Package 'PING'

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Type Package

Title Probabilistic inference for Nucleosome Positioning with MNase-based or Sonicated Short-read Data

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Depends R(>= 2.11.0),chipseq

Imports methods, graphics, grDevices, stats, GenomeGraphs, fda ,IRanges, GenomicRanges, BSgenome, stats4, BiocGenerics

Suggests snowfall, ShortRead, rtracklayer

Enhances parallel

Description Probabilistic inference of ChIP-Seq using an empirical Bayes mixture model approach.

biocViews Clustering, Statistics, Visualization, Sequencing

Collate setClasses.R setMethods.R makeRangedDataOutput.R PING.R PlotRegions.R postPING.R segmentReads.R setParaEM.R setParaPrior.R setParaSeg.R utility.R

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R topics documented:

`makeRangedDataOutput` *Create a RangedData object from a PING output*

Description

Create a list of 'RangedData' objects from a 'ping' object. The resulting RangedData object can then be analyzed with the 'IRanges' packages and/or exported to bed/wig files with the 'rtracklayer' package.

Usage

```
makeRangedDataOutput(obj, type="fixed", filter=list(delta=c(0,Inf),se=c(0,Inf),sigmaSqF=c(0,Inf)
```

Arguments

`obj`	An object of class 'pingList' as returned by 'PING' when running it on the IP/Control data.
`type`	The type of intervals to be created. The different types are 'bed', 'wig', 'ci' and 'fixed'. See details for more info.
`filter`	A list of filters to be used before computing the FDR. By default all regions are included, see details for more info on how to specify the filters.
`length`	The length to be used for the fixed type 'RangedData', see details.

Details

'bed' will generate intervals from the forward peak max to the reverse peak max. 'wig' will generate a density profile for the forward and reverse reads. 'bed' and 'wig' types should be used to be exported to wig/bed files to be used with the UCSC genome browser. 'ci' corresponds to the binding site estimates +/-3*se, while 'fixed' corresponds to the binding site estimates +/-3*length. 'bed' and 'wig' files can be exported using the 'export' function fo the 'rtracklayer' package.

Value

An object of type 'RangedData'.

Author(s)

Xuekui Zhang, <ubcxzhang@gmail.com> Sangsoon Woo, <swoo@fhcrc.org> and Raphael Gottardo, <raphael.gottardo@ircm.qc.ca>

References

Xuekui Zhang, Gordon Robertson, Sangsoon Woo, Brad G. Hoffman, and Raphael Gottardo, "Probabilistic Inference for Nucleosome Positioning with MNase-based or Sonicated Short-read Data" GenomeBiology, under review.

See Also

export

Examples

```
## Not run:
  rdBed<-makeRangedDataOutput(ping,type="bed",filter=list(delta=c(50,Inf),se=c(0,50),sigmaSqF=c(0,22500),s
  export(rbBed,"myfile.bed")
  rdBed<-makeRangedDataOutput(ping,type="wig",filter=list(delta=c(50,Inf),se=c(0,50),sigmaSqF=c(0,22500),s
  export(rbBed,"myfile.wig")
## End(Not run)
```

---

ping *Estimation of binding site positions*

Description

This object contains Estimation of binding site positions and has the following slots: segReadsList.

Usage

```
PING(segReadsList)
```

Arguments

segReadsList	This object contains segmentation of Genome

Methods

code `signature(x = "ping")`: return the error code for each list element (i.e. candidate region) of a PING object. If the string is empty, there were no errors.

plot `signature(x = "ping")`: Plot all regions in the PING object. This might be long, and should only be used to plot a few regions, so subset the object before plotting.

sigmaSqR `signature(x = "ping")`: return the variance parameter of the reverse (R) distribution for each binding event.

sigmaSqF `signature(x = "ping")`: return the variance parameter of the forward (F) distribution for each binding event.

score `signature(x = "ping")`: return the score for each binding event.

scoreF `signature(x = "ping")`: return the score of the forward (F) for each binding event.

scoreR `signature(x = "ping")`: return the score of the forward (R) for each binding event.

maxRange `signature(x = "ping")`: return the range maximum.

minRange `signature(x = "ping")`: return the range minimal.

K `signature(x = "ping")`: subset PING object.

density `signature(x = "ping")`: return the density for each binding event.

Author(s)

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Sangsoon Woo, <swoo@fhcrc.org>

See Also

ping

`ping-class` *The ping class*

Description

This object is used to gather all parameters from fitting PING to a single candidate region. The objet contains the following slots: 'estimates', 'infMat', 'Nmerged', 'converge', 'chr'. 'estimates' is a list containing all parameters estimates as well as standard errors. 'infMat' is the Cholesky decomposition of the information matrix, 'converge' is a logical value indicating whether the EM algorithm has converged, while 'chr' is a character string corresponding to a candidate region's chromosome. 'Nmerged' gives the number of binding events that were merged; binding events that overlap are merged (see the cited paper below for details).

Accessors

The PING package provide accessors to directly access to most of the parameters/standard errors and chromosome. In the code snippets below, 'x' is a 'ping' object.

'chromosome(x)' Gets the chromosome name of the candidate region.

'mu(x)' Gets the position estimates of all binding sites identified in the region.

'delta(x)' Gets the average fragment lengths of all binding sites identified in the region.

'sigmaSqF(x)' Gets the F peak variances of all binding sites identified in the region.

'sigmaSqR(x)' Gets the R peak variances of all binding sites identified in the region.

'seF(x)' Gets the standard errors of all binding site position estimates identified in the region.

'seF(x)' Gets the standard errors of all F peak modes identified in the region.

'seR(x)' Gets the standard errors of all R peak modes identified in the region.

score `signature(x = "ping")`: return the score for each binding event.

scoreF `signature(x = "ping")`: return the score of the forward (F) for each binding event.

scoreR `signature(x = "ping")`: return the score of the forward (R) for each binding event.

Constructor

newPing(w,mu,delta,sigmaSqF,sigmaSqR,seMu,seMuF,seMuR,score,Nmerged,converge,infMat,chr) construct a new 'ping' object with the following arguments:

w The mixture weights (a vector)

mu The binding site positions (a vector)

delta The DNA fragment lengths (a vector)

sigmaSqF The variance parameters for the forward distribution (vector)

sigmaSqR The variance parameters for the forward distribution (vector)

seMu The standard errors for mu (vector)

seMuF The standard errors for muF (vector)

seMuR The standard errors for muR (vector)

seMuR The standard errors for muR (vector)

score The scores for each binding event (vector)

Nmerged The number of peaks that got merged (integer)

converge A logical value, TRUE, if the EM as converged

infMat The information matrix

chr The chromosome for the region

Author(s)

Xuekui Zhang <<xzhang@stat.ubc.ca>>, Sangsoon Woo, <swoo@fhcrc.org> and Raphael Gottardo <<raphael.gottardo@ircm.qc.ca>>

References

Xuekui Zhang, Gordon Robertson, Sangsoon Woo, Brad G. Hoffman, and Raphael Gottardo, "Probabilistic Inference for Nucleosome Positioning with MNase-based or Sonicated Short-read Data" GenomeBiology, under review.

See Also

ping pingError

Examples

```
# Here is an example of how to construct such a region.
# Typically, you would not do this manually, you would use the ping function to return a 'pingList' that co
w<-1
mu<-10000
delta<-150
sigmaSqF<-5000
sigmaSqR<-5000
seMu<-10
seMuF<-10
seMuR<-10
score<-5
Nmerged<-0
converge<-TRUE
chr<-"chr1"
range<-c(1000,2000)
# Contructor
#myPING<-newPing(w,mu,delta,sigmaSqF,sigmaSqR,seMu,seMuF,seMuR,score,Nmerged,as.integer(range),chr)
```

pingError-class *The ping class*

Description

This object is used to return an error code when the PING function failed to return a valid set of estimates for a candidate regions. This could be due to non-convergence of the EM algorithm, a singular information matrix, or a number of reads below the limit specified by the user. All of these are typically due to too few reads in the region and do not affect the rest of the analysis, as such regions would most likely be labelled as false positives.

Accessors

All of the accessors defined for a 'ping' object still work for a 'pingError' object but will simply return a NULL pointer.

Constructor

newPingError(string) where 'string' is the error code.

Constructor

newPingError<-function(string)

string The mixture weights (a vector)

Author(s)

Xuekui Zhang <<xzhang@stat.ubc.ca>>, Sangsoon Woo, <swoo@fhcrc.org> and Raphael Gottardo <<raphael.gottardo@ircm.qc.ca>>

References

Xuekui Zhang, Gordon Robertson, Sangsoon Woo, Brad G. Hoffman, and Raphael Gottardo, "Probabilistic Inference for Nucleosome Positioning with MNase-based or Sonicated Short-read Data" GenomeBiology, under review.

See Also

ping

Examples

```
# Here is an example on how to construct such a pingError object
# Typically, you would not do this manually, you would use the ping function to return a 'pingList' that co
# Contructor
myPingError<-newPingError("Singular information matrix")
# Accessors
# Get the standard error of Mu
se(myPingError)
# Get the standard error of MuF
seF(myPingError)
# Get the scores
score(myPingError)
```

`pingList-class` *The ping class*

Description

This object is used to gather all parameters from fitting PING to multiple candidate regions (as returned by the 'segmentReads' function). The objet contains the following slots: 'List', 'paraPrior', 'paraEM', 'minReads', 'N', 'Nc'. 'List' is a list of 'ping' or 'pingError' objects. 'paraPrior' is a list containing the hyperparameters used for the prior, 'paraEM' is a list of convergence parameters for the EM, 'minReads' is a list containing the minimum number of reads used to fit a region with 'PING', 'N' is the total number of reads in the ChIP samples while 'Nc' is the total number of reads in the control sample.

Arguments

`object`	An object of class `ping`.

Accessors

The PING package provide accessors to directly access to most of the parameters/standard errors and chromosomes. In the code snippets below, 'x' is a 'pingList' object. For all accessors, the 'pingError' objects are omitted, so that the accessors only return values for the 'ping' objects (i.e. all valid binding events).

'chromosome(x)' Gets the chromosome names of all candidate regions.

'mu(x)' Gets the position estimates of all binding sites identified in all candidate regions.

'delta(x)' Gets the average fragment lengths of all binding sites identified in all candidate regions.

'sigmaSqF(x)' Gets the F peak variances of all binding sites identified in all candidate regions.

'sigmaSqR(x)' Gets the R peak variances of all binding sites identified in all candidate regions.

'seF(x)' Gets the standard errors of all binding site position estimates identified in all candidate regions.

'seF(x)' Gets the standard errors of all F peak modes identified in all candidate regions.

'seR(x)' Gets the standard errors of all R peak modes identified in all candidate regions.

'score(x)' Gets the scores of all binding events identified in all candidate regions.

Constructor

newPingList(List, paraEM, paraPrior, minReads, N, Nc)

List The mixture weights (a vector)

paraEM The binding site positions (a vector)

paraPrior The DNA fragment lengths (a vector)

N The variance parameters for the forward distribution (vector)

Nc The variance parameters for the forward distribution (vector)

Methods

[`signature(x = "ping")`: subset PING object.

Methods

length `signature(x = "ping")`: subset PING object.

Constructor

newPingList<-function(List, paraEM, paraPrior, minReads, N, Nc) constructs a new 'pingList' object with the following arguments.

newPingList

w The mixture weights (a vector)

mu The binding site positions (a vector)

delta The DNA fragment lengths (a vector)

sigmaSqF The variance parameters for the forward distribution (vector)

sigmaSqR The variance parameters for the reverse distribution (vector)

seMu The standard errors for mu (vector)

seMuF The standard errors for muF (vector)

seMuR The standard errors for muR (vector)

seMuR The standard errors for muR (vector)

score The scores for each binding event (vector)

Nmerged The number of peaks that were merged (integer)

converge A logical value, TRUE, if the EM as converged

infMat The information matrix

chr The chromosome for the region

Author(s)

Xuekui Zhang <<xzhang@stat.ubc.ca>>, Sangsoon Woo, <swoo@fhcrc.org> and Raphael Gottardo <<raphael.gottardo@ircm.qc.ca>>

References

Xuekui Zhang, Gordon Robertson, Sangsoon Woo, Brad G. Hoffman, and Raphael Gottardo, "Probabilistic Inference for Nucleosome Positioning with MNase-based or Sonicated Short-read Data" PlosONE, under review.

See Also

ping

Examples

```
# Here is an example of how to construct such a region
# Typically, you would not do this manually, you would use the ping function to return a 'pingList' that co
w<-1
mu<-10000
delta<-150
sigmaSqF<-5000
sigmaSqR<-5000
seMu<-10
seMuF<-10
```

```
seMuR<-10
score<-5
Nmerged<-0
converge<-TRUE
infMat<-matrix(0)
chr<-"chr1"
range<-c(1000,2000)
# Contructor
#myPING1<-newPing(w,mu,delta,sigmaSqF,sigmaSqR,seMu,seMuF,seMuR,score,Nmerged,converge,infMat,as.integer(ra
#myPING2<-newPing(w,mu+1000,delta,sigmaSqF,sigmaSqR,seMu,seMuF,seMuR,score,Nmerged,converge,infMat,as.integ

#minReads<-list(perPeak=2,perRegion=5)
#paraPrior<-list(xi=200,rho=1,alpha=20,beta=40000)
#paraEM<-list(minK=1,maxK=15,tol=10e-6,B=100)
#N<-100
#Nc<-200

#mynewPingList<-newPingList(list(myPING1,myPING2), paraEM, paraPrior, minReads, as.integer(100), as.integer
# Accessors
# Get the standard error of Mu
#se(mynewPingList)
# Get the standard error of MuF
#seF(mynewPingList)
# Get the scores
#score(mynewPingList)
```

---

postPING *Post process Estimation of binding site positions obtained from PING*

Description

Post process Estimation of binding site positions obtained from PING. Refit mixture models with stronger prior in candidate regions contain potential problems, and then convert final result into dataframe.

Usage

```
postPING(ping, seg, rho=8, sigmaB2=2500,rho1=0.8,alpha1=20,alpha2=100,beta2=100000,xi=150, min.d
```

Arguments

ping	A 'pingList' object containing estimation of nuclesome positions, result of 'PING' function.
seg	An object of class 'segmentReadsList' containing the results for all regions pre-processed, 'segmentReads' function.
rho1, sigmaB2, rho, alpha1, alpha2, beta2, xi	Integer values, the parameters in the prior of mixture models to be re-fitted.
min.dist	The minimum distance of two adjacent nucleosomes predicted from different candidate regions, smaller than that will be treated as duplicated predictions for the same nucleosomes.
lambda	The lambda control Gaussian Markov Random Field prior on the distance of adjacent nucleosomes, we do not recommend user change the default value.

Value

An dataframe containing the estimation of binding site positions.

Note

Based on our experiemt on a few real data sets, we suggestion to use following values of parameters. For sonication data we use rho1=1.2; sigmaB2=6400;rho=15;alpha1=10; alpha2=98; beta2=200000. For MNase data we use rho1=3; sigmaB2=4900; rho=8; alpha1=20; alpha2=100; beta2=100000. The value of xi depends on specy of sample, since that affect the length of linker-DNA. For example, we use xi=160 for yeast and xi=200 for mouse.

Author(s)

Xuekui Zhang <<xzhang@stat.ubc.ca>>, Sangsoon Woo, <swoo@fhcrc.org> and Raphael Gottardo <<raphael.gottardo@ircm.qc.ca>>

References

Xuekui Zhang, Gordon Robertson, Sangsoon Woo, Brad G. Hoffman, and Raphael Gottardo, "Probabilistic Inference for Nucleosome Positioning with MNase-based or Sonicated Short-read Data" PlosONE, under review.

`segmentReads` *Segment the genome into candidate regions*

Description

Pre-process bidirectional aligned reads data from a single ChIP-Seq experiment to detect candidate regions with a minimum number of forward and reverse reads. These candidate regions will then be processed by PING.

Usage

```
segmentReads(data, dataC=NULL, map=NULL,minReads=2, minReadsInRegion=3,jitter=FALSE, maxLregion=
```

Arguments

`data`	A 'GenomeData' object containing the IP reads. See details for more information on how to set up the data.
`dataC`	A 'GenomeData' object containing the control reads. Set to NULL by default, i.e. no control.
`map`	A 'RangedData' object containing the mappability profiles. Set to NULL by default, i.e. no profiles.
`minReads`	The minimum number of F/R reads to be present in the sliding window. Set to NULL by default, and this number is automatically calculated.
`minReadsInRegion`	The minimum number of F/R reads to be present in the region.
`jitter`	A logical value stating whether some noise should be added to the read locations. This is recommended if the read positions have lots of duplicates.
`maxLregion`	The maximum length. We do not suggest to use too long region, since that need to fit mixture models with too many components.
`minLregion`	The minimum length.

Value

An object of class 'segmentReadsList' containing the results for all regions pre-processed.

Author(s)

Xuekui Zhang <<xzhang@stat.ubc.ca>>, Sangsoon Woo, <swoo@fhcrc.org> and Raphael Gottardo <<raphael.gottardo@ircm.qc.ca>>

References

Xuekui Zhang, Gordon Robertson, Sangsoon Woo, Brad G. Hoffman, and Raphael Gottardo, "Probabilistic Inference for Nucleosome Positioning with MNase-based or Sonicated Short-read Data" PlosONE, under review.

See Also

segmentReads

Examples

```
# Read data
path<- system.file("extdata",package="PING")
## Note that the col name for the chromosome needs to be space and not chr
dataIP<-read.table(file.path(path, "GSM351492_R4_chr1.bed"),header=TRUE,colClasses=c("factor","integer","in
dataIP<-as(dataIP,"RangedData")
dataIP<-as(dataIP,"GenomeData")

seg<-segmentReads(dataIP, minReads=2)
```

---

segReads *Segment the genome into candidate regions*

Description

Pre-process bidirectional aligned reads data from a single ChIP-Seq experiment to detect candidate regions with a minimum number of forward and reverse reads. These candidate regions will then be processed by PING.

Usage

```
segReads(yF, yR, cF, cR, map, chr)
```

Arguments

yF	This object contains an ExpressionSet
yR	String containing the genome name used (vector).
cF	String containing the name of chromosome used (vector).
cR	String containing the Position of the sequences (vector).
map	String containing the copy number of sequence (vector).
chr	String containing the expresion data of enriched region (matrix with n column.

Methods

map `signature(x = "ping")`: subset PING object.

Author(s)

Xuekui Zhang <<xzhang@stat.ubc.ca>>, Sangsoon Woo, <swoo@fhcrc.org> and Raphael Gottardo <<raphael.gottardo@ircm.qc.ca>>

References

Xuekui Zhang, Gordon Robertson, Sangsoon Woo, Brad G. Hoffman, and Raphael Gottardo, "Probabilistic Inference for Nucleosome Positioning with MNase-based or Sonicated Short-read Data" PlosONE, under review.

See Also

ping

---

segReadsList *Segment the genome into candidate regions*

Description

Pre-process bidirectional aligned reads data from a single ChIP-Seq experiment to detect candidate regions with a minimum number of forward and reverse reads. These candidate regions will then be processed by PING.

Usage

```
segReadsList(List,paraSW,N,Nc)
```

Arguments

List	This object contains an ExpressionSet
paraSW	String containing the genome name used (vector).
N	String containing the name of chromosome used (vector).
Nc	String containing the Position of the sequences (vector).

Methods

[`signature(x = "ping")`: subset gadem object.

[`signature(x = "ping")`: subset gadem object.

Methods

length `signature(x = "ping")`: subset PING object.

Author(s)

Xuekui Zhang <<xzhang@stat.ubc.ca>>, Sangsoon Woo, <swoo@fhcrc.org> and Raphael Gottardo <<raphael.gottardo@ircm.qc.ca>>

References

Xuekui Zhang, Gordon Robertson, Sangsoon Woo, Brad G. Hoffman, and Raphael Gottardo, "Probabilistic Inference for Nucleosome Positioning with MNase-based or Sonicated Short-read Data" GenomeBiology, under review.

See Also

ping

`setParaEM` *Set convergence parameters of the EM algorithm*

Description

This function can be used to change the internal PING parameters for the EM algorithm. This function should only be called if you really now what you are doing!.

Usage

```
setParaEM(minK=0,maxK=0,tol=1e-4,B=100,mSelect="AIC3",mergePeaks=TRUE,mapCorrect=TRUE)
```

Arguments

`minK`	An integer value. The minimum number of binding events per region. If value is 0, the minimum number is automatically calculated.
`maxK`	An integer value. The maximum number of binding events per region. If value is 0, the maximum number is automatically calculated.
`tol`	The tolerance for the EM algorithm
`B`	An integer value. The maximum number of iterations to be used.
`mSelect`	A character string specifying the information criteria to be used when selecting the number of binding events.
`mergePeaks`	A logical value stating whether overlapping binding events should be picked.
`mapCorrect`	Should mappability profiles be incorporated in the estimation, that is missing reads estimated.

Value

No value returned. The function simply modifies the internal variables 'paraEMH'.

Author(s)

Xuekui Zhang <<xzhang@stat.ubc.ca>>, Sangsoon Woo, <swoo@fhcrc.org> and Raphael Gottardo <<raphael.gottardo@ircm.qc.ca>>

References

Xuekui Zhang, Gordon Robertson, Sangsoon Woo, Brad G. Hoffman, and Raphael Gottardo, "Probabilistic Inference for Nucleosome Positioning with MNase-based or Sonicated Short-read Data" GenomeBiology, under review.

See Also

setParaPrior

Examples

```
# Using mSelect="BIC"
setParaEM(minK=1,maxK=8,tol=1e-4,B=100,mSelect="BIC",mergePeaks=TRUE,mapCorrect=TRUE)
# Using mSelect="AIC"
setParaEM(minK=1,maxK=8,tol=1e-4,B=100,mSelect="AIC",mergePeaks=TRUE,mapCorrect=TRUE)
```

---

setParaPrior *Set convergence parameters of the EM algorithm*

Description

This function can be used to change the internal PING parameters for the prior distribution. This function should only be called if you really now what you are doing! In particular, you may want to specify the average DNA fragment size for your sample by changing the 'xi' parameter.

Usage

```
setParaPrior(xi=150,rho=1.2,alpha=10,beta=20000,lambda=-0.000064,dMu=200)
```

Arguments

xi	Our best guest for the average DNA fragment size.
rho	A variance parameter for the average DNA fragment size distribution.
alpha	First hyperparameter of the inverse Gamma distribution for sigma^2 in the PING model.
beta	First hyperparameter of the inverse Gamma distribution for sigma^2 in the PING model.
lambda	The precision of the prior for mu used for histone data.
dMu	Our best guess for the distance between two neighboring nucleosomes.

Value

No value returned. The function simply modifies the internal variables 'paraPriorH'.

Author(s)

Xuekui Zhang <<xzhang@stat.ubc.ca>>, Sangsoon Woo, <swoo@fhcrc.org> and Raphael Gottardo <<raphael.gottardo@ircm.qc.ca>>

References

Xuekui Zhang, Gordon Robertson, Sangsoon Woo, Brad G. Hoffman, and Raphael Gottardo, "Probabilistic Inference for Nucleosome Positioning with MNase-based or Sonicated Short-read Data" GenomeBiology, under review.

See Also

setParaEM

Examples

```
# set prior for MNase data
setParaPrior(xi=150,rho=0.8,alpha=20,beta=20000,lambda=-0.000064,dMu=200)
# set prior for sonication data
setParaPrior(xi=150,rho=1.2,alpha=10,beta=20000,lambda=-0.000064,dMu=200)
```

---

show *show PING*

Description

This methods show the objects of PING

Usage

```
## S4 method for signature 'ping'
show(object)
## S4 method for signature 'pingError'
show(object)
## S4 method for signature 'pingList'
show(object)
## S4 method for signature 'segReads'
show(object)
## S4 method for signature 'segReadsList'
show(object)
```

Arguments

object	Object returned from ping .

Details

List of the slots include in the object

Author(s)

Xuekui Zhang <<xzhang@stat.ubc.ca> Sangsoon Woo, <swoo@fhcrc.org> Raphael Gottardo <<raphael.gottardo@ircm.qc.ca>

See Also

summary

summary *summary PING*

Description

This methods summary the objects of PING.

Usage

```
## S4 method for signature 'ping'
summary(object)
## S4 method for signature 'pingList'
summary(object)
## S4 method for signature 'segReads'
summary(object)
## S4 method for signature 'segReadsList'
summary(object)
```

Arguments

object	Object returned from ping .

Author(s)

Xuekui Zhang <<xzhang@stat.ubc.ca> Sangsoon Woo, <swoo@fhcrc.org> Raphael Gottardo <<raphael.gottardo@ircm.qc.ca>

See Also

show

unique *GenomeData Unique Reads*

Description

This methods select the unique enriched regions

Arguments

object	Object returned from ping .

Author(s)

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See Also

ping

Index