

# Package ‘TargetScore’

April 10, 2015

**Type** Package

**Title** TargetScore: Infer microRNA targets using  
microRNA-overexpression data and sequence information

**Version** 1.4.0

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**Description** Infer the posterior distributions of microRNA targets by probabilistically modelling the likelihood microRNA-overexpression fold-changes and sequence-based scores. Variational Bayesian Gaussian mixture model (VB-GMM) is applied to log fold-changes and sequence scores to obtain the posteriors of latent variable being the miRNA targets. The final targetScore is computed as the sigmoid-transformed fold-change weighted by the averaged posteriors of target components over all of the features.

**Depends** pracma, Matrix

**Suggests** TargetScoreData, gplots, Biobase, GEOquery

**License** GPL-2

**URL** <http://www.cs.utoronto.ca/~yueli/software.html>

**Lazyload** yes

**biocViews** miRNA

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TargetScore-package	<i>TargetScore: Infer microRNA targets using microRNA-overexpression data and sequence information</i>
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## Description

Infer the posterior distributions of microRNA targets by probabilistically modeling the likelihood microRNA-overexpression fold-changes and sequence-based scores. Variational Bayesian Gaussian mixture model (VB-GMM) is applied to log fold-changes and sequence scores to obtain the posteriors of latent variable being the miRNA targets. The final targetScore is computed as the sigmoid-transformed fold-change weighted by the averaged posteriors of target components over all of the features.

## Details

Package: TargetScore  
 Type: Package  
 Version: 1.1.5  
 Date: 2013-10-15  
 License: GPL-2

The front-end main function `targetScore` should be used to obtain the probabilistic score of miRNA target. The workhorse function is `vbgmm`, which implementates multivariate variational Bayesian Gaussian mixture model.

## Author(s)

Yue Li <yueli@cs.toronto.edu>

## References

- Lim, L. P., Lau, N. C., Garrett-Engele, P., Grimson, A., Schelter, J. M., Castle, J., Bartel, D. P., Linsley, P. S., and Johnson, J. M. (2005). Microarray analysis shows that some microRNAs down-regulate large numbers of target mRNAs. *Nature*, 433(7027), 769-773.
- Bartel, D. P. (2009). MicroRNAs: Target Recognition and Regulatory Functions. *Cell*, 136(2), 215-233.

Bishop, C. M. (2006). Pattern recognition and machine learning. Springer, Information Science and Statistics. NY, USA. (p474-486)

### See Also

[targetScore](#)

### Examples

```
library(TargetScore)
ls("package:TargetScore")
```

---

bsxfun.se	<i>bsxfun with single expansion (real Matlab style) (Internal function)</i>
-----------	---

---

### Description

Depending on the dimension of x, repeat y in either by row or by column and apply element-wise operation defined by func.

### Usage

```
bsxfun.se(func, x, y, expandByRow = TRUE)
```

### Arguments

func	function with two or more input parameters.
x, y	two vectors, matrices, or arrays
expandByRow	expand by row or by column of x when $nrow(x) == ncol(x) == length(y)$

### Details

The function is used by vbgmm.

### Value

func(x,y)      A matrix of having the same dimension of x.

### Note

Internal function.

### Author(s)

Yue Li

### See Also

[bsxfun](#)

## Examples

```
bsxfun.se("*", matrix(c(1:10), nrow=2), matrix(c(1:5), nrow=5))
```

---

dot.ext

*Elementwise dot product (modified dot function) (Internal function)*

---

## Description

Same as dot but handle single row matrix differently by multiplying each value but not sum them up

## Usage

```
dot.ext(x, y, mydim)
```

## Arguments

x	numeric vector or matrix
y	numeric vector or matrix
mydim	Elementwise product (if 1); otherwise defined by <a href="#">dot</a>

## Details

Returns the 'dot' or 'scalar' product of vectors or columns of matrices. Two vectors must be of same length, two matrices must be of the same size. If x and y are column or row vectors, their dot product will be computed IF mydim is 1 (only difference from [dot](#)).

## Value

A scalar or vector of length the number of columns of x and y.

## Author(s)

Yue Li

## See Also

[dot](#)

## Examples

```
dot.ext(1:5, 1:5)
dot.ext(1:5, 1:5, 1)
```

---

getTargetScores	<i>Compute targetScore of an overexpressed human microRNA</i>
-----------------	---

---

### Description

Obtain for each gene the targetScore using using pre-computed (logFC) TargetScan context score and PCT as sequence score. TargetScanData package is needed.

### Usage

```
getTargetScores(mirID, logFC, ...)
```

### Arguments

mirID	A character string of microRNA ID (e.g., hsa-miR-1)
logFC	N x D numeric vector or matrix of logFC with D replicates for N genes.
...	Paramters passed to <a href="#">vbgmm</a>

### Details

This is a convenient function for computing targetScore for a human miRNA using user-supplied or pre-computed logFC and (if available) two pre-computed sequence scores namely TargetScan context score and PCT (probability of conserved targeting). The function also searches for any validated targets from the MirTarBase human validated target list. The function requires TargetScanData to be installed first.

### Value

targetScores	numeric matrix of probabilistic targetScores together with the input variable and a binary vector indicating whether each gene is a validated target (if available).
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### Author(s)

Yue Li

### References

- Lim, L. P., Lau, N. C., Garrett-Engele, P., Grimson, A., Schelter, J. M., Castle, J., Bartel, D. P., Linsley, P. S., and Johnson, J. M. (2005). Microarray analysis shows that some microRNAs down-regulate large numbers of target mRNAs. *Nature*, 433(7027), 769-773.
- Bartel, D. P. (2009). MicroRNAs: Target Recognition and Regulatory Functions. *Cell*, 136(2), 215-233.
- Bishop, C. M. (2006). Pattern recognition and machine learning. Springer, Information Science and Statistics. NY, USA. (p474-486)

**See Also**[targetScore](#)**Examples**

```

if(interactive()) {

  library(TargetScoreData)
  library(Biobase)
  library(GEOquery)

  # compute targetScore from pre-computed logFC and sequence scores
  # for hsa-miR-1
  mir1.score <- getTargetScores("hsa-miR-1", tol=1e-3, maxiter=200)

  # download fold-change data from GEO for hsa-miR-124 overexpression in HeLa
  gset <- getGEO("GSE2075", GSEMatrix =TRUE, AnnotGPL=TRUE)

  if (length(gset) > 1) idx <- grep("GPL1749", attr(gset, "names")) else idx <- 1

  gset <- gset[[idx]]

  sampleinfo <- as.character(pData(gset)$title)

  geneInfo <- fData(gset)

  # only 24h data are used (discard 12h data)
  logfc.mir124 <- as.matrix(exprs(gset)[,
  grep("HeLa transfected with miR-1 versus control transfected HeLa, 24 hours", sampleinfo)])

  rownames(logfc.mir124) <- geneInfo$Gene symbol

  mir124.score <- getTargetScores("hsa-miR-124", logfc.mir124, tol=1e-3, maxiter=200)

  head(mir124.score)
}

```

---

**initialization***Initialization of latent variable assignments (responsibility) of the VB-GMM (Internal function)*

---

**Description**

Initialize latent variables based on the number of components. The function is run before the VB-EM iteration in vbgmm.

**Usage**

```
initialization(X, init)
```

**Arguments**

X	D x N numeric vector or matrix of observations
init	Based on the dimension, init is expected to be one of the followings: scalar: number of components; vector: initial class labels; matrix: initialize with a D x K matrix for D variables and K components.

**Details**

The function is expected to be used by vbgmm to initialize assignments of latent variables before VM-EM iterations.

**Value**

R	N by K matrix for N observations and K latent components (defined by init)
---	--

**Author(s)**

Yue Li

**References**

Mo Chen (2012). Matlab code for Variational Bayesian Inference for Gaussian Mixture Model. <http://www.mathworks.com/matlabcentral/fileexchange/35362-variational-bayesian-inference-for-gaussian-mixture-model>

**See Also**

[vbgmm](#)

**Examples**

```
tmp <- initialization(matrix(c(rnorm(100,mean=2), rnorm(100,mean=3)),nrow=1), init=2)
```

---

logmvgamma

*Logarithmic multivariate Gamma function (Internal function)*

---

**Description**

Compute logarithm multivariate Gamma function.

**Usage**

```
logmvgamma(x, d)
```

**Arguments**

x	numeric vector or matrix
d	dimension

**Details**

$$\Gamma_p(x) = \pi^{p(p-1)/4} \prod_{j=1}^p \Gamma(x+(1-j)/2)$$

$$\log \Gamma_p(x) = p(p-1)/4 \log \pi + \sum_{j=1}^p \log \Gamma(x+(1-j)/2)$$

**Value**

Matrix of the same dimension as  $x$ .

**Author(s)**

Yue Li

**References**

Mo Chen (2012). Matlab code for Variational Bayesian Inference for Gaussian Mixture Model. <http://www.mathworks.com/matlabcentral/fileexchange/35362-variational-bayesian-inference-for-gaussian-mixture-model>

**See Also**

[lgamma](#)

**Examples**

```
logmvgamma(matrix(1:6,nrow=3), 2)
```

---

logsumexp

*Compute  $\log(\text{sum}(\exp(x), \text{dim}))$  while avoiding numerical underflow (Internal function)*

---

**Description**

Compute  $\log(\text{sum}(\exp(x), \text{dim}))$  while avoiding numerical underflow.

**Usage**

```
logsumexp(x, margin = 1)
```

**Arguments**

$x$                     numeric vector or matrix  
margin                dimension to apply summation

**Value**

numeric vector or matrix of the same columns or rows (depending on margin) as  $x$



**Author(s)**

Yue Li

**References**

Mo Chen (2012). Matlab code for Variational Bayesian Inference for Gaussian Mixture Model. <http://www.mathworks.com/matlabcentral/fileexchange/35362-variational-bayesian-inference-for-gaussian-mixture-model>

**Examples**

```
logsumexp(matrix(c(1:5)), 2)
```

---

sort_components	<i>Sort mixture components in increasing order of averaged means (Internal function)</i>
-----------------	--

---

**Description**

Sort Gaussian mixture components with model parameters in increasing order of averaged means of  $d$  variables.

**Usage**

```
sort_components(model)
```

**Arguments**

model            A list containing trained parameters of the Bayesian GMM (see Value section in [vbgmm](#)).

**Value**

VB-GMM model list in increasing order of averaged means.

**Author(s)**

Yue Li

**See Also**[vbgmm](#)**Examples**

```
tmp <- vbgmm(c(rnorm(100,mean=2), rnorm(100,mean=3)), tol=1e-3)
tmp$mu
```

---

targetScore	<i>Probabilistic score of genes being the targets of an overexpressed mi-croRNA</i>
-------------	---

---

### Description

Given the overexpression fold-change and sequence-scores (optional) of all of the genes, calculate for each gene the TargetScore as a probability of miRNA target.

### Usage

```
targetScore(logFC, seqScores, ...)
```

### Arguments

logFC	numeric vector of log fold-changes of N genes in treatment (miRNA overexpression) vs control (mock).
seqScores	N x D numeric vector or matrix of D sequence-scores for N genes. Each score vector is expected to be equal to or less than 0. The more negative the scores, the more likely the corresponding target.
...	Parameters passed to <a href="#">vbgmm</a>

### Details

Given expression fold-change (due to miRNA transfection), we use a three-component VB-GMM to infer down-regulated targets accounting for genes with little or positive log fold-change (due to off-target effects (Khan et al., 2009)). Otherwise, two-component VB-GMM is applied to unsigned sequence scores (seqScores). The parameters for the VB-GMM are optimized using Variational Bayesian Expectation-Maximization (VB-EM) algorithm. Presumably, the mixture component with the largest absolute means of observed negative fold-change or sequence score is associated with miRNA targets and denoted as "target component". The other components correspond to the "background component". It follows that inferring miRNA-mRNA interactions most likely explained by the observed data is equivalent to inferring the posterior distribution of the target component given the observed variables. The targetScore is computed as the sigmoid-transformed fold-change weighted by the averaged posteriors of target components over all of the features. Specifically, we define the targetScore as a composite probabilistic score of a gene being the target  $t$  of a miRNA:

$$\text{sigmoid}(-\log\text{FC}) (1/K+1) \sum_x \text{in } \{x_f, x_1, \dots, x_L\} p(t | x),$$

where  $\text{sigmoid}(-\log\text{FC}) = 1/(1 + \exp(\log\text{FC}))$  and  $p(t | x)$  is the posterior of the first component computed by [vbgmm](#).

### Value

targetScore	numeric vector of probabilistic targetScores for N genes
-------------	--

### Author(s)

Yue Li

## References

- Lim, L. P., Lau, N. C., Garrett-Engele, P., Grimson, A., Schelter, J. M., Castle, J., Bartel, D. P., Linsley, P. S., and Johnson, J. M. (2005). Microarray analysis shows that some microRNAs down-regulate large numbers of target mRNAs. *Nature*, 433(7027), 769-773.
- Bartel, D. P. (2009). MicroRNAs: Target Recognition and Regulatory Functions. *Cell*, 136(2), 215-233.
- Bishop, C. M. (2006). Pattern recognition and machine learning. Springer, Information Science and Statistics. NY, USA. (p474-486)

## See Also

[vbgmm](#)

## Examples

```
# A toy example:
# 10 down-reg, 1000 unchanged, 90 up-reg genes
# due to overexpressing a miRNA
trmt <- c(rnorm(10,mean=0.01), rnorm(1000,mean=1), rnorm(90,mean=2)) + 1e3

ctrl <- c(rnorm(1100,mean=1)) + 1e3

logFC <- log2(trmt) - log2(ctrl)

# 8 out of the 10 down-reg genes have prominent seq score A
seqScoreA <- c(rnorm(8,mean=-2), rnorm(1092,mean=0))

# 10 down-reg genes plus 10 more genes have prominent seq score B
seqScoreB <- c(rnorm(20,mean=-2), rnorm(1080,mean=0))

seqScores <- cbind(seqScoreA, seqScoreB)

p.targetScore <- targetScore(logFC, seqScores, tol=1e-3)
```

---

vbgmm

*Variational Bayesian Gaussian mixture model (VB-GMM)*

---

## Description

Given a  $N \times D$  matrix of  $N$  observations and  $D$  variables, compute VB-GMM via VB-EM.

## Usage

```
vbgmm(data, init = 2, prior, tol = 1e-20, maxiter = 2000, mirprior = TRUE, expectedTargetFreq = 0.01, ver
```

**Arguments**

<code>data</code>	$N \times D$ numeric vector or matrix of $N$ observations (rows) and $D$ variables (columns)
<code>init</code>	Based on the dimension, <code>init</code> is expected to be one of the followings: scalar: number of components; vector: initial class labels; matrix: initialize with a $D \times K$ matrix for $D$ variables and $K$ components.
<code>prior</code>	A list containing the hyperparameters including <code>alpha</code> (Dirichlet), <code>m</code> (Gaussian mean), <code>kappa</code> (Gaussian variance), <code>v</code> (Wishart degree of freedom), <code>M</code> (Wishart precision matrix).
<code>tol</code>	Threshold that defines termination/convergence of VB-EM when $\frac{\text{abs}(L[t] - L[t-1])}{\text{abs}(L[t])} < \text{tol}$
<code>maxiter</code>	Scalar for maximum number of EM iterations
<code>mirprior</code>	Boolean to indicate whether to use <code>expectedTargetFreq</code> to initialize <code>alpha0</code> for the hyperparameters of Dirichlet.
<code>expectedTargetFreq</code>	Expected target frequency within the gene population. By default, it is set to 0.01, which is consistent with the widely accepted prior knowledge that 200/20000 targets per miRNA.
<code>verbose</code>	Boolean indicating whether to show progress in terms of lower bound ( <code>vbound</code> ) of VB-EM (default: FALSE)

**Details**

The function implements variation Bayesian multivariate GMM described in Bishop (2006). Please refer to the reference below for more details. This is the workhorse of [targetScore](#). Alternatively, user can choose to apply this function to other problems other than miRNA target prediction.

**Value**

A list containing:

<code>label</code>	a vector of maximum-a-posteriori (MAP) assignments of latent discrete values based on the posteriors of latent variables.
<code>R</code>	$N \times D$ matrix of posteriors of latent variables
<code>mu</code>	Gaussian means of the latent components
<code>full.model</code>	A list containing posteriors <code>R</code> , <code>logR</code> , and the model parameters including <code>alpha</code> (Dirichlet), <code>m</code> (Gaussian mean), <code>kappa</code> (Gaussian variance), <code>v</code> (Wishart degree of freedom), <code>M</code> (Wishart precision matrix)
<code>L</code>	A vector of variational lower bound at each EM iterations (should be strictly increasing)

**Author(s)**

Yue Li

## References

Mo Chen (2012). Matlab code for Variational Bayesian Inference for Gaussian Mixture Model. <http://www.mathworks.com/matlabcentral/fileexchange/35362-variational-bayesian-inference-for-gaussian-mixture-model>

Bishop, C. M. (2006). Pattern recognition and machine learning. Springer, Information Science and Statistics. NY, USA. (p474-486)

## See Also

[targetScore](#)

## Examples

```
X <- c(rnorm(100,mean=2), rnorm(100,mean=3))
tmp <- vbgmm(X, tol=1e-3)
names(tmp)
```

---

vbound

*Variational Lower Bound Evaluation*

---

## Description

Evaluate variational lower bound to determine when to stop VB-EM iteration (convergence).

## Usage

```
vbound(X, model, prior)
```

## Arguments

X	D x N numeric vector or matrix of N observations (columns) and D variables (rows)
model	List containing model parameters (see <a href="#">vbgmm</a> )
prior	numeric vector or matrix containing the hyperparameters for the prior distributions

## Value

A continuous scalar indicating the lower bound (the higher the more converged)

## Note

X is expected to be D x N for N observations (columns) and D variables (rows)

## Author(s)

Yue Li

**References**

Mo Chen (2012). Matlab code for Variational Bayesian Inference for Gaussian Mixture Model. <http://www.mathworks.com/matlabcentral/fileexchange/35362-variational-bayesian-inference-for-gaussian-mixture-model>

Bishop, C. M. (2006). Pattern recognition and machine learning. Springer, Information Science and Statistics. NY, USA. (p474-486)

**See Also**

[vbgmm](#)

**Examples**

```
X <- c(rnorm(100,mean=2), rnorm(100,mean=3))
tmp <- vbgmm(X, tol=1e-3)
head(tmp$L) # lower bound should be strictly increasing
```

---

vexp

---

*Variational-Expectation in VB-EM (Internal function)*


---

**Description**

The E step in VB-EM iteration.

**Usage**

```
vexp(X, model)
```

**Arguments**

X	D x N numeric vector or matrix of N observations (columns) and D variables (rows)
model	List containing model parameters (see <a href="#">vbgmm</a> )

**Value**

model	A list containing the updated model parameters including alpha (Dirichlet), m (Gaussian mean), kappa (Gaussian variance), v (Wishart degree of freedom), M (Wishart precision matrix).
-------	--

**Note**

X is expected to be D x N for N observations (columns) and D variables (rows)

**Author(s)**

Yue Li

## References

Mo Chen (2012). Matlab code for Variational Bayesian Inference for Gaussian Mixture Model. <http://www.mathworks.com/matlabcentral/fileexchange/35362-variational-bayesian-inference-for-gaussian-mixture-model>

Bishop, C. M. (2006). Pattern recognition and machine learning. Springer, Information Science and Statistics. NY, USA. (p474-486)

## See Also

[vbgmm](#)

## Examples

```
X <- c(rnorm(100,mean=2), rnorm(100,mean=3))
tmp <- vbgmm(X, tol=1e-3)
dim(tmp$R); head(tmp$R)
```

---

vmax

*Variational-Maximization in VB-EM (Internal function)*


---

## Description

The M step in VB-EM iteration.

## Usage

```
vmax(X, model, prior)
```

## Arguments

X	D x N numeric vector or matrix of N observations (columns) and D variables (rows)
model	List containing model parameters (see <a href="#">vbgmm</a> )
prior	List containing the hyperparameters defining the prior distributions

## Value

model	A list containing the updated model parameters including alpha (Dirichlet), m (Gaussian mean), kappa (Gaussian variance), v (Wishart degree of freedom), M (Wishart precision matrix).
-------	--

## Note

X is expected to be D x N for N observations (columns) and D variables (rows)

## Author(s)

Yue Li

**References**

Mo Chen (2012). Matlab code for Variational Bayesian Inference for Gaussian Mixture Model.  
<http://www.mathworks.com/matlabcentral/fileexchange/35362-variational-bayesian-inference-for-gaussian-mixture-model>

Bishop, C. M. (2006). Pattern recognition and machine learning. Springer, Information Science and Statistics. NY, USA. (p474-486)

**See Also**

[vbgmm](#)

**Examples**

```
X <- c(rnorm(100,mean=2), rnorm(100,mean=3))
tmp <- vbgmm(X, tol=1e-3)
names(tmp$full.model)
```



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