Package ‘DDHFm’

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Title Variance Stabilization by Data-Driven Haar-Fisz (for Microarrays)
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Description Contains the normalizing and variance stabilizing Data-Driven Haar-Fisz algorithm. Also contains related algorithms for simulating from certain microarray gene intensity models and evaluation of certain transformations. Contains cDNA and shipping credit flow data.

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Example cDNA data

Description

cDNA data from a one-colour experiment from the Stanford Microarray Database. The data set is stored as an intensity matrix with 42624 genes (rows) and 4 replicates (columns).

The experiment numbers are 40430, 40571, 34905 and 34912.

Usage

data(cdna)

Format

A 42624x4 matrix

Source

Stanford Microarray Database

References

**cDNAdata**

Samples from the cDNA data vector

**Description**

Arranges a vector of intensities into a form amenable to analysis by the DDHF and also can restrict the number of genes analysed and also obtain a random sample

**Usage**

cDNAdata(data.vect,cdnalength,datasize,ng,nrep)

**Arguments**

data.vect  The data vector of intensities

cdnalength  Only considers the first cdnalength genes for analysis

datasize  Needs to be a power of two. The number of genes that get randomly sampled from the first cdnalengthq and then subsequently transformed.

ng  The total number of genes described by data.vect

nrep  The number of replicates (should be a power of two) contained in data.vect

**Details**

The

\[ J = ng \times nrep \]

vector data.vect should contain first the intensities of the first replicate of the ng genes’, then the second replicate of all of the ng genes in the same order, and so on.

This function first puts the one dimensional data.vect into a matrix form with ng rows and nrep columns (so the row number indices the gene and the column number the replicate).

Then the first cdnalength rows are extracted and kept, the remaining rows are discarded.

Then datasize rows at random are extracted and kept and the remaining rows are discarded.

**Value**

cDNAdata  The data vector in the proper format to perform Data-Driven Haar-Fisz algorithm

**Author(s)**

Efthimios Motakis <e.motakis@bris.ac.uk>
Description

Takes a matrix containing the results of a (e.g.) microarray experiment (rows are different genes, columns are replicates) and performs a multiscale variance stabilization and Gaussianization transform. Note, you have to have replicates to make this work.

Usage

```
DDHFm(x)
```

Arguments

- **x**: A matrix containing n rows (genes) and k columns (replicates)

Details

The data-drive Haar-Fisz transform is a multiscale variance stabilization and Gaussianization transform. The algorithm will run on a one-column matrix but the results will NOT be good. For one column of data use some other variance stabilizer (in which case why are you using one column, eh?)

However, if you have replicates then you can use this powerful multiscale algorithm which will stabilize variance and also draw the distribution of the intensities towards Gaussian extremely effectively (so skew and kurtosis will look good too).

This function forms a single vector of intensities by the following procedure. First, it computes the mean over replicates for each gene (this is why you need replicates, really). Then it orders the rows of the matrix into increasing mean order. Then it converts that matrix into a vector (which is therefore a sequence of intensities which are grouped according to gene (according to increasing mean intensity within each group)). Then this vector is padded up to the next power-of-two in length with zeroes. Then the padded vector is subjected to the `ddhft.np.2` function which actually does the data-driven Haar-Fisz transform. The results of this are unpadded and then rearranged into a matrix with an identical structure to the input matrix. This final matrix contains stabilized and Gaussianized (is this a word?) intensities.

It is important that you have replicates (ie, the number of columns of the matrix has to be greater than 1). Also, it is scientifically important that the replicates be just that (ie, although the rows might refer to the same genes the columns must be results from repeats experiments held under identical conditions). For example, you shouldn’t have results for the gene on one subject and then the same gene on another subject unless I suppose you are considering them to be replicates in some way.

Value

A single matrix with the same dimensions as the input matrix. Each entry in the resultant matrix corresponds to a variance stabilized and Gaussianized version of the entry in the input matrix.
Author(s)
Guy Nason

References


See Also
ddhft.np.2

Examples

```r
# First, let's make up some "true" intensities (these are gamma)
#
TrueInt <- genesimulator(nreps=5, nps=100)
#
# Now let us simulate data from the Durbin and Rocke (2001) model conditioning on the TrueInt
#
MAInts <- simdurbin2(TrueInt, alpha=24000, seta=0.227, seps=4800)
#
# Now put these intensities into the correct format for DDHFm. That is
# replicates across columns
#
MAm <- matrix(MAInts, ncol=5, byrow=TRUE)
#
# Apply DDHFm transform
#
MAddHFm <- DDHFm(MAm)
#
# Now look at the variances of each
#
# var(MAm))
#
# [1] 22443437 25065729 23430160 22470058 21023183
#
# var(MAm))/ mean(diag(var(MAm)))
#
# [1] 0.9806403 1.0952183 1.0237540 0.9818035 0.9185839
#
# Now for the DDHFm version
#
# var(MAmDDHFm))
```
Data-Driven Haar-Fisz transformation

Description

Forward Data-Driven Haar-Fisz transform

Usage

ddhft.np.2(data, Ccode=TRUE)

Arguments

data A vector of size $2^J$ containing the data to variance stabilize and Gaussianize.
Ccode If TRUE then fast C code is used, otherwise R code is used

Details

Performs the data-driven Haar-Fisz transform on sequence data. This consists of (i) the Haar wavelet transform of sequence; (ii) estimation of mean-variance relationship between finest level smoothing and detail wavelet coefficients using isotonic regression (see isotone); (iii) divide wavelet detail coefficients by smooth ones subjected to the estimated mean-variance relationship; (iv) perform the inverse Haar wavelet transform of the modified coefficients.

The aim is to variance stabilize and Gaussianize the sequence data which is only assumed to be positive and possess an underlying increasing mean-variance relationship.

Value

A list containing the following components

hft The data-driven Haar-Fisz transform of the input sequence
mu The mu's obtained from the input sequence used for estimating the mean-variance relationship
sigma The estimated standard deviation as a function of the mean, the result of the isotonic regression fit of sigma2 on sigma
sigma2 The local multiscale standard deviations associated with each mean
factors The numbers that divide the detail coefficients to standardize variance (obtained from the mean-variance estimation)
Author(s)

Piotr Fryzlewicz <p.fryzlewicz@imperial.ac.uk>

References


See Also
ddhft.np.inv

Examples

```r
# # Generate example Poisson data set.
# # Intensity function is steps from 1 to 32 in steps of 4 with each intensity
# # lasting for 128 observations. Then sample Poisson with these intensities
# #
v <- rpois(1024, lambda=rep(seq(from=1, to=32, by=4), rep(1024/8,8)))
# # Let's take a look at this
# #
# # Not run: ts.plot(v)
# #
# # Ok. So mean of intensity clear increasing, but variance increasing too
# #
# # Now do data-driven Haar-Fisz
# #
vhft <- ddhft.np.2(v)
# # Now plot the variance stabilized series
# #
# # Not run: ts.plot(vhft$hf)
# # The variance of the observations is much closer to 1. For example, let's
# # look a the variance of the original series and the transformed one
# #
# # For the first intensity of 1
# #
# var(v[1:128])
#[1] 0.6628322
# var(vhft$hf[1:128])
#[1] 1.025151
#```

# And for second intensity of 5
#
var(v[129:256])
#[1] 4.389518
var(vhft$hft[129:256])
#[1] 1.312953
#
# So both transformed variances near to 1
#
# Now plot the estimated variance-mean relationship
#
## Not run: plot(vhft$mu, vhft$sigma)
## Not run: lines(vhft$mu, sqrt(vhft$mu))
#
# This is an approximately square root function (because you expect the
# sd of Poisson to be the square root of the mean).
#
---

**ddhft.np.inv**

*Inverse Data-Driven Haar-Fisz transformation*

**Description**

Inverts the Data-Driven Haar-Fisz transform to obtain the raw (untransformed) data

**Usage**

```
ddhft.np.inv(hft.obj)
```

**Arguments**

- `hft.obj` An object with the same structure as that returned by the `ddhft.np.2` function.

**Details**

Merely performs the inverse of the DDHF transform see `ddhft.np.2`

**Value**

The inverted transform

**Author(s)**

Piotr Fryzlewicz <p.fryzlewicz@imperial.ac.uk>
References


See Also

ddhft.np.2

dhhrcomp

Simulated genes, apply DDHFm then compute and return variance, skewness and kurtosis values

Description

An example gene intensity simulator with given mean values mu0 which then returns the variance, skew and kurtosis of the DDHF transformed intensities. The gene intensity simulation is performed using simdurbin2

Usage

dhhrcomp(nsims = 1024, nmu = 4,
mu0 = c(0, 5, 10, 15, 20, 25, 30, 40, 50, 60,
65, 70, 80, 100, 200, 300, 500, 1000) * 1000)

Arguments

nsims Number of replicates for each mu
nmu Selects first nmu genes from mu for use
mu0 The possible gene intensity means

Details

This function simulates some gene intensities. A list of possible intensity means are supplied in mu0. The first nmu of these are selected. Then for each of the selected means nsims gene intensities are generated.

The intensities are them subjected to DDHF transformation.

Value

mu A vector of length nmu of the mean intensities considered
v.hft A vector of nmu variances, one for each mean in mu0. The variance is the variance of the DDHFm transformed simulated intensity data.
s.hft A vector of nmu skewnesses, one for each mean in mu0. The skewness is the skewness of the DDHFm transformed simulated intensity data.
k.hft A vector of nmu kurtoses, one for each mean in mu0. The kurtosis is the kurtosis of the DDHFm transformed simulated intensity data.
Author(s)

Guy Nason <g.p.nason@bris.ac.uk.

References


See Also

simdurbin2

dhhrss

Tabulates variance, skewness and kurtosis coefficients from the output of dhhrcomp

Description

Tabulates the variance, skewness and kurtosis coefficients from the output of dhhrcomp

Usage

dhhrss(dhhrobj)

Arguments

dhhrobj The results to be tabulated. The output of a call to dhhrcomp

Details

This routine merely runs summary statistics calculations on the output results from dhhrcomp

Value

None, prints a table.

Author(s)

Guy Nason <g.p.nason@bris.ac.uk.
function from vector

Function applied for the computation of the Data-Driven Haar-Fisz transform

Description

Applies the function which.min.diff to the argumentvect vector with the argument x

Usage

function from vector(x, y, argumentvect)

Arguments

x a vector of data in ascending order
y a vector with length(y) = length(x)
argumentvect can be a vector

Value

function from vector
help function for data transformation

Author(s)

Piotr Fryzlewicz <p.fryzlewicz@imperial.ac.uk>

genesimulator Gene means simulator

Description

Simulates means of the gene intensities for "nps" genes, each replicated "nreps" times. The mean is drawn from a gamma distribution with shape parameter "shape" and scale parameter "scale"

Usage

genesimulator(nreps = 3, nps = 100, shape = 4, scale = 100)

Arguments

nreps Number of replicates
nps Number of genes
shape Shape parameter
scale Scale parameter
Details

For many problems a set of reasonable gene mean intensities is useful for testing algorithms that later draw actual gene intensities with distributions that possess a gene mean intensity.

Value

A matrix containing nreps*nps rows and 3 columns. The first col contains all the gene mean intensities. The second and third col contain the gene replicate number and gene number respectively.

Author(s)

Guy Nason <g.p.nason@bris.ac.uk>

Description

Simulates gene intensities and also applies DDHFm to them

Usage

hftrialdatagen(nreps = 4, nps = 128, plot.it = FALSE, uvp = 0.8)

Arguments

- `nreps` Number of replicates
- `nps` Number of genes
- `plot.it` Takes TRUE to activate the command of the respective plot and FALSE to deactivate it
- `uvp` a parameter for the denoising

Details

The code is well commented for further information.

First, genesimulator is called to obtain a vector of mean gene intensities (for a number of genes and a number of replicates for each gene.

Then link{simdurbin2} simulates a series of gene intensities using the (log-normal type) model as described in Durbin and Rocke (2001,2002).

Then for each gene the mean of replicates for that gene is computed.

Optionally, if `plot.it` is TRUE then the mean is plotted against its standard deviation (over replicates).

Then the intensities are sorted according to increasing replicate mean.
Optionally, if \texttt{plotNit} is \texttt{TRUE} then a plot of the intensities values as a vector (sorted according to increasing replicate mean) is plotted in black, and then the true mean plotted in colour 2 (on my screen this is red) and the computed replicate mean plotted in green.

The DDHF transform of the sorted intensities is computed.

Optionally, if \texttt{plotNit} is \texttt{TRUE} then a plot of the transformed means versus the transformed standard deviations is plotted. Followed by a time series plot of the transformed sorted intensities. These can be studied to see how well DDHF has done the transformation.

Then two smoothing methods are applied the the DDHF transformed data. One method is translation invariant, Haar wavelet universal thresholding. The other method is the classical smoothing spline. If \texttt{plotNit} is \texttt{TRUE} then these smoothed estimates are plotted in different colours.

Then the mean estimated intensity for each gene is computed and this is returned as the first column of a two-column matrix (\texttt{ansm}). The second column is the true underlying mean. The object \texttt{hftssq} contains a measure of error between the estimated and true gene means.

\textbf{Value}

\begin{itemize}
  \item \texttt{ansm} Two column matrix containing the estimated gene intensities and the true ones
  \item \texttt{hftssq} Sum of squares between estimated means and true means
  \item \texttt{yhf} Simulated gene intensities
\end{itemize}

\textbf{Author(s)}

Guy Nason <g.p.nason@bris.ac.uk>

\textbf{Examples}

\begin{verbatim}
# # First run hftrialdatagen
# # Not run: v <- hftrialdatagen()
# # Now plot the Haar-Fisz transformed intensities.
# # Not run: ts.plot(v$yhf)
# # Now plot the denoised intensities
# # Note that above we have 128 genes and 4 replicates and so there are
# # 4*128 = 512 intensities to plot.
# # However, there are only 128 gene intensities, and estimates. So, for this
# # plot we choose to plot the noisy intensities and then for each replicate
# # group (which are colocated on the plot) plot the (necessarily constant)
# # true and estimated intensities (ie we plot each true/estimated intensity
# # 4 times, once for each replicate).
# # First estimates...
# # Not run: lines(1:512, rep(v$ansm[,1], rep(4,128)), col=2)
\end{verbatim}
isotone

Performs Isotone regression using "pool-adjacent-violators" algorithm

Description

It is applied in order to estimate the h() function in the Data-Driven Haar-Fisz algorithm

Usage

isotone(x, wt = rep(1, length(x)), increasing = FALSE, Ccode=TRUE)

Arguments

x the vector that will be fitted with the regression
wt a vector of weights
increasing if TRUE the curve is set to be increasing, else FALSE
Ccode if TRUE then faster C code is used rather than R

Value

isotone the regression results

Author(s)

Bernard Silverman, with C modifications by GPN

References

KURTOSIS  Kurtosis Coefficient estimator

Description
Estimates the kurtosis coefficient of a data vector

Usage
KURTOSIS(x)

Arguments
x the data vector

Value
The estimated kurtosis of x

Author(s)
Efthimios Motakis <e.motakis@bris.ac.uk

MOMENTS  Moment estimator

Description
Computes the rth central moment of the data x

Usage
MOMENTS(x, r)

Arguments
x the data vector
r parameter that describes which moment will be produced

Value
The rth central moment of x

Author(s)
Efthimios Motakis <e.motakis@bris.ac.uk.
**ShipCreditFlow**  
*Example Shipping credit flow data*

**Description**

Shipping credit flow data. A set of monthly credit transaction flow series recorded by the Central Bank of Cyprus. The time range of the data is January 2002 to December 2014 and contains 156 observations.

**Usage**

```r
data(ShipCreditFlow)
```

**Format**

A vector of length 156

**Source**

Central Bank of Cyprus

**References**


---

**simdurbin**  
*Gene intensities simulator*

**Description**

Simulates gene intensities from the two components model as in the papers of Durbin and Rocke.

**Usage**

```r
simdurbin(n, alpha, mu, seta, seps)
```

**Arguments**

- `n` number of intensities to be simulated
- `alpha` background mean of gene intensities
- `mu` the means where the gene intensities are simulated from
- `seta` standard deviation of high-level gene intensities
- `seps` standard deviation of low-level gene intensities
This function generates \( n \) intensities from the Durbin and Rocke (2001) gene intensity model with parameters \( \alpha \), \( \sigma_{\text{a}} \) and \( \sigma_{\text{p}} \).

A vector of the appropriate intensities.

Guy Nason <g.p.nason@bris.ac.uk>


Simulates gene intensities from the two components model of Durbin and Rocke.

\[
simdurbin2(\mu, \alpha, \sigma_{\text{a}}, \sigma_{\text{p}})
\]

- \( \mu \): the means where the gene intensities are simulated from
- \( \alpha \): background mean of gene intensities
- \( \sigma_{\text{a}} \): standard deviation of high-level gene intensities
- \( \sigma_{\text{p}} \): standard deviation of low-level gene intensities

Like \( \text{simdurbin} \) this function simulates gene intensities from the Durbin and Rocke two component model (see Durbin and Rocke, 2001). Unlike \( \text{simdurbin} \) this function generates each intensity with a mean specified by an entry in \( \mu \). So, \( \text{length}(\mu) \) intensities are generated with intensity \( i \) having mean \( \mu[i] \).
Author(s)
Guy Nason <g.p.nason@bris.ac.uk>

References

See Also
simdurbin

Examples
# Generate data with mu equal to 80 and mu equal to 80000 with 10 replicates each
#
#
v <- simdurbin2( c(rep(80, 10), rep(80000,10)), alpha=24800, seta=0.227, seps=4800)
#
# Let's look at the mean of the first 10 and the last 10
#
mean(v[1:10])
#[1] 27361.95
#
mean(v[11:20])
#[1] 92455.66

SKEW

Skewness coefficient estimator

Description
Estimates the skewness coefficient of the data

Usage
SKEW(x)

Arguments
x The data vector

Value
The skewness of x

Author(s)
Efthimios Motakis <e.motakis@bris.ac.uk>
which.min.diff

Find index where two vectors are closest

Description
Finds the index point where two index vectors are closest in value

Usage
which.min.diff(a, vect)

Arguments
a  input vector
vect  input vector

Value
The index where abs(a-vect) is smallest, ie where a and vect are smallest.

Author(s)
Piotr Fryzlewicz <p.fryzlewicz@imperial.ac.uk>

Examples
# Make up two vectors
#
a <- c(1,2,3)
vect <- c(3,2,1)
#
# Now see on which index are the two closest in value
#
which.min.diff(a, vect)
#[1] 2
#
# ie its the second index where both vectors are actually 2
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