Package ‘NormalGamma’

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Type Package

Title Normal-gamma convolution model

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Description The functions proposed in this package compute the density of the sum of a Gaussian and a gamma random variables, estimate the parameters and correct the noise effect in a gamma-signal and Gaussian-noise model. This package has been used to implement the background correction method for Illumina microarray data presented in Plancade S., Rozenholc Y. and Lund E. "Generalization of the normal-exponential model : exploration of a more accurate parameterization for the signal distribution on Illumina BeadArrays", BMC Bioinfo 2012, 13(329).

License GPL-2

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NormalGamma-package  Background correction using the normal+gamma model

Description

The NormalGamma package is devoted to the density convolution model \( Y = X + N \) where \( X \) and \( N \) are independent variables with respectively gamma and normal distributions. For this model called further normal-gamma convolution model, this package proposes the computation of the convoluted density, the parameter estimation by likelihood maximization and the background correction obtained by deconvolution.

This package has been used to implement the background correction method for Illumina microarray data presented in Plancade S., Rozenholc Y. and Lund E., BMC Bioinfo 2012.

Details

- Package: NormalGamma
- Type: Package
- Version: 001.0
- Date: 2011-12-20
- License: GPL-3

The NormalGamma package includes three functions and a data set:
- `dnormgam` computes the convolution product of a normal and a gamma densities.
- `normgam.fit` computes the Maximum Likelihood Estimator of the parameters.
- `normgam.signal` performs the normal-gamma background correction.
- `Intensities` provides data from one Illumina microarray.

Author(s)

Plancade S. and Rozenholc Y.
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References


Examples

```r
# Load Illumina microarray data previously transformed into two sets of intensities
# corresponding to negative and regular probes.
```
dnormgam

## Not run:

data(RegNegIntensities_Example)

X = Intensities$Regular  
N = Intensities$Negative

## Compute the maximum likelihood estimator:
parmlse = normgam.fit(X, N)$par

par(mfrow=c(2,1))  # split windows for post comparison

## plot the histogram and the estimated density:
F = dnormgam(parmlse, plot=FALSE)

H = histogram(X, type='irregular', verbose=FALSE, plot=FALSE)
plot(H, xlim=c(0,500))  
lines(F$xout, F$dout, col='red')

# Perform the normal-gamma background correction:
Shat = normgam.signal(X,parmlse)
H = histogram(Shat, type='irregular', verbose=FALSE, plot=FALSE)
plot(H, xlim=c(0,30))

## End(Not run)

---

**dnormgam**  
*Normal-gamma density*

### Description

Computes the convolution product of a normal and a gamma densities.

### Usage

```r
dnormgam(par, x = NULL, N0 = 65536, plot = TRUE,
         log = FALSE, tail.cor = TRUE, cor = 1e-15,
         mu = par[1], sigma = par[2], k = par[3], theta = par[4])
```

### Arguments

- **par**  
  vector of parameters; \((par[1], par[2])\) are the mean and standard deviation of the normal distribution and \((par[3], par[4])\) are the shape and scale parameters of the gamma distribution.
**dnormgam**

- **x**: vector of values where the density is computed; if `x == NULL`, the density is computed on a sequence of values from 0 to `par[1]+5*par[2]+q` where `q` is the quantile of probability 0.99999 of the gamma distribution.
- **n0**: number of equally spaced values in the Fast Fourier Transform (see details).
- **plot**: logical; if TRUE plot of the density.
- **log**: logical; if TRUE density `d` is given as `log(d)`.
- **tail.cor**: logical; if TRUE a linear approximation of right tail adjusts numerical instability.
- **cor**: limit of right tail correction; if `tail.cor == TRUE`, linear approximation is applied to values with density estimate smaller than `cor`.
- **mu, sigma**: alternative definition of mean and standard deviation of the normal distribution.
- **k, theta**: alternative definition of shape and scale parameters of the gamma distribution.

**Details**

The convoluted density is computed using the `fft` function (Fast Fourier Transform). See details in Plancade S., Rozenholc Y. and Lund E., BMC Bioinfo 2012.

Only one definition of the parameters is required, either `par` or `(mu, sigma, k, theta)`. If both are specified and do not match, an error message is returned.

**Value**

- **xout**: vector of values where normal-gamma density is computed; equal to `x` when `x` is not NULL.
- **dout**: vector of values of normal-gamma density.

**Author(s)**

Plancade S. and Rozenholc Y.

**References**


**See Also**

`normgam.fit` computes the Maximum Likelihood Estimator and `normgam.signal` implements the background correction using the normal-gamma model.

**Examples**

```r
## Example 1
par = c(-10, 5, 2, 20)
F = dnormgam(par)
```
## Example 2

```r
n = 50000
par = c(60, 5, 0.15, 400)
F = dnormgam(par, plot=FALSE)

X = rnorm(n, mean=par[1], sd=par[2]) + rgamma(n, shape=par[3], scale=par[4])
H = histogram(X, type='irregular', verbose=FALSE, plot=FALSE)
plot(H, xlim=c(0,500))
lines(F$xout, F$yout, col='red')
```

### Description

Provides probe intensities measured on Illumina Human HT-6 v4 Expression BeadChip, from one control in the NOWAC cohort (for more details, see Plancade S., Rozenholc Y. and Lund E. BMC Bioinfo 2012). Vectors `Regular` and `Negative` contain the intensities of regular and negative probes, respectively.

### Usage

```r
data(RegNegIntensities_Example)
```

### Format

A list `Intensities` with two elements: a vector `Regular` of length 25 519 and a vector `Negative` of length 759.

### References


### Examples

```r
data(RegNegIntensities_Example)
X = Intensities$Regular
N = Intensities$Negative
par(mfrow=c(2,1))
```
```r
HX = histogram (X, type='irregular', verbose=FALSE, plot=FALSE)
plot(HX, xlim=c(0,500))
hist(N, 30)
```

**normgam.fit**  
*Normal-gamma Maximum Likelihood Estimator*

**Description**
Computes the Maximum Likelihood Estimator for the normal-gamma distribution, either from a normal-gamma distributed sample or from two samples respectively normal-gamma and normally distributed.

**Usage**

```r
normgam.fit(X, N = NULL, par.init = NULL, lower = NULL, upper = NULL,
            control = NULL, verbose = FALSE)
```

**Arguments**

- **X**: vector of normal-gamma distributed values.
- **N**: vector of normal distributed values.
- **par.init**: vector of initial values for parameters (optional). `par.init[1]` and `par.init[2]` are the mean and standard deviation of the normal distribution, and `par.init[3]` and `par.init[4]` are the shape and scale parameters of the gamma distribution. See details for default initial values.
- **lower, upper**: Bounds on the variables for maximization (optional).
- **control**: list of control parameters (see details).
- **verbose**: logical; if TRUE initial values of the parameters are printed.

**Details**
Likelihood maximization is run by the R function `optimx`.

By default, maximization is run with the following control parameters: the maximum number of iterations is equal to 1000 and the vector of scaling values for the parameters is `(par0[1], par0[2], par0[3]*par0[4], sqrt(par0[3]*par0[4])/10)` where `par0` is the vector of default initial parameters. In case of unsuccessful convergence, maximization is run with `optimx` default control parameters. A list of control parameters can also be chosen by the user (see `optimx`).

If `par.init == NULL`, the initial parameters are computed in two ways depending if `N` is `NULL` or not. If `N != NULL`, the initial parameters are computed following the method of the moments (see...
Plancade S., Rozenholc Y. and Lund E., BMC Bioinfo 2012). If \( N = \text{NULL} \), the initial parameters \((\text{par}[1], \text{par}[2])\) of the normal distribution are computed following the RMA procedure of Xie Y., Wang X. and Story M. (2009) for the normal-exponential convolution model, and the initial parameters of the gamma distribution, computed following the method of the moments, are \((\text{par}[3])=(\text{mean}(X)-\text{par}[1])/\text{par}[2], \text{par}[4])=(\text{mean}(X)-\text{par}[1]/\text{par}[2])\). Note that the RMA procedure for initial parameter computation when \( N = \text{NULL} \) stems from an heuristic adapted to microarray data. For parameters with different magnitude, user should specify initial parameters.

**Value**

- **par**: vector of estimated parameters; \( \text{par}[1] \) and \( \text{par}[2] \) are the mean and standard deviation of the normal distribution and \( \text{par}[3] \) and \( \text{par}[4] \) are the shape and scale parameters of the gamma distribution.
- **lik**: value of the normal-gamma log-likelihood corresponding to \( \text{par} \).
- **conv**: integer code: 0 indicates successful convergence. This parameter has the value of the output parameter conv from the procedure \texttt{optimx} used for likelihood maximization (see \texttt{optimx} for details).

**Author(s)**

Plancade S. and Rozenholc Y.

**References**


**See Also**

- \texttt{dnormgam} computes the density of the normal-gamma distribution and \texttt{normgam.signal} implements the background correction using the normal-gamma model. \texttt{Intensities} provides an example of Illumina microarray data.

**Examples**

```r
# Example 1: simulated data

## Not run:

n = 1000
par = c(60,5,0.15,400)
X = rnorm(n, mean=par[1], sd=par[2]) + rgamma(n, shape=par[3], scale=par[4])
N = rnorm(100, mean=par[1], sd=par[2])

par1 = normgam.fit(X, N)$par
```
```r
par2 = normgam.fit(X)$par

F1 = dnormgam(par1, plot=FALSE)
F2 = dnormgam(par2, plot=FALSE)

par(mfrow=c(2,1))
H = histogram(X, type='irregular', verbose=FALSE, plot=FALSE)
plot(H, xlim=c(0,500))
lines(F1$xout, F1$dout, col='red')
plot(H, xlim=c(0,500))
lines(F2$xout, F2$dout, col='blue')

## End(Not run)

# Example 2: Illumina data

## Not run:
data(RegNegIntensities_Example)

X = Intensities$Regular
N = Intensities$Negative

par1 = normgam.fit(X, N)$par
par2 = normgam.fit(X)$par

F1 = dnormgam(par1, plot=FALSE)
F2 = dnormgam(par2, plot=FALSE)

par(mfrow=c(2,1))
H = histogram(X, type='irregular', verbose=FALSE, plot=FALSE)
plot(H, xlim=c(0,500))
lines(F1$xout, F1$dout, col='red')
plot(H, xlim=c(0,500))
lines(F2$xout, F2$dout, col='blue')

## End(Not run)
```

__normgam.signal__

_Normal-gamma background correction_
normgam.signal

Description

Performs background correction using the normal-gamma model.

Usage

```r
normgam.signal(x, par, tail.cor = TRUE, cor = 1e-15, gshift = FALSE,
    mu = par[1], sigma = par[2], k = par[3], theta = par[4])
```

Arguments

- `x`: vector of observed intensities.
- `par`: vector of parameters; `par[1]` and `par[2]` are the mean and standard deviation of the normal distribution and `par[3]` and `par[4]` are the shape and scale parameters of the gamma distribution.
- `tail.cor`: logical (see details).
- `cor`: limit of the right tail correction (see details).
- `gshift`: logical; if `TRUE` and `par[3]` is smaller than 1, an ad-hoc translation and a thresholding to 0 are applied to background-corrected values so that the mode of corrected value distribution is 0.
- `mu, sigma`: alternative definition of mean and standard deviation of the normal distribution.
- `k, theta`: alternative definition of shape and scale parameters of the gamma distribution.

Details

`normgam.signal` performs background correction in an additive background noise+signal model with a normal background noise and a gamma-distributed signal. The corrected value from an observed intensity `x` is the expectation of the signal given the signal and noise distributions. For a set of parameters (`mu, sigma, k, theta`), it is given by the ratio of the convolution product of `dgamma(x, shape=k+1, scale=theta)` and `dnorm(x, mean=mu, sd=sigma)` and the convolution product of `dgamma(x, shape=k, scale=theta)` and `dnorm(x, mean=mu, sd=sigma)`. For more details see Plancade S., Rozenholc Y. and Lund E., BMC Bioinfo 2012.

If `tail.cor = TRUE`, a linear approximation of right tail is applied to values with density estimate smaller than `cor` in the computation of normal-gamma convoluted densities (see `dnormgam`).

Only one definition of the parameters is required, either `par` or (`mu, sigma, k, theta`). If both are specified and do not match, an error message is returned.

Value

Vector of background noise-corrected intensities.

Author(s)

Plancade S. and Rozenholc Y.
References


See Also

dnormgam computes the density of the normal-gamma distribution and normgam.fit computes the Maximum Likelihood Estimator. Intensities provides an example of Illumina microarray data.

Examples

#Example 1: simulated data

```R
n = 50000
par = c(60, 5, 0.15, 400)
S = rgamma(n, shape=par[3], scale=par[4])
B = rnorm(n, mean=par[1], sd=par[2])
X = S + B

par(mfrow=c(2,1))
Shat1 = normgam.signal(X, par)
H1 = histogram(Shat1, type='irregular', verbose=FALSE, plot=FALSE)
plot(H1, xlim=c(0, 50))
I = seq(from=0, to=50, length=1000)
lines(I, dgamma(I, shape=0.15, scale=400), col='red')

Shat2 = normgam.signal(X, par, gshift = TRUE)
H2 = hist(Shat2, 10000, plot=FALSE)
plot(H2, xlim=c(0, 50), freq=FALSE)
lines(I, dgamma(I, shape=0.15, scale=400), col='red')
```

#Example 2: illumina data

```R
## Not run:

data(RegNegIntensities_Example)

X = Intensities$Regular
N = Intensities$Negative

# parameter estimation
parmle = normgam.fit(X, N)$par

Shat = normgam.signal(X, parmle)
H = histogram(Shat, type='irregular', verbose=FALSE, plot=FALSE)
plot(H, xlim=c(0, 30))

## End(Not run)
```
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