

Package ‘GSVA’

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Description Gene Set Variation Analysis (GSVA) is a non-parametric, unsupervised method for estimating variation of gene set enrichment through the samples of a expression data set. GSVA performs a change in coordinate systems, transforming the data from a gene by sample matrix to a gene-set by sample matrix, thereby allowing the evaluation of pathway enrichment for each sample. This new matrix of GSVA enrichment scores facilitates applying standard analytical methods like functional enrichment, survival analysis, clustering, CNV-pathway analysis or cross-tissue pathway analysis, in a pathway-centric manner.

License GPL (>= 2)

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BugReports <https://github.com/rcastelo/GSVA/issues>

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computeGeneSetsOverlap

Compute gene-sets overlap

Description

Calculates the overlap among every pair of gene-sets given as input.

This function calculates the overlap between every pair of gene sets of the input argument `gSets`. Before this calculation takes place, the gene sets in `gSets` are firstly filtered to discard genes that do not match to the identifiers in `uniqGenes`. Secondly, they are further filtered to meet the minimum and/or maximum size specified with the arguments `minSize` and `maxSize`. The overlap between two gene sets is calculated as the number of common genes between the two gene sets divided by the smallest size of the two gene sets.

Usage

```
## S4 method for signature 'list,character'  
computeGeneSetsOverlap(gSets, uniqGenes, minSize = 1, maxSize = Inf)  
  
## S4 method for signature 'list,ExpressionSet'  
computeGeneSetsOverlap(gSets, uniqGenes, minSize = 1, maxSize = Inf)  
  
## S4 method for signature 'GeneSetCollection,character'  
computeGeneSetsOverlap(gSets, uniqGenes, minSize = 1, maxSize = Inf)  
  
## S4 method for signature 'GeneSetCollection,ExpressionSet'  
computeGeneSetsOverlap(gSets, uniqGenes, minSize = 1, maxSize = Inf)
```

Arguments

gSets	Gene sets given either as a list or a GeneSetCollection object.
uniqGenes	Vector of unique genes to be considered when calculating the overlaps.
minSize	Minimum size.
maxSize	Maximum size.

Value

A gene-set by gene-set matrix of the overlap among every pair of gene sets.

Author(s)

J. Guinney

References

Hänzelmann, S., Castelo, R. and Guinney, J. GSVA: Gene set variation analysis for microarray and RNA-Seq data. *BMC Bioinformatics*, 14:7, 2013.

See Also

[filterGeneSets](#)

Examples

```
geneSets <- list(set1=as.character(1:4), set2=as.character(4:10))  
computeGeneSetsOverlap(geneSets, unique(unlist(geneSets)))
```

filterGeneSets *Filter gene sets*

Description

Filters gene sets through a given minimum and maximum set size.

This function filters the input gene sets according to a given minimum and maximum set size.

Usage

```
## S4 method for signature 'list'  
filterGeneSets(gSets, minSize = 1, maxSize = Inf)
```

```
## S4 method for signature 'GeneSetCollection'  
filterGeneSets(gSets, minSize = 1, maxSize = Inf)
```

Arguments

gSets	Gene sets given either as a list or a GeneSetCollection object.
minSize	Minimum size.
maxSize	Maximum size.

Value

A collection of gene sets that meet the given minimum and maximum set size.

Author(s)

J. Guinney

References

Hänzelmann, S., Castelo, R. and Guinney, J. GSVA: Gene set variation analysis for microarray and RNA-Seq data. *BMC Bioinformatics*, 14:7, 2013.

See Also

[computeGeneSetsOverlap](#)

Examples

```
geneSets <- list(set1=as.character(1:4), set2=as.character(4:10))  
filterGeneSets(geneSets, minSize=5)
```

Description

Estimates GSVA enrichment scores. The API of this function has changed in the Bioconductor release 3.18 and this help page describes the new API. The old API is defunct and will be removed in the next Bioconductor release. If you are looking for the documentation of the old API to the `gsva()` function, please consult [GSVA-pkg-defunct](#).

Usage

```
## S4 method for signature 'plageParam'
gsva(param, verbose = TRUE, BPPARAM = SerialParam(progressbar = verbose))

## S4 method for signature 'zscoreParam'
gsva(param, verbose = TRUE, BPPARAM = SerialParam(progressbar = verbose))

## S4 method for signature 'ssgseaParam'
gsva(param, verbose = TRUE, BPPARAM = SerialParam(progressbar = verbose))

## S4 method for signature 'gsvaParam'
gsva(param, verbose = TRUE, BPPARAM = SerialParam(progressbar = verbose))
```

Arguments

param	<p>A parameter object of one of the following classes:</p> <ul style="list-style-type: none"> • A <code>gsvaParam</code> object built using the constructor function <code>gsvaParam</code>. This object will trigger <code>gsva()</code> to use the GSVA algorithm by Hänzelmann et al. (2013). • A <code>plageParam</code> object built using the constructor function <code>plageParam</code>. This object will trigger <code>gsva()</code> to use the PLAGE algorithm by Tomfohr et al. (2005). • A <code>zscoreParam</code> object built using the constructor function <code>zscoreParam</code>. This object will trigger <code>gsva()</code> to use the combined z-score algorithm by Lee et al. (2008). • A <code>ssgseaParam</code> object built using the constructor function <code>ssgseaParam</code>. This object will trigger <code>gsva()</code> to use the ssGSEA algorithm by Barbie et al. (2009).
verbose	Gives information about each calculation step. Default: TRUE.
BPPARAM	An object of class <code>BiocParallelParam</code> specifying parameters related to the parallel execution of some of the tasks and calculations within this function.

Value

A gene-set by sample matrix (of `matrix` or `dgCMatrix` type, depending on the input) of GSVA enrichment scores.

References

- Barbie, D.A. et al. Systematic RNA interference reveals that oncogenic KRAS-driven cancers require TBK1. *Nature*, 462(5):108-112, 2009. [DOI](#)
- Hänzelmann, S., Castelo, R. and Guinney, J. GSVa: Gene set variation analysis for microarray and RNA-Seq data. *BMC Bioinformatics*, 14:7, 2013. [DOI](#)
- Lee, E. et al. Inferring pathway activity toward precise disease classification. *PLoS Comp Biol*, 4(11):e1000217, 2008. [DOI](#)
- Tomfohr, J. et al. Pathway level analysis of gene expression using singular value decomposition. *BMC Bioinformatics*, 6:225, 2005. [DOI](#)

See Also

[plageParam](#), [zscoreParam](#), [ssgseaParam](#), [gsvaParam](#)

Examples

```
library(GSVA)
library(limma)

p <- 10 ## number of genes
n <- 30 ## number of samples
nGrp1 <- 15 ## number of samples in group 1
nGrp2 <- n - nGrp1 ## number of samples in group 2

## consider three disjoint gene sets
geneSets <- list(set1=paste("g", 1:3, sep=""),
                 set2=paste("g", 4:6, sep=""),
                 set3=paste("g", 7:10, sep=""))

## sample data from a normal distribution with mean 0 and st.dev. 1
y <- matrix(rnorm(n*p), nrow=p, ncol=n,
            dimnames=list(paste("g", 1:p, sep="") , paste("s", 1:n, sep="")))

## genes in set1 are expressed at higher levels in the last 'nGrp1+1' to 'n' samples
y[geneSets$set1, (nGrp1+1):n] <- y[geneSets$set1, (nGrp1+1):n] + 2

## build design matrix
design <- cbind(sampleGroup1=1, sampleGroup2vs1=c(rep(0, nGrp1), rep(1, nGrp2)))

## fit linear model
fit <- lmFit(y, design)

## estimate moderated t-statistics
fit <- eBayes(fit)

## genes in set1 are differentially expressed
topTable(fit, coef="sampleGroup2vs1")

## build GSVA parameter object
gsvapar <- gsvaParam(y, geneSets, maxDiff=TRUE)
```

```
## estimate GSVa enrichment scores for the three sets
gsva_es <- gsva(gsvapar)

## fit the same linear model now to the GSVa enrichment scores
fit <- lmFit(gsva_es, design)

## estimate moderated t-statistics
fit <- eBayes(fit)

## set1 is differentially expressed
topTable(fit, coef="sampleGroup2vs1")
```

gsva-defunct

Gene Set Variation Analysis

Description

This is the old manual page of the defunct version of the function `gsva()`.

See Also

[GSVA-pkg-defunct](#)

GSVA-pkg-defunct

Defunct functions in package GSVA.

Description

The functions listed below are defunct and will be removed in the next release.

Details

Instead of `gsva(expr=., gset.idx.list=., method=., ...)`, use a method-specific parameter object, see [pLageParam](#) [zscoreParam](#) [ssgseaParam](#) [gsvaParam](#), followed by a call to the new `gsva()` function, see [gsva](#).

GSVA-pkg-deprecated

Deprecated functions in package GSVA.

Description

The functions listed below are deprecated and will be defunct in the near future. When possible, alternative functions with similar functionality are also mentioned.

GsvaExprData-class GsvaExprData *class*

Description

Virtual superclass of expression data classes supported by GSVA.

Details

GSVA supports expression data matrices in a growing number of containers and representations. This class union allows to store any of these in a slot of another class as well as defining common methods for all of them.

See Also

[matrix](#), [dgCMatrix](#), [ExpressionSet](#), [SummarizedExperiment](#), [SingleCellExperiment](#), [HDF5Array](#)

GsvaGeneSets-class GsvaGeneSets *class*

Description

Virtual superclass of gene set classes supported by GSVA.

Details

GSVA supports gene sets in either a list of character vectors or an object of class `GSEABase::GeneSetCollection`. This class union allows to store any of these in a slot of another class as well as defining common methods for them.

See Also

[list](#), [GeneSetCollection](#)

GsvaMethodParam-class GsvaMethodParam class

Description

Virtual superclass of method parameter classes supported by GSVA.

A virtual superclass of the GSVA packages' method-specific parameter classes.

Details

GSVA implements four single-sample gene set analysis methods: PLAGE, combined z-scores, ssGSEA, and GSVA. All of them take at least an expression data matrix and one or many gene sets as input. This virtual class provides the necessary slots for this minimum parameter set and serves as all GSVA method parameter classes,

The GSVA package implements four single-sample gene set analysis methods (PLAGE, combined z-scores, ssGSEA, and GSVA) and a respective method-specific parameter class that is used to invoke each of them with a matching set of parameters.

See Also

[GsvaExprData](#), [GsvaGeneSets](#), [zscoreParam](#), [plageParam](#), [ssgseaParam](#), [gsvaParam](#)
[plageParam](#), [zscoreParam](#), [ssgseaParam](#), [gsvaParam](#)

gsvaParam-class gsvaParam class

Description

Method-specific parameters for the GSVA method.

Objects of class gsvaParam contain the parameters for running the GSVA method.

Usage

```
gsvaParam(
  exprData,
  geneSets,
  assay = NA_character_,
  annotation = NA_character_,
  minSize = 1,
  maxSize = Inf,
  kcdf = c("Gaussian", "Poisson", "none"),
  tau = 1,
  maxDiff = TRUE,
  absRanking = FALSE
)
```

Arguments

exprData	The expression data. Must be one of the classes supported by GsvaExprData .
geneSets	The gene sets. Must be one of the classes supported by GsvaGeneSets .
assay	The name of the assay to use in case exprData is a multi-assay container, otherwise ignored. By default, the first assay is used.
annotation	The name of a Bioconductor annotation package for the gene identifiers occurring in the row names of the expression data matrix. This can be used to map gene identifiers occurring in the gene sets if those are provided in a GeneSetCollection . By default gene identifiers used in expression data matrix and gene sets are matched directly.
minSize	Minimum size of the resulting gene sets after gene identifier mapping. By default, the minimum size is 1.
maxSize	Maximum size of the resulting gene sets after gene identifier mapping. By default, the maximum size is Inf.
kcdf	Character vector of length 1 denoting the kernel to use during the non-parametric estimation of the cumulative distribution function of expression levels across samples. By default, kcdf="Gaussian" which is suitable when input expression values are continuous, such as microarray fluorescent units in logarithmic scale, RNA-seq log-CPMs, log-RPKMs or log-TPMs. When input expression values are integer counts, such as those derived from RNA-seq experiments, then this argument should be set to kcdf="Poisson".
tau	Numeric vector of length 1. The exponent defining the weight of the tail in the random walk performed by the Gsva (Hänzelmann et al., 2013) method. The default value is 1 as described in the paper.
maxDiff	Logical vector of length 1 which offers two approaches to calculate the enrichment statistic (ES) from the KS random walk statistic. <ul style="list-style-type: none"> • FALSE: ES is calculated as the maximum distance of the random walk from 0. • TRUE (the default): ES is calculated as the magnitude difference between the largest positive and negative random walk deviations.
absRanking	Logical vector of length 1 used only when maxDiff=TRUE. When absRanking=FALSE (default) a modified Kuiper statistic is used to calculate enrichment scores, taking the magnitude difference between the largest positive and negative random walk deviations. When absRanking=TRUE the original Kuiper statistic that sums the largest positive and negative random walk deviations, is used. In this latter case, gene sets with genes enriched on either extreme (high or low) will be regarded as 'highly' activated.

Details

In addition to the two common parameter slots inherited from `[GsvaMethodParam]`, this class has slots for the two method-specific parameters of the Gsva method described below.

In addition to an expression data set and a collection of gene sets, Gsva takes four method-specific parameters as described below.

Value

A new `gsvaParam` object.

Slots

`kcdf` Character vector of length 1 denoting the kernel to use during the non-parametric estimation of the cumulative distribution function of expression levels across samples. `kcdf="Gaussian"` is suitable when input expression values are continuous, such as microarray fluorescent units in logarithmic scale, RNA-seq log-CPMs, log-RPKMs or log-TPMs. When input expression values are integer counts, such as those derived from RNA-seq experiments, then this argument should be set to `kcdf="Poisson"`.

`tau` Numeric vector of length 1. The exponent defining the weight of the tail in the random walk performed by the GSVA (Hänzelmann et al., 2013) method.

`maxDiff` Logical vector of length 1 which offers two approaches to calculate the enrichment statistic (ES) from the KS random walk statistic.

- FALSE: ES is calculated as the maximum distance of the random walk from 0.
- TRUE: ES is calculated as the magnitude difference between the largest positive and negative random walk deviations.

`absRanking` Logical vector of length 1 used only when `mx.diff=TRUE`. When `abs.ranking=FALSE` a modified Kuiper statistic is used to calculate enrichment scores, taking the magnitude difference between the largest positive and negative random walk deviations. When `abs.ranking=TRUE` the original Kuiper statistic that sums the largest positive and negative random walk deviations, is used. In this latter case, gene sets with genes enriched on either extreme (high or low) will be regarded as 'highly' activated.

References

Hänzelmann, S., Castelo, R. and Guinney, J. GSVA: Gene set variation analysis for microarray and RNA-Seq data. *BMC Bioinformatics*, 14:7, 2013. [DOI](#)

See Also

[GsvaExprData](#), [GsvaGeneSets](#), [GsvaMethodParam](#), [plageParam](#), [zscoreParam](#), [ssgseaParam](#)

Examples

```
library(GSVA)
library(GSVAdata)

data(leukemia)
data(c2BroadSets)

## for simplicity, use only a subset of the sample data
ses <- leukemia_eset[1:1000, ]
gsc <- c2BroadSets[1:100]
gp1 <- gsvaParam(ses, gsc)
gp1
```

Description

Starts an interactive GSVA shiny web app.

GSVA assesses the relative enrichment of gene sets across samples using a non-parametric approach. Conceptually, GSVA transforms a p-gene by n-sample gene expression matrix into a g-geneset by n-sample pathway enrichment matrix. This facilitates many forms of statistical analysis in the 'space' of pathways rather than genes, providing a higher level of interpretability.

The `igsva()` function starts an interactive shiny web app that allows the user to configure the arguments of the `gsva()` function and runs it on the computer. Please see the manual page of the `gsva()` function for a description of the arguments and their default and alternative values.

The input data may be loaded from the users workspace or by selecting a CSV file for the expression data, and a GMT file for the gene sets data.

Usage

```
igsva()
```

Value

A gene-set by sample matrix of GSVA enrichment scores after pressing the button 'Save & Close'. This result can be also downloaded as a CSV file with the 'Download' button.

Author(s)

J. Fernández and R. Castelo

References

Hänzelmann, S., Castelo, R. and Guinney, J. GSVA: Gene set variation analysis for microarray and RNA-Seq data. *BMC Bioinformatics*, 14:7, 2013.

See Also

[gsva\(\)](#)

Examples

```
## Not run:  
res <- igsva() ## this will open your browser with the GSVA shiny web app  
  
## End(Not run)
```

plageParam-class	plageParam <i>class</i>
------------------	-------------------------

Description

Method-specific parameters for the PLAGE method.

Objects of class `plageParam` contain the parameters for running the PLAGE method.

Usage

```
plageParam(
  exprData,
  geneSets,
  assay = NA_character_,
  annotation = NA_character_,
  minSize = 1,
  maxSize = Inf
)
```

Arguments

<code>exprData</code>	The expression data. Must be one of the classes supported by GsvaExprData .
<code>geneSets</code>	The gene sets. Must be one of the classes supported by GsvaGeneSets .
<code>assay</code>	The name of the assay to use in case <code>exprData</code> is a multi-assay container, otherwise ignored. By default, the first assay is used.
<code>annotation</code>	The name of a Bioconductor annotation package for the gene identifiers occurring in the row names of the expression data matrix. This can be used to map gene identifiers occurring in the gene sets if those are provided in a GeneSetCollection . By default gene identifiers used in expression data matrix and gene sets are matched directly.
<code>minSize</code>	Minimum size of the resulting gene sets after gene identifier mapping. By default, the minimum size is 1.
<code>maxSize</code>	Maximum size of the resulting gene sets after gene identifier mapping. By default, the maximum size is <code>Inf</code> .

Details

Since this method does not take any method-specific parameters, the parameter class does not add any slots to the common slots inherited from [GsvaMethodParam](#).

PLAGE does not take any method-specific parameters in addition to an expression data set and a collection of gene sets.

Value

A new `plageParam` object.

References

Tomfohr, J. et al. Pathway level analysis of gene expression using singular value decomposition. *BMC Bioinformatics*, 6:225, 2005. [DOI](#)

See Also

[GsvaExprData](#), [GsvaGeneSets](#), [GsvaMethodParam](#), [zscoreParam](#), [ssgseaParam](#), [gsvaParam](#)

Examples

```
library(GSVA)
library(GSVAdata)

data(leukemia)
data(c2BroadSets)

## for simplicity, use only a subset of the sample data
ses <- leukemia_eset[1:1000, ]
gsc <- c2BroadSets[1:100]
pp1 <- plageParam(ses, gsc)
pp1
```

ssgseaParam-class *ssgseaParam class*

Description

Method-specific parameters for the ssGSEA method.

Objects of class `ssgseaParam` contain the parameters for running the ssGSEA method.

Usage

```
ssgseaParam(
  exprData,
  geneSets,
  assay = NA_character_,
  annotation = NA_character_,
  minSize = 1,
  maxSize = Inf,
  alpha = 0.25,
  normalize = TRUE
)
```

Arguments

exprData	The expression data. Must be one of the classes supported by GsvaExprData .
geneSets	The gene sets. Must be one of the classes supported by GsvaGeneSets .
assay	The name of the assay to use in case exprData is a multi-assay container, otherwise ignored. By default, the first assay is used.
annotation	The name of a Bioconductor annotation package for the gene identifiers occurring in the row names of the expression data matrix. This can be used to map gene identifiers occurring in the gene sets if those are provided in a GeneSetCollection . By default gene identifiers used in expression data matrix and gene sets are matched directly.
minSize	Minimum size of the resulting gene sets after gene identifier mapping. By default, the minimum size is 1.
maxSize	Maximum size of the resulting gene sets after gene identifier mapping. By default, the maximum size is Inf.
alpha	Numeric vector of length 1. The exponent defining the weight of the tail in the random walk performed by the ssGSEA (Barbie et al., 2009) method. The default value is 0.25 as described in the paper.
normalize	Logical vector of length 1; if TRUE runs the ssGSEA method from Barbie et al. (2009) normalizing the scores by the absolute difference between the minimum and the maximum, as described in their paper. Otherwise this last normalization step is skipped.

Details

In addition to the two common parameter slots inherited from `[GsvaMethodParam]`, this class has slots for the two method-specific parameters of the ssGSEA method described below.

In addition to an expression data set and a collection of gene sets, ssGSEA takes two method-specific parameters as described below.

Value

A new `ssgseaParam` object.

Slots

alpha Numeric vector of length 1. The exponent defining the weight of the tail in the random walk performed by the ssGSEA (Barbie et al., 2009) method.

normalize Logical vector of length 1. If TRUE runs the ssGSEA method from Barbie et al. (2009) normalizing the scores by the absolute difference between the minimum and the maximum, as described in their paper. Otherwise this last normalization step is skipped.

References

Barbie, D.A. et al. Systematic RNA interference reveals that oncogenic KRAS-driven cancers require TBK1. *Nature*, 462(5):108-112, 2009. [DOI](#)

See Also

[GsvaExprData](#), [GsvaGeneSets](#), [GsvaMethodParam](#), [plageParam](#), [zscoreParam](#), [gsvaParam](#)

Examples

```
library(GSVA)
library(GSVAdata)

data(leukemia)
data(c2BroadSets)

## for simplicity, use only a subset of the sample data
ses <- leukemia_eset[1:1000, ]
gsc <- c2BroadSets[1:100]
sp1 <- ssgseaParam(ses, gsc)
sp1
```

zscoreParam-class zscoreParam *class*

Description

Method-specific parameters for the combined z-scores method.

Objects of class `zscoreParam` contain the parameters for running the combined z-scores method.

Usage

```
zscoreParam(
  exprData,
  geneSets,
  assay = NA_character_,
  annotation = NA_character_,
  minSize = 1,
  maxSize = Inf
)
```

Arguments

<code>exprData</code>	The expression data. Must be one of the classes supported by GsvaExprData .
<code>geneSets</code>	The gene sets. Must be one of the classes supported by GsvaGeneSets .
<code>assay</code>	The name of the assay to use in case <code>exprData</code> is a multi-assay container, otherwise ignored. By default, the first assay is used.
<code>annotation</code>	The name of a Bioconductor annotation package for the gene identifiers occurring in the row names of the expression data matrix. This can be used to map gene identifiers occurring in the gene sets if those are provided in a GeneSetCollection . By default gene identifiers used in expression data matrix and gene sets are matched directly.

minSize	Minimum size of the resulting gene sets after gene identifier mapping. By default, the minimum size is 1.
maxSize	Maximum size of the resulting gene sets after gene identifier mapping. By default, the maximum size is Inf.

Details

Since this method does not take any method-specific parameters, the parameter class does not add any slots to the common slots inherited from [GsvaMethodParam](#).

The combined z-scores method does not take any method-specific parameters in addition to an expression data set and a collection of gene sets.

Value

A new [zscoreParam](#) object.

References

Lee, E. et al. Inferring pathway activity toward precise disease classification. *PLoS Comp Biol*, 4(11):e1000217, 2008. [DOI](#)

See Also

[GsvaExprData](#), [GsvaGeneSets](#), [GsvaMethodParam](#), [plageParam](#), [ssgseaParam](#), [gsvaParam](#)

Examples

```
library(GSVA)
library(GSVAdata)

data(leukemia)
data(c2BroadSets)

## for simplicity, use only a subset of the sample data
ses <- leukemia_eset[1:1000, ]
gsc <- c2BroadSets[1:100]
zp1 <- zscoreParam(ses, gsc)
zp1
```

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