

# Package ‘birte’

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**Title** Bayesian Inference of Regulatory Influence on Expression (biRte)

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**Depends** R(>= 3.0.0), RcppArmadillo (>= 0.3.6.1), Rcpp

**Imports** MASS, limma(>= 3.22.0), glmnet, Biobase, nem, graphics, stats, utils

**Reference** H. Froehlich, biRte: Bayesian Inference of Context Specific Regulator Activities and Transcriptional Networks, Bioinformatics, 2015, in press.

**Suggests** knitr

**Enhances** Rgraphviz

**LinkingTo** RcppArmadillo, Rcpp

**NeedsCompilation** yes

**SystemRequirements** BLAS, LAPACK

**Materials** Please enable BLAS and LAPACK for armadillo library (see <http://arma.sourceforge.net/faq.html>). The file config.hpp can be found under library/RcppArmadillo/include/armadillo\_bits.

**Description** Expression levels of mRNA molecules are regulated by different processes, comprising inhibition or activation by transcription factors and post-transcriptional degradation by microRNAs. biRte uses regulatory networks of TFs, miRNAs and possibly other factors, together with mRNA, miRNA and other available expression data to predict the relative influence of a regulator on the expression of its target genes. Inference is done in a Bayesian modeling framework using Markov-Chain-Monte-Carlo. A special feature is the possibility for follow-up network reverse engineering between active regulators.

**License** GPL (>= 2)

**biocViews** Microarray, Sequencing, GeneExpression, Transcription, Network, Bayesian, Regression, NetworkInference

**LazyLoad** yes

**VignetteBuilder** knitr

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birteFitRidge	<i>Fit ridge regression model given a defined set of active regulators.</i>
---------------	---

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### Description

Given a most likely configuration of active regulators identified by biRte, this method fits a conventional ridge regression model to explain gene expression. This function is required, if one would like to use MAP based prediction of gene expression instead of Bayesian predictions (see [birtePredict](#)). To fit the ridge regression model the R-package `ridge` is employed, which provides an efficient tuning of the regularization hyperparameter.

### Usage

```
birteFitRidge(model, mRNA.train, ref.cond=1)
```

### Arguments

<code>model</code>	output of <a href="#">birteRun</a>
<code>mRNA.train</code>	vector of gene expression values
<code>ref.cond</code>	condition to consider

### Details

In order to make predictions with the fitted ridge regression model ([birtePredict](#)) store it into a slot "fit.ridge" of the object returned by [birteRun](#) and [birtLimma](#), respectively.

### Value

an object of class "cv.glmnet" (see [cv.glmnet](#))

### Author(s)

Holger Froehlich

**Examples**

```
# artificial data
data(humanNetworkSimul)
sim = simulateData(affinities2)
limmamRNA = limmaAnalysis(sim$dat.mRNA, design=NULL, "treated - control")

# burnin and sampling size is much too small in reality
result = birteLimma(dat.mRNA=sim$dat.mRNA, data.regulators=NULL,
limmamRNA=limmamRNA,
affinities=affinities2, niter=100, nburnin=100, thin=2)

fit.ridge = birteFitRidge(result, sim$dat.mRNA[,1])
```

---

birtePredict	<i>Prediction of gene expression via biRte.</i>
--------------	---

---

**Description**

Given a biRte model, this function makes posterior inference about gene expression data.

**Usage**

```
birtePredict(model, test.genes, method=c("Bayes", "MAP"), knock.out=NULL)
```

**Arguments**

model	output of <a href="#">birteRun</a>
test.genes	Set of gene IDs. Gene IDs should be contained into the defined regulator-target gene network. Note that expression data is generally not required to be available for these genes.
method	Bayes: estimate expectation of posterior predictive distribution. MAP: Use previously fitted ridge regression model ( <a href="#">birteFitRidge</a> ), which has to be stored into a slot "fit.ridge".
knock.out	optionally: A character vector of those regulators, which should be removed from the network before making predictions, hence simulating a knock.out

**Value**

#conditions x #replicates matrix containing data.frame objects with

gene	gene, for which predictions are made
mean	expected expression
sd	SD of predictions (only for method="Bayes")

**Author(s)**

Holger Froehlich

## Examples

```
# artificial data
data(humanNetworkSimul)
sim = simulateData(affinities2)
limmamRNA = limmaAnalysis(sim$dat.mRNA, design=NULL, "treated - control")

# burnin and sampling size is much too small in reality
result = birteLimma(dat.mRNA=sim$dat.mRNA, data.regulators=NULL,
limmamRNA=limmamRNA,
affinities=affinities2, niter=100, nburnin=100, thin=2)

est = birtePredict(result, rownames(sim$dat.mRNA))
```

---

birteRun

*Main interface for Bayesian Inference of Regulatory Influence on Expression (biRte).*

---

## Description

The function estimates regulator activities via MCMC sampling. The function assumes experimental data of two conditions to be given. If desired, influences on mRNA log fold changes can be estimated rather than on expression levels itself.

Besides miRNA, mRNA and TF expression data, biRte also allows to integrate other data types (e.g. CNV data - data type 'other').

birteLimma is a convenience function, which allows to directly pass results from a previous limma analysis (see [limmaAnalysis](#)) to birteRun. When working with relative expression levels (log fold changes) birteLimma allows to deal with arbitrary complex statistical designs, including e.g. time as a covariate.

## Usage

```
birteRun(dat.mRNA, mRNA.Sigma=NULL, nrep.mRNA=c(5, 5),
df.mRNA=sum(nrep.mRNA)-2,
data.regulators=NULL, sigma.regulators=NULL,
nrep.regulators=NULL, diff.regulators=NULL,
init.regulators=NULL, theta.regulators=NULL,
reg.interactions=FALSE, affinities, use.affinities=FALSE,
niter=100000, nburnin=100000, thin=50,
potential_swaps=NULL, only_switches=FALSE, only.diff.TFs=TRUE,
explain.LFC=TRUE, model=c("no-plug-in", "all-plug-in"))

birteLimma(dat.mRNA, limmamRNA,
data.regulators=NULL, limma.regulators=NULL,
fdr.regulators=NULL, lfc.regulators=NULL,
init.regulators=NULL, theta.regulators=NULL,
reg.interactions=FALSE, affinities, use.affinities=FALSE,
niter=100000, nburnin=100000, thin=50,
potential_swaps=NULL, only_switches=FALSE, only.diff.TFs=TRUE,
explain.LFC=TRUE, model=c("no-plug-in", "all-plug-in"))
```

**Arguments**

<code>dat.mRNA</code>	mRNA expression data matrix. <b>IMPORTANT:</b> Replicates must be ordered according to <code>nrep.mRNA</code>
<code>mRNA.Sigma</code>	gene expression variances (array data). <b>IMPORTANT:</b> Names have to match the row names in <code>dat.mRNA</code> . If <code>mRNA.Sigma = NULL</code> , <code>birte.run</code> tries to deduce variances from a <code>limma</code> analysis (see <a href="#">limmaAnalysis</a> )
<code>nrep.mRNA</code>	number of replicates per condition.
<code>df.mRNA</code>	residual degrees of freedom of linear model for mRNA data.
<code>data.regulators</code>	list with at most 3 components (miRNA, TF, other). Each component contains one data matrix. <b>IMPORTANT:</b> Samples in data matrices have to be grouped according to conditions. That means first there are all samples from the first condition, then those from the second condition, etc.
<code>sigma.regulators</code>	list with at most 3 components (miRNA, TF, other). Each component contains one named vector of expression variances (array data) or dispersion parameters (RNAseq data). <b>IMPORTANT:</b> Names have to fit to the row names of the data matrix.
<code>nrep.regulators</code>	list with at most 3 components (miRNA, TF, other). Each component contains the number of replicates per condition
<code>diff.regulators</code>	list with at most 3 components (miRNA, TF, other). Each component is a character vector with differentially expressed regulators. Has to be subset of row names of the data matrix
<code>init.regulators</code>	list with at most 3 components (miRNA, TF, other). Each component is matrix of <code>#conditions x length(affinities[[regulator type]])</code> : initial states for regulators. In case this matrix is not provided (i.e. <code>NULL</code> ) initial states are assumed to be 0. <b>IMPORTANT:</b> column names have to match names( <code>affinities[[regulator type]]</code> )
<code>theta.regulators</code>	list with at most 3 components (miRNA, TF, other). If single numbers are provided, each component contains the expected fraction of active regulators. If vectors are provided, each vector entry corresponds to the individual probability of a specific regulator to be active. Accordingly, vectors should be named in agreement with the regulator-target gene network. If <code>affinities\$other</code> corresponds to interaction terms between regulators, <code>theta.regulators</code> can also be provided as a <code>#regulators x #regulators</code> matrix.
<code>reg.interactions</code>	If <code>TRUE</code> , entries of <code>affinities\$other</code> are interpreted as interaction terms between regulators.
<code>affinities</code>	Regulator-target gene interactions. This is a list with at most three components (TF, miRNA, other). Each of these lists again contains a weighted adjacency list representation. See <a href="#">humanNetworkSimul</a> for an example. <b>IMPORTANT:</b> gene names used in this network have to match with row names of <code>dat.mRNA</code> . Moreover, regulator names have to fit to row names of the corresponding data matrices.
<code>use.affinities</code>	Should weights given in the bipartite regulator-target gene graph given a specific meaning? If yes, it is assumed that weights correspond to quantitative influences of regulators on their targets.

niter	Number of MCMC iterations (AFTER burnin).
nburnin	Number of MCMC iterations UNTIL burnin is assumed to be finished.
thin	Thinning of Markov chain: only use every thin's sample for posterior computation.
potential_swaps	Pre-computed potential swaps (OPTIONAL, see <code>get_potential_swaps</code> ).
only_switches	Should only switches be performed?
only.diff.TFs	Should, in case of TF expression data, only the information for differentially expressed TFs be considered? Note that this makes fewer assumption about the relation of mRNA and protein expression data, but typically leads to less conservative results (i.e. more TFs predicted to be active).
limmamRNA	results of limma analysis for mRNA data according to <a href="#">limmaAnalysis</a>
limma.regulators	list with at most 3 components (miRNA, TF, other). Each component contains the results of a limma analysis for regulator data according to <a href="#">limmaAnalysis</a>
lfc.regulators	list with at most 3 components (miRNA, TF, other). Each component contains the log fold change cutoff for differential expression. It is assumed to be 0, if not provided.
fdr.regulators	list with at most 3 components (miRNA, TF, other). Each component contains the FDR cutoff for differential expression (DEFAULT: 0.05).
explain.LFC	If yes, biRte tries to explain mRNA log fold changes rather than expression levels itself.
model	If "no-plug-in", for marginal log likelihoods are considered for regulator specific expression data. Otherwise, (posterior) variance estimates are used directly.

## Value

The function returns a list containing the following entries:

post	#regulators x #conditions matrix containing the marginal probability for each regulator to influence mRNA expression.
map	#regulators x #conditions matrix containing the regulator configuration with highest joint probability.
coef	matrix of #conditions x #replicates: Each entry is itself a matrix (embedded into a list) of #coefficients x #effective samples. The data contains the expected regression coefficients.
log_lik_trace	(Marginal) log-likelihood trace of MCMC sampling.
eff_sample_size	effective sample size after burnin and thinning
contains.interactions	TRUE, if <code>affinities\$other</code> corresponds to interaction terms between regulators, FALSE otherwise
explain.LFC	TRUE, if model explains mRNA log fold change, FALSE otherwise
nburnin	number of burnin iterations - as provided as an argument
affinities	original regulator-target gene network
C_cnt	number of conditions
design	design matrix effectively used for model training
param	estimated parameters for mRNA precision (i.e. inverse variance) distribution

**Author(s)**

Holger Froehlich

**Examples**

```

# artificial data
data(humanNetworkSimul)
sim = simulateData(affinities2)
limmamRNA = limmaAnalysis(sim$dat.mRNA, design=NULL, "treated - control")
limmamiRNA = limmaAnalysis(sim$dat.miRNA, design=NULL, "treated - control")
limmaTF = limmaAnalysis(sim$dat.TF, design=NULL, "treated - control")

# burnin and sampling size is much too small in reality
result = birteLimma(dat.mRNA=sim$dat.mRNA,
data.regulators=list(miRNA=sim$dat.miRNA, TF=sim$dat.TF),
limmamRNA=limmamRNA, limma.regulators=list(miRNA=limmamiRNA, TF=limmaTF),
affinities=affinities2, niter=100, nburnin=100, thin=2)
plotConvergence(result)
pred = birtePredict(result, rownames(sim$dat.mRNA))
MSE.Bayes = mean((pred[[1]][[1]]$mean - limmamRNA$pvalue.tab[rownames(sim$dat.mRNA), "logFC"])^2)
MSE.Bayes

# real data
library(Biobase)
data(EColiOxygen)
# prepare network
affinities = list(TF=sapply(names(EColiNetwork$TF), function(tf){
w = rep(1, length(EColiNetwork$TF[[tf]]));
names(w)= EColiNetwork$TF[[tf]]; w}))
# prepare data
mydat = exprs(EColiOxygen)
colnames(mydat) = make.names(paste(pData(EColiOxygen)$GenotypeVariation,
pData(EColiOxygen)$GrowthProtocol, sep="."))
mydat = cbind(mydat[,colnames(mydat) == "wild.type.aerobic"],
exprs(EColiOxygen)[,colnames(mydat) == "wild.type.anaerobic"])

# more realistic sampling
## Not run:
result = birteRun(dat.mRNA=mydat,
nrep.mRNA=c(3,4), affinities=affinities, niter=10000, nburnin=10000)
plotConvergence(result)

## End(Not run)

```

EColiNetwork

*Example TF-target graph from Regulon DB.***Description**

This list contains the TF-target graph used in the vignette.

**Usage**

```
EColiNetwork
```

**Format**

A list containing the target gene sets of 160 TFs.

**Value**

A list containing the target gene sets of 160 TFs.

**Source**

This TF-target graph was taken from (R. Castelo and A. Roverato, 2009). It is a pre-filtered version of RegulonDB 6.1.

**References**

R. Castelo and A. Roverato. Reverse engineering molecular regulatory networks from microarray data with qp-graphs. *J Comput Biol*, 16(2):213227, Feb 2009.

---

EColiOxygen

*Example data set from E. Coli to sample TF activities.*

---

**Description**

This data set gives expression values for three experiments of the E. Coli K12 strain under aerobic and three experiments under anaerobic growth. It is used in the vignette to illustrate application of birta to TFs only.

**Usage**

EColiOxygen

**Format**

ExpressionSet

**Value**

ExpressionSet

**Source**

The original data comes from (Covert et al., 2004) The normalized data set used here is taken from the qpgraph package by R. Castelo and A. Roverato.

**References**

M. W. Covert, E. M. Knight, J. L. Reed, M. J. Herrgard, and B. O. Palsson. Integrating high-throughput and computational data elucidates bacterial networks. *Nature*, 429(6987):9296, May 2004.



---

estimateNetwork	<i>Estimate network between active regulators using Nested Effects Models (NEMs).</i>
-----------------	---

---

### Description

Given a biRte model, this function makes posterior inference about possible upstream-downstream relationships between active regulators. This is done based on observed differential expression of putative target genes. The idea is that regulator A acts upstream of regulator B, if differentially expressed targets of B are a subset of those of A.

### Usage

```
estimateNetwork(model, thresh=0.1, select=c("marginal", "MAP"), method="pairwise",  
de.genes, bootstrap=0, typeII=0.1)
```

### Arguments

model	biRte model
thresh	cutoff for marginal posterior probabilities
select	"marginal": select regulators based on marginal posterior probabilities; "MAP": select regulators based on MAP configuration
method	algorithm used for NEM based network inference, see <a href="#">nem</a>
de.genes	set of differentially expressed genes
bootstrap	optional: number of bootstrap replicates to draw (non-parameteric bootstrap)
typeII	assumed type-II error rate

### Value

nem-model

### Author(s)

Holger Froehlich

### Examples

```
# see vignette
```

---

getPotentialSwaps	<i>Calculate swap partner for TF-/miRNA-target graph. This function is usually only called internally, but may be used to speed up repetitive calls to <a href="#">birteRun</a>.</i>
-------------------	--

---

### Description

Calculates for TF-/miRNA-target graph all potential swap partner.

### Usage

```
getPotentialSwaps(genesets, perc.overlap.cutoff=0.8, integer.id=TRUE)
```

### Arguments

genesets	Each entry corresponds to a regulator (miRNA, TF, other) and contains its target genes.
perc.overlap.cutoff	Percentage cutoff of minimal overlap between two miRNAs or TFs to be possible swap partner.
integer.id	If TRUE, the swap partner are not output as characters, but as integer indices.

### Value

A list object, where each element corresponds to one regulator.

### Author(s)

Holger Froehlich

### Examples

```
# artificial data
data(humanNetworkSimul)
genesets = c(sapply(affinities2$TF, names),
sapply(affinities2$miRNA, names), sapply(affinities2$other, names))
swaps = getPotentials(genesets)
```

---

humanNetworkSimul	<i>Subset of regulator-target gene network for human</i>
-------------------	--

---

### Description

The human regulatory network was constructed as follows: For miRNA target gene prediction we used MiRmap (Vejnar and Zdobnov, 2012) and converted the reported scores into z-scores. P-values were then calculated based on the observed approximate normality of z-scores under the null hypothesis and corrected for multiple testing via the FDR method under dependencies of tests (Benjamini and Yekutieli, 2001). In consequence we arrived at 356 miRNAs regulating between 1 and 318 target genes (median: 5).

A TF-target gene network was compiled by computing TF binding affinities to promoter sequences of all human genes according to the TRAP model (Roeder et al., 2007) via the author's R implementation. Upstream sequences of genes were retrieved here from the ENSEMBL database via biomaRt (Durinck et al., 2009). We assumed that promoter sequences were located in the range 0 - 2Kbp upstream to the transcription start site of a gene. 556 TRANSFAC (Wingender, 2008; public version) as well as 130 JASPAR (Bryne et al., 2008; accessed Dec. 2011) TFBS matrices were used. As significant we considered those TFBS, for which a FDR < 5% was reported (Benjamini-Yekutieli method).

In a subsequent step from each significant TFBS we extracted the set of TFs, for which the corresponding TFBS matrix had been defined by parsing the original TRANSFAC and JASPAR files, respectively. Ambiguities were corrected via manual curation with the help of the commercial MetaCore software. In consequence we arrived at a TF-target gene network of 344 TFs regulating between 1 and 19,392 target genes (median: 155).

For simulation purposes we randomly selected subset of 999 human genes together with the set of corresponding regulators. After network simplification ([simplify](#)) we arrived at 13 miRNA and 111 TF clusters.

## Usage

```
humanNetworkSimul
```

## Format

**affinities2** TF and miRNA target gene network. For miRNAs scores from z-scores derived from MiRmap are reported. For TFs  $-\log_{10}(\text{p-values})$ .

## Details

- **affinities2**
  - TTF-target gene graph – list object
  - miRNAmiRNA-target gene graph – list object

Both, the TF-target and the miRNA target gene graphs are given in form of a weighted adjacency list representation.

## Value

see above

## Note

The object 'affinities2' may be extended by one further component 'other' containing additional regulatory information (e.g. CNVs, predefined interaction terms between regulators).

## References

- Vejnar, C. E. and Zdobnov, E. M. (2012). Mirmap: comprehensive prediction of microrna target repression strength. *Nucleic Acids Res*, 40(22):11673-11683.
- Roeder, H. G., Kanhere, A., Manke, T., and Vingron, M. (2007). Predicting transcription factor affinities to dna from a biophysical model. *Bioinformatics*, 23(2):134-141.

---

`limmaAnalysis`*Simple limma analysis on expression data with one contrast.*

---

### Description

This is a convenience function, which can be used to perform a limma analysis with one contrast. Subsequently results may be passed to `birteLimma`

### Usage

```
limmaAnalysis(dat, design=NULL, contrast)
```

### Arguments

<code>dat</code>	A matrix or ExpressionSet containing the expression values.
<code>design</code>	A design matrix. If no design matrix is provided, the method tries to infer a design matrix by taking column names as a factor. That means the design matrix is constructed according to <code>~0 + factor(colnames(dat))</code> .
<code>contrast</code>	Contrast for the linear model. Currently only one contrast is supported. If more contrasts are desired separate birte analyses should be run for each of them.

### Value

Returns a list containing the following entries:

<code>pvalue.tab</code>	Containing the result of the topTable function from limma.
<code>lm.fit</code>	Linear fit to the model, i.e. output of function 'eBayes'.
<code>design</code>	The design used.
<code>contrast</code>	The contrasts used.

### Author(s)

Holger Froehlich

### References

G. K. Smyth. Limma : Linear Models for Microarray Data. *Bioinformatics*, (2005):397-420.

### Examples

```
# see birte.run
```

---

plotConvergence	<i>Plot the marginal log-likelihood of the model along MCMC samples (after thinning).</i>
-----------------	---

---

**Description**

Plot the marginal log-likelihood of the model along MCMC samples (after thinning).

**Usage**

```
plotConvergence(res, title="")
```

**Arguments**

res	The output of birte.run (a list object).
title	Optional title of the plot.

**Value**

none

**Author(s)**

Holger Froehlich

**See Also**

[birteRun](#)

**Examples**

```
# see birteRun
```

---

proposeInteractions	<i>Propose possible regulator-regulator interactions that could be worthwhile to be tested into the biRte model.</i>
---------------------	--

---

**Description**

The purpose is to identify interesting interactions terms for our model. Assuming the design matrix to be binary, the interaction term between two variables X1 and X2 is 1, if X1=1 AND X2=1 (zero, otherwise). The function computes the relative overlap between all pairs of variables X1 and X2 via the Tanimoto-Jaccard index. Variable pairs with  $\text{cutoff.lower} < \text{Tanimoto-Jaccard} < \text{cutoff.upper}$  are considered interesting candidates.

**Usage**

```
proposeInteractions(affinities, cutoff.lower=0.1, cutoff.upper=0.8)
```

**Arguments**

`affinities`      original regulator-target gene network  
`cutoff.lower`    lower range for Tanimoto-Jaccard index  
`cutoff.upper`    upper range for Tanimoto-Jaccard index

**Value**

A list of the same format as `affinities$TF` and `affinities$miRNA`: Each list entry corresponds to the intersection of two target gene sets.

**Author(s)**

Holger Froehlich

**Examples**

```
# artificial data
data(humanNetworkSimul)
affinities.int = proposeInteractions(affinities2)
```

---

simplify

*Simplify regulator-target gene network via clustering.*

---

**Description**

Several regulators (specifically TFs) might have extremely overlapping target genes. In order to identify clusters of highly similar regulators (mainly TFs) we implemented a network simplification algorithm in `biRte`: We construct the biadjacency matrix of the complete bipartite regulator target-gene graph and then calculate a single linkage clustering of regulators based on the Tanimoto-Jaccard similarity of their target genes. The dendrogram is cut at a defined height (default: 0.1) to identify resulting groups. The algorithm is meant to simplify the inference of active regulators, because the resulting regulator clusters have more dissimilar target gene profiles.

**Usage**

```
simplify(affinities, cutoff=0.9)
```

**Arguments**

`affinities`      original regulator-target gene network  
`cutoff`            cut dendrogram at height 1 - cutoff (i.e. similarity cutoff)

**Value**

clustered / simplified network

**Author(s)**

Holger Froehlich

**Examples**

```
# artificial data
data(humanNetworkSimul)
affinities2 = simplify(affinities2)
```

---

simulateData	<i>Simulate expression data.</i>
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---

**Description**

The function draws expression data from a multivariate normal distribution with block structured co-variance matrix. First, data is drawn for a control condition (no active regulators). Then data is generated for the situation that a certain fraction of regulators is turned 'on' (treatment condition). Regulator activity states are sampled from a Bernoulli distribution.

**Usage**

```
simulateData(affinities, nrep = 5, miRNAExpressions = TRUE, fn.targets = 0.1,
fp.targets = 0.2, exp.nTF = 5, exp.nmiR = 5, exp.interact = 5)
```

**Arguments**

affinities	regulator-target gene network (see <a href="#">humanNetworkSimul</a> )
nrep	number of replicates per condition
miRNAExpressions	Should miRNA expression data be simulated?
fn.targets	fraction of false negative target predictions (i.e. missing edges per regulator in the bipartite regulator-gene graph)
fp.targets	fraction of false positive target predictions
exp.nTF	expected number of active TFs
exp.nmiR	expected number of active miRNAs
exp.interact	expected number of active interaction terms

**Details**

If active interaction terms should be simulated, a set of possible interaction terms has to be defined in `affinities$other`.

**Value**

dat.mRNA	mRNA data – active regulators are expected to induce a log FC of 1
dat.miRNA	miRNA data – active miRNAs are expected to show a log FC of 1
dat.TF	TF expression data – active miRNAs are expected to show a log FC of 0.5
miRNAsstates	simulated miRNA activities in treatment condition
TFstates	simulated TF activities in treatment condition
inter.states	simulated regulator interaction activities in treatment condition

**Author(s)**

Holger Froehlich

**Examples**

```
data(humanNetworkSimul)
sim = simulateData(affinities2)
```

---

suggestThreshold	<i>Automatically suggest suitable threshold for marginal regulator activities.</i>
------------------	--

---

**Description**

The algorithm fits a mixture of a  $\text{beta}(1, \beta)$  and  $\text{beta}(\alpha, 1)$  distribution to observed marginal regulator activities. Based on this mixture a cutoff is chosen such that the expected false positive rate is below a defined threshold.

**Usage**

```
suggestThreshold(prob, fpr=0.001)
```

**Arguments**

prob	marginal probability obtained from <a href="#">birteRun</a>
fpr	threshold for accepted false positive rate

**Value**

a cutoff for marginal activity probabilities

**Author(s)**

Holger Froehlich

**References**

Froehlich, H. and Klau, G. (2013). Reconstructing Consensus Bayesian Network Structures with Application to Learning Molecular Interaction Networks. In: Beissbarth, T., Kollmar, M., Leha, A., Morgenstern, B., Schultz, A.-K., Waack, S., and Wingender, E., editors, Proc. German Conference on Bioinformatics, Open Access Series in Informatics, pages 46 - 55. Schloss Dagstuhl - Leibniz-Zentrum fuer Informatik, Dagstuhl Publishing, Germany.

**Examples**

```
freq = 0.2*rbeta(100, 1, 10) + 0.8*rbeta(100, 5, 1)
thresh = suggestThreshold(freq)
```



---

TFexpr	<i>Transcription factor expression values for the aerobic-anaerobic growth experiment.</i>
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**Description**

This data set gives expression values for the 160 TF of the TF-target graph EColiNetwork used in the vignette.

**Usage**

TFexpr

**Format**

ExpressionSet. Rownames in the assayData correspond to entries in TF-target graph.

**Value**

ExpressionSet. Rownames in the assayData correspond to entries in TF-target graph.

**Source**

See EColiOxygen and EColiNetwork (see reference for details).

**References**

M. W. Covert, E. M. Knight, J. L. Reed, M. J. Herrgard, and B. O. Palsson. Integrating high-throughput and computational data elucidates bacterial networks. *Nature*, 429(6987):92-96, May 2004.

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