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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URL https://github.com/rcastelo/GSVA
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computeGeneSetsOverlap

**computeGeneSetsOverlap**

Compute gene-sets overlap

**Description**

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

**Usage**

```r
## S4 method for signature 'list,character'
computeGeneSetsOverlap(gSets, uniqGenes, min.sz=1, max.sz=Inf)

## S4 method for signature 'list,ExpressionSet'
computeGeneSetsOverlap(gSets, uniqGenes, min.sz=1, max.sz=Inf)

## S4 method for signature 'GeneSetCollection,character'
computeGeneSetsOverlap(gSets, uniqGenes, min.sz=1, max.sz=Inf)

## S4 method for signature 'GeneSetCollection,ExpressionSet'
computeGeneSetsOverlap(gSets, uniqGenes, min.sz=1, max.sz=Inf)
```
computeGeneSetsOverlap

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.
min.sz      Minimum size.
max.sz      Maximum size.

Details

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 min.sz and max.sz. 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.

Value

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

Author(s)

J. Guinney

References


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.

Usage

## S4 method for signature 'list'
filterGeneSets(gSets, min.sz=1, max.sz=Inf)
## S4 method for signature 'GeneSetCollection'
filterGeneSets(gSets, min.sz=1, max.sz=Inf)

Arguments

gSets Gene sets given either as a list or a GeneSetCollection object.
min.sz Minimum size.
max.sz Maximum size.

Details

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

Value

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

Author(s)

J. Guinney

References


See Also

computeGeneSetsOverlap

Examples

geneSets <- list(set1=as.character(1:4), set2=as.character(4:10))
filterGeneSets(geneSets, min.sz=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 deprecated and will become defunct in the next Bioconductor release. If you are looking for the documentation of the old API to the gsva() function, please consult GSVA-pkg-deprecated.

Usage

## S4 method for signature 'plageParam,missing'
gsva(
  expr, 
  gset.idx.list, 
  verbose = TRUE, 
  BPPARAM = SerialParam(progressbar = verbose) 
)

## S4 method for signature 'zscoreParam,missing'
gsva(
  expr, 
  gset.idx.list, 
  verbose = TRUE, 
  BPPARAM = SerialParam(progressbar = verbose) 
)

## S4 method for signature 'ssgseaParam,missing'
gsva(
  expr, 
  gset.idx.list, 
  verbose = TRUE, 
  BPPARAM = SerialParam(progressbar = verbose) 
)

## S4 method for signature 'gsvaParam,missing'
gsva(
  expr, 
  gset.idx.list, 
  verbose = TRUE, 
  BPPARAM = SerialParam(progressbar = verbose) 
)

Arguments

expr A parameter object of one of the following classes:
• A `gsvaParam` object built using the constructor function `gsvaParam`. This object will trigger `gsva()` to use the GSVA algorithm by Hänzelmann et al. (2013).

• A `plageParam` object built using the constructor function `plageParam`. This object will trigger `gsva()` to use the PLAGE algorithm by Tomfohr et al. (2005).

• A `zscoreParam` object built using the constructor function `zscoreParam`. This object will trigger `gsva()` to use the combined z-score algorithm by Lee et al. (2008).

• A `ssgseaParam` object built using the constructor function `ssgseaParam`. This object will trigger `gsva()` to use the ssGSEA algorithm by Barbie et al. (2009).

`gset.idx.list`  Dummy parameter, only present for backward compatibility, do not use it. It will be removed once the deprecated version of `gsva()` is defunct.

`verbose`  Gives information about each calculation step. Default: FALSE.

`BPPARAM`  An object of class `BiocParallelParam` 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


See Also

`plageParam`, `zscoreParam`, `ssgseaParam`, `gsvaParam`

Examples

```r
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= newX::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 <- newX::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 'ngrpl+1' to 'n' samples

## build design matrix
design <- newX::cbind(sampleGroup1=1, sampleGroup2vs1=rep(0, ngrpl), rep(1, ngrpl2))

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

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

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

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

## estimate GSVA enrichment scores for the three sets
gsva_es <- newX::gsva(gsvapar)

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

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

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

---

### gsva-deprecated

**Gene Set Variation Analysis**

**Description**

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

**Usage**

```r
gsva(expr, gset.idx.list, ...)
```
See Also

GSVA-pkg-deprecated

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. Help pages for deprecated functions are available at gsva-deprecated.

Usage

```r
## S4 method for signature 'HDF5Array,list'
gsva(
  expr,
  gset.idx.list,
  annotation,
  method = c("gsva", "ssgsea", "zscore", "plage"),
  kcdf = c("Gaussian", "Poisson", "none"),
  abs.ranking = FALSE,
  min.sz = 1,
  max.sz = Inf,
  parallel.sz = 1L,
  mx.diff = TRUE,
  tau = switch(method, gsva = 1, ssgsea = 0.25, NA),
  ssgsea.norm = TRUE,
  verbose = TRUE,
  BPPARAM = SerialParam(progressbar = verbose)
)
```

```r
## S4 method for signature 'SingleCellExperiment,GeneSetCollection'
gsva(expr, gset.idx.list, ...)
```

```r
## S4 method for signature 'SingleCellExperiment,list'
gsva(
  expr,
  gset.idx.list,
  annotation,
  method = c("gsva", "ssgsea", "zscore", "plage"),
  kcdf = c("Gaussian", "Poisson", "none"),
  abs.ranking = FALSE,
  min.sz = 1,
  max.sz = Inf,
  parallel.sz = 1L,
  ```
mx.diff = TRUE,
tau = switch(method, gsva = 1, ssgsea = 0.25, NA),
ssgsea.norm = TRUE,
verbose = TRUE,
BPPARAM = SerialParam(progressbar = verbose)
)

## S4 method for signature 'dgCMatrix,list'
gsva(
  expr,
  gset.idx.list,
  annotation,
  method = c("gsva", "ssgsea", "zscore", "plage"),
kcdf = c("Gaussian", "Poisson", "none"),
  abs.ranking = FALSE,
  min.sz = 1,
  max.sz = Inf,
  parallel.sz = 1L,
  mx.diff = TRUE,
  tau = switch(method, gsva = 1, ssgsea = 0.25, NA),
  ssgsea.norm = TRUE,
  verbose = TRUE,
  BPPARAM = SerialParam(progressbar = verbose)
)

## S4 method for signature 'SummarizedExperiment,GeneSetCollection'
gsva(
  expr,
  gset.idx.list,
  annotation,
  method = c("gsva", "ssgsea", "zscore", "plage"),
kcdf = c("Gaussian", "Poisson", "none"),
  abs.ranking = FALSE,
  min.sz = 1,
  max.sz = Inf,
  parallel.sz = 1L,
  mx.diff = TRUE,
  tau = switch(method, gsva = 1, ssgsea = 0.25, NA),
  ssgsea.norm = TRUE,
  verbose = TRUE,
  BPPARAM = SerialParam(progressbar = verbose)
)

## S4 method for signature 'SummarizedExperiment,list'
gsva(
  expr,
  gset.idx.list,
  annotation,
method = c("gsva", "ssgsea", "zscore", "plage"),
kcdf = c("Gaussian", "Poisson", "none"),
abs.ranking = FALSE,
min.sz = 1,
max.sz = Inf,
parallel.sz = 1L,
mx.diff = TRUE,
tau = switch(method, gsva = 1, ssgsea = 0.25, NA),
ssgsea.norm = TRUE,
verbose = TRUE,
BPPARAM = SerialParam(progressbar = verbose)
)

## S4 method for signature 'ExpressionSet,list'
gsva(
    expr,
    gset.idx.list,
    annotation,
    method = c("gsva", "ssgsea", "zscore", "plage"),
kcdf = c("Gaussian", "Poisson", "none"),
abs.ranking = FALSE,
min.sz = 1,
max.sz = Inf,
parallel.sz = 1L,
mx.diff = TRUE,
tau = switch(method, gsva = 1, ssgsea = 0.25, NA),
ssgsea.norm = TRUE,
verbose = TRUE,
BPPARAM = SerialParam(progressbar = verbose)
)

## S4 method for signature 'ExpressionSet,GeneSetCollection'
gsva(
    expr,
    gset.idx.list,
    annotation,
    method = c("gsva", "ssgsea", "zscore", "plage"),
kcdf = c("Gaussian", "Poisson", "none"),
abs.ranking = FALSE,
min.sz = 1,
max.sz = Inf,
parallel.sz = 1L,
mx.diff = TRUE,
tau = switch(method, gsva = 1, ssgsea = 0.25, NA),
ssgsea.norm = TRUE,
verbose = TRUE,
BPPARAM = SerialParam(progressbar = verbose)
)
## 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`.
**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.
gsvaParam-class

See Also

GsvaExprData, GsvaGeneSets, zscoreParam, plageParam, ssgseaParam, gsvaParam

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`.

Description

Method-specific parameters for the GSVA method.

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

- 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.
Gene Set Variation Analysis

**Description**

Starts an interactive GSVA shiny web app.

**Usage**

```r
igsva()
```
Details

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.

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


See Also

`gsva`

Examples

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

## End(Not run)
```

plageParam-class  PlageParam class

Description

Method-specific parameters for the PLAGE method.

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

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

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`.

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


See Also

`GsvaExprData, GsvaGeneSets, GsvaMethodParam, zscoreParam, ssgseaParam, gsvaParam`
Examples

```r
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
```

**Description**

Method-specific parameters for the ssGSEA method.

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

**Usage**

```r
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.
ssgseaParam-class

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


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

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
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.

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


See Also

`GsvaExprData, GsvaGeneSets, GsvaMethodParam, plageParam, ssgseaParam, gsvaParam`

Examples

```r
library(GSVA)
library(GSVAdataset)

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
```
**Index**

- **GSVA**
  - igsva, 15

- **Gene set**
  - computeGeneSetsOverlap, 2
  - filterGeneSets, 4

- **internal**
  - gsva-deprecated, 7
  - GSVA-pkg-deprecated, 8

- **shiny**
  - igsva, 15

**BiocParallelParam**, 6

computeGeneSetsOverlap, 2, 4
computeGeneSetsOverlap, GeneSetCollection, character-method (computeGeneSetsOverlap), 2
computeGeneSetsOverlap, GeneSetCollection, ExpressionSet-method (computeGeneSetsOverlap), 2
computeGeneSetsOverlap, list, character-method (computeGeneSetsOverlap), 2
computeGeneSetsOverlap, list, ExpressionSet-method (computeGeneSetsOverlap), 2

dgCMatrix, 6, 12

ExpressionSet, 12

filterGeneSets, 3, 4
filterGeneSets, GeneSetCollection-method (filterGeneSets), 4
filterGeneSets, list-method (filterGeneSets), 4

GeneSetCollection, 12, 13, 17, 18, 20

gsva, 5, 11, 16

gsva, dgCMatrix, list-method (GSVA-pkg-deprecated), 8

gsva, ExpressionSet, GeneSetCollection-method (GSVA-pkg-deprecated), 8

gsva, ExpressionSet, list-method (GSVA-pkg-deprecated), 8

gsva, gsvaParam, missing-method (gsva), 5
gsva, HDF5Array, list-method (GSVA-pkg-deprecated), 8
gsva, matrix, GeneSetCollection-method (GSVA-pkg-deprecated), 8
gsva, matrix, list-method (GSVA-pkg-deprecated), 8
gsva, plageParam, missing-method (gsva), 5
gsva, SingleCellExperiment, GeneSetCollection-method (GSVA-pkg-deprecated), 8
gsva, SingleCellExperiment, list-method (GSVA-pkg-deprecated), 8
gsva, ssgseaParam, missing-method (gsva), 5
gsva, SummarizedExperiment, GeneSetCollection-method (GSVA-pkg-deprecated), 8
gsva, SummarizedExperiment, list-method (GSVA-pkg-deprecated), 8
gsva, zscoreParam, missing-method (gsva), 5

gsva-deprecated, 7
GSVA-pkg-deprecated, 8
GsvaExprData, 13, 15, 17–21
GsvaExprData-class, 11
GsvaGeneSets, 13, 15, 17–21
GsvaGeneSets-class, 12
GsvaMethodParam, 15, 17, 19–21
GsvaMethodParam-class, 12
gsvaParam, 6, 13, 14, 17, 19, 21
gsvaParam (gsvaParam-class), 13
gsvaParam-class, 13

HDF5Array, 12

igsva, 15

list, 12

matrix, 12

plageParam, 6, 13, 15, 17, 19, 21
plageParam (plageParam-class), 16
plageParam-class, 16

SingleCellExperiment, 12
ssgseaParam, 6, 13, 15, 17, 19, 21
ssgseaParam (ssgseaParam-class), 18
ssgseaParam-class, 18
SummarizedExperiment, 12

zscoreParam, 6, 13, 15, 17, 19, 21
zscoreParam (zscoreParam-class), 20
zscoreParam-class, 20