## Package: MVR (via r-universe)

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Type Package

Title Mean-Variance Regularization

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Description Implements a non-parametric method for joint adaptive mean-variance regularization and variance stabilization of high-dimensional data. It is suited for handling difficult problems posed by high-dimensional multivariate datasets (p >> n paradigm). Among those are that the variance is often a function of the mean, variable-specific estimators of variances are not reliable, and tests statistics have low powers due to a lack of degrees of freedom. Key features include: (i)

Normalization and/or variance stabilization of the data, (ii)

Computation of mean-variance-regularized t-statistics
(F-statistics to follow), (iii) Generation of diverse diagnostic plots, (iv) Computationally efficient implementation using C/C++ interfacing and an option for parallel computing to enjoy a faster and easier experience in the R environment.

**Depends** R (>= 3.5.0)

Imports parallel, methods, statmod

NeedsCompilation yes

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**License** GPL (>= 3) | file LICENSE

Archs i386, x64

**RemoteUrl** https://jedazard.r-universe.dev **RemoteUrl** https://github.com/jedazard/mvr

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### **Description**

Implements a non-parametric method for joint adaptive mean-variance regularization and variance stabilization of high-dimensional data (Dazard and Rao, 2012).

It is suited for handling difficult problems posed by high-dimensional multivariate datasets ( $p \gg n$  paradigm), such as in omics-type data, among which are that the variance is often a function of the mean, variable-specific estimators of variances are not reliable, and tests statistics have low powers due to a lack of degrees of freedom.

Key features include:

- 1. Normalization and/or variance stabilization of the data
- 2. Computation of mean-variance-regularized *t*-statistics (*F*-statistics to come)
- 3. Generation of diverse diagnostic plots
- 4. Computationally efficient implementation using C/C++ interfacing and an option for parallel computing to enjoy a fast and easy experience in the R environment

#### Details

The following describes all the end-user functions, and internal R subroutines needed for running a complete MVR procedure. Other internal subroutines are not to be called by the end-user at any time. For computational efficiency, end-user regularization functions offer the option to configure a cluster. This is indicated by an asterisk (\* = optionally involving cluster usage). The R functions are categorized as follows:

END-USER REGULARIZATION & VARIANCE STABILIZATION FUNCTION
 mvr (\*) Function for Mean-Variance Regularization and Variance Stabilization.
 End-user function for Mean-Variance Regularization (MVR) and Variance Stabilization by similarity statistic under sample group homoscedasticity or heteroscedasticity assumption.

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The function takes advantage of the R package **parallel**, which allows users to create a cluster of workstations on a local and/or remote machine(s), enabling parallel execution of this function and scaling up with the number of CPU cores available.

#### 2. END-USER REGULARIZED TESTS-STATISTICS FUNCTIONS

## mvrt.test (\*) Function for Computing Mean-Variance Regularized T-test Statistic and Its Significance.

End-user function for computing MVR t-test statistic and its significance (p-value) under sample group homoscedasticity or heteroscedasticity assumption. The function takes advantage of the R package **parallel**, which allows users to create a cluster of workstations on a local and/or remote machine(s), enabling parallel execution of this function and scaling up with the number of CPU cores available.

### 3. END-USER DIAGNOSTIC PLOTS FOR QUALITY CONTROL

## cluster.diagnostic Function for Plotting Summary Cluster Diagnostic Plots.

Plot similarity statistic profiles and the optimal joint clustering configuration for the means and the variances by group. Plot quantile profiles of means and standard deviations by group and for each clustering configuration, to check that the distributions of first and second moments of the MVR-transformed data approach their respective null distributions under the optimal configuration found, assuming independence and normality of all the variables.

### target.diagnostic Function for Plotting Summary Target Moments Diagnostic Plots.

Plot comparative distribution densities of means and standard deviations of the data before and after Mean-Variance Regularization to check for location shifts between observed first and second moments and their expected target values under a target centered homoscedastic model. Plot comparative QQ scatterplots to look at departures between observed distributions of first and second moments of the MVR-transformed data and their theoretical distributions assuming independence and normality of all the variables.

## stabilization.diagnostic Function for Plotting Summary Variance Stabilization Diagnostic Plots.

Plot comparative variance-mean plots to check the variance stabilization across variables before and after Mean-Variance Regularization.

## ${\color{blue} \textbf{normalization. diagnostic Function for Plotting Summary Normalization Diagnostic Plots.} \\$

Plot comparative Box-Whisker and Heatmap plots of variables across samples check the effectiveness of normalization before and after Mean-Variance Regularization.

#### 4. OTHER END-USER FUNCTIONS

## MVR.news Display the MVR Package News

Function to display the log file NEWS of updates of the  $\boldsymbol{MVR}$  package.

#### 5. END-USER DATASETS

A Real dataset coming from a quantitative proteomics experiment, consisting of n=6 samples split into a control ("M") and a treated group ("S") with p=9052 unique peptides or predictor variables. This is a balanced design with two sample groups (G=2), under unequal

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sample group variance.

A Synthetic dataset with n=10 observations (samples) and p=100 variables, where nvar=20 of them are significantly different between the two sample groups. This is a balanced design with two sample groups (G=2), under unequal sample group variance.

Known Bugs/Problems: None at this time.

### Acknowledgments

This work made use of the High Performance Computing Resource in the Core Facility for Advanced Research Computing at Case Western Reserve University. This project was partially funded by the National Institutes of Health (P30-CA043703).

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#### References

- Dazard J-E. and J. S. Rao (2010). "Regularized Variance Estimation and Variance Stabilization of High-Dimensional Data." In JSM Proceedings, Section for High-Dimensional Data Analysis and Variable Selection. Vancouver, BC, Canada: American Statistical Association IMS JSM, 5295-5309.
- Dazard J-E., Hua Xu and J. S. Rao (2011). "R package MVR for Joint Adaptive Mean-Variance Regularization and Variance Stabilization." In JSM Proceedings, Section for Statistical Programmers and Analysts. Miami Beach, FL, USA: American Statistical Association IMS - JSM, 3849-3863.
- Dazard J-E. and J. S. Rao (2012). "Joint Adaptive Mean-Variance Regularization and Variance Stabilization of High Dimensional Data." Comput. Statist. Data Anal. 56(7):2317-2333.

#### See Also

- makeCluster (R package parallel)
- justvsn (R package **vsn**) Variance stabilization and calibration for microarray data *Huber*, 2002
- eBayes (R package limma) Bayesian Regularized t-test statistic Smyth, 2004
- samr (R package samr) SAM Regularized t-test statistic Tusher et al., 2001, Storey, 2003
- matest (R package **maanova**) James-Stein shrinkage estimator-based Regularized t-test statistic *Cui et al.*, 2005
- ebam (R package siggenes) Empirical Bayes Regularized z-test statistic Efron, 2001
- bayesT Hierarchical Bayesian Regularized t-test statistic Baldi et al., 2001

cluster.diagnostic

Function for Plotting Summary Cluster Diagnostic Plots

## **Description**

Plot similarity statistic profiles and the optimal joint clustering configuration for the means and the variances by group.

Plot quantile profiles of means and standard deviations by group and for each clustering configuration, to check that the distributions of first and second moments of the MVR-transformed data approach their respective null distributions under the optimal configuration found, assuming independence and normality of all the variables.

## Usage

#### **Arguments**

obj	Object of class "MVR" returned by mvr.
title	Title of the plot. Defaults to "Cluster Diagnostic Plots".
span	Span parameter of the loess() function (R package <b>stats</b> ), which controls the degree of smoothing. Defaults to 0.75.
degree	Degree parameter of the loess() function (R package <b>stats</b> ), which controls the degree of the polynomials to be used. Defaults to 2. (Normally 1 or 2. Degree 0 is also allowed, but see the "Note" in loess stats package.)
family	Family distribution in "gaussian", "symmetric" of the loess() function (R package <b>stats</b> ), used for local fitting. If "gaussian" fitting is by least-squares, and if "symmetric" is used, a re-descending M estimator is used with Tukey's biweight function. Defaults to "gaussian".
device	Graphic display device in {NULL, "PS", "PDF"}. Defaults to NULL (standard output screen). Currently implemented graphic display devices are "PS" (Postscript) or "PDF" (Portable Document Format).
file	File name for output graphic. Defaults to "Cluster Diagnostic Plots".
path	Absolute path (without final (back)slash separator). Defaults to working directory path.

horizontal Logical scalar. Orientation of the printed image. Defaults to FALSE, that is

potrait orientation.

width Numeric scalar. Width of the graphics region in inches. Defaults to 8.5.

height Numeric scalar. Height of the graphics region in inches. Defaults to 11.

... Generic arguments passed to other plotting functions.

#### **Details**

In a plot of a similarity statistic profile, one checks the goodness of fit of the transformed data relative to the hypothesized underlying reference distribution with mean-0 and standard deviation-1 (e.g. N(0,1)). The red dashed line depicts the LOESS scatterplot smoother estimator. The subroutine internally generates reference null distributions for computing the similarity statistic under each cluster configuration. The optimal cluster configuration (indicated by the vertical red arrow) is found where the similarity statistic reaches its minimum plus/minus one standard deviation (applying the conventional one-standard deviation rule). A smaller cluster number configuration indicates under-regularization, while over-regularization starts to occur at larger numbers. This over/underregularization must be viewed as a form of over/under-fitting (see Dazard, J-E. and J. S. Rao (2012) for more details). The quantile diagnostic plots uses empirical quantiles of the transformed means and standard deviations to check how closely they are approximated by theoretical quantiles derived from a standard normal equal-mean/homoscedastic model (solid green lines) under a given cluster configuration. To assess this goodness of fit of the transformed data, theoretical null distributions of the mean and variance are derived from a standard normal equal-mean/homoscedastic model with independence of the first two moments, i.e. assuming i.i.d. normality of the raw data. However, we do not require i.i.d. normality of the data in general: these theoretical null distributions are just used here as convenient ones to draw from. Note that under the assumptions that the raw data is i.i.d. standard normal (\$N(0, 1)\$) with independence of first two moments, the theoretical null distributions of means and standard deviations for each variable are respectively:  $N(0,\frac{1}{n})$  and

 $\sqrt{\frac{\chi_{n-G}^2}{n-G}}$ , where G denotes the number of sample groups. The optimal cluster configuration found is indicated by the most horizontal red curve. The single cluster configuration, corresponding to no transformation, is the most vertical curve, while the largest cluster number configuration reaches horizontality. Notice how empirical quantiles of transformed pooled means and standard deviations converge (from red to black) to the theoretical null distributions (solid green lines) for the optimal configuration. One should see a convergence towards the target null, after which overfitting starts to occur (see *Dazard*, *J-E. and J. S. Rao* (2012) for more details). Both cluster diagnostic plots help determine (i) whether the minimum of the *Similarity Statistic* is observed within the range of clusters (i.e. a large enough number of clusters has been accommodated), and (ii) whether the corresponding cluster configuration is a good fit. If necessary, run the procedure again with larger value of the nc.max parameter in the mvr as well as in mvrt.test functions until the minimum of the similarity statistic profile is reached.

Option file is used only if device is specified (i.e. non NULL).

## Value

None. Displays the plots on the chosen device.

#### Acknowledgments

This work made use of the High Performance Computing Resource in the Core Facility for Advanced Research Computing at Case Western Reserve University. This project was partially funded by the National Institutes of Health (P30-CA043703).

#### Note

End-user function.

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#### References

- Dazard J-E. and J. S. Rao (2010). "Regularized Variance Estimation and Variance Stabilization of High-Dimensional Data." In JSM Proceedings, Section for High-Dimensional Data Analysis and Variable Selection. Vancouver, BC, Canada: American Statistical Association IMS JSM, 5295-5309.
- Dazard J-E., Hua Xu and J. S. Rao (2011). "R package MVR for Joint Adaptive Mean-Variance Regularization and Variance Stabilization." In JSM Proceedings, Section for Statistical Programmers and Analysts. Miami Beach, FL, USA: American Statistical Association IMS - JSM, 3849-3863.
- Dazard J-E. and J. S. Rao (2012). "Joint Adaptive Mean-Variance Regularization and Variance Stabilization of High Dimensional Data." Comput. Statist. Data Anal. 56(7):2317-2333.

#### See Also

loess (R package **stats**) Fit a polynomial surface determined by one or more numerical predictors, using local fitting.

## **Examples**

```
citation("MVR")
# Loading of the Synthetic and Real datasets
# (see description of datasets)
data("Synthetic", "Real", package="MVR")
?Synthetic
?Real
# Mean-Variance Regularization (Real dataset)
# Multi-Group Assumption
# Assuming unequal variance between groups
# Without cluster usage
_____
nc.min <- 1
nc.max <- 30
probs <- seq(0, 1, 0.01)
n <- 6
GF \leftarrow factor(gl(n = 2, k = n/2, length = n),
          ordered = FALSE,
          labels = c("M", "S"))
mvr.obj <- mvr(data = Real,</pre>
           block = GF,
            log = FALSE,
            nc.min = nc.min,
            nc.max = nc.max,
            probs = probs,
            B = 100,
            parallel = FALSE,
            conf = NULL,
            verbose = TRUE,
            seed = 1234)
#=========
# Summary Cluster Diagnostic Plots (Real dataset)
# Multi-Group Assumption
# Assuming unequal variance between groups
cluster.diagnostic(obj = mvr.obj,
               title = "Cluster Diagnostic Plots
               (Real - Multi-Group Assumption)",
               span = 0.75,
               degree = 2,
               family = "gaussian",
               device = NULL,
               horizontal = FALSE,
               width = 8.5,
               height = 11)
```

```
## End(Not run)
```

mvr

Function for Mean-Variance Regularization and Variance Stabiliza-

## Description

End-user function for Mean-Variance Regularization (MVR) and Variance Stabilization by similarity statistic under sample group homoscedasticity or heteroscedasticity assumptions.

Return an object of class "MVR". Offers the option of parallel computation for improved efficiency.

## Usage

```
mvr(data,
    block = rep(1,nrow(data)),
    tolog = FALSE,
    nc.min = 1,
    nc.max = 30,
    probs = seq(0, 1, 0.01),
    B = 100,
    parallel = FALSE,
    conf = NULL,
    verbose = TRUE,
    seed = NULL)
```

## **Arguments**

data	numeric matrix of untransformed (raw) data, where samples are by rows and variables (to be clustered) are by columns, or an object that can be coerced to a matrix (such as a numeric vector or a data. frame with all numeric columns). Missing values (NA), NotANumber values (NaN) or Infinite values (Inf) are not allowed.
block	character or numeric vector, or factor of group membership indicator variable (grouping/blocking variable) of length the data sample size with as many different values or levels as the number of data sample groups. Defaults to single group situation. See details.
tolog	logical scalar. Is the data to be log2-transformed first? Optional, defaults to FALSE. Note that negative or null values will be changed to 1 before taking log2-transformation.
nc.min	Positive integer scalar of the minimum number of clusters, defaults to 1
nc.max	Positive integer scalar of the maximum number of clusters, defaults to 30
probs	numeric vector of probabilities for quantile diagnostic plots. Defaults to $seq(0, 1, 0.01)$ .
В	Positive integer scalar of the number of Monte Carlo replicates of the inner loop of the sim statistic function (see details).

parallel

logical scalar. Is parallel computing to be performed? Optional, defaults to FALSE.

conf

list of 5 fields containing the parameters values needed for creating the parallel backend (cluster configuration). See details below for usage. Optional, defaults to NULL, but all fields are required if used:

- type: character vector specifying the cluster type ("SOCKET", "MPI").
- spec : A specification (character vector or integer scalar) appropriate to the type of cluster.
- homogeneous: logical scalar to be set to FALSE for inhomogeneous clusters
- verbose: logical scalar to be set to FALSE for quiet mode.
- outfile: character vector of an output log file name to direct the stdout and stderr connection output from the workernodes. "" indicates no redirection.

verbose

logical scalar. Is the output to be verbose? Optional, defaults to TRUE.

seed

Positive integer scalar of the user seed to reproduce the results.

#### **Details**

Argument block will be converted to a factor, whose levels will match the data groups. It defaults to a single group situation, that is, under the assumption of equal variance between sample groups. All group sample sizes must be greater than 1, otherwise the program will stop.

Argument nc.max currently defaults to 30. Empirically, we found that this is enough for most datasets tested. This depends on (i) the dimensionality/sample size ratio  $\frac{p}{n}$ , (ii) the signal/noise ratio, and (iii) whether a pre-transformation has been applied (see *Dazard*, *J-E. and J. S. Rao* (2012) for more details). See the cluster diagnostic function cluster.diagnostic for more details, whether larger values of nc.max may be required.

The function mvr relies on the R package **parallel** to create a parallel backend within an R session. This enables access to a cluster of compute cores and/or nodes on a local and/or remote machine(s) and scaling-up with the number of CPU cores available and efficient parallel execution. To run a procedure in parallel (with parallel RNG), argument parallel is to be set to TRUE and argument conf is to be specified (i.e. non NULL). Argument conf uses the options described in function makeCluster of the R packages **parallel** and **snow**. **PRIMsrc** supports two types of communication mechanisms between master and worker processes: 'Socket' or 'Message-Passing Interface' ('MPI'). In **PRIMsrc**, parallel 'Socket' clusters use sockets communication mechanisms only (no forking) and are therefore available on all platforms, including Windows, while parallel 'MPI' clusters use high-speed interconnects mechanism in networks of computers (with distributed memory) and are therefore available only in these architectures. A parallel 'MPI' cluster also requires R package **Rmpi** to be installed first. Value type is used to setup a cluster of type 'Socket' ("SOCKET") or 'MPI' ("MPI"), respectively. Depending on this type, values of spec are to be used alternatively:

• For 'Socket' clusters (conf\$type="SOCKET"), spec should be a character vector naming the hosts on which to run the job; it can default to a unique local machine, in which case, one may use the unique host name "localhost". Each host name can potentially be repeated to the number of CPU cores available on the local machine. It can also be an integer scalar specifying the number of processes to spawn on the local machine; or a list of machine specifications (a character value named host specifying the name or address of the host to use).

• For 'MPI' clusters (conf\$type="MPI"), spec should be an integer scalar specifying the total number of processes to be spawned across the network of available nodes, counting the workernodes and masternode.

The actual creation of the cluster, its initialization, and closing are all done internally. For more details, see the reference manual of R package **snow** and examples below.

When random number generation is needed, the creation of separate streams of parallel RNG per node is done internally by distributing the stream states to the nodes. For more details, see the vignette of R package **parallel**. The use of a seed allows to reproduce the results within the same type of session: the same seed will reproduce the same results within a non-parallel session or within a parallel session, but it will not necessarily give the exact same results (up to sampling variability) between a non-parallelized and parallelized session due to the difference of management of the seed between the two (see parallel RNG and value of returned seed below).

### Value

Xraw numeric matrix of original data.

Xmvr numeric matrix of MVR-transformed data.

centering numeric vector of centering values for standardization (cluster mean of pooled

sample mean).

scaling numeric vector of scaling values for standardization (cluster mean of pooled

sample std dev).

MVR list (of size the number of groups) containing for each group:

• membership numeric vector of cluster membership of each variable

• nc Positive integer scalar of number of clusters found in optimal cluster configuration

- gap numeric vector of the similarity statistic values
- sde numeric vector of the standard errors of the similarity statistic values
- mu.std numeric matrix (K x p) of the vector of standardized means by groups (rows), where K = \#groups and p = \#variables
- sd.std numeric matrix (K x p) of the vector of standardized standard deviations by groups (rows), where K = \#groups and p = \#variables
- mu.quant numeric matrix (nc.max nc.min + 1) x (length(probs)) of quantiles of means
- sd.quant numeric matrix (nc.max nc.min + 1) x (length(probs)) of quantiles of standard deviations

block Value of argument block.
tolog Value of argument tolog.
nc.min Value of argument nc.min.
nc.max Value of argument nc.max.
probs Value of argument probs.

seed User seed(s) used: integer of a single value, if parallelization is used. integer

vector of values, one for each replication, if parallelization is not used.

#### Acknowledgments

This work made use of the High Performance Computing Resource in the Core Facility for Advanced Research Computing at Case Western Reserve University. This project was partially funded by the National Institutes of Health (P30-CA043703).

#### Note

End-user function.

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- Dazard J-E. and J. S. Rao (2012). "Joint Adaptive Mean-Variance Regularization and Variance Stabilization of High Dimensional Data." Comput. Statist. Data Anal. 56(7):2317-2333.

## See Also

- makeCluster (R package parallel).
- justvsn (R package vsn) Variance stabilization and calibration for microarray data Huber, 2002

## **Examples**

```
# MVR package citation
   citation("MVR")
  # Loading of the Synthetic and Real datasets
  # Use help for descriptions
  data("Synthetic", "Real", package="MVR")
  ?Synthetic
  ?Real
## End(Not run)
# Mean-Variance Regularization (Synthetic dataset)
# Single-Group Assumption
# Assuming equal variance between groups
# Without cluster usage
data("Synthetic", package="MVR")
nc.min <- 1
nc.max <- 10
probs <- seq(0, 1, 0.01)
n <- 10
mvr.obj <- mvr(data = Synthetic,</pre>
          block = rep(1,n),
          tolog = FALSE,
          nc.min = nc.min,
          nc.max = nc.max,
          probs = probs,
          B = 100,
          parallel = FALSE,
          conf = NULL,
          verbose = TRUE,
          seed = 1234)
## Not run:
  # Examples of parallel backend parametrization
  if (require("parallel")) {
    cat("'parallel' is attached correctly \n")
  } else {
    stop("'parallel' must be attached first \n")
  # Ex. #1 - Multicore PC
  # Running WINDOWS
  # SOCKET communication cluster
  # Shared memory parallelization
```

```
cpus <- parallel::detectCores(logical = TRUE)</pre>
conf <- list("spec" = rep("localhost", cpus),</pre>
           "type" = "SOCKET",
           "homo" = TRUE,
           "verbose" = TRUE,
           "outfile" = "")
# Ex. #2 - Master node + 3 Worker nodes cluster
# All nodes equipped with identical setups of multicores
# (8 core CPUs per machine for a total of 32)
# SOCKET communication cluster
# Distributed memory parallelization
masterhost <- Sys.getenv("HOSTNAME")</pre>
slavehosts <- c("compute-0-0", "compute-0-1", "compute-0-2")
nodes <- length(slavehosts) + 1</pre>
cpus <- 8
conf <- list("spec" = c(rep(masterhost, cpus),</pre>
                     rep(slavehosts, cpus)),
           "type" = "SOCKET",
           "homo" = TRUE,
           "verbose" = TRUE,
           "outfile" = "")
# Ex. #3 - Enterprise Multinode Cluster w/ multicore/node
# Running LINUX with SLURM scheduler
# MPI communication cluster
# Distributed memory parallelization
# Below, variable 'cpus' is the total number of requested
# taks (threads/CPUs), which is specified from within a
# SLURM script.
if (require("Rmpi")) {
   print("Rmpi is loaded correctly \n")
   stop("Rmpi must be installed first to use MPI\n")
cpus <- as.numeric(Sys.getenv("SLURM_NTASKS"))</pre>
conf <- list("spec" = cpus,</pre>
           "type" = "MPI",
           "homo" = TRUE,
           "verbose" = TRUE,
           "outfile" = "")
# Mean-Variance Regularization (Real dataset)
# Multi-Group Assumption
# Assuming unequal variance between groups
data("Real", package="MVR")
nc.min <- 1
nc.max <- 30
probs <- seq(0, 1, 0.01)
n <- 6
```

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MVR.news

Function to Display the NEWS File

## Description

Function to display the NEWS file of the MVR package.

## Usage

```
MVR.news(...)
```

### **Arguments**

... Further arguments passed to or from other methods.

## Value

None.

## Acknowledgments

This work made use of the High Performance Computing Resource in the Core Facility for Advanced Research Computing at Case Western Reserve University. This project was partially funded by the National Institutes of Health (P30-CA043703).

#### Note

End-user function.

### Author(s)

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#### References

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- Dazard J-E. and J. S. Rao (2012). "Joint Adaptive Mean-Variance Regularization and Variance Stabilization of High Dimensional Data." Comput. Statist. Data Anal. 56(7):2317-2333.

mvrt.test

Function for Computing Mean-Variance Regularized T-test Statistic and Its Significance

## **Description**

End-user function for computing MVR t-test statistic and its significance (p-value) under sample group homoscedasticity or heteroscedasticity assumption.

Return an object of class "MVRT". Offers the option of parallel computation for improved efficiency.

## Usage

```
mvrt.test(data,
    obj=NULL,
    block,
    tolog = FALSE,
    nc.min = 1,
    nc.max = 30,
    pval = FALSE,
    replace = FALSE,
    n.resamp = 100,
    parallel = FALSE,
    conf = NULL,
    verbose = TRUE,
    seed = NULL)
```

#### **Arguments**

data

numeric matrix of untransformed (raw) data, where samples are by rows and variables (to be clustered) are by columns, or an object that can be coerced to a matrix (such as a numeric vector or a data. frame with all numeric columns). Missing values (NA), NotANumber values (NaN) or Infinite values (Inf) are not allowed.

obj

Object of class "MVR" returned by mvr.

block

character or numeric vector, or factor of group membership indicator variable (grouping/blocking variable) of length the data sample size with as many different values or levels as the number of data sample groups. Defaults to single group situation. See details.

tolog

logical scalar. Is the data to be log2-transformed first? Optional, defaults to FALSE. Note that negative or null values will be changed to 1 before taking log2-transformation.

nc.min

Positive integer scalar of the minimum number of clusters, defaults to 1

nc.max

Positive integer scalar of the maximum number of clusters, defaults to 30

pval

logical scalar. Shall p-values be computed? If not, n. resamp and replace will be ignored. If FALSE (default), t-statistic only will be computed, If TRUE, exact (permutation test) or approximate (bootstrap test) p-values will be computed.

replace

logical scalar. Shall permutation test (default) or bootstrap test be computed? If FALSE (default), permutation test will be computed with null permutation distribution, If TRUE, bootstrap test will be computed with null bootstrap distribution.

n.resamp

Positive integer scalar of the number of resamplings to compute (default=100) by permutation or bootstsrap (see details).

parallel

logical scalar. Is parallel computing to be performed? Optional, defaults to FALSE.

conf

list of 5 fields containing the parameters values needed for creating the parallel backend (cluster configuration). See details below for usage. Optional, defaults to NULL, but all fields are required if used:

- type: character vector specifying the cluster type ("SOCKET", "MPI").
- spec : A specification (character vector or integer scalar) appropriate to the type of cluster.
- homogeneous: logical scalar to be set to FALSE for inhomogeneous clusters.
- verbose : logical scalar to be set to FALSE for quiet mode.
- outfile: character vector of an output log file name to direct the stdout and stderr connection output from the workernodes. "" indicates no redirection.

verbose

logical scalar. Is the output to be verbose? Optional, defaults to TRUE.

seed

Positive integer scalar of the user seed to reproduce the results.

#### **Details**

Argument block will be converted to a factor, whose levels will match the data groups. It defaults to a single group situation, that is, under the assumption of equal variance between sample groups. All group sample sizes must be greater than 1, otherwise the program will stop.

Argument nc.max currently defaults to 30. Empirically, we found that this is enough for most datasets tested. This depends on (i) the dimensionality/sample size ratio  $\frac{p}{n}$ , (ii) the signal/noise ratio, and (iii) whether a pre-transformation has been applied (see *Dazard*, *J-E. and J. S. Rao* (2012) for more details). See the cluster diagnostic function cluster.diagnostic for more details, whether larger values of nc.max may be required.

To save un-necessary computations, previously computed MVR clustering can be provided through option obj (i.e. obj is fully specified as a mvr object). In this case, arguments data, block, tolog, nc.min, nc.max are ignored. If obj is fully specified (i.e. an object of class "MVR" returned by mvr), the the MVR clustering provided by obj will be used for the computation of the regularized t-test statistics. If obj=NULL, a MVR clustering computation for the regularized t-test statistics and/or p-values will be performed.

The function mvrt.test relies on the R package **parallel** to create a parallel backend within an R session, enabling access to a cluster of compute cores and/or nodes on a local and/or remote machine(s) and scaling-up with the number of CPU cores available and efficient parallel execution. To run a procedure in parallel (with parallel RNG), argument parallel is to be set to TRUE and argument conf is to be specified (i.e. non NULL). Argument conf uses the options described in function makeCluster of the R packages **parallel** and **snow**. **PRIMsrc** supports two types of communication mechanisms between master and worker processes: 'Socket' or 'Message-Passing Interface' ('MPI'). In **PRIMsrc**, parallel 'Socket' clusters use sockets communication mechanisms only (no forking) and are therefore available on all platforms, including Windows, while parallel 'MPI' clusters use high-speed interconnects mechanism in networks of computers (with distributed memory) and are therefore available only in these architectures. A parallel 'MPI' cluster also requires R package **Rmpi** to be installed first. Value type is used to setup a cluster of type 'Socket' ("SOCKET") or 'MPI' ("MPI"), respectively. Depending on this type, values of spec are to be used alternatively:

- For 'Socket' clusters (conf\$type="SOCKET"), spec should be a character vector naming the hosts on which to run the job; it can default to a unique local machine, in which case, one may use the unique host name "localhost". Each host name can potentially be repeated to the number of CPU cores available on the local machine. It can also be an integer scalar specifying the number of processes to spawn on the local machine; or a list of machine specifications (a character value named host specifying the name or address of the host to use).
- For 'MPI' clusters (conf\$type="MPI"), spec should be an integer scalar specifying the total number of processes to be spawned across the network of available nodes, counting the workernodes and masternode.

The actual creation of the cluster, its initialization, and closing are all done internally. For more details, see the reference manual of R package **snow** and examples below.

When random number generation is needed, the creation of separate streams of parallel RNG per node is done internally by distributing the stream states to the nodes. For more details, see the vignette of R package **parallel**. The use of a seed allows to reproduce the results within the same type of session: the same seed will reproduce the same results within a non-parallel session or within a parallel session, but it will not necessarily give the exact same results (up to sampling variability)

between a non-parallelized and parallelized session due to the difference of management of the seed between the two (see parallel RNG and value of returned seed below).

In case p-values are desired (pval=TRUE), the use of a cluster is highly recommended. It is ideal for computing embarassingly parallel tasks such as permutation or bootstrap resamplings. Note that in case both regularized t-test statistics and p-values are desired, in order to maximize computational efficiency and avoid multiple configurations (since a cluster can only be configured and used one session at a time, which otherwise would result in a run stop), the cluster configuration will only be used for the parallel computation of p-values, but not for the MVR clustering computation of the regularized t-test statistics.

#### Value

statistic	vector, of size the number of variables, where entries are the t-statistics values of each variable.
p.value	vector, of size the number of variables, where entries are the p-values (if requested, otherwise NULL value) of each variable.
seed	User seed(s) used: integer of a single value, if parallelization is used. integer vector of values, one for each replication, if parallelization is not used.

## Acknowledgments

This work made use of the High Performance Computing Resource in the Core Facility for Advanced Research Computing at Case Western Reserve University. This project was partially funded by the National Institutes of Health (P30-CA043703).

#### Note

End-user function.

#### Author(s)

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#### References

- Dazard J-E. and J. S. Rao (2010). "Regularized Variance Estimation and Variance Stabilization of High-Dimensional Data." In JSM Proceedings, Section for High-Dimensional Data Analysis and Variable Selection. Vancouver, BC, Canada: American Statistical Association IMS JSM, 5295-5309.
- Dazard J-E., Hua Xu and J. S. Rao (2011). "R package MVR for Joint Adaptive Mean-Variance Regularization and Variance Stabilization." In JSM Proceedings, Section for Statistical Programmers and Analysts. Miami Beach, FL, USA: American Statistical Association IMS - JSM, 3849-3863.
- Dazard J-E. and J. S. Rao (2012). "Joint Adaptive Mean-Variance Regularization and Variance Stabilization of High Dimensional Data." Comput. Statist. Data Anal. 56(7):2317-2333.

### See Also

- makeCluster (R package parallel)
- eBayes (R package **limma**) Bayesian Regularized t-test statistic Smyth, 2004
- samr (R package samr) SAM Regularized t-test statistic Tusher et al., 2001, Storey, 2003
- matest (R package **maanova**) James-Stein shrinkage estimator-based Regularized t-test statistic *Cui et al.*, 2005
- ebam (R package siggenes) Empirical Bayes Regularized z-test statistic Efron, 2001
- bayesT Hierarchical Bayesian Regularized t-test statistic Baldi et al., 2001

## **Examples**

```
# Loading the library and its dependencies
library("MVR")
## Not run:
  # MVR package news
  MVR.news()
  # MVR package citation
  citation("MVR")
  # Loading of the Synthetic and Real datasets
  # Use help for descriptions
  data("Synthetic", "Real", package="MVR")
  ?Synthetic
  ?Real
## End(Not run)
# Regularized t-test statistics (Synthetic dataset)
# Multi-Group Assumption
# Assuming unequal variance between groups
# With option to use prior MVR clustering results
# Without computation of p-values
# Without cluster usage
data("Synthetic", package="MVR")
nc.min <- 1
nc.max <- 10
probs <- seq(0, 1, 0.01)
n <- 10
```

```
GF \leftarrow factor(gl(n = 2, k = n/2, length = n),
          ordered = FALSE,
          labels = c("G1", "G2"))
mvr.obj <- mvr(data = Synthetic,</pre>
            block = GF,
            tolog = FALSE,
            nc.min = nc.min,
            nc.max = nc.max,
            probs = probs,
            B = 100,
            parallel = FALSE,
            conf = NULL,
            verbose = TRUE,
            seed = 1234)
mvrt.obj <- mvrt.test(data = NULL,</pre>
                  obj = mvr.obj,
                  block = NULL,
                  pval = FALSE,
                  replace = FALSE,
                  n.resamp = 100,
                  parallel = FALSE,
                  conf = NULL,
                  verbose = TRUE,
                  seed = 1234)
## Not run:
   # Examples of parallel backend parametrization
   if (require("parallel")) {
     cat("'parallel' is attached correctly \n")
   } else {
     stop("'parallel' must be attached first \n")
   # Ex. #1 - Multicore PC
   # Running WINDOWS
   # SOCKET communication cluster
   # Shared memory parallelization
   cpus <- parallel::detectCores(logical = TRUE)</pre>
   conf <- list("spec" = rep("localhost", cpus),</pre>
              "type" = "SOCKET",
              "homo" = TRUE,
              "verbose" = TRUE,
              "outfile" = "")
   # Ex. #2 - Master node + 3 Worker nodes cluster
   # All nodes equipped with identical setups of multicores
   # (8 core CPUs per machine for a total of 32)
   # SOCKET communication cluster
   # Distributed memory parallelization
   masterhost <- Sys.getenv("HOSTNAME")</pre>
```

```
slavehosts <- c("compute-0-0", "compute-0-1", "compute-0-2")</pre>
nodes <- length(slavehosts) + 1</pre>
cpus <- 8
conf <- list("spec" = c(rep(masterhost, cpus),</pre>
                      rep(slavehosts, cpus)),
            "type" = "SOCKET",
            "homo" = TRUE,
            "verbose" = TRUE,
            "outfile" = "")
#===========
                             -----
# Ex. #3 - Enterprise Multinode Cluster w/ multicore/node
# Running LINUX with SLURM scheduler
# MPI communication cluster
# Distributed memory parallelization
# Below, variable 'cpus' is the total number of requested
# taks (threads/CPUs), which is specified from within a
# SLURM script.
if (require("Rmpi")) {
   print("Rmpi is loaded correctly \n")
} else {
   stop("Rmpi must be installed first to use MPI\n")
}
cpus <- as.numeric(Sys.getenv("SLURM_NTASKS"))</pre>
conf <- list("spec" = cpus,</pre>
            "type" = "MPI",
            "homo" = TRUE,
            "verbose" = TRUE,
            "outfile" = "")
# Mean-Variance Regularization (Real dataset)
# Multi-Group Assumption
# Assuming unequal variance between groups
data("Real", package="MVR")
nc.min <- 1
nc.max <- 30
probs <- seq(0, 1, 0.01)
n <- 6
GF \leftarrow factor(gl(n = 2, k = n/2, length = n),
            ordered = FALSE,
            labels = c("M", "S"))
mvr.obj <- mvr(data = Real,</pre>
              block = GF,
              tolog = FALSE,
              nc.min = nc.min,
              nc.max = nc.max,
              probs = probs,
              B = 100,
              parallel = TRUE,
              conf = conf,
              verbose = TRUE,
              seed = 1234)
```

```
# Regularized t-test statistics (Real dataset)
   # Multi-Group Assumption
   # Assuming unequal variance between groups
   # With option to use prior MVR clustering results
   # With computation of p-values
   mvrt.obj <- mvrt.test(data = NULL,</pre>
                       obj = mvr.obj,
                       block = NULL,
                       pval = TRUE,
                       replace = FALSE,
                       n.resamp = 100,
                       parallel = TRUE,
                       conf = conf,
                       verbose = TRUE,
                       seed = 1234)
## End(Not run)
```

normalization.diagnostic

Function for Plotting Summary Normalization Diagnostic Plots

## **Description**

Plot comparative Box-Whisker and Heatmap plots of variables across samples check the effectiveness of normalization before and after Mean-Variance Regularization.

## Usage

## Arguments

obj	Object of class"MVR" returned by mvr.
title	Title of the plot. Defaults to "Normalization Diagnostic Plots".
pal	Color palette.

device	Graphic display device in {NULL, "PS", "PDF"}. Defaults to NULL (standard output screen). Currently implemented graphic display devices are "PS" (Postscript) or "PDF" (Portable Document Format).
file	File name for output graphic. Defaults to "Normalization Diagnostic Plots".
path	Absolute path (without final (back)slash separator). Defaults to working directory path.
horizontal	Logical scalar. Orientation of the printed image. Defaults to FALSE, that is potrait orientation.
width	Numeric scalar. Width of the graphics region in inches. Defaults to 7.
height	Numeric scalar. Height of the graphics region in inches. Defaults to 8.

... Generic arguments passed to other plotting functions.

#### **Details**

Option file is used only if device is specified (i.e. non NULL). The argument pal can be any color palette, e.g. as provided by R package **RColorBrewer**.

#### Value

None. Displays the plots on the chosen device.

## Acknowledgments

This work made use of the High Performance Computing Resource in the Core Facility for Advanced Research Computing at Case Western Reserve University. This project was partially funded by the National Institutes of Health (P30-CA043703).

#### Note

End-user function.

#### Author(s)

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- "Alberto Santana, MBA." <ahs4@case.edu>

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## References

- Dazard J-E. and J. S. Rao (2010). "Regularized Variance Estimation and Variance Stabilization of High-Dimensional Data." In JSM Proceedings, Section for High-Dimensional Data Analysis and Variable Selection. Vancouver, BC, Canada: American Statistical Association IMS JSM, 5295-5309.
- Dazard J-E., Hua Xu and J. S. Rao (2011). "R package MVR for Joint Adaptive Mean-Variance Regularization and Variance Stabilization." In JSM Proceedings, Section for Statistical Programmers and Analysts. Miami Beach, FL, USA: American Statistical Association IMS - JSM, 3849-3863.

• Dazard J-E. and J. S. Rao (2012). "Joint Adaptive Mean-Variance Regularization and Variance Stabilization of High Dimensional Data." Comput. Statist. Data Anal. 56(7):2317-2333.

#### See Also

justvsn (R package **vsn**) Variance stabilization and calibration for microarray data. loess (R package **stats**) Fit a polynomial surface determined by one or more numerical predictors, using local fitting.

## **Examples**

```
## Not run:
  # Loading the library and its dependencies
  library("MVR")
  library("RColorBrewer")
  # MVR package news
  MVR.news()
  # MVR package citation
  citation("MVR")
  # Loading of the Synthetic and Real datasets
  # (see description of datasets)
  data("Synthetic", "Real", package="MVR")
  ?Synthetic
  ?Real
  # Mean-Variance Regularization (Real dataset)
  # Multi-Group Assumption
  # Assuming unequal variance between groups
  # Without cluster usage
  nc.min <- 1
 nc.max <- 30
 probs <- seq(0, 1, 0.01)
  n <- 6
  GF \leftarrow factor(gl(n = 2, k = n/2, length = n),
         ordered = FALSE,
         labels = c("M", "S"))
 mvr.obj <- mvr(data = Real,</pre>
          block = GF,
          log = FALSE,
```

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```
nc.min = nc.min,
                 nc.max = nc.max,
                 probs = probs,
                 B = 100,
                 parallel = FALSE,
                 conf = NULL,
                 verbose = TRUE,
                 seed = 1234)
   # Summary Normalization Diagnostic Plots (Real dataset)
   # Multi-Group Assumption
   # Assuming unequal variance between groups
   normalization.diagnostic(obj = mvr.obj,
                          title = "Normalization Diagnostic Plots
                          (Real - Multi-Group Assumption)",
                          pal = brewer.pal(n=11, name="RdYlGn"),
                          device = NULL,
                          horizontal = FALSE,
                          width = 7,
                          height = 8)
## End(Not run)
```

Real

Real Proteomics Dataset

#### **Description**

The dataset comes from a quantitative Liquid Chromatography/Mass-Spectrometry (LC/MS) shotgun (bottom-up) proteomics experiment. It consists of n=6 independent cell cultures of human of Myeloid Dendritic Cells (MDCs) from normal subjects. Samples were split into a control ("M") and a treated group ("S"), stimulated with either media alone or a Toll-Like receptor-3 Ligand respectively. The goal was to identify differentially expressed peptides (or proteins) between the two groups involved in the immune response of human MDCs upon TLR-3 Ligand binding.

The dataset is assumed to have been pre-processed for non-ignorable missing values, leaving a complete dataset with p=9052 unique peptides or predictor variables.

This is a balanced design with two sample groups (G = 2), under unequal sample group variance.

## Usage

```
data("Real", package="MVR")
```

#### **Format**

A numeric matrix containing n=6 observations (samples) by rows and p=9052 variables by columns, named after peptide names  $(diffset_1,...,diffset_p)$ . Samples are balanced  $(n_1=3,n_2=3)$  between the two groups ("M", "S"). Compressed Rda data file.

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### Acknowledgments

This work made use of the High Performance Computing Resource in the Core Facility for Advanced Research Computing at Case Western Reserve University. This project was partially funded by the National Institutes of Health (P30-CA043703).

#### Author(s)

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Maintainer: "Jean-Eudes Dazard, Ph.D." < jean-eudes.dazard@case.edu>

#### Source

See real proteomics data application in Dazard et al., 2011, 2012.

#### References

- Dazard J-E. and J. S. Rao (2010). "Regularized Variance Estimation and Variance Stabilization of High-Dimensional Data." In JSM Proceedings, Section for High-Dimensional Data Analysis and Variable Selection. Vancouver, BC, Canada: American Statistical Association IMS JSM, 5295-5309.
- Dazard J-E., Hua Xu and J. S. Rao (2011). "R package MVR for Joint Adaptive Mean-Variance Regularization and Variance Stabilization." In JSM Proceedings, Section for Statistical Programmers and Analysts. Miami Beach, FL, USA: American Statistical Association IMS - JSM, 3849-3863.
- Dazard J-E. and J. S. Rao (2012). "Joint Adaptive Mean-Variance Regularization and Variance Stabilization of High Dimensional Data." Comput. Statist. Data Anal. 56(7):2317-2333.

stabilization.diagnostic

Function for Plotting Summary Variance Stabilization Diagnostic Plots

### **Description**

Plot comparative variance-mean plots to check the variance stabilization across variables before and after Mean-Variance Regularization.

## Usage

## **Arguments**

obj	Object of class "MVR" returned by mvr.
title	Title of the plot. Defaults to "Stabilization Diagnostic Plots".
span	Span parameter of the loess() function (R package $stats$ ), which controls the degree of smoothing. Defaults to 0.75.
degree	Degree parameter of the loess() function (R package <b>stats</b> ), which controls the degree of the polynomials to be used. Defaults to 2. (Normally 1 or 2. Degree 0 is also allowed, but see the "Note" in loess stats package.)
family	Family distribution in "gaussian", "symmetric" of the loess() function (R package $stats$ ), used for local fitting . If "gaussian" fitting is by least-squares, and if "symmetric" a re-descending M estimator is used with Tukey's biweight function.
device	Graphic display device in {NULL, "PS", "PDF"}. Defaults to NULL (standard output screen). Currently implemented graphic display devices are "PS" (Postscript) or "PDF" (Portable Document Format).
file	File name for output graphic. Defaults to "Stabilization Diagnostic Plots".
path	Absolute path (without final (back)slash separator). Defaults to working directory path.
horizontal	Logical scalar. Orientation of the printed image. Defaults to FALSE, that is potrait orientation.
width	Numeric scalar. Width of the graphics region in inches. Defaults to 7.
height	Numeric scalar. Height of the graphics region in inches. Defaults to 5.
	Generic arguments passed to other plotting functions.

## Details

In the plots of standard deviations vs. means, standard deviations and means are calculated in a feature-wise manner from the expression matrix. The scatterplot allows to visually verify whether there is a dependence of the standard deviation (or variance) on the mean. The black dotted line depicts the LOESS scatterplot smoother estimator. If there is no variance-mean dependence, then this line should be approximately horizontal.

Option file is used only if device is specified (i.e. non NULL).

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#### Value

None. Displays the plots on the chosen device.

### Acknowledgments

This work made use of the High Performance Computing Resource in the Core Facility for Advanced Research Computing at Case Western Reserve University. This project was partially funded by the National Institutes of Health (P30-CA043703).

### Note

End-user function.

#### Author(s)

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#### References

- Dazard J-E. and J. S. Rao (2010). "Regularized Variance Estimation and Variance Stabilization of High-Dimensional Data." In JSM Proceedings, Section for High-Dimensional Data Analysis and Variable Selection. Vancouver, BC, Canada: American Statistical Association IMS JSM, 5295-5309.
- Dazard J-E., Hua Xu and J. S. Rao (2011). "R package MVR for Joint Adaptive Mean-Variance Regularization and Variance Stabilization." In JSM Proceedings, Section for Statistical Programmers and Analysts. Miami Beach, FL, USA: American Statistical Association IMS - JSM, 3849-3863.
- Dazard J-E. and J. S. Rao (2012). "Joint Adaptive Mean-Variance Regularization and Variance Stabilization of High Dimensional Data." Comput. Statist. Data Anal. 56(7):2317-2333.

#### See Also

justvsn (R package **vsn**) Variance stabilization and calibration for microarray data. loess (R package **stats**) Fit a polynomial surface determined by one or more numerical predictors, using local fitting.

## **Examples**

```
# MVR package news
MVR.news()
# MVR package citation
citation("MVR")
# Loading of the Synthetic and Real datasets
# (see description of datasets)
data("Synthetic", "Real", package="MVR")
?Synthetic
?Real
# Mean-Variance Regularization (Real dataset)
# Multi-Group Assumption
# Assuming unequal variance between groups
# Without cluster usage
nc.min <- 1
nc.max <- 30
probs <- seq(0, 1, 0.01)
GF \leftarrow factor(gl(n = 2, k = n/2, length = n),
         ordered = FALSE,
         labels = c("M", "S"))
mvr.obj <- mvr(data = Real,</pre>
          block = GF,
          log = FALSE,
          nc.min = nc.min,
          nc.max = nc.max,
          probs = probs,
          B = 100,
          parallel = FALSE,
          conf = NULL,
          verbose = TRUE,
          seed = 1234)
# Summary Stabilization Diagnostic Plots (Real dataset)
# Multi-Group Assumption
# Assuming unequal variance between groups
stabilization.diagnostic(obj = mvr.obj,
                 title = "Stabilization Diagnostic Plots
                 (Real - Multi-Group Assumption)",
                 span = 0.75,
                 degree = 2,
                 family = "gaussian",
```

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```
device = NULL,
horizontal = FALSE,
width = 7,
height = 5)
```

## End(Not run)

Synthetic

Multi-Groups Synthetic Dataset

## **Description**

Generation of a synthetic dataset with n=10 observations (samples) and p=100 variables, where nvar=20 of them are significantly different between the two sample groups.

This is a balanced design with two sample groups (G = 2), under unequal sample group variance.

## Usage

```
data("Synthetic", package="MVR")
```

## **Format**

A numeric matrix containing n=10 observations (samples) by rows and p=100 variables by columns, named  $v_1,...,v_p$ . Samples are balanced ( $n_1=5,n_2=5$ ) between the two groups ( $G_1,G_2$ ). Compressed Rda data file.

## Acknowledgments

This work made use of the High Performance Computing Resource in the Core Facility for Advanced Research Computing at Case Western Reserve University. This project was partially funded by the National Institutes of Health (P30-CA043703).

## Author(s)

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- "Alberto Santana, MBA." <ahs4@case.edu>

Maintainer: "Jean-Eudes Dazard, Ph.D." < jean-eudes.dazard@case.edu>

#### Source

See model #2 in Dazard et al., 2011, 2012.

### References

Dazard J-E. and J. S. Rao (2010). "Regularized Variance Estimation and Variance Stabilization of High-Dimensional Data." In JSM Proceedings, Section for High-Dimensional Data Analysis and Variable Selection. Vancouver, BC, Canada: American Statistical Association IMS - JSM, 5295-5309.

- Dazard J-E., Hua Xu and J. S. Rao (2011). "R package MVR for Joint Adaptive Mean-Variance Regularization and Variance Stabilization." In JSM Proceedings, Section for Statistical Programmers and Analysts. Miami Beach, FL, USA: American Statistical Association IMS - JSM, 3849-3863.
- Dazard J-E. and J. S. Rao (2012). "Joint Adaptive Mean-Variance Regularization and Variance Stabilization of High Dimensional Data." Comput. Statist. Data Anal. 56(7):2317-2333.

target.diagnostic

Function for Plotting Summary Target Moments Diagnostic Plots

## **Description**

Plot comparative distribution densities of means and standard deviations of the data before and after Mean-Variance Regularization to check for location shifts between observed first and second moments and their expected target values under a target centered homoscedastic model.

Plot comparative QQ scatterplots to look at departures between observed distributions of first and second moments of the MVR-transformed data and their theoretical distributions assuming independence and normality of all the variables.

## Usage

### **Arguments**

obj	Object of class "MVR" returned by mvr.
title	Title of the plot. Defaults to "Target Moments Diagnostic Plots".
device	Graphic display device in {NULL, "PS", "PDF"}. Defaults to NULL (standard output screen). Currently implemented graphic display devices are "PS" (Postscript) or "PDF" (Portable Document Format).
file	File name for output graphic. Defaults to "Target Moments Diagnostic Plots".
path	Absolute path (without final (back)slash separator). Defaults to working directory path.

horizontal Logical scalar. Orientation of the printed image. Defaults to FALSE, that is potrait orientation.

width Numeric scalar. Width of the graphics region in inches. Defaults to 8.5.

Numeric scalar. Width of the graphics region in inches. Defaults to 8.5.

Numeric scalar. Height of the graphics region in inches. Defaults to 6.5.

... Generic arguments passed to other plotting functions.

#### **Details**

The plots of the density distribution of means and standard deviations checks that the distributions of means and standard deviations of the MVR-transformed data have correct target first moments, i.e. with mean  $\sim 0$  and mean  $\sim 1$ . The expected target mean and standard deviation are shown in red (before and) after MVR-transformation. Caption shows the p-values from the parametric two-sample two-sided t-tests for the equality of parameters to their expectations (assuming normality since usually sample sizes are large :  $p \gg 1$ , or a relative robustness to moderate violations of the normality assumption).

In the general case, the variables are not normally distributed and not even independent and identically distributed before and after MVR-transformation. Therefore, the distributions of untransformed first and second moments usually differ from their respective theoretical null distributions,

i.e., from  $N(0,\frac{1}{n})$  for the means and from  $\sqrt{\frac{\chi^2_{n-G}}{n-G}}$  for the standard deviations, where G denotes the number of sample groups (see *Dazard*, *J-E. and J. S. Rao (2012)* for more details). Also, the observed distributions of transformed first and second moments are unknown. This is reflected in the QQ plots, where theoretical and empirical quantiles do not necessarily align with each other. Caption shows the p-values from the nonparametric two-sample two-sided Kolmogorov-Smirnov tests of the null hypothesis that a parameter distribution differs from its theoretical distribution. Each black dot represents a variable. The red solid line depicts the interquartile line, which passes through the first and third quartiles.

Option file is used only if device is specified (i.e. non NULL).

## Value

None. Displays the plots on the chosen device.

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#### Note

End-user function.

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### References

Dazard J-E. and J. S. Rao (2010). "Regularized Variance Estimation and Variance Stabilization of High-Dimensional Data." In JSM Proceedings, Section for High-Dimensional Data Analysis and Variable Selection. Vancouver, BC, Canada: American Statistical Association IMS - JSM, 5295-5309.

- Dazard J-E., Hua Xu and J. S. Rao (2011). "R package MVR for Joint Adaptive Mean-Variance Regularization and Variance Stabilization." In JSM Proceedings, Section for Statistical Programmers and Analysts. Miami Beach, FL, USA: American Statistical Association IMS - JSM, 3849-3863.
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#### See Also

justvsn (R package **vsn**) Variance stabilization and calibration for microarray data. loess (R package **stats**) Fit a polynomial surface determined by one or more numerical predictors, using local fitting.

## **Examples**

```
## Not run:
  # Loading the library and its dependencies
  library("MVR")
  library("RColorBrewer")
  # MVR package news
  MVR.news()
  # MVR package citation
  citation("MVR")
  # Loading of the Synthetic and Real datasets
  # (see description of datasets)
  data("Synthetic", "Real", package="MVR")
  ?Synthetic
  ?Real
  # Mean-Variance Regularization (Real dataset)
  # Multi-Group Assumption
  # Assuming unequal variance between groups
  # Without cluster usage
```

```
nc.min <- 1
   nc.max <- 30
   probs <- seq(0, 1, 0.01)
   n <- 6
   GF \leftarrow factor(gl(n = 2, k = n/2, length = n),
              ordered = FALSE,
              labels = c("M", "S"))
   mvr.obj <- mvr(data = Real,</pre>
                block = GF,
                log = FALSE,
                nc.min = nc.min,
                nc.max = nc.max,
                probs = probs,
                B = 100,
                parallel = FALSE,
                conf = NULL,
                verbose = TRUE,
                seed = 1234)
   # Summary Target Moments Diagnostic Plots (Real dataset)
   # Multi-Group Assumption
   # Assuming unequal variance between groups
   target.diagnostic(obj = mvr.obj,
                   title = "Target Moments Diagnostic Plots
                   (Real - Multi-Group Assumption)",
                   device = NULL,
                   horizontal = FALSE,
                   width = 8.5,
                   height = 6.5)
## End(Not run)
```

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