# Package 'geva'

## January 20, 2021

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## R topics documented:

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geva.cluster

GEVA Cluster Analysis

#### **Description**

Performs a cluster analysis from summarized data.

#### Usage

```
geva.cluster(
    sv,
    cluster.method = options.cluster.method,
    cl.score.method = options.cl.score.method,
    resolution = 0.3,
    distance.method = options.distance,
    ...,
    grouped.return = FALSE
)

options.cluster.method
# c("hierarchical", "density", "quantiles")

options.cl.score.method
# c("auto", "hclust.height", "density", "centroid")

options.distance
# c("euclidean", "manhattan")
```

#### **Arguments**

sv a numeric SVTable object (usually GEVASummary) cluster.method character, one of the main grouping methods (see 'Details') cl.score.method

character, method used to calculate the cluster scores for each point. Ignored if cluster.method is quantiles

resolution

numeric (0 to 1), used as a "zoom" parameter for cluster detection. A zero value returns the minimum number of clusters that can detected by the cluster.method, while 1 returns the maximum amount of clusters. Ignored if cluster.method is quantiles

distance.method

character, two-point distance calculation method. Options are "eucludian" or "manhattan" distances

further arguments passed to geva.dcluster(), geva.hcluster(), or geva.quantiles(). In addition, the following arguments are accepted:

- eps: numeric, defines the *epsilon* coefficient for density clustering (see 'Details')
- mink.p: numeric, parameter for the Minkowsky metric used in hierarchial clustering. Used as the p argument for fastcluster::hclust.vector()
- verbose : logical, whether to print the current progress (default is TRUE)

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grouped.return logical, whether to concatenate the clustered and summarized data into a single object

#### **Details**

The cluster.method determines which grouping subroutine is used to classify the summarized data points based on distance and partitioning. Each option has their equivalent functions that can be called directly: "density" uses <code>geva.dcluster()</code>; "hierarchical" uses <code>geva.hcluster()</code>; and "quantiles" calls <code>geva.quantiles()</code>. However, this wrapper function can also be used to join <code>GEVASummary</code> and <code>GEVAGroupSet</code> objects into a single <code>GEVAGroupedSummary</code> object by setting <code>grouped.return</code> to <code>TRUE</code>.

The cl.score.method argument defines how scores are calculated for each SV point (row in sv) that was assigned to a cluster, (i.e., excluding non-clustered points). If specified as "auto", the parameter will be selected based on the cluster.method: "density" (rate of neighbor points) for the density method; and "hclust.height" (local hierarchy height) for the hierarchical method. The "centroid" method calculates the scores based on the proportional distance between each point to its cluster's centroid. Note that the cl.score.method argument is ignored if cluster.method is "quantiles", since quantile scores are always based on their local centroid distances.

The resolution value is a more accessible way to define the cluster separation threshold used in density and hierarchical clustering methods. Density clusters uses an *epsilon* value that represents the minimum distance of separation, whereas hierarchical clusters are defined by cutting the hierarchy tree wherever there is a minimum distance between two hierarchies. In this sense, resolution translates a value between 0 and 1 to propotional value for *epsilon* or hierarchical height (depending on the cluster.method) that would result in the least number of possible clusters for 0 and the highest number for 1. Nevertheless, if *epsilon* is specified as eps in the optinal arguments, its value is used and resolution is ignored.

#### Value

This function produces a GEVAGroupSet-derived object, particularly a GEVACluster for the "hierarchical" and "density" cluster methods or a GEVAQuantiles for the "quantiles" method.

However, if grouped.return is TRUE and sv is a GEVASummary object, the produced GEVAGroupSet data will be concatenated to the input and returned as a GEVAGroupedSummary

#### See Also

```
Other geva.cluster: geva.dcluster(), geva.hcluster(), geva.quantiles()
```

#### **Examples**

```
## Cluster analysis from a randomly generated input

# Preparing the data
ginput <- geva.ideal.example()  # Generates a random input example
gsummary <- geva.summarize(ginput)  # Summarizes with the default parameters

# Hierarchical clustering
gclust <- geva.cluster(gsummary, cluster.method="hierarchical")
plot(gclust)

# Density clustering
gclust <- geva.cluster(gsummary, cluster.method="density")
plot(gclust)</pre>
```

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geva.dcluster

GEVA Density Clustering

## **Description**

Performs a density cluster analysis from summarized data.

## Usage

```
geva.dcluster(
   sv,
   resolution = 0.3,
   dcluster.method = options.dcluster.method,
   cl.score.method = options.cl.score.method,
   minpts = 2,
   ...,
   eps = NA_real_,
   include.raw.results = FALSE
)

options.dcluster.method
# c("dbscan", "optics")
```

#### **Arguments**

sv a numeric SVTable object (usually GEVASummary)

 $\mbox{resolution} \qquad \mbox{numeric (0 to 1), used as a "zoom" parameter for cluster detection. A zero value}$ 

returns the minimum number of clusters that can detected, while 1 returns the

maximum amount of detectable clusters. Ignored if eps is specified

dcluster.method

character, density-based method for cluster separation

 ${\tt cl.score.method}$ 

character, method used to calculate the cluster scores for each point. If "auto",

the "density" method is selected

minpts integer, minimum number of points required to form a cluster

... additional arguments. Accepts verbose (logical, default is TRUE) to enable or

disable printing the current progress

eps numeric, maximum neighborhood distance between points to be clustered

include.raw.results

logical, whether to attach intermediate results to the returned object

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#### **Details**

This function performs a density cluster analysis with the aid of implemented methods from the dbscan::dbscan package. The available methods for the dcluster.method arguments are "dbscan" and "options", which internally call dbscan::dbscan() and dbscan::optics(), respectively.

The resolution value is an accessible way to define the cluster separation threshold used in density clustering. The *DBSCAN* algorithm uses an *epsilon* value that represents the minimum distance of separation, and resolution translates a value between 0 and 1 to a propotional value within the acceptable range of *epsilon* values. This allows defining the rate of clusters from 0 to 1, which results in the least number of possible clusters for 0 and the highest number for 1. Nevertheless, if *epsilon* is specified as eps in the optinal arguments, its value is used and resolution is ignored.

The cl.score.method argument defines how scores are calculated for each SV point (row in sv) that was assigned to a cluster, (*i.e.*, excluding non-clustered points). If specified as "auto", the parameter will be selected based on the rate of neighbor points ("density").

If include.raw.results is TRUE, some additional data will be attached to the info slot of the returned GEVACluster objects, including the kNN tree generated during the intermediate steps.

#### Value

A GEVACluster object

#### Note

In density clustering, only the most dense points are clustered. For the unclustered points, the grouping value is set to NA.

#### See Also

```
Other geva.cluster: geva.cluster(), geva.hcluster(), geva.quantiles()
```

#### **Examples**

```
## Density clustering from a randomly generated input

# Preparing the data
ginput <- geva.ideal.example()  # Generates a random input example
gsummary <- geva.summarize(ginput)  # Summarizes with the default parameters

# Density clustering
gclust <- geva.dcluster(gsummary)
plot(gclust)

# Density clustering with slightly more resolution
gclust <- geva.dcluster(gsummary, resolution=0.35)
plot(gclust)</pre>
```

6 geva.finalize

geva.finalize

Concatenating GEVA calculations into the final results

#### **Description**

Merges the obtained information (Summarization, Clustering, and Quantiles), then applies the final steps to produce the classification results for the SV points (genes).

## Usage

```
geva.finalize(
   gsummary,
   ...,
   p.value = 0.05,
   p.val.adjust = options.factoring.p.adjust,
   constraint.factors = TRUE
)

options.factoring.p.adjust
# c("partial.quantiles", "holm", "hochberg", "hommel",
# "bonferroni", "BH", "BY", "fdr", "none")
```

#### **Arguments**

```
a GEVASummary object

Intermediate results produced from the gsummary object, such as clusters (GEVACluster), quantiles (GEVAQuantiles), or any other object inherited from GEVAGroupSet

p.value numeric (0 to 1), p-value cutoff used in the ANOVA procedures (factor analysis only)

p.val.adjust character, p-value correction method (factor analysis only). Possible values are: "partial.quantiles", "holm", "hochberg", "hommel", "bonferroni", "BH", "BY", "fdr", "none"

constraint.factors

logical. If TRUE, the S values are restricted to the range within the quantile centroids (factor analysis only)
```

## Details

In this procedure, the SV points (*i.e.*, each row in the GEVASummary object) are classified according to the detected quantiles (see geva.quantiles), whose results can be adjusted using other grouping analysis results such as clusters (see geva.cluster). To achieve the best statistical accuracy, both GEVAQuantiles and GEVACluster objects must be given in the . . . as optional arguments. If a GEVAQuantiles argument is not present, it is automatically calculated using the default parameters.

If multiple factors are present in the GEVASummary object (retrieved by factors(gsummary)), a factor analysis is also performed, giving two additional possible classifications (*factor-dependent* and *factor-specific*) besides the default ones (*similar*, *basal*, and *sparse*).

In factor analysis, an ANOVA is applied for each gene using Fisher's and Levene's tests to distinguish genes whose *logFC* (differential expression) variation is dependent or specific to the analyzed factors based on the p-value cutoff. The p.val.adjust argument defines how these p-values will

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be adjusted: by quantile separation between each factor ("partial.quantiles" method); or by one of the default methods listed in stats::p.adjust.methods.

The constraint.factors argument determines if the S values (summarized *logFC*) will be limited to the range between the quantile centroids during factor analysis. For example, if the quantile centroids were -0.90, 0.00, and 0.90 in the S axis, values such as -1.53 and 2.96 would be converted to -0.90 and 0.90, respectively. This constraint is particularly applied to avoid significative observations from ANOVA based on multiple degrees of differential expression.

In another example to illustrate the constraint of factors, given two sets of values: A = (-1.00, -1.10, 0.00, 0.20, 1.00, 1.15), and B = (0.00, 0.12, 1.11, 1.00, 1.95, 2.00), with the centroids located in C = (-0.90, 0.00, 0.90), and the factors F = (Cond1, Cond2, Cond2, Cond3, Cond3). If constraint factors is FALSE, both A and B are considered as significantly separated factors, whereas if TRUE, only A will present a significant separation, since in B the values 1.11, 1.00, 1.95, and 2.00 are converted to 0.90. In qualitative terms, if constraint factors is TRUE, all values above 0.90 are considered the same over-expressed values, ensuring that they will fit in the same degree of differential expression. Hence, in this example using the constrained values, B would not represent a significant separation between the factors Cond1, Cond2, and Cond3.

#### Value

A GEVAResults object, containing the entire set of results. The relevant genes can be retrieved using top.genes()

#### Note

To perform factor analysis, the following observations must be considered:

- The factors must be defined in the provided data. They can be retrieved using the factors
  accessor. If factors are not present or are entirelly composed by NA, they can be assigned
  through factors<- by providing a factor or character vector of the same length of the
  input columns;</li>
- Each factor must include two or more values, since the factor analysis is based on ANOVA and at least two values are needed to variance calculation;
- · Columns whose factor value is NA are not considered.

#### See Also

p.adjust.methods

#### **Examples**

```
## Finalizing example using a random generated input
ginput <- geva.ideal.example()  # Generates a random input (for testing purposes only)
gsummary <- geva.summarize(ginput)  # Summarizes the input
gquant <- geva.quantiles(gsummary)  # Calculates the quantiles
gclust <- geva.cluster(gsummary)  # Calculates the clusters
gresults <- geva.finalize(gsummary, gquant, gclust)  # Finishes the results
head(top.genes(gresults))  # Prints the final results
plot(gresults)  # Plots the final SV-plot</pre>
```

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geva.hcluster

GEVA Hierarchical Clustering

## **Description**

Performs a hierarchical cluster analysis from summarized data.

## Usage

```
geva.hcluster(
  SV,
  resolution = 0.3,
  hc.method = options.hc.method,
  hc.metric = options.hc.metric,
  cl.score.method = options.cl.score.method,
  include.raw.results = FALSE
)
options.hc.metric
# c("euclidean", "maximum", "manhattan", "canberra",
    "binary", "minkowski")
options.hc.method
# c("centroid", "median", "ward", "single")
```

## **Arguments**

a numeric SVTable object (usually GEVASummary) sv resolution numeric (0 to 1), used as a "zoom" parameter for cluster detection. A zero value returns the minimum number of clusters that can detected, while 1 returns the maximum amount of detectable clusters hc.method character, the agglomeration method to be used. Used as the method argument for fastcluster::hclust.vector() hc.metric character, the distance measure to be used. Used as the metric argument for fastcluster::hclust.vector() cl.score.method character, method used to calculate the cluster scores for each point. If "auto", the "hclust.height" method is selected additional arguments: • mink.p: numeric, parameter for the Minkowsky metric. Used as the p argument for fastcluster::hclust.vector()

• verbose : logical, whether to print the current progress (default is TRUE)

include.raw.results

logical, whether to attach intermediate results to the returned object

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#### **Details**

This function performs a hierarchical cluster analysis with the aid of implemented methods from the fastcluster::fastcluster package, particularly the fastcluster::hclust.vector() function. The available methods for the hc.method and hc.metric are described in the function's documentation page (see fastcluster::hclust.vector()).

The resolution value is an accessible way to define the cluster separation threshold used in hierarchical clustering. The algorithm produces a dendrogram-like hierarchy in which each level/node is separated by a distance (sometimes called "height") to the next level/node, and the resolution translates a value between 0 and 1 to a proportional value within the total hierarchy height. This allows defining the rate of clusters from 0 to 1, which results in the least number of possible clusters (usually two) for 0, and the highest number (approximately one cluster per point) for 1.

If include.raw.results is TRUE, some additional data will be attached to the info slot of the returned GEVACluster objects, including the kNN tree generated during the intermediate steps.

#### Value

A GEVACluster object

#### Note

In hierarchical clustering, all points are clustered. Therefore, setting resolution to 1 will result into one cluster per point, where the cluster analysis may become pointless (no pun intended).

#### See Also

```
Other geva.cluster: geva.cluster(), geva.dcluster(), geva.quantiles()
```

#### **Examples**

```
geva.ideal.example GEVA "Ideal" Example for Package Testing
```

## **Description**

Generates a random example of GEVAInput object that simulates an ideal analysis dataset. Used for testing purposes only.

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#### Usage

```
geva.ideal.example(probecount = 10000, nfactors = 3, colsperfactor = 3)
```

## **Arguments**

```
probecount integer, number of probes (i.e., table rows)

nfactors integer, number of factors (e.g., experimental groups)

colsperfactor integer, number of columns (e.g., experiments) per factor
```

#### Value

A GEVAInput object. The included tables are composed by probecount rows and nfactors \* colsperfactor columns

#### See Also

```
geva.summarize
```

## **Examples**

```
## "Ideal" input example
ginput <- geva.ideal.example()  # Generates a random example
gsummary <- geva.summarize(ginput) # Summarizes the generated data
plot(gsummary)  # Plots the summarized data</pre>
```

geva.input.correct GEVA Input Post-processing

## **Description**

Helper functions used to edit the contents from a GEVAInput.

## Usage

```
geva.input.correct(ginput, na.rm = TRUE, inf.rm = TRUE, invalid.col.rm = TRUE)

geva.input.filter(
    ginput,
    p.value.cutoff = 0.05,
    by.any = FALSE,
    na.val = 0,
    ...
)

geva.input.rename.rows(
    ginput,
    attr.column,
    dupl.rm.method = c("least.p.vals", "order")
)
```

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## **Arguments**

ginput	A GEVAInput object
na.rm	logical; if TRUE, removes all rows containing NA
inf.rm	logical; if TRUE, removes all rows containing infinite values (Inf or -Inf)
invalid.col.rm	$\log$ ical; if TRUE, searches for any column that is entirely composed by invalid values (according to the other arguments) and removes it before checking the rows
p.value.cutoff	numeric (0 to 1), the p-value cutoff. Rows containing values above this threshold are removed
by.any	logical, set to TRUE to delete the rows with at least one occurrence above the cutoff; or FALSE to delete only those rows in which all values are above the specified threshold
na.val	numeric, the replacement for NA values
•••	optional arguments. Accepts verbose (logical, default is TRUE) to enable or disable printing the progress $$
attr.column	character, target column with the values that will replace the current row names $% \left( 1\right) =\left( 1\right) \left( 1\right) $
dupl.rm.method	character, method to remove duplicate names. The possible options are:
	<ul> <li>"least.p.vals": Keeps the duplicate that contains the least sum of p-values</li> <li>"order": Keeps the first occurrence of the duplicate in the current row</li> </ul>
	order

#### Details

geva.input.correct corrects the numeric input data (values and weights), removing rows that include invalid values such as NA or infinite.

geva.input.filter attempts to select the most relevant part of the input data, removing rows containing p.values (1 - weights) above a specific threshold.

geva.input.rename.rows replaces the row names with a column from the feature table (see GEVAInput). The column name specified for attr.column must be included in the names(featureTable(ginput)). Any duplicates are removed according to the dupl.rm.method, and the selected duplicates are stored as a new column named "renamed\_id" inside the feature table from the returned object.

## Value

A modified GEVAInput object

## **Examples**

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```
print(nrow(ginput))
                       # Returns 1000
# Applies the correction (removes rows with NA's)
ginput <- geva.input.correct(ginput)</pre>
# After the correction:
                      # Returns less than 1000
print(nrow(ginput))
## ---
## geva.input.filter example
ginput <- geva.ideal.example(1000) # Generates a random input</pre>
# Before the filter:
print(nrow(ginput))
                        # Returns 1000
# Applies the filter
ginput <- geva.input.filter(ginput)</pre>
# After the filter:
                        # Returns less than 1000
print(nrow(ginput))
## ---
## geva.input.rename.rows example
ginput <- geva.ideal.example() # Generates a random input</pre>
# Renames to 'Symbol'
ginput <- geva.input.rename.rows(ginput,</pre>
                                 attr.column = "Symbol")
print(head(ginput))
                                 # The row names are set now as the gene symbols
```

geva.merge.input

GEVA Input Processing and Merge

## **Description**

Functions to read, load, and concatenate the experimental comparisons from the data input. This is the initial step to proceed with any GEVA analysis.

## Usage

```
geva.merge.input(
    ...,
    col.values = "logFC",
    col.pvals = "adj.P.Val",
    col.other = NULL
)

geva.read.tables(
    filenames = NULL,
    dirname = ".",
    col.values = "logFC",
    col.pvals = "adj.P.Val",
    col.other = NULL,
    ...,
    files.pattern = "\\.txt$",
    p.value.cutoff = 0.05,
    read.args = list()
```

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#### **Arguments**

multiple matrix or data. frame objects. At least two arguments are required for geva.merge.input, but it's optional for geva.read.tables. The optional arguments in geva. read. tables are also passed to its internal call to geva. merge. input and geva.input.filter.

In addition, the following optional arguments are accepted:

- na.val: (numeric) value between 0 and 1 used as replacement when a p-value column is not present (default is NA)
- use.regex: (logical) whether to match the column names using regular expressions (default is FALSE)
- verbose: (logical) whether to print the current loading and merge progress

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above this cutoff (i.e., no significant logFC) are removed after the final merge. Ignored if NA or NULL

## **Details**

read.args

The geva.merge.input function takes multiple tables as arguments (e.g., matrix or data.frame objects), extracts the logFC columns from each table and merges them into a single GEVAInput dataset.

list of additional arguments passed to utils::read.table

The column names are specified in the col.values and col.pvals arguments (character) and must correctly match the column names for logFC and p-value columns, respectively, in the inputs to be extracted. Multiple values for column names can also be specified as valid name possibilities if they differ among the tables.

The function geva.merge.input reads multiple tab-delimited text files containing, extracts the logFC columns from each table and merges into a single GEVAInput dataset.

#### Value

A GEVAInput object

## Note

The inclusion of p-value columns is not technically required, but strongly recommended as they improve the statistical accuracy in the summarization steps. If the p-value (or adjusted p-value) columns are present, their values are converted to weights by applying 1 -pvalue for each pvalue 14 geva.merge.input

element, otherwise an optional na.val optional argument can specified as replacement to the absent values (default is NA). Weights are used to accommodate the central logFC values towards the most significant observations and penalize potential statistical innacuracies.

## **Examples**

```
### EXAMPLE 1
## geva.merge.input example with three randomly generated tables
## (For demonstration purposes only)
# Number of rows
n <- 10000
# Random row (probe) names
probnms <- sprintf("PROBE_%s", 1:n)</pre>
# Random gene names (optional)
genenms <- paste0(sprintf("GENE_%s", 1:n), LETTERS[1:n %% (length(LETTERS)+1)])</pre>
# Random table 1
dt1 <- data.frame(row.names=probnms,</pre>
                  logfc=(rnorm(n, 0, sd=2) * rnorm(n, 0, sd=0.5)),
                   pvalues = runif(n, max=0.08),
                   genesymbol = genenms)
# Random table 2
dt2 <- data.frame(row.names=probnms,</pre>
                   logfc=(rnorm(n, 0, sd=2) * rnorm(n, 0, sd=0.5)),
                   pvalues = runif(n, max=0.08),
                   genesymbol = genenms)
# Random table 3
dt3 <- data.frame(row.names=probnms,</pre>
                  logfc=(rnorm(n, 0, sd=2) * rnorm(n, 0, sd=0.5)),
                   pvalues = runif(n, max=0.08),
                  genesymbol = genenms)
# Merges the three tables
ginput <- geva.merge.input(exp1=dt1, exp2=dt2, exp3=dt3,</pre>
                            col.values="logfc",
                            col.pvals="pvalues",
                            col.other="genesymbol")
# Prints the first rows from the merged table
print(head(ginput))
                                   # values
print(head(inputweights(ginput))) # weights
## Not run:
### EXAMPLE 2
## geva.read.tables example with three tab-delimited files
# Table file examples. Each one has 3 columns: "logfc", "pvalues", and "genesymbol"
# Replace it with your tab-delimited files (e.g. exported from limma's topTable)
fnames <- c("dt1.txt", "dt2.txt", "dt3.txt")</pre>
ginput <- geva.read.tables(fnames,</pre>
                            col.values="logfc",
```

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```
col.pvals="pvalues",
                            col.other="genesymbol")
# Prints the first rows from the merged table
print(head(ginput))
                                   # values
print(head(inputweights(ginput))) # weights
# ---
### EXAMPLE 3
## geva.read.tables example with tab-delimited files in a directory
# Directory name (replace it with a directory containing the table files)
dirnm <- "C:/User/robertplant123/Documents/R/gevaexamples"</pre>
# In this example, table files contain 3 columns: "logfc", "pvalues", and "genesymbol"
# Reads all txt files in the directory
ginput <- geva.read.tables(dirname=dirnm,</pre>
                           col.values="logfc",
                           col.pvals="pvalues",
                            col.other="genesymbol")
# (Optional step)
# Let's assume that all table file names start with "dt" and ends with the ".txt" extension,
# such as dt1.txt, dt2.txt and so on...
fname\_pattern \leftarrow c("^dt.+?\\) # Defines a RegEx pattern to find the files
\# Loads only files that match the file name pattern
ginput <- geva.read.tables(dirname=dirnm,</pre>
                           files.pattern=fname_pattern,
                           col.values="logfc",
                            col.pvals="pvalues",
                            col.other="genesymbol")
# Prints the first rows from the merged table
print(head(ginput))
                                   # values
print(head(inputweights(ginput))) # weights
## End(Not run)
```

geva.quantiles

GEVA Quantiles Detection Calculates the quantiles of a SVTable

## **Description**

**GEVA Quantiles Detection** 

Calculates the quantiles of a SVTable

Returns a vector with the supported methods of quantiles separation

## Usage

```
geva.quantiles(
   sv,
```

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```
quantile.method = options.quantiles,
  initial.thresholds = c(S = NA_real_, V = NA_real_),
  nq.s = 3L,
  nq.v = 2L,
  comb.score.fn = prod,
  ...
)

options.quantiles
# c("range.slice", "proportional", "density", "k.max.sd",
# "custom")
```

#### **Arguments**

sv a SVTable object (usually GEVASummary)

quantile.method

character, method to detect the initial quantile thresholds. Ignored if initial.thresholds is specified with no NA elements

initial.thresholds

named numeric vector with the threshold that delimits the initial quantile

nq.s integer, number of quantiles in S-axis (experimental, see 'Note')

ng.v integer, number of quantiles in V-axis (experimental, see 'Note')

comb. score.fn function applied to merge S and V score columns into a single column. The

function must require only one argument of numeric vector type and return a single numeric value. Examples include prod or mean

.. additional arguments include:

• qslice: numeric (0 to 1), the axis fraction used by "range.slice" and "density" methods (see 'Details'). Default is 0.25

- k: integer, neighbor points used by "density" and "k.max.sd" methods (see 'Details'). Default is 16
- verbose : logical, whether to print the current progress. Default is TRUE

#### **Details**

The quantile.method defines how the initial quantile (usually the one at the bottom center) is calculated. Each method has a specific way to estimate the first spatial delimiter, as described below:

- "range.slice" (**default**) Separation is set at the nearest point to a fraction of the spatial range. This fraction can be specified by the qslice optional argument (numeric, default is 0.25, or 25%);
- "density" Separation is set at the point with the most proportional density by k neighbor points to its current spatial fraction. This method uses the optional arguments qslice (numeric, default is 0.25, or 25%) for the desired spatial fraction, and k (numeric, default is 16) for the number of neighbor points;
- "k.max.sd" Separation is set at the point with the greatest standard deviation of distance to its *k* neighbor points. The number of neighbor points can be specified by the k optional argument (numeric, default is 16);

<sup>&</sup>quot;proportional" Separation is set at the exact axis division so that all quantiles have the size;

<sup>&</sup>quot;custom" Uses the values specified in the initial.thresholds argument.

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A custom initial separation point can be specified in the initial.thresholds as a numeric vector of two elements, where the first element refers to S axis and the second, to V axis. If one of the elements is NA, the initial quantile is calculated for that axis only. If both values are not NA, the quantile separation method is ignored and automatically set to "custom".

The nq.s and nq.v arguments determine the number of quantiles for the S and V axes, respectively. These parameters can be used to increase the number of possible partitions in the SV space, but their applicability is currently being tested (see 'Note').

The comb.score.fn is a function applied to the partial scores for each SV point to combine them into a single value. The result value is defined as the "quantile score" for a SV point. The function is applied iteratively to two-element numeric vectors.

#### Note

Customizing the number of quantiles by nq.s and nq.v is a **experimental feature** and the remaining analysis steps are mostly based on the default parameters for these arguments. Tests are being conducted to determine this feature's applicability for the next releases.

#### See Also

```
geva.cluster
```

```
Other geva.cluster: geva.cluster(), geva.dcluster(), geva.hcluster()
```

#### **Examples**

```
## Quantile detection from a randomly generated input
# Preparing the data
ginput <- geva.ideal.example()</pre>
                                     # Generates a random input example
gsummary <- geva.summarize(ginput) # Summarizes with the default parameters
# Default usage
gquants <- geva.quantiles(gsummary) # Detects the quantiles</pre>
plot(gquants)
                                     # Plots the quantiles
# Custom initial delimiters
gquants <- geva.quantiles(gsummary,</pre>
                           initial.thresholds = c(S=1.00, V=0.5))
plot(gquants)
                                     # Plots the quantiles
# Quantile detection using densities
gquants <- geva.quantiles(gsummary, quantile.method = 'density')</pre>
plot(gquants)
                                     # Plots the quantiles
```

geva.quick

All-In-One Function for GEVA Intermediate Procedures

## Description

Given a GEVAInput object, applies the geva.summarize(), geva.quantiles, geva.cluster, and geva.finalize in a single call. Optional arguments are passed to the internal calls of these functions.

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#### **Usage**

```
geva.quick(gobject, ...)
```

#### **Arguments**

```
gobject A GEVAInput, or any object that returns a GEVAInput upon calling inputdata(gobject) (e.g., GEVASummary or GEVAResults).

Optional arguments passed to geva.summarize(), geva.quantiles(), geva.cluster(), and geva.finalize()
```

#### **Details**

This function performs the summarization, quantile detection, and clustering of an input data, then merges the results together and, if applicable, performs a factor analysis. If the gobject is not a GEVAInput, it must provide a valid GEVAInput object when called by inputdata(gobject). Moreover, all parameters used in previous analysis will be taken into account. For instance, if gobject is a GEVASummary obtained by using variation.method='mad', the internal call to geva.summarize in this function will use variation.method='mad' as well, unless if another parameter for variation.method is specified in the . . . arguments.

Therefore, this function can be useful not only as a shortcut to analyze GEVAInput but also for parameter testing when applied to a GEVAResults object, since the previous parameters are reused, while the specified parameters are overriden.

#### **Examples**

```
## Basic usage using a random generated input
ginput <- geva.ideal.example()  # Generates a random input example</pre>
gresults <- geva.quick(ginput) # Performs the entire analysis (default parameters)</pre>
print(head(top.genes(gresults))) # Prints the results
plot(gresults)
                                       # Plots the final SV-plot
## Example with non-default parameters
ginput <- geva.ideal.example()</pre>
                                 # Generates a random input example
gresults <- geva.quick(ginput,</pre>
                        summary.method="median",
                        variation.method="mad",
                        quantiles.method="density",
                        cluster.method="density",
                        resolution=0.32)
print(head(top.genes(gresults))) # Prints the results
plot(gresults)
                                  # Plots the final SV-plot
```

geva.summarize

Summarizes the GEVAInput

## **Description**

Performs the summarization step by calculating the central points and variation estimates of *logFC* values from the input data.

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#### Usage

```
geva.summarize(
   ginput,
   summary.method = options.summary,
   variation.method = options.variation,
   ...
)

options.summary
# c("mean", "median")

options.variation
# c("sd", "var", "mad")
```

#### **Arguments**

```
ginput a GEVAInput object summary.method single character, method used to calculate the central (summarized) logFC values variation.method single character, method used to calculate the distribution degree (variation) of the logFC values ... additional arguments. Accepts verbose (logical, default is TRUE) to enable or disable printing the current progress
```

## **Details**

The options.summary refer to the available operations to calculate central logFC values (mean or median), whereas options.variation presents three functions to calculate logFC variation (sd: Standard Deviation; var: Variance; and mad: Median Absolute Deviation). Moreover, all those operations include a weighted counterpart applied using the weights table from the GEVAInput object.

#### Value

A GEVASummary object

#### See Also

```
base::mean(), stats::median()
stats::var(), stats::sd(), stats::mad()
```

#### **Examples**

```
## Summarization of a randomly generated input
ginput <- geva.ideal.example()  # Generates a random input example
gsummary <- geva.summarize(ginput) # Summarizes with the default parameters
plot(gsummary)  # Plots the summarized data</pre>
```

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GEVACluster-class

GEVA Clustering Results

## **Description**

The GEVACluster class represents the classification results from a cluster analysis. For each probe/gene, there is a assigned cluster among the g defined clusters.

This class inherits from GEVAGroupSet.

#### **Slots**

```
grouping factor (m elements, g levels), cluster assignment for each gene/probe
    (Inherited from GEVAGroupSet)

scores numeric vector (m elements) comprising a score value for each cluster assignment
    (Inherited from GEVAGroupSet)

ftable data.frame (m lines) with additional cluster assignment features
    (Inherited from GEVAGroupSet)

centroids numeric SVTable (g lines) with the S and V centroid coordinates for each cluster
    (Inherited from GEVAGroupSet)

offsets numeric SVTable (m lines) with the S and V coordinate offsets each gene/probe from its cluster centroid
    (Inherited from GEVAGroupSet)

info list of supplementary information
    (Inherited from GEVAGroupSet)
```

cluster.method character, method used in the cluster analysis (see geva.cluster)

#### Methods

(See also the inherited methods from GEVAGroupSet)

## **Dimension accessors**

lines (x, ...) Draws convex hulls around the clustered points

## Slot accessors

cluster.method(object) Gets the character from the cluster.method slot

GEVAGroupedSummary-class

GEVA Grouped Summary-Variation Table

## **Description**

The GEVAGroupedSummary class inherits the GEVASummary class and includes group analysis data (*e.g.*, clustering and quantile detection).

## **Slots**

## Methods

 ${\tt cluster.method(object)} \ \ {\tt Gets\ a\ character\ vector\ listing\ the\ cluster.method\ from\ each\ group\ set}$ 

#### **Dimension accessors**

lines(x, ...) Draws delimiters within quantiles and convex hulls around the clustered points

#### **Properties**

analysis.params(gobject) Returns a list of analysis parameters passed to geva.cluster to obtain this object

#### Slot accessors

```
groupsets(object) Gets the TypedList from the groupsetlist slot
quantiles(object) Gets the GEVAQuantiles, or NULL if not present
```

GEVAGroupSet-class

GEVA Grouping Results

#### **Description**

The GEVAGroupSet class represents the classification of summarized values from a SVTable, where each gene/probe has one assigned group among g defined groups. This is an abstract class. Inherits the GEVACluster and GEVAQuantiles classes.

#### **Slots**

grouping factor (m elements, g levels) used to group the genes/probes scores numeric vector (m elements) with the assigned grouping scores for each gene/probe ftable data.frame (m lines) with additional grouping features centroids numeric SVTable (g lines) with the S and V centroid coordinates for each group offsets numeric SVTable (m lines) with the S and V coordinate offsets each gene/probe from its group centroid info list of additional information

#### Methods

sv(object) Returns the numeric matrix in the SVTable from sv.data(object)

#### **Plotting**

color.values(x, point.col = NULL, ...) Gets the colors associated to the grouped data points. If not present, generates random group colors.

If point.col is a single character or an vector of the same length of data points, adjusts the color values to web RGBA

points(x, which, ..., classif) Draws the grouped points

## **Properties**

analysis.params(gobject) Returns a list of analysis parameters passed to geva.cluster to obtain this object

## Slot accessors

centroids(object) Gets the SVTable from the centroids slot
featureTable(object) Gets the data.frame from the ftable slot
groups(object) Gets the value from the groups slot
infolist(object, field, ...) Gets the list from the info slot.
 If field is a character, returns the element with the matching name(infolist(object)\$<field
 name>)
infolist(object) <- value Sets a value to the info slot
offsets(object) Gets the SVTable from the offsets slot
scores(object, group) Gets the value from the If slot. scores is a group name, returns only
 the scores from this group
sv.data(object) Returns a SVTable with the source SV coordinates</pre>

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GEVAInput-class

GEVA Input Data

#### **Description**

The GEVAInput class contains the initial data for GEVA usage. It stores numeric matrices of *logFC* values from differential expression comparison results. Options for calculations and summarizing are also included.

#### **Slots**

values numeric matrix (m\*n) of log-ratio values, usually logFC

weights numeric matrix (m\*n) of weighted values. If not defined, all weight values are equal to 1

factors factor (n elements) representing the grouping of the n columns. If not defined, all factors are equal to NA

ftable data.frame with m rows containing attribute columns associated to the features (e.g., probes or genes)

info list of supplementary information related to the input

#### Methods

#### **Dimension accessors**

dim(x) Gets the dimensions defined for both matrices in values and weights slots

dimnames(x) Gets a list with the row and column names.

Individual dimension names can also be accessed through rownames and colnames

 $dimnames(x) \leftarrow value$  Sets the list with the row and column names.

Individual dimension names can also be set using rownames<- and colnames<-

## **Properties**

analysis.params(gobject) Returns a list of analysis parameters passed to geva.merge.input or geva.read.tables to obtain this object

#### **Slot accessors**

factors(object) Gets the factor from the factors slot

factors(object) <- value Sets a value to the factors slot</pre>

featureTable(object) Gets the data.frame from the ftable slot

featureTable(object) <- value Sets a value to the ftable slot</pre>

infolist(object, field = NULL, ...) Gets the list from the info slot.

If field is a character, returns the element with the matching name (infolist(object) \$<field name>)

infolist(object) <- value Sets a value to the info slot</pre>

inputvalues(object) Gets the matrix from the values slot

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inputweights(object, normalized = FALSE) Gets the matrix from the weights slot.

If normalized is TRUE, returns the weights matrix in the normalized form

#### **Sub-slot accessors**

inputnames(object) Gets the input column names (same as colnames(object))

GEVAQuantiles-class

GEVA Quantiles Grouping Results

#### **Description**

The GEVAQuantiles class represents the results of a quantile detection analysis. For each probe/gene, there is a assigned quantile among the *g* defined quantiles.

This class inherits from GEVAGroupSet and is inherited by GEVAQuantilesAdjusted.

#### **Slots**

grouping factor (*m* elements, *g* levels), quantile assignment for each gene/probe (Inherited from GEVAGroupSet)

scores numeric vector (*m* elements) with the assigned quantile scores for each gene/probe (Inherited from GEVAGroupSet)

ftable data.frame (m lines) with additional quantile assignment features (Inherited from GEVAGroupSet)

centroids numeric SVTable (g lines) with the S and V centroid coordinates for each quantile (Inherited from GEVAGroupSet)

offsets numeric SVTable (m lines) with the S and V coordinate offsets each gene/probe from its quantile centroid

(Inherited from GEVAGroupSet)

info list of additional information

(Inherited from GEVAGroupSet)

syscores numeric SVTable (m lines) with individual partial scores for the assigned quantiles

qareasizes numeric SVTable (g lines) with the S and V sizes for each quantile

qindexes integer SVTable (g lines) representing the position index to each quantile, in terms of summary and variation

 $\begin{array}{c} \text{qcount integer attributes (SVIntAttribute) with the defined number of quantiles for the $S$ and $V$} \\ \text{axes} \end{array}$ 

qcutoff numeric attributes (SVNumAttribute) with the initial quantile cutoff in S and V, starting from the point zero

## Methods

(See also the inherited methods from GEVAGroupSet)

## **Dimension accessors**

lines (x, ...) Draws the quantile delimiter lines

#### Slot accessors

```
qareasizes(object) Gets the SVTable from the qareasizes slot
qcount(object) Gets the SVIntAttribute from the qcount slot
qindexes(object) Gets the SVTable from the qindexes slot
quantiles(object) Gets the unique quantile names
quantiles.method(object) Gets the character from the qmethod slot
sv.scores(object) Gets the SVTable from the svscores slot
```

GEVAQuantilesAdjusted-class

GEVA Adjusted Quantiles Results

#### **Description**

The GEVAQuantilesAdjusted class represents the results of a quantile detection analysis with adjusted assignments based on relationships with other GEVAGroupSet objects. For each probe/gene, there is a assigned quantile among the g defined quantiles.

This class inherits from GEVAQuantiles.

(Inherited from GEVAQuantiles)

#### Slots

```
grouping factor (m elements, g levels), quantile assignment for each gene/probe
     (Inherited from GEVAGroupSet)
scores numeric vector (m elements) with the assigned quantile scores for each gene/probe
     (Inherited from GEVAGroupSet)
ftable data. frame (m lines) with additional quantile assignment data
     (Inherited from GEVAGroupSet)
centroids numeric SVTable (g lines) with the S and V centroid coordinates for each quantile
     (Inherited from GEVAGroupSet)
offsets numeric SVTable (m lines) with the S and V coordinate offsets each gene/probe from its
     quantile centroid
     (Inherited from GEVAGroupSet)
info list of additional information
     (Inherited from GEVAGroupSet)
syscores numeric SVTable (m lines) with individual partial scores for the assigned quantiles
     (Inherited from GEVAQuantiles)
gareasizes numeric SVTable (g lines) with the S and V sizes for each quantile
     (Inherited from GEVAQuantiles)
qindexes integer SVTable (g lines) representing the position index to each quantile, in terms of
     summary and variation
     (Inherited from GEVAQuantiles)
qcount integer attributes (SVIntAttribute) with the defined number of quantiles for the S and V
```

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```
qcutoff numeric attributes (SVNumAttribute) with the initial quantile cutoff in S and V, starting from the point zero (Inherited from GEVAQuantiles)
```

grouprels TypedList of named factor elements representing external group relationships to the current quantiles

#### Methods

(See also the inherited methods from GEVAQuantiles and GEVAGroupSet)

#### Slot accessors

group.rels(object) Gets the TypedList from the grouprels slot

GEVAResults-class

GEVA Results Table

## **Description**

The GEVAResults class contains the final results from GEVA analyses. It represents the results of multiple statistical approaches from summary/variation data, clustering, quantile detection, and factor analysis (if applicable).

## **Slots**

```
results table data.frame (m lines) with classification results for the genes/probes svdata GEVASummary used as input
```

quantdata GEVAQuantiles or GEVAQuantilesAdjusted with the final quantile assignments for the summarized data

factoring data.frame (*m* lines) with detailed results for the factor analyses, such as p-values for each factor. If there was no factor analysis, this slot is NULL or empty

 ${\tt classiftable\ data.frame\ used\ as\ reference\ for\ the\ final\ classification}$ 

info list of supplementary information

#### Methods

#### **Dimension accessors**

```
dim(x) Gets the dimensions from the results.table slot
```

dimnames(x) Gets a list with the row and column names from the results.table slot. Individual dimension names can also be accessed through rownames and colnames

#### **Plotting**

```
points(x, which, ..., classif) Draws the results points.

If which (character vector) is given, plots only the matching genes/probes.

If classif (character vector) is given, plots only points with the matching classification
```

GEVASummary-class 27

## **Properties**

analysis.params(gobject) Returns a list of analysis parameters passed to geva.finalize or geva.quick to obtain this object

#### **Slot accessors**

```
infolist(object, field, ...) Gets the list from the info slot
infolist(object, field, ...) Gets the list from the info slot
quantiles(object) Gets the GEVAQuantiles from the quantdata slot
results.table(gres) Gets the data.frame from the resultstable slot
sv.data(object) Gets the GEVASummary from the svdata slot
```

#### **Sub-slot accessors**

```
featureTable(object) Returns the features data.frame from the internal GEVAInput head(x, ...) Returns the first lines of results.table(x) inputdata(object) Returns the internal GEVAInput inputvalues(object) Returns the values matrix from the internal GEVAInput inputweights(object, normalized) Returns the weights matrix from the internal GEVAInput levels(x) Returns the factors used in factor analysis, if present
```

GEVASummary-class

GEVA Summary-Variation Table

## **Description**

The GEVASummary class represents the calculation results for summary and variation from a GEVAInput. This class inherits from SVTable.

## **Slots**

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#### Methods

(See also the inherited methods from SVTable

## **Properties**

analysis.params(gobject) Returns a list of analysis parameters passed to geva.summarize to obtain this object

get.summary.method(gevasummary) Gets a character for the summarization method name
get.variation.method(gevasummary) Gets a character for the variation calculation method
name

#### **Slot accessors**

```
infolist(object, field, ...) Gets the list from the info slot.

If recursive is TRUE, appends the contents from the info slot in the internal GEVAInput inputdata(object) Gets the GEVAInput from the inputdata slot
```

#### **Sub-slot accessors**

factors(object) Gets the factor defined in the factors slot in the internal GEVAInput factors(object) <- value Sets the value to the factor slot in the internal GEVAInput featureTable(object) Gets the data.frame from the ftable slot in the internal GEVAInput inputvalues(object) Gets the matrix from the values slot in the internal GEVAInput inputweights(object, normalized) Gets the matrix from the weights slot in the internal GEVAInput

SVAttribute-class

Summary-Variation Attribute Field

## **Description**

This S4 class stores two character slots representing attribute fields for summary and variation. The SVAttribute class is abstract and must be instantiated as SVChrAttribute (for character), SVNumAttribute (for numeric), or SVIntAttribute (for integer).

#### Usage

```
## $4 method for signature 'character, character'
svattr(S, V)

## $4 method for signature 'numeric, numeric'
svattr(S, V)

## $4 method for signature 'integer, integer'
svattr(S, V)
```

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#### **Arguments**

S the *summary* value
V the *variation* value

#### **Slots**

S either character or numeric or integer of length one V either character or numeric or integer of length one

#### Methods

#### Slot accessors

```
summary(object, ...) Gets the value from the S slot variation(object, ...) Gets the value from the V slot
```

#### Note

The slots S and V must be of the same class (either character, numeric, or integer).

SVTable-class

Summary-Variation Table

## **Description**

The SVTable class stores a matrix composed by two columns: S (for *summary*) and V (for *variation*).

This class is inherited by GEVASummary.

## **Slots**

```
sv matrix composed by two columns: S (summary) and V (variation)
```

#### Methods

## Constructor

```
svtable(S, V, row.names = NULL) Creates a SVTable from the vectors S and V
```

## **Dimension accessors**

```
dim(x) Gets the dimensions from the sv slot
```

dimnames(x) Gets a list with the row and column names from the sv slot.

Individual dimension names can also be accessed through rownames and colnames

## **Plotting**

```
points(x, which, ..., classif) Draws the SV points in the plot
```

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#### Slot accessors

```
sv(object) Gets the matrix from the sv slot
```

#### Note

The matrix from sv slot can numeric, character, or any other supported type by matrix. The same slot from GEVASummary, however, is always a numeric matrix.

top.genes

Top Results from GEVA

## **Description**

Extracts the genes with a relevant classification according to the GEVA results.

#### Usage

```
top.genes(
  gevaresults,
  classif = c("similar", "factor-dependent", "factor-specific"),
  which.spec = levels(gevaresults),
  add.cols = NULL,
   ...,
  names.only = FALSE
)
```

## **Arguments**

```
gevaresults a GEVAResults object

classif character vector, filters the returned genes by their final classification. Possible options are "similar", "factor-dependent", "factor-specific", "sparse", and "basal". Multiple options can be combined

which.spec factor, filters the specific factors to be returned

add.cols character vector with column names from the feature table (accessed by featureTable(gevaresul The matching columns will be added to the returned table

optional arguments (not used in this version)

logical, set to TRUE to return only the table row names
```

#### Value

If names only is FALSE (the default), returns a subset of the resultstable slot (data.frame) from the gevaresults that includes only the filtered genes according to the function parameters.

Otherwise, if names.only is TRUE, returns only the row names (character vector) of this table subset.

TypedList-class 31

#### **Examples**

```
## Basic usage with a random generated input
ginput <- geva.ideal.example() # Generates a random input example</pre>
gresults <- geva.quick(ginput) # Performs the entire analysis (default parameters)</pre>
# Gets a table that includes all the top genes
dtgenes <- top.genes(gresults) # Gets the top genes table</pre>
head(dtgenes)
                                # Prints the first results
# Appends the "Symbol" column to the results table
dtgenes <- top.genes(gresults, add.cols="Symbol")</pre>
head(dtgenes)
                                # Prints the first results
# Appends all feature columns to the results table
dtgenes <- top.genes(gresults, add.cols=names(featureTable(gresults)))</pre>
head(dtgenes)
                                # Prints the first results
# Gets only the factor-specific genes
dtgenes <- top.genes(gresults, "factor-specific")</pre>
head(dtgenes)
                                # Prints the first results
# Gets only the factor-specific genes for "Cond_1" factor (if any)
dtgenes <- top.genes(gresults, "factor-specific", "Cond_1")</pre>
head(dtgenes)
                                # Prints the first results
```

TypedList-class

Type-strict List (TypedList-class)

## Description

List containing elements of the same class or inheritance.

#### **Slots**

elem.class character representing the class related to the elements

## Methods

```
typed.list(..., elem.class = NA_character_) Creates a TypedList from the elements in ...
derived from the class elem.class
```

## Slot accessors

```
elem.class(typedlist) Gets the character from the elem.class slot
elem.class(typedlist) <- value Sets a value to the elem.class slot</pre>
```