Package ‘PICS’

April 26, 2017

Type Package

Title Probabilistic inference of ChIP-seq

Version 2.20.0

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Depends R (>= 2.14.0), BiocGenerics (>= 0.1.3)

Imports methods, stats4, IRanges, GenomicRanges, graphics, grDevices,
stats, Rsamtools, GenomicAlignments, S4Vectors

Suggests ShortRead, rtracklayer, parallel

SystemRequirements GSL (GNU Scientific Library)

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

License Artistic-2.0

biocViews Clustering, Visualization, Sequencing, ChIPSeq

NeedsCompilation yes

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bam2gr

Description

Reads a bam file using Rsamtools and extract the reads for each chromosome.

Usage

bam2gr(bamFile, chr=NULL, PE=FALSE, verbose=FALSE)

Arguments

bamFile A character string, the name of the .bam file to read.
chr An optional character string. If specified, only the selected chromosome will be returned. Speed up the computation.
PE A logical. This should be set to TRUE for paired-end sequencing data.
verbose A logical. Print additional information about the data.

Value

Returns a GRanges of all the reads for each chromosome.

Note

The user might encounter a memory allocation error when using bam files of bigger sizes. Splitting the file by chromosome before calling bam2gr will solve this issue.

For Paired-End data, non matched reads are discarded.

Author(s)

Renan Sauteraud

See Also

segmentPICS
**makeRangedDataOutput**

Create a RangedData object from a PICS output

**Description**

Create a list of ‘RangedData’ objects from a ‘pics’ 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**

```r
makeRangedDataOutput(obj, type="fixed", filter=list(delta=c(0,Inf),se=c(0,Inf),sigmaSqF=c(0,Inf),sigmaSqR=c(0,Inf)),length=100)
```

**Arguments**

- `obj` An object of class ‘picsList’ as returned by ‘PICS’ 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, Arnaud Droit <<arnaud.droit@crchuq.ualaval.ca>> and Raphael Gottardo <<rgottard@fhcrc.org>

**References**


**See Also**

export
## Not run:

rdBed<-makeRangedDataOutput(pics,type="bed",filter=list(delta=c(50,Inf),se=c(0,50),sigmaSqF=c(0,22500),sigmaSqR=c(0,22500),score=c(10,Inf)))
export(rdBed,"myfile.bed")

rdBed<-makeRangedDataOutput(pics,type="wig",filter=list(delta=c(50,Inf),se=c(0,50),sigmaSqF=c(0,22500),sigmaSqR=c(0,22500),score=c(10,Inf)))
export(rdBed,"myfile.wig")

## End(Not run)

---

**Description**

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

**Usage**

```
PICS(segReadsList,dataType=NULL, paraEM=NULL, paraPrior=NULL, nCores=1)
```

**Arguments**

- segReadsList: This object contains segmentation of Genome
- dataType: The type of data you are processing: specified ‘TF’ for transcription factor.
- paraEM: A list of parameters for the EM algorithm as returned by the setParaEm function. The default parameters should be good enough for most usages.
  - minK: an integer, default=1. The minimum number of binding events per region. If the value is 0, the minimum number is automatically calculated.
  - maxK: an integer, default=15. The maximum number of binding events per region. If the value is 0, the maximum number is automatically calculated.
  - tol: a numeric, default=1e-4. The tolerance for the EM algorithm.
  - B: an integer, default=100. 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. Default="BIC"
  - mergePeaks: a logical stating whether overlapping binding events should be picked. Default=TRUE
  - mapCorrect: a logical stating whether mappability profiles should be incorporated in the estimation, i.e: missing reads estimated. Default=TRUE
- paraPrior: A list of parameters for the prior distribution as returned by the setParaPrior function. The default parameters should be good enough for most usages.
  - xi: an integer, default=200. The average DNA fragment size.
  - rho: an integer, default=1. A variance parameter for the average DNA fragment size distribution.
  - alpha: an integer, default=20. First hyperparameter of the inverse Gamma distribution for sigma^2 in the PICS model
beta: an integer, default=40000. Second hyperparameter of the inverse
Gamma distribution for sigma^2 in the PING model
lambda: an integer, default=0. The precision of the prior for mu used for
histone data.
dMu: an integer, default=0. Our best guess for the distance between two
neighboring nucleosomes.
ncores: An integer. The number of cores that should be used in parallel by the func-
tion.

Methods

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

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

sigmaSqR signature(x = `\'pics\'\'): return the variance parameter of the reverse (R) distribu-
tion for each binding event.

sigmaSqF signature(x = `\'pics\'\'): return the variance parameter of the forward (F) distribu-
tion for each binding event.

score signature(x = `\'pics\'\'): return the score for each binding event.

scoreF signature(x = `\'pics\'\'): return the score of the forward (F) for each binding event.

scoreR signature(x = `\'pics\'\'): return the score of the forward (R) for each binding event.

maxRange signature(x = `\'pics\'\'): return the range maximum.

minRange signature(x = `\'pics\'\'): return the range minimal.

K signature(x = `\'pics\'\'): subset PICS object.

wigDensity signature(x = `\'pics\'\'): return the density for each binding event.

Author(s)

Xuekui Zhang, Arnaud Droit <<arnaud.droit@crchuq.ualaval.ca>> and Raphael Gottardo <<rgottard@fhcrc.org>

References

X. Zhang, G. Robertson, M. Krzywinski, K. Ning, A. Droit, S. Jones, and R. Gottardo, “PICS:

See Also

pics
The pics class

Description

This object is used to gather all parameters from fitting PICS to a single candidate region. The object 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 PICS package provide accessors to directly access to most of the parameters/standard errors and chromosome. In the code snippets below, ‘x’ is a ‘pics’ 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 = "pics"): return the score for each binding event.
scoreF signature(x = "pics"): return the score of the forward (F) for each binding event.
scoreR signature(x = "pics"): return the score of the forward (R) for each binding event.

Constructor

newPics(w,mu,delta,sigmaSqF,sigmaSqR,seMuF,seMuR,score,Nmerged,converge,infMat,chr)
construct a new ‘pics’ 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, Arnaud Droit <<arnaud.droit@crchuq.ualaval.ca>> and Raphael Gottardo <<rgottardo@fhcrc.org>>

References


See Also

pics picsError

Examples

# Here is an example of how to construct such a region.
# Typically, you would not do this manually, you would use the pics function to return a 'picsList' that contains
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)
# Constructor
#myPICS<-newPics(w,mu,delta,sigmaSqF,sigmaSqR,seMu,seMuF,seMuR,score,Nmerged,as.integer(range),chr)

---

Description

This object is used to return an error code when the PICS 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 ‘pics’ object still work for a ‘picsError’ object but will simply return a NULL pointer.

Constructor

newPicsError(string) where ‘string’ is the error code.
Constructor

newPicsError<-function(string)

  string  The mixture weights (a vector)

Author(s)

Xuekui Zhang, Arnaud Droit <<arnaud.droit@crchuq.ualaval.ca>> and Raphael Gottardo <rgottard@fhcrc.org>

References


See Also

pics

Examples

# Here is an example on how to construct such a picsError object
# Typically, you would not do this manually, you would use the pics function to return a 'picsList' that contains
# Constructor
myPicsError<-newPicsError("Singular information matrix")
# Accessors
# Get the standard error of Mu
se(myPicsError)
# Get the standard error of MuF
seF(myPicsError)
# Get the scores
score(myPicsError)

picsFDR          Estimate the FDR.

Description

Estimate the false detection rate for an object of class pics or picsList.

Usage

picsFDR(picsIP,picsCont,filter=list(delta=c(0,Inf),se=c(0,Inf),sigmaSqF=c(0,Inf),sigmaSqR=c(0,Inf)))

Arguments

picsIP          An object of class pics or picsList containing the informations for the IP reads.
picsCont       An object of class pics or picsList containing the informations for the control reads.
filter          filterA list of ranges for filtering regions based on PICS parameters. By default filter is set to 'NULL' and all regions are used.
delta         Length of the binding sites.
**Value**

A 3 columns data.frame with the following columns: FDR, score, N.

**Author(s)**

Xuekui Zhang

**See Also**

`picsList pics`

---

### Description

This object is used to gather all parameters from fitting PICS 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 ‘pics’ or ‘picsError’ 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 ‘PICS’, ‘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 `pics`.

### Accessors

The PICS package provide accessors to directly access to most of the parameters/standard errors and chromosomes. In the code snippets below, ‘x’ is a ‘picsList’ object. For all accessors, the ‘picsError’ objects are omitted, so that the accessors only return values for the ‘pics’ 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

newPicsList(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 = `pic`): subset PICS object.

Methods

length signature(x = `pic`): subset PICS object.

Constructor

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

newPicsList

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)
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, Arnaud Droit <<arnaud.droit@crchuq.ualaval.ca>> and Raphael Gottardo <<rgottard@fhcrc.org

References

See Also

picks

Examples

# Here is an example of how to construct such a region
# Typically, you would not do this manually, you would use the pics function to return a 'picsList' that contains
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)
# Constructor
#myPICS1<-newPics(w,mu,delta,sigmaSqF,sigmaSqR,seMu,seMuF,seMuR,score,Nmerged,converge,infMat,as.integer(range),chr)
#myPICS2<-newPics(w,mu+1000,delta,sigmaSqF,sigmaSqR,seMu,seMuF,seMuR,score,Nmerged,converge,infMat,as.integer(range),chr)
#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

#mynewPicsList<-newPicsList(list(myPICS1,myPICS2), paraEM, paraPrior, minReads, as.integer(100), as.integer(200))

# Accessors
# Get the standard error of Mu
#se(mynewPicsList)
# Get the standard error of MuF
#seF(mynewPicsList)
# Get the scores
#score(mynewPicsList)

plot-FDR

FDR plot for PICS

Description

This method plots an FDR curve showing the FDR as a function of the PICS scores.

Usage

## S4 method for signature 'picsList,picsList'
plot(x, y, filter=NULL, h=.1, ...)
segmentPICS

Arguments

x A picsList object as returned by the function PICS run on the treatment data.
y A picsList object as returned by the function PICS run on the control data.
filter A list of ranges for filtering regions based on PICS parameters. By default filter is set to ‘NULL’ and all regions are used.
h A value between 0 and 1, representing the desired FDR. This simply draws a horizontal line at the given value.
... Further graphical parameters passed to the generic function plot.

Author(s)

Xuekui Zhang, Arnaud Droit <<arnaud.droit@crchuq.ualaval.ca>> and Raphael Gottardo <<rgottard@fhcrc.org>>

References


See Also

PICS

Description

These two functions are part of the segmentation step for paired-end sequencing data and are exported to be used in PING package.

segmentPICS

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 PICS.

Usage

segmentPICS(data, dataC=NULL, map=NULL, minReads=2, minReadsInRegion=3, jitter=FALSE, dataType="TF", maxLregion=0, minLregion=100)
Arguments

- **data**: A linkS4class(GRanges) object containing the IP reads. See details for more information on how to set up the data.
- **dataC**: A linkS4class(GRanges) 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.
- **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.
- **dataType**: Type of experiment. "TF" or "H".
- **maxLregion**: The maximum length.
- **minLregion**: The minimum length.

Value

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

Author(s)

Xuekui Zhang, Arnaud Droit <arnaud.droit@crchuq.ualaval.ca> and Raphael Gottardo <rgottard@fhcrc.org>

References


See Also

segReadsList

Examples

```r
# Read data
path<-system.file("extdata",package="PICS")
## Note that the col name for the chromosome needs to be space and not chr
dataIP<-read.table(file.path(path,"Treatment_tags_chr21_sort.bed"),header=TRUE,colClasses=c("factor","integer","integer","factor"))
dataIP<-as(dataIP,"GRanges")
dataCont<-read.table(file.path(path,"Input_tags_chr21_sort.bed"),header=TRUE,colClasses=c("factor","integer","integer","factor"))
dataCont<-as(dataCont,"GRanges")
map<-read.table(file.path(path,"mapProfileShort"),header=TRUE,colClasses=c("factor","integer","integer","NULL"))
map<-as(map,"GRanges")
seg<-segmentPICS(dataIP, dataC=dataCont, map=map, minReads=1)
```
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 PICS.

Methods
map signature(x = `pics`): subset PICS object.

Author(s)
Xuekui Zhang, Arnaud Droit <arnaud.droit@crchuq.ualaval.ca> and Raphael Gottardo <rgottard@fhcrc.org>

References

See Also
pics
segReadsListPE

References


See Also

pics

segReadsListPE List of segReadsPE objects

Description

A list of segReadsPE. The class also store information related to the segmentation process, keeping a trace of the parameters used and the proportion of forward and reverse reads for the input and the control.

Methods

[ signature(x = "pics")]: subset gadem object.
[ [ signature(x = "pics")]: subset gadem object.

Extends

Class segReadsList, directly.

Author(s)

Xuekui Zhang

See Also

segReadsPE segReadsList

segReadsPE Class to store post-segmentation result

Description

This class stores the information of the segmentation performed by segmentPING. It is used as the input of the PING function.

Extends

Class segReadsList, directly.

Author(s)

Xuekui Zhang
See Also

`segReads` `segReadsListPE`
setParaPrior

Function that returns a list of parameters that can be used as an argument of PICS.

Description

This function takes from 0 to 6 parameters as argument, check if they are valid and returns a list to be used in a call to PICS.

Usage

```r
setParaPrior(xi=200, rho=1, alpha=20, beta=40000, lambda=0, dMu=0, dataType=NULL, PExi=0)
```

Arguments

- **xi**: An integer. The average DNA fragment size.
- **rho**: An integer. A variance parameter for the average DNA fragment size distribution.
- **alpha**: An integer. First hyperparameter of the inverse Gamma distribution for sigma^2 in the PICS model.
- **beta**: An integer. Second hyperparameter of the inverse Gamma distribution for sigma^2 in the PICS model.
- **lambda**: An integer. The precision of the prior for mu used for histone data.
- **dMu**: An integer. Our best guess for the distance between two neighboring nucleosomes.
- **dataType**: A character string. If a valid dataType is specified, use our suggested parameters. "MNase" or "sonicated".
- **PExi**: A numeric. With paired end data, `xi` can be calculated directly from the reads. If PExi is set, it will overwrite the xi determined by the dataType.

Value

Returns a list of 6 parameters to be used in PICS.

Author(s)

Renan Sauteraud

See Also

PICS

Examples

```r
# set prior for PICS data
paraPrior<-setParaPrior()

# set prior for sonicated data using our selected default parameters
paraPrior<-setParaPrior(dataType="sonicated")
```
show

Description

This methods show the objects of PICS

Usage

```r
## S4 method for signature 'pics'
show(object)
## S4 method for signature 'picsError'
show(object)
## S4 method for signature 'picsList'
show(object)
## S4 method for signature 'segReads'
show(object)
## S4 method for signature 'segReadsList'
show(object)
```

Arguments

- `object`: Object returned from `pics`.

Details

List of the slots include in the object

Author(s)

Xuekui Zhang, Arnaud Droit <arnaud.droit@crchuq.ualaval.ca> and Raphael Gottardo <rgottard@fhcrc.org>

See Also

- `summary`

---

summary

Description

This methods summarized ‘pics’, ‘picsList’, ‘seg’ or ‘segList’ objects.
summarySeg

Usage

```r
## S4 method for signature 'pics'
summary(object)
## S4 method for signature 'picsList'
summary(object)
## S4 method for signature 'segReads'
summary(object)
## S4 method for signature 'segReadsList'
summary(object)
```

Arguments

object Object returned from `pics`.

Author(s)

Xuekui Zhang, Arnaud Droit <<arnaud.droit@crchuq.ualaval.ca>> and Raphael Gottardo <<rgottard@fhcrc.org>>

See Also

`show`

summarySeg

`Summary a segReadsList object.`

Description

Returns info about a segReadsList object in a data.frame containing the following informations:
- `chr` : chromosome id
- NF : number of forward reads
- NR : number of reverse reads
- L : length of segment
- min: start location of segments
- max: end location of segments

Usage

```r
summarySeg(seg)
```

Arguments

seg An object of class `segReadsList`

Value

A six columns data.frame.

Author(s)

Xuekui Zhang

See Also

`segReadsList`
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