Package ‘GenoGAM’

November 20, 2016

Type Package

Title A GAM based framework for analysis of ChIP-Seq data

Version 1.2.1

Date 2016-10-05

Description This package allows statistical analysis of genome-wide data with smooth functions using generalized additive models based on the implementation from the R-package 'mgcv'. It provides methods for the statistical analysis of ChIP-Seq data including inference of protein occupancy, and pointwise and region-wise differential analysis. Estimation of dispersion and smoothing parameters is performed by cross-validation. Scaling of generalized additive model fitting to whole chromosomes is achieved by parallelization over overlapping genomic intervals.

License GPL-2

LazyData true

Depends R (>= 3.3), Rsamtools (>= 1.18.2), SummarizedExperiment (>= 1.1.19), GenomicRanges (>= 1.23.16), methods

Imports BiocParallel (>= 1.5.17), data.table (>= 1.9.4), DESeq2 (>= 1.11.23), futile.logger (>= 1.4.1), GenomeInfoDb (>= 1.7.6), GenomicAlignments (>= 1.7.17), IRanges (>= 2.5.30), mgcv (>= 1.8), reshape2 (>= 1.4.1), S4Vectors (>= 0.9.34), Biostrings (>= 2.39.14)

Suggests BiocStyle, chipseq (>= 1.21.2), LSD (>= 3.0.0), genefilter (>= 1.54.2), ggplot2 (>= 2.1.0), testthat, knitr

VignetteBuilder knitr

NeedsCompilation no

RoxygenNote 5.0.1

biocViews Regression, DifferentialPeakCalling, ChIPSeq, DifferentialExpression, Genetics, Epigenetics

Collate 'GenomicTiles-class.R' 'GenoGAMSettings-class.R' 'GenoGAM-class.R' 'GenoGAM-package.R' 'GenoGAMDataSet-class.R' 'cv.R' 'devel.R' 'diffBinding.R' 'filter.R' 'genogam.R' 'helper.R' 'peakCalling.R' 'plotting.R' 'qc.R' 'readData.R' 'sf.R'

URL https://github.com/gstricker/GenoGAM
BugReports  https://github.com/gstricker/GenoGAM/issues

Author  Georg Stricker [aut, cre], Alexander Engelhardt [aut], Julien Gagneur [aut]

Maintainer  Georg Stricker <georg.stricker@in.tum.de>

R topics documented:

<table>
<thead>
<tr>
<th>Function</th>
<th>Documented Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>asDataFrame</td>
<td>3</td>
</tr>
<tr>
<td>callPeaks</td>
<td>3</td>
</tr>
<tr>
<td>changeSettings</td>
<td>4</td>
</tr>
<tr>
<td>checkSettings</td>
<td>5</td>
</tr>
<tr>
<td>computeRegionSignificance</td>
<td>6</td>
</tr>
<tr>
<td>computeSignificance</td>
<td>6</td>
</tr>
<tr>
<td>computeSizeFactors</td>
<td>7</td>
</tr>
<tr>
<td>dataRange</td>
<td>8</td>
</tr>
<tr>
<td>design,GenoGAMDataSet-method</td>
<td>8</td>
</tr>
<tr>
<td>filterData</td>
<td>9</td>
</tr>
<tr>
<td>GenoGAM</td>
<td>10</td>
</tr>
<tr>
<td>genogam</td>
<td>10</td>
</tr>
<tr>
<td>GenoGAM-class</td>
<td>11</td>
</tr>
<tr>
<td>GenoGAM-methods</td>
<td>12</td>
</tr>
<tr>
<td>GenoGAMDataSet</td>
<td>13</td>
</tr>
<tr>
<td>GenoGAMDataSet-class</td>
<td>14</td>
</tr>
<tr>
<td>GenoGAMDataSetToDataFrame</td>
<td>15</td>
</tr>
<tr>
<td>GenoGAMSets</td>
<td>15</td>
</tr>
<tr>
<td>GenoGAMSets-class</td>
<td>16</td>
</tr>
<tr>
<td>GenomicTiles</td>
<td>16</td>
</tr>
<tr>
<td>GenomicTiles-class</td>
<td>17</td>
</tr>
<tr>
<td>getChromosomes</td>
<td>18</td>
</tr>
<tr>
<td>getChunkIndex</td>
<td>19</td>
</tr>
<tr>
<td>getCoordinates</td>
<td>20</td>
</tr>
<tr>
<td>getIndex</td>
<td>20</td>
</tr>
<tr>
<td>getIndexCoordinates</td>
<td>21</td>
</tr>
<tr>
<td>getTile</td>
<td>22</td>
</tr>
<tr>
<td>makeTestGenoGAM</td>
<td>22</td>
</tr>
<tr>
<td>makeTestGenoGAMDataSet</td>
<td>23</td>
</tr>
<tr>
<td>makeTestGenomicTiles</td>
<td>23</td>
</tr>
<tr>
<td>plot,GenoGAM</td>
<td>24</td>
</tr>
<tr>
<td>qualityCheck</td>
<td>24</td>
</tr>
<tr>
<td>sizeFactors,GenoGAMDataSet-method</td>
<td>25</td>
</tr>
<tr>
<td>subset,GenoGAM-method</td>
<td>26</td>
</tr>
<tr>
<td>subset,GenoGAMDataSet-method</td>
<td>26</td>
</tr>
<tr>
<td>subset,GenomicTiles-method</td>
<td>27</td>
</tr>
<tr>
<td>subsetByOverlaps,GenoGAM,ANY-method</td>
<td>28</td>
</tr>
<tr>
<td>subsetByOverlaps,GenoGAMDataSet,GRanges-method</td>
<td>28</td>
</tr>
<tr>
<td>subsetByOverlaps,GenomicTiles,GRanges-method</td>
<td>29</td>
</tr>
<tr>
<td>Summary,GenomicTiles-method</td>
<td>30</td>
</tr>
<tr>
<td>tileSettings</td>
<td>32</td>
</tr>
<tr>
<td>untile</td>
<td>32</td>
</tr>
<tr>
<td>view</td>
<td>33</td>
</tr>
<tr>
<td>view,GenoGAM-method</td>
<td>34</td>
</tr>
</tbody>
</table>
asDataFrame

writeToBEDFile .......................................................... 34
[,GenoGAMDataSet,GRanges,ANY,ANY-method ................................ 35
[,][,GenomicTiles,numeric,ANY-method ................................... 35

Index 37

genscan 86

callPeaks Call peaks on a GenoGAM object

Description
Call narrow or broad peaks on the GenoGAM fit and computing significance, respectively

Usage
callPeaks(fit, smooth = NULL, range = NULL, peakType = c("narrow", "broad"),
threshold = NULL, thresholdType = c("fdr", "pvalue"),
maxgap = 500, cutoff = 0.05, minregion = 1)

Arguments
fit A GenoGAM object
smooth The name of the smooth, i.e. the 'by' variables in the GenoGAMDataSet design.
By default the last one will be taken.
range A GRanges object specifying a range. By default the complete fit is taken.
peakType The type of the peak (narrow or broad). Default is narrow, see details.
threshold The significance threshold. Keep in mind that the threshold depends on the
thresholdType. By default this is 0.05 for 'pvalue' and 0.1 for 'fdr'.
thresholdType The threshold type. Either 'fdr'(default) or 'pvalue'. If the threshold is not
provided it, will be set accordingly to the thresholdType.
maxgap For broad peaks only. The maximum gap between two broad peaks, that can be
tolerated in order to identify both as part of one broad peak. All broad peaks
with distances smaller or equal to the maxgap will be merged.
cutoff A separate threshold for broad peaks. Since pointwise pvalues are available, this
threshold is used to identify all significantly high positions, which then make up
a broad peak.
minregion For broad peaks only. The minimum length of a broad peak. By default 1, thus
catching also narrow peaks.
changeSettings

Details

Note that broad peaks don’t provide a specific highest location, but a region. Whereas narrow peaks provide both. However, the borders of narrow peaks are not necessarily informative. Additionally, narrow peaks provide a 95% confidence interval for the position, namely 'start' and 'end', which gives a more informative uncertainty measure to the peak position. Also, narrow peaks provide an occupancy estimate at the peak position, while broad peaks give the average occupancy across the region. The columns returned are:

Value

A data.table of identified peaks. The different columns loosely resemble the narrow and broad peak format (with different column order), such that it is easy to write them to a 'narrowPeak', 'broadPeak' file. See details for column description.

Author(s)

Georg Stricker <georg.stricker@in.tum.de>

Examples

```r
load(system.file("extdata/GenoGAM/fit.rda", package="GenoGAM"))
## calling narrow peaks
peaks <- callPeaks(fit, smooth = "genotype", threshold = 1)

## calling broad peaks
peaks <- callPeaks(fit, smooth = "genotype", threshold = 1,
                  peakType = "broad", cutoff = 0.75)
```

changeSettings

Check data compliance with tile settings

Description

Check if the indices were build correctly, according to the specified parameters. This is the recommended way of changing tile settings, as it triggers instant recomputation of the index.

Usage

```r
changeSettings(object, param, value)
```

Arguments

- **object**: A `GenomicTiles` object.
- **param**: The name of a tile settings parameter.
- **value**: An appropriate value. In most cases integer.
checkSettings

Value
A GenomicTiles object

Author(s)
Georg Stricker <georg.stricker@in.tum.de>

Examples
```r
gt <- makeTestGenomicTiles()
gt2 <- changeSettings(gt, "chunkSize", 20)
```

checkSettings

Check data compliance with tile settings

Description
Check if the indices were built correctly, according to the specified parameters

Usage
```r
checkSettings(object)
```

## S4 method for signature 'GenomicTiles'
checkSettings(object)

Arguments

object A GenomicTiles object.

Value
A logical value

Author(s)
Georg Stricker <georg.stricker@in.tum.de>

Examples
```r
gt <- makeTestGenomicTiles()
checkSettings(gt)
```
computeRegionSignificance

Compute significance for given regions

Description
For a given set of regions, region-wise p-values and FDR is computed

Usage
computeRegionSignificance(fit, regions, what = NULL)

Arguments
- fit: A GenoGAM object containing the fit
- regions: A GRanges object of regions of interest
- what: Which fit should be used. The names should be equivalent to the column names used in the config file. Lookup with names(colData(my_GenoGAMDataSet_object))

Details
For a given set of regions, region-wise p-values are computed by applying familywise hochberg correction and taking the minimal p-value. FDR is computed by further applying Benjamini-Hochberg correction.

Value
The GRanges object from the 'region' parameter extended by two columns: pvalue and FDR

Author(s)
Georg Stricker <georg.stricker@in.tum.de>

Examples
gg <- makeTestGenoGAM()
gr <- GRanges("chr1", IRanges(1,100))
computeRegionSignificance(gg, gr)

computeSignificance

Compute significance.

Description
Based on the model fits this functions computes pointwise pvalues.

Usage
computeSignificance(gg, log.p = FALSE)
computeSizeFactors

Arguments

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>gg</td>
<td>A fitted GenoGAM object.</td>
</tr>
<tr>
<td>log.p</td>
<td>Should pvalues be returned in log scale?</td>
</tr>
</tbody>
</table>

Value

A GenoGAM object which fits has been updated by the pvalue columns.

Author(s)

Georg Stricker <georg.stricker@in.tum.de>

Examples

```r

## Example 1
ggd <- makeTestGenoGAM()
ggd <- computeSignificance(ggd)
head(getFits(ggd))

## Example 2
computeSizeFactors(ggd)
```

Description

The function computes the size factors for given factor groups based on the DESeq2 package.

Usage

```r
computeSizeFactors(ggd, factorGroups = NULL)
```

Arguments

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ggd</td>
<td>A GenoGAMDataSet object.</td>
</tr>
<tr>
<td>factorGroups</td>
<td>A list of grouped IDs (same as the colnames of the GenoGAMDataSet object). Each element of the list represents a group of samples within which size factors are computed. If NULL all samples are regarded to belong to one group. Size factors are not computed between groups.</td>
</tr>
</tbody>
</table>

Value

An updated GenoGAMDataSet object.

Author(s)

Georg Stricker <georg.stricker@in.tum.de>

Examples

```r

## Example 1
ggd <- makeTestGenoGAMDataSet()
ggd <- computeSizeFactors(ggd)
```
dataRange  The `GRanges` of the underlying data

**Description**

Just like the `coordinates` slot but returns the genomic ranges of the underlying data.

**Usage**

```r
dataRange(object)
```

## S4 method for signature 'GenomicTiles'
dataRange(object)

## S4 method for signature 'GPos'
dataRange(object)

**Arguments**

- `object` A `GenomicTiles` object.

**Value**

A `GRanges` object of genomic ranges of the underlying data

**Author(s)**

Georg Stricker <georg.stricker@in.tum.de>

**Examples**

```r
gt <- makeTestGenomicTiles()
dataRange(gt)
```

design,GenoGAMDataSet-method

Access the design slot

**Description**

The design slot contains the formula object which is used to fit the model

**Usage**

```r
## S4 method for signature 'GenoGAMDataSet'
design(object)
```

```r
## S4 replacement method for signature 'GenoGAMDataSet,ANY'
design(object) <- value
```
filterData

Arguments

object A GenoGAMDataSet object.
value A formula object

Value

A formula object

Author(s)

Georg Stricker <georg.stricker@in.tum.de>

Examples

ggd <- makeTestGenoGAMDataSet()
design(ggd)
design(ggd) <- ~1

filterData A filter function for \codeGenoGAMDataSet

Description

A function to filter the \codeGenoGAMDataSet by the sum or mean of counts to significantly reduce
the amount of models to compute

Usage

filterData(ggd, threshold = NULL, windowsize = 201, mode = c("sum",
"mean"))

Arguments

ggd A GenoGAMDataSet object
threshold A value for the mean or sum of counts, which will be used to filter on basepair
level. By default it is taken as median + 3*MAD
windowsize The sliding window size. Should be an odd value.
mode Should the sum or the mean of counts be used?

Value

A GenoGAMDataSet object containing the filtered regions

Author(s)

Georg Stricker <georg.stricker@in.tum.de>

Examples

ggd <- makeTestGenoGAMDataSet()
fdata <- filterData(ggd, windowsize = 10)
fdata
GenoGAM: A package providing a framework to analyse ChIP-Seq data

Description

This is the fitting function for GenoGAMDataSet. It processes the data in GenoGAMDataSet, estimates the overdispersion and the penalization parameter, passes all information to mgcv::gam in parallel fashion and extracts the results. So far the model is restricted to Negativ Binomial distribution (mgcv::nb()).

Usage

```r
genogam(ggd, lambda = NULL, family = mgcv::nb(), bpknots = 20,
        kfolds = 10, intervallSize = 20, m = 2)
```

Arguments

- `ggd` A GenoGAMDataSet object to be fitted.
- `lambda` The penalization parameter. Will be estimated if missing.
- `family` A distribution family object. So far only mgcv::nb() is allowed.
- `bpknots` Number of basepairs per one knot, that is, how dense should the knots be placed. The denser the knots, the more sensitive the fit. Note however, that computation time increases approximately cubic with every additional knot.
- `kfolds` An integer number giving the number of k-folds to be used in cross validation, if parameters need to be estimated.
- `intervallSize` The size of the intervalls to be used in cross validation. Short intervalls are used instead of single points to be left out due to spatial correlation. If replicates are present it is advised to make them bigger, e.g. 2*fragment size. Otherwise, depending on the density of the data, they should not exceed the size of a short read.
- `m` The penalization order of the P-Splines.

Value

A GenoGAM object containing the fits and parameters.

Author(s)

Georg Stricker <georg.stricker@in.tum.de>
## Examples

```r
## Not run:
## simple example
config <- data.frame(ID = c("input", "IP"),
                      file = c("myInput.bam", "myIP.bam"),
                      paired = c(FALSE, FALSE),
                      type = c(0,1), stringsAsFactors = FALSE)
bpk <- 100 ## basepairs per one knot
chunkSize <- 5000
overhang <- round(7*chunkSize/bpk) # overhang with 7 knots
knots <- chunkSize/bpk
## build the GenoGAMDataSet
gtiles <- GenoGAMDataSet(config = config, chunkSize = chunkSize, overhangSize = overhang,
                         design = ~ s(x) + s(x, by = type))
gtiles <- computeSizeFactors(gtiles)
fits <- genogam(gtiles, bpknots = bpk)
## End(Not run)
```

---

**GenoGAM-class**

### Description

This class is designed to represent the model object containing the estimate parameters, arguments and finals fits of the model on a basepair level.

### Slots

- **design** A mgcv-type formula object.
- **fits** A data.frame of the fits, the standard error and the first and second derivative of the fits for each experiment.
- **positions** A GPos object of the positions and seqnames corresponding to the rows in the 'fits' slot.
- **smooths** A data.frame of knot positions and base function coefficients, in order to reproduce the splines and compute derivatives.
- **vcov** A list of covariance matrices for each tile fit.
- **experimentDesign** The design matrix according to which the fitting was performed.
- **fitparams** Global parameters 'lambda', 'theta', 'Coefficient of Variation' and the 'penalty order' used to compute the model.
- **family** The distribution family.
- **cvparams** Parameters used for cross validation.
- **settings** The global and local settings that were used to compute the model.
- **tileSettings** A list of settings used to compute tiles.

### Author(s)

Georg Stricker <georg.stricker@in.tum.de>
**Description**

The different accessor functions for the GenoGAM object

- The 'positions' slot holds the positions of the fit in GPos format
- The 'design' slot holds the formula of the fit
- The 'fits' slot contains the fitted values of the model
- The 'experimentDesign' slot contains the experimental design of the model as specified in the config file

**Usage**

```r
## S4 method for signature 'GenoGAM'
rowRanges(x)

## S4 method for signature 'GenoGAM'
design(object)

getFits(x)

## S4 method for signature 'GenoGAM'
colData(x)
```

**Arguments**

`x`, `object`  A GenoGAM object.

**Value**

The respective slot

**Author(s)**

Georg Stricker <georg.stricker@in.tum.de>

**Examples**

```r
gg <- makeTestGenoGAM()
ranges <- rowRanges(gg)
gg <- makeTestGenoGAM()
res <- design(gg)
gg <- makeTestGenoGAM()
fits <- getFits(gg)
gg <- makeTestGenoGAM()
exdesign <- colData(gg)
```
Description

This is the constructor function for GenoGAMDataSet. So far a GenoGAMDataSet can be constructed from either an experiment design file or data.frame or directly from a RangedSummarizedExperiment with a GPos object being the rowRanges.

Usage

GenoGAMDataSet(experimentDesign, chunkSize, overhangSize, design, directory = ".", settings = NULL, ...)

Arguments

- experimentDesign
  Either a character object specifying the path to a delimited text file (the delimiter will be determined automatically), or a data.frame specifying the experiment design. See details for the structure of the experimentDesign.

- chunkSize
  An integer specifying the size of one chunk in bp.

- overhangSize
  An integer specifying the size of the overhang in bp. As the overhang is taken to be symmetrical, only the overhang of one side should be provided.

- design
  A mgcv-like formula object. See details for its structure.

- directory
  The directory from which to read the data. By default the current working directory is taken.

- settings
  A GenoGAMSettings object. This class is already present but not yet fully tested and therefore not accessible to the user. This argument exists however in order to allow some workarounds if necessary. See the vignette for a possible use.

- ...
  Further parameters, mostly for arguments of custom processing functions or to specify a different method for fragment size estimation. See details for further information.

Details

The experimentDesign file/data.frame must contain at least three columns with fixed names: 'ID', 'file' and 'paired'. The field 'ID' stores a unique identifier for each alignment file. It is recommended to use short and easy to understand identifiers because they are subsequently used for labelling data and plots. The field 'file' stores the BAM file name. The field 'paired', values TRUE for paired-end sequencing data, and FALSE for single-end sequencing data. All other columns are stored in the colData slot of the GenoGAMDataSet object. Note that all columns which will be used for analysis must have at most two conditions, which are for now restricted to 0 and 1. For example, if the IP data should be corrected for input, then the input will be 0 and IP will be 1, since we are interested in the corrected IP. See examples.

Design must be a mgcv-like formula. At the moment only the following is possible: Either '~ 1' for a constant. ~ s(x) for a smooth fit over the entire data. s(x, by = "myColumn"), where 'myColumn' is a column name in the experimentDesign. This type of formula will then only fit the samples annotated with 1 in this column. Or ~ s(x) + s(x, by = "myColumn") + s(x, by = ...) + ... The last formula lets you combine any number of columns, given they are binary with 0 and 1. For example
the formula for correcting IP for input would look like this: \( ~s(x) + s(x, \text{by} = \"experiment\") \), where 'experiment' is a column with 0s and 1s, with the ip samples annotated with 1 and input samples with 0. In case of single-end data in might be usefull to specify a different method for fragment size estimation. The argument 'shiftMethod' can be supplied with the values 'coverage' (default), 'correlation’ or 'SISSR’. See \(?\text{chipseq}::\text{estimate.mean.fraglen}\) for explanation.

**Value**

An object of class GenoGAMDataSet.

**Author(s)**

Georg Stricker <georg.stricker@in.tum.de>

**Examples**

```r
## Not run:
myConfig <- data.frame(ID = c("input","ip"),
file = c("myInput.bam", "myIP.bam"),
paired = c(FALSE, FALSE),
experiment = factor(c(0,1)),
stringsAsFactors = FALSE)
myConfig2 <- data.frame(ID = c("wildtype1","wildtype2",
"mutant1", "mutant2"),
file = c("myWT1.bam", "myWT2.bam"
"myMutant1.bam", "myMutant2.bam"),
paired = c(FALSE, FALSE, FALSE, FALSE),
experiment = factor(c(0, 0, 1, 1)),
stringsAsFactors = FALSE)
gtiles <- GenoGAMDataSet(myConfig, chunkSize = 2000,
overhang = 250, design = ~ s(x) + s(x, by = "experiment")
gtiles <- GenoGAMDataSet(myConfig2, chunkSize = 2000,
overhang = 250, design = ~ s(x) + s(x, by = "experiment"))
## End(Not run)
```
GenoGAMDataSetToDataFrame

**Slots**

- **settings**  The global and local settings that were used to compute the model.
- **design**  The formula describing how to evaluate the data.
- **sizeFactors**  The normalized values for each sample.

**Author(s)**

Georg Stricker <georg.stricker@in.tum.de>

---

**Description**

GenoGAMDataSet to DataFrame

**See Also**

Other res: asDataFrame

---

GenoGAMSettings  

*The constructor function for GenoGAMSettings*

**Description**

The constructor function for GenoGAMSettings

**Usage**

GenoGAMSettings(...)  

**Arguments**

...  Any parameters corresponding to the slots and their possible values. See GenoGAM-Settings

**Value**

A GenoGAMSettings object.

**Author(s)**

Georg Stricker <georg.stricker@in.tum.de>
**GenoGAMSettings-class**  

**GenoGAMSettings**

**Description**

This class is designed to store settings for the computation of the GenoGAM package.

**Details**

Center can have three values: TRUE, FALSE, NULL. TRUE will trigger the center function, FALSE will trigger the use of the entire fragment. NULL should be used in case a custom process function is used.

**Slots**

- **center**  
  A logical or NULL value to specify if the raw data should be centered, i.e. only the midpoint of the fragment will be used to represent its coverage. See details.

- **chromosomeList**  
  A character vector of chromosomes to be used. NULL for all chromosomes.

- **bamParams**  
  An object of class ScanBamParam. See ?Rsamtools::ScanBamParam.

- **parallel**  
  A parallel backend of the respective class. See BiocParallel for the options.

- **processFunction**  
  A custom function on how to process raw data. Not used if center is TRUE/FALSE.

- **optimMethod**  
  The optimization method to be used in cross validation.

- **optimControl**  
  Settings for the optim() function.

**Author(s)**

Georg Stricker <georg.stricker@in.tum.de>

---

**GenomicTiles**  

**GenomicTiles constructor.**

**Description**

This is the constructor function for GenomicTiles. The easiest construction is from SummarizedExperiment. However as the class operates on basepair level, the rowRanges are restricted to the GPos class.

**Usage**

GenomicTiles(assays, chunkSize = 10000, overhangSize = 0, ...)

---
GenomicTiles-class

Arguments

assays
One of two things. Either directly an object of type 'RangedSummarizedExperiment'. Or in case the object is created from raw data, a 'list' or 'SimpleList' of matrix-like elements, or a matrix-like object. All elements of the list must have the same dimensions, and dimension names (if present) must be consistent across elements and with the row names of 'rowRanges' and 'colData'.

chunkSize
An integer specifying the size of one chunk in bp.

overhangSize
An integer specifying the size of the overhang in bp. The overhang is regarded to be symmetric, such that only the overhang of one side should be provided.

... Further parameters passed to the SummarizedExperiment constructor.

Details

Most, but not necessary all functionalities of SummarizedExperiment are yet provided.

Value

An object of class GenomicTiles.

Author(s)

Georg Stricker <georg.stricker@in.tum.de>

Examples

## from raw data
gp <- GPos(GRanges(c("chrI", "chrII"), IRanges(c(1,1), c(5,5))))
assay <- matrix(1:10, 10, 1)
gt <- GenomicTiles(assay, chunkSize = 3, rowRanges = gp)

## from SummarizedExperiment
se <- SummarizedExperiment(assay, rowRanges = gp)
gt <- GenomicTiles(se, chunkSize = 3)

Description

This class is designed to represent the entire genome (or a subset of it) and any additional data associated with the samples or positions. It extends the RangedSummarizedExperiment class and adds two additional index slots to keep track of the data. The main change compared to RangedSummarizedExperiment is the use of a GPos (basepair level) instead of GRanges (ranges level) object as rowRanges and the use of two GRanges objects as indices. The GPos object allows to store raw instead of summarized data in the assays. Because of this the size of genomic data can increase tremendously. Thus the GenomicTiles class automatically divides the data in (overlapping) tiles, making any operation on this data easy executable in parallel.

Details

For all other slots see SummarizedExperiment.
getChromosomes

Slots

index  A GRanges object that stores the tiles ranges and their index in the genome space. That is, ranges are the positions on the genome.
coordinates  A GRanges object that stores the tiles ranges and their index in the DataFrame space. That is ranges are the row positions in the DataFrame.

Author(s)

Georg Stricker <georg.stricker@in.tum.de>

Description

Returns the single elements of the tile settings

Usage

getchromosomes(object)

## S4 method for signature 'GenomicTiles'
getchromosomes(object)

gettileSize(object)

## S4 method for signature 'GenomicTiles'
getchileSize(object)

getChunkSize(object)

## S4 method for signature 'GenomicTiles'
getchunkSize(object)

getOverhangSize(object)

## S4 method for signature 'GenomicTiles'
getchoverhangSize(object)

getchileNumber(object, ...)

## S4 method for signature 'GenomicTiles'
getchileNumber(object)

Arguments

object  A GenomicTiles object.
...  Additional arguments
**getChunkIndex**

**Value**

An integer value, or in case of `getChromosomes` a `GRanges` object

**Author(s)**

Georg Stricker <georg.stricker@in.tum.de>

**Examples**

```r
gt <- makeTestGenomicTiles()
getChromosomes(gt)
getTileSize(gt)
getChunkSize(gt)
getOverhangSize(gt)
getTileNumber(gt)
```

```r
getChunkIndex(gt)
```

**Description**

The chunk index holds the `Granges` object that splits the entire dataset in chunk, that is non-overlapping intervals.

**Usage**

```r
getChunkIndex(object, ...)  
## S4 method for signature 'GenomicTiles'
getChunkIndex(object, id = NULL)
```

**Arguments**

- `object` A `GenomicTiles` object.
- `...` Additional arguments
- `id` A vector if tile ids. By default the complete index is returned.

**Value**

A `GRanges` object representing the index

**Author(s)**

Georg Stricker <georg.stricker@in.tum.de>

**Examples**

```r
gt <- makeTestGenomicTiles()
getChunkIndex(gt)
```
getCoordinates

Accessor to the `coordinates` slot

**Description**

The `coordinates` slot contains the row coordinates of each chromosome in the data. Such that taken a genomic position from a chromosome it’s easy to detect the correct row in the assay.

**Usage**

```
getCoordinates(object)
```

```r
## S4 method for signature 'GenomicTiles'
getCoordinates(object)
```

**Arguments**

- `object` A `GenomicTiles` object.

**Value**

A `GRanges` object of row coordinates

**Author(s)**

Georg Stricker &lt;georg.stricker@in.tum.de&gt;

**Examples**

```
gt <- makeTestGenomicTiles()
getCoordinates(gt)
```

getIndex

**Accessor to the 'index' slot**

**Description**

The index holds the Granges object that splits the entire dataset in tiles.

**Usage**

```
getIndex(object, ...)
```

```r
## S4 method for signature 'GenomicTiles'
getIndex(object, id = NULL)
```

**Arguments**

- `object` A `GenomicTiles` object.
- `...` Additional arguments
- `id` A vector if tile ids. By default the complete index is returned.
**getIndexCoordinates**

*Compute the row coordinates for a given index*

**Value**

A GRanges object representing the index

**Author(s)**

Georg Stricker <georg.stricker@in.tum.de>

**Examples**

```r
gt <- makeTestGenomicTiles()
getIndex(gt)
getIndex(gt, 1:3)
```

**Description**

Given an index of genomic positions, this method computes the corresponding row positions in the assay

**Usage**

```r
getIndexCoordinates(object, ...)  
## S4 method for signature 'GenomicTiles'
getIndexCoordinates(object, id = NULL, index = NULL)
```

**Arguments**

- `object`: A GenomicTiles object.
- `...`: Additional arguments Usually the original index or the chunk index.
- `id`: A vector if tile ids. By default the complete index is returned.
- `index`: A Granges object representing an index of genomic positions.

**Value**

A GRanges object of row coordinates

**Author(s)**

Georg Stricker <georg.stricker@in.tum.de>

**Examples**

```r
gt <- makeTestGenomicTiles()
getIndexCoordinates(gt)
```
**getTile**  
*Tile extraction as a DataFrame*

**Description**
Extracting one or multiple tiles from a `GenomicTiles` object and coercing them to a `DataFrameList`.

**Usage**
```r
getTile(object, id, ...) 
## S4 method for signature 'GenomicTiles'
getTile(object, id, size = 3e+09)
```

**Arguments**
- `object`: A `GenomicTiles` object
- `id`: A vector of tile ids
- `...`: Additional arguments
- `size`: The maximal number of rows that should be handled at once. If the dataset is bigger it will be processed in chunks. This is to lower memory consumption on big datasets, which in turn is slower.

**Value**
A `SimpleDataFrameList`

**Author(s)**
Georg Stricker <georg.stricker@in.tum.de>

**Examples**
```r
gt <- makeTestGenomicTiles()
getTile(gt, 1:3)
```

---

**makeTestGenoGAM**  
*Make an example /codeGenoGAM*

**Description**
Make an example /codeGenoGAM

**Usage**
```r
makeTestGenoGAM() 
```

**Value**
A /codeGenoGAM object
makeTestGenoGAMDataSet

Examples

test <- makeTestGenoGAM()

Description
Make an example GenoGAMDataSet

Usage
makeTestGenoGAMDataSet()

Value
A GenoGAMDataSet object

Examples

test <- makeTestGenoGAMDataSet()

makeTestGenomicTiles

Description
Make an example GenomicTile

Usage
makeTestGenomicTiles()

Value
A GenomicTiles object

Examples

test <- makeTestGenomicTiles()
**plot.GenoGAM**  
*The pot function for a GenoGAM object*

**Description**
This function plots the fit of a given region and optionally the read counts from the GenoGAM-DataSet object.

**Usage**
```
plot.GenoGAM(x, ggd = NULL, ranges = NULL, seqnames = NULL, 
start = NULL, end = NULL, scale = TRUE, ...)
```

**Arguments**
- `x`: A GenoGAM object
- `ggd`: A GenoGAMDataSet object to plot raw counts
- `ranges`: A GRanges object specifying a particular region
- `seqnames`: A chromosome name. Together with start and end it is an alternative way of selecting a region
- `start`: The start of a region
- `end`: The end of a region
- `scale`: Logical, should all tracks be scaled to the same y-axis?
- `...`: Additional parameters that will be passed to the basic plot routine

**Value**
A plot of all tracks either using the ggplot2 or the base R framework

**Author(s)**
Georg Stricker <georg.stricker@in.tum.de>

---

**qualityCheck**  
*A function to quality check the data*

**Description**
This function checks some data attributes in the given class. Check details for more information.

**Usage**
```
qualityCheck(object, ...)
```

**Arguments**
- `object`: Any object for which this methods is implemented
- `...`: Further parameters. See details.
Details

So far this method is only implemented for the class GenoGAMDataSet. In this case some general metrics are printed and some plots are stored in the folder "qc", which will be created in the working directory.

Additional parameters: factorGroups (for GenoGAMDataSet), which is used to specify factor groups for normalization plots. By default the groups will be identified automatically. See ?computeSizeFactors for parameter description.

Value

Based on the object provided, see details.

Author(s)

Georg Stricker <georg.stricker@in.tum.de>

Description

The sizeFactor slot contains the vector of normalization values for each sample

Usage

```r
## S4 method for signature 'GenoGAMDataSet'
sizeFactors(object)
```

```r
## S4 replacement method for signature 'GenoGAMDataSet,ANY'
sizeFactors(object) <- value
```

Arguments

- **object**: A GenoGAMDataSet object.
- **value**: A named numeric vector

Value

A named numeric vector

Author(s)

Georg Stricker <georg.stricker@in.tum.de>

Examples

```r
ggd <- makeTestGenoGAMDataSet()
sizeFactors(ggd)
sizeFactors(ggd) <- c(a = 5, b = 1/5)
```
Subset method for GenoGAM

Description

Subsetting the GenoGAM by a logical statement

Usage

```r
## S4 method for signature 'GenoGAM'
subset(x, ...)
```

Arguments

- `x` A GenoGAM object.
- `...` Further arguments. Mostly a logical statement. Note that the columnnames for chromosomes and positions are: seqnames and pos.

Value

A subsetted GenoGAM object.

Author(s)

Georg Stricker <georg.stricker@in.tum.de>

Examples

```r
gg <- makeTestGenoGAM()
subset(gg, pos <= 40)
```

Subset method for GenoGAMDataSet

Description

Subsetting the GenoGAMDataSet by a logical statement

Usage

```r
## S4 method for signature 'GenoGAMDataSet'
subset(x, ...)
```

Arguments

- `x` A GenoGAMDataSet object.
- `...` Further arguments. Mostly a logical statement. Note that the columnnames for chromosomes and positions are: seqnames and pos.
Description
Subsetting the GenomicTiles by a logical statement

Usage
```
## S4 method for signature 'GenomicTiles'
subset(x, ...)
```

Arguments
- `x`: A GenomicTiles object.
- `...`: Further arguments. Mostly a logical statement. Note that the columnnames for chromosomes and positions are: seqnames and pos.

Value
A subsetted GenomicTiles object.

Author(s)
Georg Stricker <georg.stricker@in.tum.de>

Examples
```r
gt <- makeTestGenomicTiles()
res <- subset(gt, seqnames == "chrI" & pos <= 50)
```
**Description**

Subsetting the GenoGAM by a GRanges object

**Usage**

```r
## S4 method for signature 'GenoGAM,ANY'
subsetByOverlaps(query, subject)
```

**Arguments**

- `query` A GenoGAM object.
- `subject` A GRanges object
- `...` Additional parameters

**Value**

A subsetted GenoGAM object.

**Author(s)**

Georg Stricker <georg.stricker@in.tum.de>

**Examples**

```r
gg <- makeTestGenoGAM()
gr <- GRanges("chr1", IRanges(1,40))
subsetByOverlaps(gg, gr)
```

---

**Description**

Subsetting the GenoGAMDataSet by a GRanges object

**Usage**

```r
## S4 method for signature 'GenoGAMDataSet,GRanges'
subsetByOverlaps(query, subject, maxgap = 0L, minoverlap = 1L, type = c("any", "start", "end", "within", "equal"), ...)
```

---
subsetByOverlaps, GenomicTiles, GRanges-method

Arguments

query A GenoGAMDataSet object.
subject A GRanges object
maxgap, minoverlap
Intervals with a separation of maxgap or less and a minimum of minoverlap overlapping positions, allowing for maxgap, are considered to be overlapping. maxgap should be a scalar, non-negative, integer. minoverlap should be a scalar, positive integer.
type By default, any overlap is accepted. By specifying the type parameter, one can select for specific types of overlap. The types correspond to operations in Allen’s Interval Algebra (see references). If type is start or end, the intervals are required to have matching starts or ends, respectively. While this operation seems trivial, the naive implementation using outer would be much less efficient. Specifying equal as the type returns the intersection of the start and end matches. If type is within, the query interval must be wholly contained within the subject interval. Note that all matches must additionally satisfy the minoverlap constraint described above.
The maxgap parameter has special meaning with the special overlap types. For start, end, and equal, it specifies the maximum difference in the starts, ends or both, respectively. For within, it is the maximum amount by which the query may be wider than the subject.

Value
A subsetted GenoGAMDataSet object.

Author(s)
Georg Stricker <georg.stricker@in.tum.de>

Examples

```r
ggd <- makeTestGenoGAMDataSet()
gr <- GRanges("chrI", IRanges(1,50))
res <- subsetByOverlaps(ggd, gr)
```

Description
Subsetting the GenomicTiles by a GRanges object

Usage

```r
# S4 method for signature 'GenomicTiles, GRanges'
subsetByOverlaps(query, subject, maxgap = 0L,
                 minoverlap = 1L, type = c("any", "start", "end", "within", "equal"), ...)```
Arguments

query A GenomicTiles object.
subject A GRanges object
maxgap, minoverlap
Intervals with a separation of maxgap or less and a minimum of minoverlap overlapping positions, allowing for maxgap, are considered to be overlapping. maxgap should be a scalar, non-negative, integer. minoverlap should be a scalar, positive integer.
type By default, any overlap is accepted. By specifying the type parameter, one can select for specific types of overlap. The types correspond to operations in Allen’s Interval Algebra (see references). If type is start or end, the intervals are required to have matching starts or ends, respectively. While this operation seems trivial, the naïve implementation using outer would be much less efficient. Specifying equal as the type returns the intersection of the start and end matches. If type is within, the query interval must be wholly contained within the subject interval. Note that all matches must additionally satisfy the minoverlap constraint described above.

The maxgap parameter has special meaning with the special overlap types. For start, end, and equal, it specifies the maximum difference in the starts, ends or both, respectively. For within, it is the maximum amount by which the query may be wider than the subject.

Value

A subsetted GenomicTiles object.

Author(s)

Georg Stricker <georg.stricker@in.tum.de>

Examples

```r
gt <- makeTestGenomicTiles()
gr <- GRanges(c("chrI", "chrII"), IRanges(c(1, 120), c(40, 150)))
res <- subsetByOverlaps(gt, gr)
```

Description

Computing metrics on each tile of the GenomicTiles object. So far all metrics from the Summary generics group, as well as mean, var, sd, median, mad and IQR are supported.
Summary.GenomicTiles-method

Usage

## S4 method for signature 'GenomicTiles'
Summary(x, ..., na.rm = FALSE)

## S4 method for signature 'GenomicTiles'
mean(x)

## S4 method for signature 'GenomicTiles,ANY'
var(x)

## S4 method for signature 'GenomicTiles'
sd(x)

## S4 method for signature 'GenomicTiles'
median(x)

## S4 method for signature 'GenomicTiles'
mad(x)

## S4 method for signature 'GenomicTiles'
IQR(x)

Arguments

x A GenomicTiles object

... Additional arguments

na.rm Should NAs be dropped. Otherwise the result is NA

Value

A list of as many elements as there are assays. Each element contains a matrix with the specified metric computed per tile per column of the assay data.

Author(s)

Georg Stricker <georg.stricker@in.tum.de>

Examples

gt <- makeTestGenomicTiles()
sum(gt)
min(gt)
max(gt)
mean(gt)
var(gt)
sd(gt)
median(gt)
mad(gt)
IQR(gt)
tileSettings

Return tile settings

Description
Returns a list settings used to generate the tile index

Usage
tileSettings(object)

## S4 method for signature 'GenomicTiles'
tileSettings(object)

Arguments
object A /codeGenomicTiles object.

Value
A list of tile settings

Author(s)
Georg Stricker <georg.stricker@in.tum.de>

Examples
gt <- makeTestGenomicTiles()
tileSettings(gt)

untile
Set index to chunkIndex

Description
Replace the tile index with the chunk index in /codeGenomicTiles object

Usage
untile(object, ...)

## S4 method for signature 'GenomicTiles'
untile(object, id = NULL)

Arguments
object A /codeGenomicTiles object.
... Additional arguments
id A vector if tile ids. By default the complete index is taken.
A modified `codeGenomicTiles` object

Georg Stricker <georg.stricker@in.tum.de>

```r
gt <- makeTestGenomicTiles()
newGT <- untile(gt)
```

View the dataset

Cbinding the columns all together and coercing to data.frame

```r
view(object, ...)  
## S4 method for signature 'GenomicTiles'
view(object, ranges = NULL, seqnames = NULL,  
     start = NULL, end = NULL)
```

**Arguments**

- `object`: A `GenomicTiles` object
- `...`: Additional arguments
- `ranges`: A `GRanges` object. Makes it possible to select regions by `GRanges`. Either ranges or seqnames, start and end must be supplied
- `seqnames`: A chromosomes name. Either ranges or seqnames, start and end must be supplied
- `start`: A start site. Either ranges or seqnames, start and end must be supplied
- `end`: An end site. Either ranges or seqnames, start and end must be supplied

A data.frame of the selected data.

Georg Stricker <georg.stricker@in.tum.de>

```r
gt <- makeTestGenomicTiles()
gr <- GRanges(c("chrI", "chrII"), IRanges(c(1, 10), c(40, 30)))
head(view(gt, ranges = gr))
head(view(gt, seqnames = "chrI", start = 1, end = 20))
```
**view,GenoGAM-method**  
*View the dataset*

### Description

Cbinding the columns all together and coercing to data.frame

### Usage

```r
## S4 method for signature 'GenoGAM'
view(object, ranges = NULL, seqnames = NULL,
     start = NULL, end = NULL)
```

### Arguments

- **object**
  A GenoGAM object

- **ranges**
  A GRanges object. Makes it possible to select regions by GRanges. Either ranges or seqnames, start and end must be supplied

- **seqnames**
  A chromosomes name. Either ranges or seqnames, start and end must be supplied

- **start**
  A start site. Either ranges or seqnames, start and end must be supplied

- **end**
  An end site. Either ranges or seqnames, start and end must be supplied

### Value

A data.frame of the selected data.

### Author(s)

Georg Stricker <georg.stricker@in.tum.de>

### Examples

```r
gg <- makeTestGenoGAM()
gr <- GRanges("chrI", IRanges(1,40))
head(view(gg, gr))
```

---

**writeToBEDFile**  
*Write peaks to BED6+3/4 format*

### Description

A function to write the data.table of peaks into a narrowPeaks or broadPeaks file

### Usage

```r
writeToBEDFile(peaks, file = NULL)
```
Arguments

peaks A data.table or data.frame of peaks as produced by callPeaks()

file A file name without suffix. It will be determined automatically. If no file is
given, it will be written to a generic `peaks_[timestamp]` file in the current working
directory

Value

Nothing. A narrowPeaks or broadPeaks file written to 'file'

Author(s)

Georg Stricker <georg.stricker@in.tum.de>

Description

Providing subsetting by GRanges through the single-bracket operator

Usage

```r
## S4 method for signature 'GenoGAMDataSet,GRanges,ANY,ANY'
x[i]
```

Arguments

- `x` A GenoGAMDataSet object
- `i` A GRanges object

Value

A subsetted GenoGAMDataSet object

Description

Getting a specific tile

Usage

```r
## S4 method for signature 'GenomicTiles,numeric,ANY'
x[[i]]
```

```r
## S4 method for signature 'GenomicTiles,GRanges,ANY,ANY'
x[i]
```
Arguments

x  A GenomicTiles object

i  An integer (for `[[]`) or a GRanges object (for `['`)

Value

A DataFrame (for `[[`) or a subsetting GenomicTiles object (for `['`)
Index

[,GenoGAMDataSet, GRanges, ANY, ANY-method, 35
[,GenomicTiles, GRanges, ANY, ANY-method 35
[[[,GenomicTiles, numeric, ANY-method), 35
[[,GenomicTiles, numeric, ANY-method, 35
asDataFrame, 3, 75
callPeaks, 3
changeSettings, 4
changeSettings, GenomicTiles, character-method (changeSettings), 4
checkSettings, 5
checkSettings, GenomicTiles-method (checkSettings), 5
colData, GenoGAM-method (GenoGAM-methods), 12
computeRegionSignificance, 6
computeSignificance, 6
computeSizeFactors, 7
dataRange, 8
dataRange, GenomicTiles-method (dataRange), 8
design, GenoGAM-method (GenoGAM-methods), 12
design, GenoGAMDataSet-method, 8
design<-, GenoGAMDataSet, ANY-method (design, GenoGAMDataSet-method), 8

gIndex, 20
getCoordinates, 20
getCoordinates, GenomicTiles-method (getCoordinates), 20
getChromosomes, GenomicTiles-method (getChromosomes), 18
getChunkIndex, 19
getChunkIndex, GenomicTiles-method (getChunkIndex), 19
getChunkSize (getChromosomes), 18
getChunkSize, GenomicTiles-method (getChromosomes), 18
getIndex, 20
getIndex, GenomicTiles-method (getIndex), 20
getIndexCoordinates, 21
getIndexCoordinates, GenomicTiles-method (getIndexCoordinates), 21
getOverhangSize (getChromosomes), 18
getOverhangSize, GenomicTiles-method (getChromosomes), 18
gTile, 22
gTile, GenomicTiles-method (gTile), 22
gTileNumber (getChromosomes), 18
gTileNumber, GenomicTiles-method (getChromosomes), 18
gTileSize, GenomicTiles-method (getChromosomes), 18
getTileSize, GenomicTiles-method (getChromosomes), 18
IQR, GenomicTiles-method (Summary, GenomicTiles-method), 30
mad, GenomicTiles-method (Summary, GenomicTiles-method), 30
makeTestGenoGAM, 22
makeTestGenoGAMDataSet, 23

GenoGAM, 10
genogam, 10
GenoGAM-class, 11
GenoGAM-methods, 12
GenoGAMDataSet, 13
GenoGAMDataSet-class, 14
GenoGAMDataSetToDataFrame, 3, 15
GenoGAMSettings, 15, 15
GenoGAMSettings-class, 16
GenomicTiles, 16

GenoGAM-class, 17
getChromosomes, 18
getChromosomes, GenomicTiles-method (getChromosomes), 18
getChunkIndex, 19
getChunkIndex, GenomicTiles-method (getChunkIndex), 19
getChunkSize (getChromosomes), 18
getChunkSize, GenomicTiles-method (getChromosomes), 18
getCoordinates, 20
getCoordinates, GenomicTiles-method (getCoordinates), 20
getFits (GenoGAM-methods), 12
getFits, GenoGAM-method (GenoGAM-methods), 12
getOverhangSize (getChromosomes), 18
getOverhangSize, GenomicTiles-method (getChromosomes), 18
getTile, 22
getTile, GenomicTiles-method (getTile), 22
getTileNumber (getChromosomes), 18
getTileNumber, GenomicTiles-method (getChromosomes), 18
getTileSize, GenomicTiles-method (getChromosomes), 18
getTileSize, GenomicTiles-method (getChromosomes), 18
IQR, GenomicTiles-method (Summary, GenomicTiles-method), 30
mad, GenomicTiles-method (Summary, GenomicTiles-method), 30
makeTestGenoGAM, 22
makeTestGenoGAMDataSet, 23

37
makeTestGenomicTiles, 23
mean, GenomicTiles-method
  (Summary, GenomicTiles-method), 30
median, GenomicTiles-method
  (Summary, GenomicTiles-method), 30
plot.GenomGAM, 24
qualityCheck, 24
rowRanges, GenoGAM-method
  (GenoGAM-methods), 12
sd, GenomicTiles-method
  (Summary, GenomicTiles-method), 30
sizeFactors, GenoGAMDataSet-method, 25
sizeFactors<-, GenoGAMDataSet, ANY-method
  (sizeFactors, GenoGAMDataSet-method), 25
subset, GenoGAM-method, 26
subset, GenoGAMDataSet-method, 26
subset, GenomicTiles-method, 27
subsetByOverlaps, GenoGAM, ANY-method,
  28
subsetByOverlaps, GenoGAMDataSet, GRanges-method,
  28
subsetByOverlaps, GenomicTiles, GRanges-method,
  29
SummarizedExperiment, 17
Summary, GenomicTiles-method, 30
tileSettings, 32
tileSettings, GenomicTiles-method
  (tileSettings), 32
untile, 32
untile, GenomicTiles-method (untile), 32
var, GenomicTiles, ANY-method
  (Summary, GenomicTiles-method), 30
view, 33
view, GenoGAM-method, 34
view, GenomicTiles-method (view), 33
writeToBEDFile, 34