA proceeds by comparing the intersecting subset of the proposed edges with a reference network composed of regulator-genes pairs. Edges that don't exist between any regulator and any target gene in the reference network are used to complete the larger set P of all possible edges for the comparison. Only the subset of network edges that belong to P is considered. There are issues in handling known edges hardcoded in the modeling, for which a detailed explanation is given in the package vignette.

#### Value

The contingency table for the the intersection of network and reference with edges in known removed.

#### References

Uncovering regulatory relationships in yeast using networkBMA, networkBMA Bioconductor package vignette.

#### See Also

```
networkBMA,contabs.prelim,contabs
```

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## End(Not run)

contabs.prelim

Preliminary calculation for network assessment.

#### Description

Computes the quantities to be used for assessment from a proposed and a set of reference edges. For cases where there is incomplete information about the true underlying network.

## Usage

contabs.prelim(network, reference, known = NULL)

#### **Arguments**

network A network represented as a data frame in which each row corresponds to a di-

rected edge (regulator-gene pair) with nonzero estimated probability. The first column gives the name of the regulator, the second column gives the name of the regulated gene, and the third column gives the estimated probability for the regulator-gene pair. If the third column is omitted it is assumed that all edges

are assigned probability 1.

reference A reference network represented as a two-column data frame in which each row

corresponds to a regulator-gene pair (or network edge), and the columns give the corresponding regulator and target gene names, respectively. This reference

network is used as the standard for determining contingency table entries.

known A 2-column matrix of regulatory relationships that were known (hard-coded) in

the modeling process that produced network. Each row corresponds to a known regulator-gene pair (edge in the network), and the columns give the corresponding regulator and target gene names, respectively. These known regulatory relationships should all be included in network (this is checked), and they may also

have regulator-gene pairs in common with reference.

#### **Details**

This function accomplishes the preprocessing step from contabs.newtBMA to produce the appropriate input to contabs to produce contingency tables.

#### Value

A list with the following components:

network

A network represented as a data frame in which each row corresponds to an edge with nonzero estimated probability. This is the input network with edges from the known regulatory relationships and edges outside of the domain defined by the output version of reference removed.

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reference A reference network represented as a two-column data frame in which each row

corresponds to an edge, and the columns give the regulator and target genes, respectively. This is the input reference reduced by the known regulatory rela-

tionships.

size The size of the network formed by pairs (r,g) in which r is any regulator g is any

gene from the output version of reference, reduced by any known regulatory

relationships.

## See Also

networkBMA, contabs.netwBMA, contabs

## **Examples**

```
## Not run:
data(vignette)
dim(timeSeries)
colnames(timeSeries)
table(timeSeries$replicate)
table(timeSeries$time)
dim(reg.known)
colnames(reg.known)
dim(reg.prob)
edges <- networkBMA(data = timeSeries[,-(1:2)],</pre>
                    nTimePoints = length(unique(timeSeries$time)),
                    prior.prob = reg.prob, known = reg.known)
prelim <- contabs.prelim( network = edges, reference = referenceNetwork,</pre>
                       known = reg.known)
contabs( network = prelim$network, reference = prelim$reference,
         size = prelim$size, thresholds = prelim$thresholds)
contabs.netwBMA( network = edges, reference = referenceNetwork,
                 known = reg.known)
## End(Not run)
```

dream4

DREAM 4 (Stolovitsky et al. 2007) 'gold standard' reference network specifications, simulated time series perturbation subsets, and steady state (wild-type) gene expression levels.

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## Description

Contains six objects: dream4gold10, dream4gold100, dream4ts10, dream4ts100, dream4wild10, dream4wild100, each in the form of a list of matrices, in which each element corresponds to one of 5 different datasets.

dream4gold10 and dream4gold100 are lists of gold standard network specifications for the 10-gene and 100-gene simulated networks. The list elements are three-column data frames, in which the first and second column represent all possible regulator-gene pairs in the network, excluding self edges. The third column is a boolean variable indicating whether or not the genes in the first two columns are a regulatory pair and thus consitute an edge in the network.

dream4ts10 and dream4ts100 are lists of time course datasets showing how the simulated network responds to a perturbation and how it relaxes upon removal of the perturbation. For both size 10 and size 100, 5 different datasets are available. For networks of size 10, each of the 5 datasets consists of 5 different time series replicates, and for networks of size 100, each of the 5 datasets consists of 10 time series replicates. Each time series has 21 time points. In both cases, there are 5 list components corresponding to the datasets, each of which is a data frame in which the first two columns give the replicate and time, and the remaining columns give the measured expression levels.

The initial condition always corresponds to a steady-state measurement of the wild-type. At t=0, a perturbation is applied to the network as described below. The first half of the time series (until t=500) shows the response of the network to the perturbation. At t=500, the perturbation is removed (the wild-type network is restored). The second half of the time series (until t=1000) shows how the gene expression levels go back from the perturbed to the wild-type state.

dream4wild10 and dream4wild100 are lists giving the steady state (wild-type) expression levels for the genes in each dataset.

#### Usage

data(dream4)

#### **Details**

The perturbations applied here only affect about a third of all genes, but basal activation of these genes can be strongly increased or decreased. For example, these experiments could correspond to physical or chemical perturbations applied to the cells, which would cause (via regulatory mechanisms not explicitly modeled here) some genes to have an increased or decreased basal activation. The genes that are directly targeted by the perturbation may then cause a change in the expression level of their downstream target genes.

The time series datasets included in this package are a subset of the DREAM 4 data available for the reference networks.

## References

Stolovitzky G, Monroe D and Califano A. (2007), Dialogue on Reverse-Engineering Assessment and Methods. Annals of the New York Academy of Sciences,1115(1),1–22.

Stolovitzky G, Califano A, Prill RJ and Saez Rodriguez J.(2009), DREAM: Dialogue for Reverse Engineering Assessments and Methods, http://wiki.c2b2.columbia.edu/dream/

Marbach D, Prill RJ, Schaffter T, Mattiussi C, Floreano D, and Stolovitzky G. Revealing strengths and weaknesses of methods for gene network inference. PNAS, 107(14):6286-6291, 2010.

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Marbach D, Schaffter T, Mattiussi C, and Floreano D. Generating Realistic in silico Gene Networks for Performance Assessment of Reverse Engineering Methods. Journal of Computational Biology, 16(2) pp. 229-239, 2009.

Prill RJ, Marbach D, Saez-Rodriguez J, Sorger PK, Alexopoulos LG, Xue X, Clarke ND, Altan-Bonnet G, and Stolovitzky G. Towards a rigorous assessment of systems biology models: the DREAM3 challenges. PLoS ONE, 5(2):e9202, 2010.

#### See Also

networkBMA

fastBMAcontrol

Control parameters for networkBMA when using fastBMA algorithm

#### **Description**

Assigns default control parameters for networkBMA when using fastBMA algorithm, and allows setting control parameter values.

#### Usage

## **Arguments**

OR	A number specifying the maximum ratio for excluding models in Occam's window.
timeSeries	A logical value indicating whether the input the input data set is a time series data or static data.
rankOnly	A logical value indicating use priors to rank variables but uniform prior otherwise
noPrune	A logical value indicating whether not applying transitive reduction on the output edges or not
edgeMin	Threshold for the posterior probability to be shown
edgeTol	the error tolerance for determining whether an indirect path is as good as a direct path
nThreads	The number of threads used in the parallel computing of fastBMA
selfie	A logical value indicating whether showing self-loop edges or not
showPrune	A logical value indicating whether showing removed edges in transitive reduction or not. Ignored if noPrune is TRUE

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nVars the number of variables analyzed

fastgCtrl A list of control variables affecting fastBMA computations when using Zellner's

g-prior in model likelihhod evaluation. A function called fastgCtrl is provided

to facilitate this setting, and the default is fastgCtrl().

start start point of eval subset. end end point of eval subset.

pruneFilterMin minimum posterior prob (0-1) before an edge will be included in the network to

be pruned

timeout maximum number of seconds for the regression before it stops the search. 0 if

not apply.

#### Value

A list of values for the named control parameters to be passed to fastBMA.

#### References

K. Lo, A. E. Raftery, K. M. Dombek, J. Zhu, E. E. Schadt, R. E. Bumgarner and K. Y. Yeung (2011), Integrating External Biological Knowledge in the Construction of Regulatory Networks from Time-series Expression Data, unpublished manuscript, University of Washington.

K. Y. Yeung, K. M. Dombek, K. Lo, J. E. Mittler, J. Zhu, E. E. Schadt, R. E. Bumgarner and A. E. Raftery (2011), Construction of regulatory networks using expression time-series data of a genotyped population, Proceedings of the National Academy of Sciences, 108(48):19436-41.

K. Y. Yeung, R. E. Bumgarner and A. E. Raftery (2005). Bayesian Model Averaging: Development of an improved multi-class, gene selection and classification tool for microarray data. Bioinformatics 21:2394-2402.

J. A. Hoeting, D. Madigan, A. E. Raftery, and C. T. Volinsky (1999). Bayesian Model Averaging: a tutorial, Statistical Science 14(4): 382-417.

L. H. Hong, M. Wu1, A. Lee, W. C. Young, A. E. Raftery and K. Y. Yeung, FastBMA and Transitive Reduction for Gene Network Inference. [in preparation]

#### See Also

fastgControl, networkBMA

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fastgControl	Control parameters for using Zellner's g-prior in fastBMA algorithm in networkBMA

## **Description**

Assigns default control parameters for the use of Zellner's g-prior in fastBMA algorithm in networkBMA, and allows setting control parameter values.

#### Usage

```
fastgControl( optimize = 0, g0 = NULL, iterlim = 20 )
```

## **Arguments**

optimize	optimize bits - an int value determines how accurate the optimization of g is. 0 means not optimize.
g0	An initial value of g to use if optimize is TRUE, or the fixed value to use without optimization.
iterlim	If optimize is non-zero, the maximum number of iterations of the optimization algorithm to use. Ignored otherwise.

#### Value

A list of values for the named control parameters to be passed to fastBMAcontrol and networkBMA using fastBMA algorithm.

## References

A. Zellner (1986), On assessing prior distributions and Bayesian regression analysis with g-prior distributions, Bayesian inference and decision techniques: Essays in Honor of Bruno De Finetti, 6:233-243.

M. Clyde and E.I. George (2004), Model Uncertainty, Statistical Science, 81-94.

L. H. Hong, M. Wu1, A. Lee, W. C. Young, A. E. Raftery and K. Y. Yeung, FastBMA and Transitive Reduction for Gene Network Inference. [in preparation]

## See Also

```
fastBMAcontrol, networkBMA
```

```
data(dream4)
network <- 1
nTimePoints <- length(unique(dream4ts10[[network]]$time))</pre>
```

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gControl

Control parameters for using Zellner's g-prior in ScanBMA

## Description

Assigns default control parameters for the use of Zellner's g-prior in ScanBMA, and allows setting control parameter values.

## Usage

#### **Arguments**

optimize	A logical value indicating whether to optimze g using an iterative EM algorithm or use a fixed value of g.
optMethod	A character string indicating how to optimize g. Currently, only perTarget is supported, indicating that g should be optimized individually for each target.
g0	An initial value of g to use if optimize is TRUE, or the fixed value to use without optimization.
iterlim	If optimize is TRUE, the maximum number of iterations of the EM algorithm to use. Ignored otherwise.
epsilon	If optimize is TRUE, the precision with which to find g using the EM algorithm. Ignored otherwise.

## Value

A list of values for the named control parameters to be passed to ScanBMAcontrol and ScanBMA.

#### References

A. Zellner (1986), On assessing prior distributions and Bayesian regression analysis with g-prior distributions, Bayesian inference and decision techniques: Essays in Honor of Bruno De Finetti, 6:233-243.

M. Clyde and E.I. George (2004), Model Uncertainty, Statistical Science, 81-94.

## See Also

ScanBMAcontrol, ScanBMA, networkBMA

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#### **Examples**

iBMAcontrolLM

Control parameters for iterateBMAlm

#### **Description**

Assigns default control parameters for iterateBMAlm, and allows setting control parameter values.

## Usage

#### **Arguments**

OR A number specifying the maximum ratio for excluding models i	in Occam's win-
---	-----------------

dow.

nbest A positive integer specifying the number of models of each size to be consid-

ered by leaps-and-bounds in determining the model space for Bayesian Model

Averaging. The default value is 10.

maxNvar A positive integer specifying the maximum number of variables (excluding the

intercept) used in each iteration of BMA. The default value is 30.

thresProbne0 Threshold (in percent) for the posterior probability that each variable is has a

non-zero coefficient (in percent). Variables with posterior probability less than thresProbne0 are removed in future BMA iterations. The default value is 1

percent.

keepModels A logical value indicating whether or not to keep the BMA models from all

of the iterations and apply Occam's window using OR at the end, or to apply Occam's window in all BMA iterations and return the final model. The default is not to keep the models. Setting the argument to TRUE requires more memory

and may slow the computation as a result.

maxIter A positive integer giving a limit on the number of iterations of iterateBMAlm.

The default value is 20000. iterateBMAlm will terminate in fewer than maxIter iterations if the iterative BMA modeling process has seen all available variables.

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#### Value

A list of values for the named control parameters to be passed to a version of the function bicreg from the BMA package that has been modified to handle prior probabilities.

#### References

- K. Lo, A. E. Raftery, K. M. Dombek, J. Zhu, E. E. Schadt, R. E. Bumgarner and K. Y. Yeung (2012), Integrating External Biological Knowledge in the Construction of Regulatory Networks from Time-series Expression Data, BMC Systems Biology, 6:101.
- K. Y. Yeung, K. M. Dombek, K. Lo, J. E. Mittler, J. Zhu, E. E. Schadt, R. E. Bumgarner and A. E. Raftery (2011), Construction of regulatory networks using expression time-series data of a genotyped population, Proceedings of the National Academy of Sciences, 108(48):19436-41.
- K. Y. Yeung (with contributions from A. E. Raftery and I. Painter), iterativeBMA: The Iterative Bayesian Model Averaging (BMA) algorithm, Bioconductor R package, version 1.8.0 posted in 2009.
- K. Y. Yeung, R. E. Bumgarner and A. E. Raftery (2005). Bayesian Model Averaging: Development of an improved multi-class, gene selection and classification tool for microarray data. Bioinformatics 21:2394-2402.
- A. E. Raftery, J. A. Hoeting, C. T. Volinsky, I. Painter and K. Y. Yeung (2005), BMA: Bayesian Model Averaging, Comprehensive R Archhive Network (CRAN), package version 3.15.1 posted in 2012.
- J. A. Hoeting, D. Madigan, A. E. Raftery, and C. T. Volinsky (1999). Bayesian Model Averaging: a tutorial, Statistical Science 14(4): 382-417.

#### See Also

iterateBMAlm, networkBMA do.call

## **Examples**

iterateBMAlm

*Iterative BMA for linear modeling with prior variable probabilities.* 

#### **Description**

An iterative version of Bayesian Model Averaging (BMA) for linear models with many variables. Incorporates prior probabilities for inclusion of variables in models.

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## Usage

## Arguments

x A matrix of real-valued predictor variables. Rows correspond to observations

and columns to variables.

y A real-valued response vector.

prior.prob An optional vector of prior probabilities for each predictor variable belonging to

a linear model for the data. If not specified, predictor variables are assumed to

have equal prior probability.

control A list of values controling the underlying algorithm. The default is given by

iBMAcontrolLM().

verbose A logical variable indicating whether or not the details of the method's progress

shoul be printed during computation. The default value is FALSE.

#### **Details**

iterateBMAlm is intended for datasets that have more variables (e.g. gene expression values) than observations (e.g. subjects). There is currently no mechanism for handling factor variables in iterateBMAlm, as there is in the underlying function bicreg in the BMA package. However factors can be encoded by users and included with other variables as input.

#### Value

A list with the following components, similar to the output of function bicreg in the BMA package:

bic values of BIC for the models

postprob the posterior probabilities of the models selected priorprob the prior probabilities of the variables in the models

namesx the names of the variables

label labels identifying the models selected

r2 R2 values for the models

size the number of independent variables in each of the models

which a logical matrix with one row per model and one column per variable indicating

whether that variable is in the model

probne0 the posterior probability that each variable is non-zero (in percent) postmean the posterior mean of each coefficient (from model averaging)

condpostmean the posterior mean of each coefficient conditional on the variable being included

in the model

condpostsd the posterior standard deviation of each coefficient conditional on the variable

being included in the model

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ols matrix with one row per model and one column per variable giving the OLS

estimate of each coefficient for each model

mle the same as ols

n.models the number of modelsn.vars the number of variables

#### References

K. Y. Yeung, R. E. Bumgarner and A. E. Raftery (2005), Bayesian model averaging: development of an improved multi-class, gene selection and classification tool for microarray data, Bioinformatics 21(10) 2394-2402.

K. Lo, A. E. Raftery, K. M. Dombek, J. Zhu, E. E. Schadt, R. E. Bumgarner and K. Y. Yeung (2012), Integrating External Biological Knowledge in the Construction of Regulatory Networks from Time-series Expression Data, BMC Systems Biology, 6:101.

K. Y. Yeung, K. M. Dombek, K. Lo, J. E. Mittler, J. Zhu, E. E. Schadt, R. E. Bumgarner and A. E. Raftery (2011), Construction of regulatory networks using expression time-series data of a genotyped population, Proceedings of the National Academy of Sciences, 108(48):19436-41.

#### See Also

iBMAcontrolLM, varord, bicreg

```
data(dream4)
network <- 1
Time <- as.numeric(dream4ts100[[network]]$time)
xIndex <- which(Time != max(Time))
yIndex <- which(Time != min(Time))
gene <- "G1"

x <- dream4ts100[[network]][xIndex,-(1:2)]
y <- dream4ts100[[network]][yIndex,gene]

nvar <- 50
ord <- varord( x, y, ordering = "bic1")[1:nvar]
result <- iterateBMAlm( x = x[,ord], y = y)</pre>
```

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networkBMA	Gene network inference from time series data via BMA.
networkBMA	Gene network inference from time series data via BMA.

## Description

Estimates a probabilistic network of regulator-gene pairs from time series data via ScanBMA or iterative BMA.

## Usage

## Arguments

_	
data	A matrix whose columns correspond to variables or genes and whose rows correspond to the observations at different time points. The row names should be the gene names, to used in conjunction with prob and known as appropriate.
nTimePoints	The number of time points at which expression measurements are available. The number of columns in data should be a multiple of nTimePoints, which could be greater than 1 if there are replicates.
prior.prob	If included as input, either a single positive fraction representing the probability of an regulator-gene pair in the network, or else a matrix in which the (i,j) entry is the estimated prior probability that gene i regulates gene j. The default value is NULL, which implies that no prior information will be used in modeling the network.
known	An optional 2-column matrix of known (hard-coded) regulatory relationships. The first column gives the name of the regulator, and the second column gives the name of the target gene. The gene names should be consistent with the data.
ordering	A character string indicating the ordering to be used for the genes or variables, referring to the options for ordering in function varord. The default is option "bic1+prior" for varord.  If a prior is provided, genes with prob=1 are always included first in modeling
	regardless of the specified ordering, while genes with prior = 0 are excluded.
nvar	The number of top-ranked (see ordering) genes to be considered in the modeling. The default is determined by the length of ordering if it is greater than 1, otherwise it is min(nrow(data),ncol(data)-1). The maximum number of genes for which measurements are available is nrow(data). If fastBMA algorithm is choosen, this parameter ignored, nVars in fastBMAcontrol used instead
self	A logical variable indicating whether or not to allow self edges in modeling. The default is to allow self edges.

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An optional estimate of the maximum number of regulators for any gene in the maxreg network. If provided, this is used to help reduce the amount of memory used for the computations. A list of control variables affecting the BMA computations. The functions control ScanBMAcontrol for optimize="ScanBMA" and iBMAcontrolLM for optimize="iBMA" and fastBMAcontrol for optimize="fastBMA" are provided to faciltate this setting, and the default is ScanBMAcontrol(). diff0 A logical variable indicating whether to differentiate between edges with posterior probability of 0. This includes regulators not included from when nvar is less than the total number of possible regulators. If known is not NULL, then diff0 must be FALSE. If fastBMA algorithm used, then diff0 must be FALSE. diff100 A logical variable indicating whether to differentiate between edges with posterior probability of 1.0. If known is not NULL, then diff100 must be FALSE. If fastBMA algorithm used, then diff100 must be FALSE. A logical variable indicating whether or not a detailed information should be verbose output as the computation progresses. The default value is FALSE.

#### **Details**

networkBMA is intended for time-series data in which there are more variables (gene expression values) than observations (experiments). For each gene, a linear model is fit to the expression data for all genes at a particular time point to predict the expression of a particular gene at the next time point. BMA is used to fit the linear model to identify the candidate regulators (variables) in the model. The inferred network consists of candidate regulators and their corresponding posterior probabilities for each gene.

It is assumed that data is available for all replicates at the same set of time points.

#### Value

A network represented as a data frame in which each row corresponds to a directed edge for which the probability is estimated to be nonzero. The first column gives the name of the regulator, the second column gives the name of the regulated gene, and the third column gives the estimated probability for the regulator-gene pair. Rows are ordered by decreasing probability estimate.

The summary function gives the number of inferred edges at posterior probabilities 0, .5, .75, .90, .95 and 1.0

## References

- K. Lo, A. E. Raftery, K. M. Dombek, J. Zhu, E. E. Schadt, R. E. Bumgarner and K. Y. Yeung (2012), Integrating External Biological Knowledge in the Construction of Regulatory Networks from Time-series Expression Data, BMC Systems Biology, 6:101.
- K. Y. Yeung, K. M. Dombek, K. Lo, J. E. Mittler, J. Zhu, E. E. Schadt, R. E. Bumgarner and A. E. Raftery (2011), Construction of regulatory networks using expression time-series data of a genotyped population, Proceedings of the National Academy of Sciences, 108(48):19436-41.
- K. Y. Yeung, A. E. Raftery and C. Fraley (2012), Uncovering regulatory relationships in yeast using networkBMA, networkBMA Bioconductor package vignette.
- L. H. Hong, M. Wu1, A. Lee, W. C. Young, A. E. Raftery and K. Y. Yeung, FastBMA and Transitive Reduction for Gene Network Inference. [in preparation]

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#### See Also

summary.networkBMA, varord, ScanBMAcontrol, iBMAcontrolLM, contabs

#### **Examples**

roc

Receiver Operating Characteristic and Precision-Recall Curves

#### **Description**

Computes the Receiver Operating Characteristic (ROC) or precision-recall curves from contingencies tables (confusion matrices) and their associated probabilities, and optionally plots them.

#### Usage

```
roc( contabs, plotit = TRUE)
prc( contabs, plotit = TRUE, ymax = max(y))
```

## **Arguments**

contabs A data frame representing a contingency tables (confusion matrices) for a bi-

nary classification experiment. The column names should include TP (for true positive), FN (for false negative), FP (for false positive), TN (for true negative);

these can be given in any order.

plotit A logical variable indicating whether or not the ROC curve should be plotted.

ymax Upper vertical axis value for plotting precision-recall curves with prc. The de-

fault is max(y), (the maximum value for precision derived from the contingency

table). ymax should be no larger than 1.

#### **Details**

The estimated area may be inaccurate when the sector covered by the contingency tables is small, and should be used with caution in such cases.

20 roc

#### Value

A vector with the following named components:

area The area under the extended curve (covered by the black solid and dotted lines).

sector The estimated area under the sector (below the curve and within the red lines)

covered by the contingency table.

width The width of the sector (within the red vertical lines) covered by the contingency

table.

As a side-effect, the ROC (roc) or precision-recall curve (prc) is plotted if plotit = TRUE. The red vertical lines highlight the sector covered by the contingency table. The black lines approximate the curve. They are dotted beyond the endpoints of the sector, where there is no information from the contingency table. The diagonal blue line in the ROC curve indicates the line between (0,0) and (1,1).

#### References

J. Davis and M. Goadrich, The relationship between Precision-Recall and ROC curves, manuscript, Department of Computer Science, University of Wisconsin.

#### See Also

contabs

```
data(dream4)
network <- 1
nTimePoints <- length(unique(dream4ts10[[network]]$time))</pre>
edges1ts10 <- networkBMA( data = dream4ts10[[network]][,-(1:2)],
                       nTimePoints = nTimePoints, prior.prob = 0.1)
# check for self loops in estimated network
selfN <- any(as.character(edges1ts10[,1]) == as.character(edges1ts10[,2]))</pre>
selfN
reference <- dream4gold10[[network]]</pre>
# check for self loops in reference (there are none)
selfR <- any(as.character(reference[,1]) == as.character(reference[,2]))</pre>
selfR
# restrict reference to edges; first two columns (gene) only
reference <- reference[reference[,3] == 1,1:2]</pre>
contingencyTables <- contabs(network = edges1ts10, reference = reference,</pre>
                               size = 100)
```

ScanBMA 21

```
roc(contingencyTables)
prc(contingencyTables)
```

ScanBMA

Bayesian Model Averaging for linear regression models.

#### **Description**

Bayesian Model Averaging accounts for the model uncertainty inherent in the variable selection problem by averaging over the best models in the model class according to approximate posterior model probability.

## Usage

#### **Arguments**

x A matrix of independent variables.

y A vector of values for the dependent variable.

prior.prob If included as input, either a single positive fraction representing the probabil-

ity of an independent variable being present in the true model, or else a vector assigning an estimated prior probability for each independent variable individually. The default value is NULL, which implies that no prior information will be

used.

control A list of control variables affecting the ScanBMA computations. The func-

tion ScanBMAcontrol is provided to faciltate this setting, and the default is

ScanBMAcontrol().

verbose A logical variable indicating whether or not a detailed information should be

output as the computation progresses. The default value is FALSE.

#### **Details**

Bayesian Model Averaging accounts for the model uncertainty inherent in the variable selection problem by averaging over the best models in the model class according to approximate posterior model probability. ScanBMA is an algorithm for searching the model space efficiently when a large number of independent variables are present.

## Value

Returns an object of classbicreg (see the BMA package). In addition, it adds nmodelschecked, which gives the number of models looked at in the ScanBMA model search, and g, which gives the final value of g used if Zellner's g-prior was used to evaluate model likelihood.

22 ScanBMAcontrol

#### References

Raftery, Adrian E. (1995). Bayesian model selection in social research (with Discussion). Sociological Methodology 1995 (Peter V. Marsden, ed.), pp. 111-196, Cambridge, Mass.: Blackwells.

#### See Also

```
networkBMA, ScanBMAcontrol, gControl
```

## **Examples**

ScanBMAcontrol

Control parameters for ScanBMA

#### **Description**

Assigns default control parameters for ScanBMA, and allows setting control parameter values.

#### Usage

```
ScanBMAcontrol( OR = 100, useg = TRUE, gCtrl = gControl(), thresProbne0 = 1 )
```

#### **Arguments**

OR	A number specifying the maximum ratio for excluding models in Occam's win-
	dow.

useg A logical value indicating whether to use Zellner's g-prior in model likelihood

evaluation. If set to FALSE, ScanBMA will use BIC to approximate the likeli-

hood.

gCtrl A list of control variables affecting ScanBMA computations when using Zell-

ner's g-prior in model likelihhod evaluation. A function called gControl is

provided to facilitate this setting, and the default is gControl().

thresProbne0 Threshold (in percent) for the posterior probability that each variable is has a

non-zero coefficient (in percent). Variables with posterior probability less than thresProbne0 are removed in future BMA iterations. The default value is 1

percent.

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#### Value

A list of values for the named control parameters to be passed to ScanBMA.

#### References

K. Lo, A. E. Raftery, K. M. Dombek, J. Zhu, E. E. Schadt, R. E. Bumgarner and K. Y. Yeung (2011), Integrating External Biological Knowledge in the Construction of Regulatory Networks from Time-series Expression Data, unpublished manuscript, University of Washington.

K. Y. Yeung, K. M. Dombek, K. Lo, J. E. Mittler, J. Zhu, E. E. Schadt, R. E. Bumgarner and A. E. Raftery (2011), Construction of regulatory networks using expression time-series data of a genotyped population, Proceedings of the National Academy of Sciences, 108(48):19436-41.

K. Y. Yeung, R. E. Bumgarner and A. E. Raftery (2005). Bayesian Model Averaging: Development of an improved multi-class, gene selection and classification tool for microarray data. Bioinformatics 21:2394-2402.

J. A. Hoeting, D. Madigan, A. E. Raftery, and C. T. Volinsky (1999). Bayesian Model Averaging: a tutorial, Statistical Science 14(4): 382-417.

#### See Also

gControl, ScanBMA, networkBMA

## **Examples**

scores

Scores for assessment from contingency tables.

#### **Description**

Gives scores for assessment and other values associated with contingency tables for network inference.

## Usage

24 scores

#### **Arguments**

contabs

A data frame representing a contingency tables (confusion matrices) for a binary classification experiment. The column names should include TP (for true positive), FN (for false negative) FP (for false positive), TN (for true negative); these can be given in any order.

what

A character string specifying one or more desired output quantities from among:

"TP" Number of edges that are correctly identified as such (true positives).

"FP" Number of unlinked pairs that are incorrectly identified as edges (false positives).

"TN" Number of unlinked pairs that are correctly identified as such (true negatives).

"FN" Number of edges that are not identified as such (false negatives).

"TPR", "sensitivity", "recall" True positive rate, sensitivity, or recall. TP/(# edges).

"FPR" False positive or false alarm rate. FP/(# edges).

"TNR", "specificity" True negative rate or specificity. TN/(# unlinked pairs).

"FDR" False discovery rate. FP/(# estimated links).

"PPV","precision" Positive predictive value or precision. TP/(# estimated links).

"NPV" Negative predictive value. TN/(# estimated unlinked pairs).

"F1" F1 score, F-measure, balanced F-score. Harmonic mean of precision and recall.

"MCC" Matthews correlation coefficient.

"ACC" Accuracy. (TP + TN)/(# edges + # unlinked pairs).

"expected" Expected number of links under random assortment.

"O/E" Ratio of estimated (observed) number of edges to expected number of links under random assortment. TP/"expected".

## Value

A data frame in which the variables are the desired quantities derived the specified contingency tables. The rows correspond to the rows of the contingency tables supplied as input (contabs).

#### See Also

```
contabs, roc, prc
```

```
data(dream4)
network <- 1
reference <- dream4gold10[[network]]
nGenes <- length(unique(c(reference[,1],reference[,2])))
nPossibleEdges <- nGenes^2</pre>
```

summary.networkBMA 25

summary.networkBMA

Summarizes a networkBMA object.

## **Description**

Counts the number of edges in a networkBMA object that are at or above specified probability thresholds.

## Usage

```
## S3 method for class 'networkBMA'
summary(object, thresholds = c(0,.5,.75,.90,.95,1), ...)
```

## **Arguments**

object A networkBMA object.

thresholds Threshold probabilities. The number of edges at or above these values are in-

cluded in the output.

... Not used. For generic/method consistency.

#### Value

A vector giving the number of edges in the object that have probability at or above the values given in thresholds.

## See Also

networkBMA

26 varord

#### **Examples**

varord

Variable orderings for linear regression.

## Description

Gives variable orderings for linear regression in high-dimensional data by various approaches.

#### Usage

```
varord(x, y, prior.prob = NULL, ordering = c("bic1","prior","bic1+prior"))
```

## Arguments

x	A matrix whose columns correspond to variables or genes and whose rows correspond to the observations.	
У	A vector of response values for fitting a linear model to a subset of the variables in x.	
prior.prob	A vector of prior probabilities corresponding to the variables (genes).	
ordering	A character string specifying the method to be used for the ordering the variables.	
	"bic1" Variables are ordered in by the BIC for the univariate linear model with that variable as predictor. (Yeung et~al. 2011)	
	"prior" The variables are ordered according to the log odds of their prior values. (Lo et~al. 2011)	

"bic1+prior" The variables are ordered according to sum of the univarite BIC values and the log odds of their prior values.

## Value

A vector of integers corresponding to the variable indexes in the specified order.

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#### References

K. Lo, A. E. Raftery, K. M. Dombek, J. Zhu, E. E. Schadt, R. E. Bumgarner and K. Y. Yeung (2012), Integrating External Biological Knowledge in the Construction of Regulatory Networks from Time-series Expression Data, BMC Systems Biology, 6:101.

K. Y. Yeung, K. M. Dombek, K. Lo, J. E. Mittler, J. Zhu, E. E. Schadt, R. E. Bumgarner and A. E. Raftery (2011), Construction of regulatory networks using expression time-series data of a genotyped population, Proceedings of the National Academy of Sciences, 108(48):19436-41.

#### See Also

```
networkBMA, iterateBMAlm
```

#### **Examples**

```
data(dream4)
network <- 1
Time <- as.numeric(dream4ts100[[network]]$time)
xIndex <- which(Time != max(Time))
yIndex <- which(Time != min(Time))
gene <- "G1"

x <- dream4ts100[[network]][xIndex,-(1:2)]
y <- dream4ts100[[network]][yIndex,gene]

nvar <- 50
ord <- varord( x, y, ordering = "bic1")[1:nvar]
## Not run:
result <- iterateBMAlm( x = x[,ord], y = y)
## End(Not run)</pre>
```

vignette

The subsets of the yeast-rapamycin time-series data from Yeung et al. (2011) and Lo et al. (2011), and of the static yeast gene-expression data from Brem et al. (2002, 2005), that are used in the networkBMA package vignette.

## **Description**

Contains four data objects used to illustrate the networkBMA package in the accompanying vignette.

**brem.data** An 85 by 111 subset of the data used for network inference in yeast in Brem et~al. (2002) and Brem and Kruglyak (2005). The rows correspond to genes and the columns to experiments. Provided courtesy of Rachel Brem.

28 vignette

**referencePairs** A 2-column data frame giving 287 regulator-gene pairs among the selected set of genes reported from the literature. The known regulatory relationships are not necessarily included in the reference network.

**reg.known** A 2-column matrix of known (hard-coded) regulatory relationships among the 100 gene subset. The first column gives the name of the regulator, and the second column gives the name of the target gene. The gene names should be consistent with the data.

**reg.prob** A 100 by 100 matrix in which the (i,j) entry is the estimated prior probability that gene i regulates gene j (from Lo et al. 2011).

**timeSeries** A data frame in which the first two columns are factors identifying the replicate and time (in minutes) after drug perturbation, and the remaining 100 columns are the expression measurements for a subset of 100 genes from the yeast-rapamycin experiment described in Yeung et al. (2011).

#### Usage

```
data(vignette)
```

#### References

- R. B. Brem and G. Yvert and R. Clinton and L. Kruglyak (2002), Genetic dissection of transcriptional regulation in budding yeast, Science 296(5568):752-755.
- R. B. Brem and L. Kruglyak (2005), The landscape of genetic complexity across 5,700 gene expression traits in yeast, Proceedings of the National Academy of Sciences 102(5):1572-1577.
- K. Lo, A. E. Raftery, K. M. Dombek, J. Zhu, E. E. Schadt, R. E. Bumgarner and K. Y. Yeung (2012), Integrating External Biological Knowledge in the Construction of Regulatory Networks from Time-series Expression Data, BMC Systems Biology, 6:101.
- K. Y. Yeung, K. M. Dombek, K. Lo, J. E. Mittler, J. Zhu, E. E. Schadt, R. E. Bumgarner and A. E. Raftery (2011), Construction of regulatory networks using expression time-series data of a genotyped population, Proceedings of the National Academy of Sciences, 108(48):19436-41.

## See Also

iterateBMAlm

writeEdges 29

writeEdges	Output network edges to text in Cytoscape-readable format.	

## Description

Outputs a data frame of probabilistic network edges to a text file suitable as input to Cytoscape for visualization.

## Usage

```
writeEdges( network, threshhold = .5, fileName = "edges.txt")
```

## **Arguments**

network A network represented as a data frame in which each row corresponds to an edge

for which the probability is estimated to be nonzero. The first column gives the name of the regulator, the second column gives the name of the regulated gene, and the third column gives the estimated probability for the regulator-gene pair.

threshhold A threshhold on the probability that the variables in x. The default value is .5

fileName A character string given the desired name of the output text file. The default is

"edges.txt".

#### Value

The data frame of edges with those having probabilities below the specified threshhold removed. As a side effect, this data from is output to a text file named fileName in a format suitable for use with Cytoscape for visualization (see <a href="https://www.cytoscape.org">www.cytoscape.org</a>).

## References

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

## See Also

networkBMA

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writeEdges(edges1ts10)

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