

# Package ‘MVR’

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## Description

MVR is 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 ( $p \gg n$  paradigm), 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: (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 ( $\geq 2.15.0$ ), parallel, statmod

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**Repository** CRAN

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**LazyData** yes

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MVR-package

*Mean-Variance Regularization Package*


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## Description

MVR is 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 ( $p \gg n$  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:

1. NEWS

[MVR.news](#) **Function to display the NEWS file of the MVR package.**

2. 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. 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 REGULARIZED TESTS-STATISTICS FUNCTIONS

[mvr.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.

4. 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.

[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.

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 sample group variance.

A Synthetic dataset with  $n = 10$  observations (samples) and  $p = 200$  variables, where  $nvar = 40$  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

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Acknowledgments: This project was partially funded by the National Institutes of Health (P30-CA043703 to J-E.DAZARD).

#### References

- 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*

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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

```
cluster.diagnostic(obj,
                   title = "",
                   span = 0.75,
                   degree = 2,
                   family = "gaussian",
                   device = NULL,
                   file = "Cluster Diagnostic Plots")
```

### Arguments

obj	Object of class "mvr" returned by <a href="#">mvr</a> .
title	Title of the plot. Defaults to the empty string.
span	Span parameter of the <code>loess()</code> function (R package <b>stats</b> ), which controls the degree of smoothing. Defaults to 0.75.
degree	Degree parameter of the <code>loess()</code> 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 <code>loess stats</code> package.)
family	Family distribution in "gaussian", "symmetric" of the <code>loess()</code> function (R package <b>stats</b> ), 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 (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".

### 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 sub-routine 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/under-regularization 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  $\sqrt{\frac{\chi^2_{n-G}}{n-G}}$ , 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 `mvt.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.

### Note

End-user function.

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## References

- 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

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")

#####
# Loading of the Synthetic and Real datasets
# (see description of datasets)
#####
data("Synthetic", "Real", package="MVR")

#####
# 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 <- factor(gl(n = 2, k = n/2, len = n),
             ordered = FALSE,
             labels = c("M", "S"))
mvr.obj <- mvr(data = Real,
              block = GF,
              log = FALSE,
              nc.min = nc.min,
              nc.max = nc.max,
              probs = probs,
              B = 100,
              parallel = FALSE,
              conf = NULL,
              verbose = TRUE)
```

```

#####
# 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 = "PS")

#####
# Mean-Variance Regularization (Real dataset)
# Single-Group Assumption
# Assuming equal variance between groups
# Without cluster usage
#####
nc.min <- 1
nc.max <- 30
probs <- seq(0, 1, 0.01)
n <- 6
mvr.obj <- mvr(data = Real,
               block = rep(1,n),
               log = FALSE,
               nc.min = nc.min,
               nc.max = nc.max,
               probs = probs,
               B = 100,
               parallel = FALSE,
               conf = NULL,
               verbose = TRUE)

#####
# Summary Cluster Diagnostic Plots (Real dataset)
# Single-Group Assumption
# Assuming equal variance between groups
#####
cluster.diagnostic(obj = mvr.obj,
                   title = "Cluster Diagnostic Plots
                             (Real - Single-Group Assumption)",
                   span = 0.75,
                   degree = 2,
                   family = "gaussian",
                   device = NULL)

## End(Not run)

```



**Description**

Internal subroutine called by end-user `mvr` and `mvr.test` functions to represent the empty array, matrix, or vector of zero dimension or length. Often returned by expressions and functions whose value is undefined.

**Usage**

```
is.empty(x)
```

**Arguments**

x                    array, matrix or vector of any type.

**Details**

None

**Value**

logical scalar. Returns TRUE if its argument is empty and FALSE otherwise.

**Note**

Internal function not to be called by end-user.

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**References**

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**See Also**

`is.null` from R package **base**.

---

`is.valid`*Validation Subroutine to Test the Bootstrap Set of Indices*

---

**Description**

Internal subroutine called by end-user `mVRT.test` function to validate the bootstrap set of indices if a bootstrap test is undertaken in `mVRT.test`. Check that the bootstrapped indices of samples (from all-groups samples) are unique per sample group in a multiple sample group situation.

**Usage**

```
is.valid(x, def, ng)
```

**Arguments**

<code>x</code>	vector of bootstrap set of indices.
<code>def</code>	list of samples indices per sample group in original data.
<code>ng</code>	Positive integer scalar of the number of sample groups.

**Details**

None

**Value**

`ok` logical scalar, taking on value TRUE if valid and FALSE otherwise.

**Note**

Internal function not to be called by end-user.

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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.

## See Also

[mvert.test](#) Mean-Variance Regularized t-Test Statistic with Significance.

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km.clustering	<i>Wrapper Subroutine Around C Subroutine for 'K-means' Clustering Algorithm</i>
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---

## Description

Perform 'K-means' clustering on a data matrix.

## Usage

```
km.clustering(data, k, ns, maxiter)
```

## Arguments

data	numeric matrix of data where variables are by columns and samples to cluster are by rows.
k	Positive integer scalar of number of centroids to start with.
ns	Positive integer scalar of how many random seedings should be done.
maxiter	Positive integer scalar of maximum number of iterations in 'K-means' clustering algorithm (convergence criteria).

## Details

The 'K-means' clustering algorithm (current default implementation) is derived from *MacQueen, 1967*.

## Value

lwk	numeric scalar of Log-transformed within cluster dispersion statistic.
centers	numeric vector of cluster centers.
membership	numeric vector of cluster membership of each variable.
obj	Object of class similar to the one returned by "kmeans" in R package <b>stats</b> .

**Note**

Internal subroutine of [sim.dis](#), and [MeanVarReg](#), not to be called by end-user.

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**References**

- 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.
- MacQueen, J. (1967). "*Some methods for classification and analysis of multivariate observations.*" In Proceedings of the Fifth Berkeley Symposium on Mathematical Statistics and Probability, eds L. M. Le Cam and J. Neyman, pp. 281-297. Berkeley, CA: University of California Press.

**See Also**

- [sim.dis](#) Similarity Statistic.
- [MeanVarReg](#) Mean-Variance Regularization Core Function.
- [withinsumsq](#) Within-Cluster Sum of Squares Distances.
- [kmeans](#) (R package **stats**) for partition clustering in R.

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MeanVarReg

*Mean-Variance Regularization Core Subroutine*

---

**Description**

Core subroutine of [mvr](#) and [mvrt.test](#) functions for mean-variance regularization and variance stabilization, and the computation of regularized test-statistics. Returns optimal cluster configuration. Internal function called by [mvr](#) and internally by [mvrt](#).

**Usage**

```
MeanVarReg(data, nc.min, nc.max, probs, B, parallel, conf, verbose)
```

**Arguments**

<code>data</code>	numeric data matrix, where points to cluster are by rows (usually samples), or an object that can be coerced to such a matrix (such as a vector or a <code>data.frame</code> with all numeric entries). Missing values (NA), NotANumber values (NaN), or Infinite values (Inf) are not allowed.
<code>nc.min</code>	Positive integer scalar of the minimum number of clusters.
<code>nc.max</code>	Positive integer scalar of the maximum number of clusters.
<code>B</code>	Positive integer scalar of the number of Monte Carlo replicates of the inner loop of the sim statistic function.
<code>probs</code>	numeric vector of probabilities for quantile diagnostic plots.
<code>parallel</code>	logical scalar. Is parallel computing to be performed? Optional, defaults to FALSE.
<code>conf</code>	list of parameters for cluster configuration, passed from <code>mvr</code> or <code>mVRT.test</code> functions for parallel computing. Inputs for R package <b>parallel</b> function <code>makeCluster</code> (R package <b>parallel</b> ) for cluster setup. See details for usage.
<code>verbose</code>	logical scalar. Is the output to be verbose?

**Details**

See details in `mvr` and `mVRT.test`.

**Value**

<code>membership</code>	numeric vector of cluster membership of each variable
<code>nc</code>	Positive integer scalar of number of clusters found in optimal cluster configuration
<code>gap</code>	numeric vector of the similarity statistic values
<code>sde</code>	numeric vector of the standard errors of the similarity statistic values
<code>mu.quant</code>	numeric matrix $(nc.max - nc.min + 1) \times (\text{length}(probs))$ of quantiles of means
<code>sd.quant</code>	numeric matrix $(nc.max - nc.min + 1) \times (\text{length}(probs))$ of quantiles of standard deviations

**Note**

Internal function not to be called by end-user.

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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

- [mvr](#) Mean-Variance Regularization and Variance Stabilization.
- [mvrt.test](#) Mean-Variance Regularized t-Test Statistic with Significance.
- [mvrt](#) Mean-Variance Regularized t-test statistic.

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 merging.cluster

*Variable-Cluster Configuration Merging Subroutine*


---

## Description

Merging subroutine of variable-cluster configurations, determined for each group. Internal function called by [mvr](#) and internally by [mvrt.test](#). Takes as argument the cluster membership matrix for each variable by group, which is returned by the membership value of [MeanVarReg](#).

## Usage

```
merging.cluster(M)
```

## Arguments

M Cluster membership matrix for each variable by group, where variables are by rows, and groups by columns. Returned by the membership value of [MeanVarReg](#).

## Details

None

## Value

clus numeric vector representing the merged-clusters membership of each variable.

## Note

Internal function not to be called by end-user.

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**See Also**

- [mvr](#) Mean-Variance Regularization and Variance Stabilization.
- [mvr.t.test](#) Mean-Variance Regularized t-Test Statistic with Significance.
- [kmeans](#) (R package **stats**) for partition clustering in R.

---

mvr

*Function for Mean-Variance Regularization and Variance Stabilization*

---

**Description**

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

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)
```

## Arguments

<code>data</code>	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 such a matrix (such as a numeric vector or a <code>data.frame</code> with all numeric columns). Missing values (NA), NotANumber values (NaN) or Infinite values (Inf) are not allowed.
<code>block</code>	character or numeric vector or factor grouping/blocking variable of length the sample size. Defaults to single group situation (see details).
<code>tolog</code>	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.
<code>nc.min</code>	Positive integer scalar of the minimum number of clusters, defaults to 1
<code>nc.max</code>	Positive integer scalar of the maximum number of clusters, defaults to 30
<code>probs</code>	numeric vector of probabilities for quantile diagnostic plots. Defaults to <code>seq(0, 1, 0.01)</code> .
<code>B</code>	Positive integer scalar of the number of Monte Carlo replicates of the inner loop of the sim statistic function (see details).
<code>parallel</code>	logical scalar. Is parallel computing to be performed? Optional, defaults to FALSE.
<code>conf</code>	list of parameters for cluster configuration. Inputs for R package <b>parallel</b> function <code>makeCluster</code> (R package <b>parallel</b> ) for cluster setup. Optional, defaults to NULL. See details for usage.
<code>verbose</code>	logical scalar. Is the output to be verbose? Optional, defaults to TRUE.

## Details

Argument `block` is a vector or a factor grouping/blocking variable. It must be of length sample size with as many different character or numeric values as the number of levels or sample groups. It defaults to single group situation, i.e. under the assumption of equal variance between sample groups. All group sample sizes must be greater than 1, otherwise the program will stop.

Argument `B` is reset to `conf$cpus*ceiling(B/conf$cpus)` in case the cluster is used (i.e. `conf` is non NULL), where `conf$cpus` denotes the total number of CPUs to be used (see below).

Argument `nc.max` currently defaults to 30. We found in our hands 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 run a parallel session (and parallel RNG) of the MVR procedures (`parallel=TRUE`), argument `conf` is to be specified (i.e. non NULL). It must list the specifications of the following parameters for cluster configuration: "names", "cpus", "type", "homo", "verbose", "outfile". These match the arguments described in function `makeCluster` of the R package **parallel**. All fields are required to properly configure the cluster, except for "names" and "cpus", which are the values used alternatively in the case of a cluster of type "SOCK" (socket), or in the case of a cluster of type other than "SOCK" (socket), respectively.



- "names": names : character vector specifying the host names on which to run the job. Could default to a unique local machine, in which case, one may use the unique host name "local-host". Each host name can potentially be repeated to the number of CPU cores available on the corresponding machine.
- "cpus": spec : integer scalar specifying the total number of CPU cores to be used across the network of available nodes, counting the workernodes and masternode.
- "type": type : character vector specifying the cluster type ("SOCK", "PVM", "MPI").
- "homo": homogeneous : logical scalar to be set to FALSE for inhomogeneous clusters.
- "verbose": verbose : logical scalar to be set to FALSE for quiet mode.
- "outfile": outfile : character vector of the output log file name for the workernodes.

Note that the actual creation of the cluster, its initialization, and closing are all done internally. In addition, 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 function `makeCluster` (R package **parallel**) and/or <http://www.stat.uiowa.edu/~luke/R/cluster/cluster.html>).

### 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 <code>MeanVarReg</code> values.
block	Value of argument <code>block</code> .
tolog	Value of argument <code>tolog</code> .
nc.min	Value of argument <code>nc.min</code> .
nc.max	Value of argument <code>nc.max</code> .
probs	Value of argument <code>probs</code> .

### Note

End-user function.

### Author(s)

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- "Hua Xu, Ph.D." <huaxu77@gmail.com>
- "Alberto Santana, MBA." <ahs4@case.edu>

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Acknowledgments: This project was partially funded by the National Institutes of Health (P30-CA043703 to J-E.DAZARD).

## References

- 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*

## Examples

```

=====
# Loading the library and its dependencies
=====
library("MVR")

=====
# 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")

=====
# Mean-Variance Regularization (Synthetic dataset)
# Single-Group Assumption
# Assuming equal variance between groups
# Without cluster usage
=====
nc.min <- 1
nc.max <- 20
probs <- seq(0, 1, 0.01)
n <- 10
mvr.obj <- mvr(data = Synthetic,
               block = rep(1,n),
               tolog = FALSE,
               nc.min = nc.min,

```

```

        nc.max = nc.max,
        probs = probs,
        B = 100,
        parallel = FALSE,
        conf = NULL,
        verbose = TRUE)

## Not run:
#####
# Setup of a SOCKET cluster:
# With 1 masternode and 3 workernodes
# All hosts run identical setups
# Same number of core CPUs (8) per node
#####
masterhost <- Sys.getenv("HOSTNAME")
slavehosts <- c("compute-0-0", "compute-0-1", "compute-0-2")
nodes <- length(slavehosts) + 1
cpus <- 8
conf <- list("names" = c(rep(masterhost, cpus),
                          rep(slavehosts, cpus)),
            "cpus" = nodes * cpus,
            "type" = "SOCK",
            "homo" = TRUE,
            "verbose" = TRUE,
            "outfile" = "")

#####
# Setup of a PVM cluster (requires rpvm commands):
# With 1 masternode and 3 workernodes
# All hosts run identical setups
# Same number of core CPUs (8) per node
#####
if (.Platform$OS.type == "unix") {
  if (!is.loaded("rpvm")) {
    library("rpvm")
  }
}
masterhost <- Sys.getenv("HOSTNAME")
slavehosts <- c("compute-0-0", "compute-0-1", "compute-0-2")
nodes <- length(slavehosts) + 1
cpus <- 8
conf <- list("cpus" = nodes * cpus,
            "type" = "PVM",
            "homo" = TRUE,
            "verbose" = TRUE,
            "outfile" = "")
.PVM.start.pvmd(hosts = masterhost)
.PVM.addhosts(hosts = slavehosts)
#####
# Run:
# Mean-Variance Regularization (Real dataset)
# Multi-Group Assumption
# Assuming unequal variance between groups
#####

```

```

nc.min <- 1
nc.max <- 30
probs <- seq(0, 1, 0.01)
n <- 6
GF <- factor(gl(n = 2, k = n/2, len = n),
             ordered = FALSE,
             labels = c("M", "S"))
mvr.obj <- mvr(data = Real,
              block = GF,
              tolog = FALSE,
              nc.min = nc.min,
              nc.max = nc.max,
              probs = probs,
              B = 100,
              parallel = TRUE,
              conf = conf,
              verbose = TRUE)

#####
# If PVM cluster used (requires rpvm commands):
#####
.PVM.delhosts(hosts = slavehosts)
.PVM.delhosts(hosts = masterhost)
.PVM.halt()
#####

## End(Not run)

```

---

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.

### Note

End-user function.

**Author(s)**

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

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Acknowledgments: This project was partially funded by the National Institutes of Health (P30-CA043703 to J-E.DAZARD).

**References**

- 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.

---

mvert

*Mean-Variance Regularized t-Test Statistic Subroutine*


---

**Description**

Internal subroutine called by `mvert.test` for computing the mean-variance regularized test-statistic.

**Usage**

```
mvert(x, obj, lev, tab, ng, def, nc.min, nc.max, parallel, conf, verbose)
```

**Arguments**

x	Input matrix with variables in columns
obj	Object of class "mvr" returned by <code>mvr</code> .
lev	levels of the group/blocking factor used in <code>mvert.test()</code>
tab	numeric scalar of the number of samples per group
ng	numeric scalar of the number of sample groups
def	list of samples indices per sample group
nc.min	numeric scalar of the minimum number of clusters
nc.max	numeric scalar of the maximum number of clusters
parallel	Is parallel computing to be performed? Optional, defaults to FALSE.
conf	List of parameters for cluster configuration, passed from <code>mvert.test</code> function for parallel computing. Inputs for R package <b>parallel</b> function <code>makeCluster</code> (R package <b>parallel</b> ) for cluster setup. See details for usage.
verbose	Is the output to be verbose?

**Details**

See details in [mvrt.test](#).

**Value**

numeric scalar of the test statistic.

**Note**

Internal subroutine of [mvrt.test](#), not to be called by end-user.

**Author(s)**

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Acknowledgments: This project was partially funded by the National Institutes of Health (P30-CA043703 to J-E.DAZARD).

**References**

- 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**

[mvrt.test](#) Mean-Variance Regularized t-Test Statistic with Significance

---

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.test". Offers the option of parallel computation for improved efficiency.

**Usage**

```
mvr.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)
```

**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 such 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 <code>mvr</code> .
block	character or numeric vector or factor grouping/blocking variable of length the sample size. (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, <code>n.resamp</code> and <code>replace</code> 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 bootstrap (see details).
parallel	logical scalar. Is parallel computing to be performed? Optional, defaults to FALSE.
conf	list of parameters for cluster configuration. Inputs for R package <b>parallel</b> function <code>makeCluster</code> (R package <b>parallel</b> ) for cluster setup. Optional, defaults to NULL. See details for usage.
verbose	logical scalar. Is the output to be verbose? Optional, defaults to TRUE.

## Details

Argument `block` is a vector or a factor grouping/blocking variable. It must be of length sample size with as many different character or numeric values as the number of levels or sample groups. The number of sample groups must be greater or equal to 2, and all group sample sizes must be greater than 1, otherwise the program will stop.

Argument `nc.max` currently defaults to 30. We found in our hands 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.

Argument `n.resamp` is reset to `conf$cpus*ceiling(n.resamp/conf$cpus)` in case the cluster is used (i.e. `conf` is non NULL), where `conf$cpus` denotes the total number of CPUs to be used (see below).

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.

To run a parallel session (and parallel RNG) of the MVR procedures (`parallel=TRUE`), argument `conf` is to be specified (i.e. non NULL). It must list the specifications of the following parameters for cluster configuration: "names", "cpus", "type", "homo", "verbose", "outfile". These match the arguments described in function `makeCluster` of the R package **parallel**. All fields are required to properly configure the cluster, except for "names" and "cpus", which are the values used alternatively in the case of a cluster of type "SOCK" (socket), or in the case of a cluster of type other than "SOCK" (socket), respectively.

- "names": `names` : character vector specifying the host names on which to run the job. Could 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 corresponding machine.
- "cpus": `spec` : integer scalar specifying the total number of CPU cores to be used across the network of available nodes, counting the workernodes and masternode.
- "type": `type` : character vector specifying the cluster type ("SOCK", "PVM", "MPI").
- "homo": `homogeneous` : logical scalar to be set to FALSE for inhomogeneous clusters.
- "verbose": `verbose` : logical scalar to be set to FALSE for quiet mode.
- "outfile": `outfile` : character vector of the output log file name for the workernodes.

Note that the actual creation of the cluster, its initialization, and closing are all done internally. In addition, 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 function `makeCluster` (R package **parallel**) and/or <http://www.stat.uiowa.edu/~luke/R/cluster/cluster.html>).

In case p-values are desired (`pval=TRUE`), the use of the 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.

### Note

End-user function.

### Author(s)

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Acknowledgments: This project was partially funded by the National Institutes of Health (P30-CA043703 to J-E.DAZARD).

### References

- 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")

#####
# 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")

#####
# 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
#####
nc.min <- 1
nc.max <- 20
probs <- seq(0, 1, 0.01)
n <- 10
GF <- factor(gl(n = 2, k = n/2, len = n),
             ordered = FALSE,
             labels = c("G1", "G2"))
mvr.obj <- mvr(data = Synthetic,
              block = GF,
              tolog = FALSE,
              nc.min = nc.min,
              nc.max = nc.max,
              probs = probs,
              B = 100,
              parallel = FALSE,
              conf = NULL,
              verbose = TRUE)
mvrt.obj <- mvrt.test(obj = mvr.obj,
                    pval = FALSE,
                    parallel = FALSE,
                    conf = NULL,
                    verbose = TRUE)

```

```

## Not run:
#####
# If setup of a SOCKET cluster:
# With 1 masternode and 3 workernodes
# All hosts run identical setups
# Same number of core CPUs (8) per node
#####
masterhost <- Sys.getenv("HOSTNAME")
slavehosts <- c("compute-0-0", "compute-0-1", "compute-0-2")
nodes <- length(slavehosts) + 1
cpus <- 8
conf <- list("names" = c(rep(masterhost, cpus),
                          rep(slavehosts, cpus)),
            "cpus" = nodes * cpus,
            "type" = "SOCK",
            "homo" = TRUE,
            "verbose" = TRUE,
            "outfile" = "")

#####
# If setup of a PVM cluster (requires rpvm commands):
# With 1 masternode and 3 workernodes
# All hosts run identical setups
# Same number of core CPUs (8) per node
#####
if (.Platform$OS.type == "unix") {
  if (!is.loaded("rpvm")) {
    library("rpvm")
  }
}
masterhost <- Sys.getenv("HOSTNAME")
slavehosts <- c("compute-0-0", "compute-0-1", "compute-0-2")
nodes <- length(slavehosts) + 1
cpus <- 8
conf <- list("cpus" = nodes * cpus,
            "type" = "PVM",
            "homo" = TRUE,
            "verbose" = TRUE,
            "outfile" = "")

.PVM.start.pvmd(hosts = masterhost)
.PVM.addhosts(hosts = slavehosts)
#####
# Mean-Variance Regularization (Real dataset)
# Multi-Group Assumption
# Assuming unequal variance between groups
#####
nc.min <- 1
nc.max <- 30
probs <- seq(0, 1, 0.01)
n <- 6
GF <- factor(gl(n = 2, k = n/2, len = n),
            ordered = FALSE,
            labels = c("M", "S"))

```

```

mvr.obj <- mvr(data = Real,
              block = GF,
              tolog = FALSE,
              nc.min = nc.min,
              nc.max = nc.max,
              probs = probs,
              B = 100,
              parallel = TRUE,
              conf = conf,
              verbose = TRUE)

#=====
# 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(obj = mvr.obj,
                    pval = TRUE,
                    replace = FALSE,
                    n.resamp = 100,
                    parallel = TRUE,
                    conf = conf,
                    verbose = TRUE)

#=====
# If PVM cluster used (requires rpvm commands):
#=====
.PVM.delhosts(hosts = slavehosts)
.PVM.delhosts(hosts = masterhost)
.PVM.halt()
#=====

## 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

```

normalization.diagnostic(obj,
                        title = "",
                        pal,
                        device = NULL,
                        file = "Normalization Diagnostic Plots")

```

## Arguments

obj	Object of class "mvr" returned by <code>mvr</code> .
title	Title of the plot. Defaults to the empty string.
pal	Color palette.
device	Graphic display device in {NULL, "PS", "PDF"}. Defaults to NULL (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".

## 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.

## Note

End-user function.

## Author(s)

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- "Hua Xu, Ph.D." <huaxu77@gmail.com>
- "Alberto Santana, MBA." <ahs4@case.edu>

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Acknowledgments: This project was partially funded by the National Institutes of Health (P30-CA043703 to J-E.DAZARD).

## References

- 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 libraries
#####
library("MVR")
library("RColorBrewer")

#####
# 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 <- factor(gl(n = 2, k = n/2, len = n),
             ordered = FALSE,
             labels = c("M", "S"))
mvr.obj <- mvr(data = Real,
              block = GF,
              log = FALSE,
              nc.min = nc.min,
              nc.max = nc.max,
              probs = probs,
              B = 100,
              parallel = FALSE,
              conf = NULL,
              verbose = TRUE)

#####
# 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 = "PS")

#####
# Mean-Variance Regularization (Real dataset)
# Single-Group Assumption
# Assuming equal variance between groups
# Without cluster usage
#####
nc.min <- 1
nc.max <- 30
probs <- seq(0, 1, 0.01)

```

```

n <- 6
mvr.obj <- mvr(data = Real,
               block = rep(1,n),
               log = FALSE,
               nc.min = nc.min,
               nc.max = nc.max,
               probs = probs,
               B = 100,
               parallel = FALSE,
               conf = NULL,
               verbose = TRUE)

#####
# Summary Normalization Stabilization Diagnostic Plots (Real dataset)
# Single-Group Assumption
# Assuming equal variance between groups
#####
normalization.diagnostic(obj = mvr.obj,
                        title = "Normalization Diagnostic Plots
                                (Real - Single-Group Assumption)",
                        pal = brewer.pal(n=11, name="RdYlGn"),
                        device = NULL)

## End(Not run)

```

---

pooled.mean

*Pooled Group Sample Mean Subroutine*


---

## Description

Internal subroutine called by end-user function `mvr` and internally by `MeanVarReg` subroutine.

## Usage

```
pooled.mean(x, block)
```

## Arguments

<code>x</code>	numeric vector or matrix with variables in columns.
<code>block</code>	vector or factor grouping/blocking variable. Must Have length equal to the sample size. All group sample sizes must be greater than 1.

## Details

If `block` describes a unique sample group, ordinary sample mean will be computed.

**Value**

numeric vector of size the dimensionality where each entry is the variable-wise pooled group sample mean.

**Note**

Internal function not to be called by end-user.

**Author(s)**

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- "Hua Xu, Ph.D." <huaxu77@gmail.com>
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Maintainer: "Jean-Eudes Dazard, Ph.D." <jxd101@case.edu>

Acknowledgments: This project was partially funded by the National Institutes of Health (P30-CA043703 to J-E.DAZARD).

**References**

- 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**

- [pooled.mean](#) Pooled group sample mean
- [mvr](#) Mean-Variance Regularization and Variance Stabilization.
- [MeanVarReg](#) Mean-Variance Regularization Core Function.

---

pooled.sd

*Pooled Group Sample Standard Deviation Subroutine*

---

**Description**

Internal subroutine called by end-user function [mvr](#) and internally by [MeanVarReg](#) subroutine.

**Usage**

```
pooled.sd(x, block)
```



**Arguments**

- |       |  |
|-------|--|
| x     | numeric vector or matrix with variables in columns.  |
| block | vector or factor grouping/blocking variable. Must Have length equal to the sample size. All group sample sizes must be greater than 1. |

**Details**

If block describes a unique sample group, ordinary sample standard deviation will be computed.

**Value**

numeric vector of size the dimensionality where each entry is the variable-wise pooled group sample standard deviation.

**Note**

Internal function not to be called by end-user.

**Author(s)**

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Maintainer: "Jean-Eudes Dazard, Ph.D." <jxd101@case.edu>

Acknowledgments: This project was partially funded by the National Institutes of Health (P30-CA043703 to J-E.DAZARD).

**References**

- 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**

- [pooled.mean](#) Pooled group sample mean
- [mvr](#) Mean-Variance Regularization and Variance Stabilization.
- [MeanVarReg](#) Mean-Variance Regularization Core Function.

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 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**

Real

**Format**

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

**Author(s)**

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Acknowledgments: This project was partially funded by the National Institutes of Health (P30-CA043703 to J-E.DAZARD).

**Source**

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

**References**

- 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.

---

sim.dis	<i>Similarity Statistic Subroutine</i>
---------	--

---

### Description

Internal subroutine called by [MeanVarReg](#) subroutine. Computes similarity statistic with sampling variability under a standard Gaussian reference distribution. Offers parallel computation option for computational efficiency.

### Usage

```
sim.dis(data, k, B, parallel, conf, verbose)
```

### Arguments

data	Standardized numeric data matrix, where points to cluster are by rows (usually samples), or an object that can be coerced to such a matrix (such as a vector or a data.frame with all numeric entries). Missing values are not allowed. NaN or Inf are not allowed.
k	Positive integer scalar of the fixed number of clusters.
B	Positive integer scalar of the number of Monte Carlo replicates of the inner loop of the gap statistic function.
parallel	logical scalar. Is parallel computing to be performed? Optional, defaults to FALSE.
conf	list of parameters for cluster configuration, passed from <a href="#">MeanVarReg</a> subroutine for parallel computing. Inputs for R package <b>parallel</b> function <code>makeCluster</code> (R package <b>parallel</b> ) for cluster setup. See details for usage.
verbose	logical scalar. Is the output to be verbose?

### Details

See details in [mvr](#) or [mvrt.test](#).

### Value

gapk	numeric scalar of the similarity statistic value.
sk	numeric scalar of the standard error of the similarity statistic value.

### Note

Internal subroutine of [MeanVarReg](#), not to be called by end-user.

**Author(s)**

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Acknowledgments: This project was partially funded by the National Institutes of Health (P30-CA043703 to J-E.DAZARD).

**References**

- 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**

- [MeanVarReg](#) Mean-Variance Regularization Core Function.
- [withinsumsq](#) Within-Cluster Sum of Squares Distances.

---

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**

```
stabilization.diagnostic(obj,  
                          title = "",  
                          span = 0.5,  
                          degree = 2,  
                          family = "gaussian",  
                          device = NULL,  
                          file = "Stabilization Diagnostic Plots")
```

**Arguments**

obj	Object of class "mvr" returned by <code>mvr</code> .
title	Title of the plot. Defaults to the empty string.
span	Span parameter of the <code>loess()</code> function (R package <b>stats</b> ), which controls the degree of smoothing. Defaults to 0.75.
degree	Degree parameter of the <code>loess()</code> 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 <code>loess stats</code> package.)
family	Family distribution in "gaussian", "symmetric" of the <code>loess()</code> function (R package <b>stats</b> ), used for local fitting . If "gaussian" fitting is by least-squares, and "symmetric" a re-descending M estimator is used with Tukey's biweight function.
device	Graphic display device in {NULL, "PS", "PDF"}. Defaults to NULL (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".

**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).

**Value**

None. Displays the plots on the chosen device.

**Note**

End-user function.

**Author(s)**

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Maintainer: "Jean-Eudes Dazard, Ph.D." <jxd101@case.edu>

Acknowledgments: This project was partially funded by the National Institutes of Health (P30-CA043703 to J-E.DAZARD).

## References

- 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 **vs**n) 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")

#####
# Loading of the Synthetic and Real datasets
# (see description of datasets)
#####
data("Synthetic", "Real", package="MVR")

#####
# 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 <- factor(gl(n = 2, k = n/2, len = n),
             ordered = FALSE,
             labels = c("M", "S"))
mvr.obj <- mvr(data = Real,
              block = GF,
              log = FALSE,
              nc.min = nc.min,
              nc.max = nc.max,
              probs = probs,
              B = 100,
              parallel = FALSE,
              conf = NULL,
              verbose = TRUE)
```

```
#####  
# 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",  
                          device = "PS")  
  
#####  
# Mean-Variance Regularization (Real dataset)  
# Single-Group Assumption  
# Assuming equal variance between groups  
# Without cluster usage  
#####  
nc.min <- 1  
nc.max <- 30  
probs <- seq(0, 1, 0.01)  
n <- 6  
mvr.obj <- mvr(data = Real,  
               block = rep(1,n),  
               log = FALSE,  
               nc.min = nc.min,  
               nc.max = nc.max,  
               probs = probs,  
               B = 100,  
               parallel = FALSE,  
               conf = NULL,  
               verbose = TRUE)  
  
#####  
# Summary Stabilization Diagnostic Plots (Real dataset)  
# Single-Group Assumption  
# Assuming equal variance between groups  
#####  
stabilization.diagnostic(obj = mvr.obj,  
                          title = "Stabilization Diagnostic Plots  
                          (Real - Single-Group Assumption)",  
                          span = 0.75,  
                          degree = 2,  
                          family = "gaussian",  
                          device = NULL)  
  
## End(Not run)
```

---

Synthetic

*Multi-Groups Synthetic Dataset*

---

### Description

Generation of a synthetic dataset with  $n=10$  observations (samples) and  $p = 200$  variables, where  $nvar = 40$  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

Synthetic

### Format

A numeric matrix containing  $n = 10$  observations (samples) by rows and  $p = 200$  variables by columns, named  $v_1, \dots, v_p$ . Samples are balanced ( $n_1 = 5, n_2 = 5$ ) between the two groups ( $G_1, G_2$ ). Compressed Rda data file.

### Author(s)

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

Maintainer: "Jean-Eudes Dazard, Ph.D." <jxd101@case.edu>

Acknowledgments: This project was partially funded by the National Institutes of Health (P30-CA043703 to J-E.DAZARD).

### Source

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

### References

- 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	<i>Function for Plotting Summary Target Moments Diagnostic Plots</i>
-------------------	--

---

## 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

```
target.diagnostic(obj,
                  title = "",
                  device = NULL,
                  file = "Target Moments Diagnostic Plots")
```

## Arguments

obj	Object of class "mvr" returned by <code>mvr</code> .
title	Title of the plot. Defaults to the empty string.
device	Graphic display device in {NULL, "PS", "PDF"}. Defaults to NULL (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".

## 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  $\sqrt{\frac{\chi_{n-G}^2}{n-G}}$  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.

### Note

End-user function.

### Author(s)

- "Jean-Eudes Dazard, Ph.D." <jxd101@case.edu>
- "Hua Xu, Ph.D." <huaxu77@gmail.com>
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Maintainer: "Jean-Eudes Dazard, Ph.D." <jxd101@case.edu>

Acknowledgments: This project was partially funded by the National Institutes of Health (P30-CA043703 to J-E.DAZARD).

### References

- 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 **vs**n) 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")

#####
# Loading of the Synthetic and Real datasets
# (see description of datasets)
#####
```

```

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

#=====
# 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 <- factor(gl(n = 2, k = n/2, len = n),
             ordered = FALSE,
             labels = c("M", "S"))
mvr.obj <- mvr(data = Real,
              block = GF,
              log = FALSE,
              nc.min = nc.min,
              nc.max = nc.max,
              probs = probs,
              B = 100,
              parallel = FALSE,
              conf = NULL,
              verbose = TRUE)

#=====
# 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 = "PS")

#=====
# Mean-Variance Regularization (Real dataset)
# Single-Group Assumption
# Assuming equal variance between groups
# Without cluster usage
#=====
nc.min <- 1
nc.max <- 30
probs <- seq(0, 1, 0.01)
n <- 6
mvr.obj <- mvr(data = Real,
              block = rep(1,n),
              log = FALSE,
              nc.min = nc.min,
              nc.max = nc.max,
              probs = probs,
              B = 100,

```

```

parallel = FALSE,
conf = NULL,
verbose = TRUE)

#=====
# Summary Target Moments Diagnostic Plots (Real dataset)
# Single-Group Assumption
# Assuming equal variance between groups
#=====
target.diagnostic(obj = mvr.obj,
                  title = "Target Moments Diagnostic Plots
(Real - Single-Group Assumption)",
                  device = NULL)

## End(Not run)

```

---

withinsumsq

*Within-Cluster Sum of Squares Distances Subroutine*


---

### Description

Wrapping subroutine around internal C subroutine for returning Monte-Carlo replicates of within-cluster sum of squares distances for a given number of clusters and under a standard Gaussian reference distribution.

### Usage

```
withinsumsq(n, p, B, k)
```

### Arguments

n	Positive integer scalar of the number of rows in the data matrix (where points to cluster are by rows (usually samples)).
p	Positive integer scalar of the number of columns in the data matrix (where variables are by columns).
k	Positive integer scalar of the fixed number of clusters.
B	Positive integer scalar of the number of Monte Carlo replicates of the inner loop of the gap statistic function.

### Details

None

### Value

lWk.mc	numeric B-vector of Monte Carlo replicates of within-cluster sum of squares.
--------	--

**Note**

Internal subroutine of `sim.dis`, not to be called by end-user.

**Author(s)**

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

Maintainer: "Jean-Eudes Dazard, Ph.D." <jxd101@case.edu>

Acknowledgments: This project was partially funded by the National Institutes of Health (P30-CA043703 to J-E.DAZARD).

**References**

- 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**

`sim.dis` Similarity Statistic.

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