

Package ‘cn.mops’

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License LGPL (>= 2.0)

Type Package

Title cn.mops - Mixture of Poissons for CNV detection in NGS data

Description cn.mops (Copy Number estimation by a Mixture Of PoissonS) is a data processing pipeline for copy number variations and aberrations (CNVs and CNAs) from next generation sequencing (NGS) data. The package supplies functions to convert BAM files into read count matrices or genomic ranges objects, which are the input objects for cn.mops. cn.mops models the depths of coverage across samples at each genomic position. Therefore, it does not suffer from read count biases along chromosomes. Using a Bayesian approach, cn.mops decomposes read variations across samples into integer copy numbers and noise by its mixture components and Poisson distributions, respectively. cn.mops guarantees a low FDR because wrong detections are indicated by high noise and filtered out. cn.mops is very fast and written in C++.

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URL <http://www.bioinf.jku.at/software/cnmops/cnmops.html>

Depends R (>= 2.12), BiocGenerics, Biobase, IRanges, GenomicRanges

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Suggests snow, DNACopy

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 'normalizeChromosomes.R' 'normalizeGenome.R' 'plot-methods.R'
 'show-methods.R' 'segment.R' 'zzz.R' 'AllGenerics.R'
 'methodsAccess.R' 'getSegmentReadCountsFromBAM.R'
 'haplocn.mops.R' 'segPlot.R' 'exomecn.mops.R'
 'calcIntegerCopyNumbers.R' 'makeRobustCNVR.R'
 'referencecn.mops.R' 'calcFractionalCopyNumbers.R' 'singlecn.mops.R'

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R topics documented:

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`calcFractionalCopyNumbers`*Calculation of fractional copy numbers for the CNVs and CNV regions.*

Description

This generic function calculates the fractional copy numbers of a CNV detection method stored in an instance of `CNVDetectionResult-class`. Must be a result of "referencecn.mops".

Arguments

<code>object</code>	An instance of "CNVDetectionResult"
<code>segStat</code>	Which statistic per segment should be used. Can be either "mean" or "median". (Default="mean").

Value

`calcFractionalCopyNumbers` returns an instance of "CNVDetectionResult".

Author(s)

Guenter Klambauer <klambauer@bioinf.jku.at>

Examples

```
data(cn.mops)
r <- referencecn.mops(X[,1:2], rowMedians(X))
calcFractionalCopyNumbers(r)
```

`calcIntegerCopyNumbers`*Calculation of integer copy numbers for the CNVs and CNV regions.*

Description

This generic function calculates the integer copy numbers of a CNV detection method stored in an instance of `CNVDetectionResult-class`.

Arguments

<code>object</code>	An instance of "CNVDetectionResult"
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Value

`calcIntegerCopyNumbers` returns an instance of "CNVDetectionResult".

Author(s)

Guenter Klambauer <klambauer@bioinf.jku.at>

Examples

```
data(cn.mops)
r <- cn.mops(X[1:100,1:5])
calcIntegerCopyNumbers(r)
```

cn.mops

Copy number detection in NGS data.

Description

This function performs the cn.mops algorithm for copy number detection in NGS data.

Usage

```
cn.mops(input,
  I = c(0.025, 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4),
  classes = c("CN0", "CN1", "CN2", "CN3", "CN4", "CN5", "CN6", "CN7", "CN8"),
  priorImpact = 1, cyc = 20, parallel = 0,
  normType = "poisson", normQu = 0.25, norm = 1,
  upperThreshold = 0.5, lowerThreshold = -0.9,
  minWidth = 3, segAlgorithm = "fast", minReadCount = 5,
  useMedian = FALSE, returnPosterior = FALSE, ...)
```

Arguments

input	Either an instance of "GRanges" or a raw data matrix, where columns are interpreted as samples and rows as genomic regions. An entry is the read count of a sample in the genomic region.
I	Vector positive real values that contain the expected fold change of the copy number classes. Length of this vector must be equal to the length of the "classes" parameter vector. For human copy number polymorphisms we suggest to use the default $I = c(0.025, 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4)$.
classes	Vector of characters of the same length as the parameter vector "I". One vector element must be named "CN2". The names reflect the labels of the copy number classes. Default = $c("CN0", "CN1", "CN2", "CN3", "CN4", "CN5", "CN6", "CN7", "CN8")$.
priorImpact	Positive real value that reflects how strong the prior assumption affects the result. The higher the value the more samples will be assumed to have copy number 2. Default = 1.
cyc	Positive integer that sets the number of cycles for the algorithm. Usually after less than 15 cycles convergence is reached. Default = 20.

parallel	How many cores are used for the computation. If set to zero than no parallelization is applied. The package "snow" has to be installed for this option. Default = 0.
normType	Mode of the normalization technique. Possible values are "mean", "min", "median", "quant", "poisson" and "mode". Read counts will be scaled sample-wise. Default = "poisson".
normQu	Real value between 0 and 1. If the "normType" parameter is set to "quant" then this parameter sets the quantile that is used for the normalization. Default = 0.25.
norm	The normalization strategy to be used. If set to 0 the read counts are not normalized and cn.mops does not model different coverages. If set to 1 the read counts are normalized. If set to 2 the read counts are not normalized and cn.mops models different coverages. (Default=1).
upperThreshold	Positive real value that sets the cut-off for copy number gains. All CNV calling values above this value will be called as "gain". The value should be set close to the log2 of the expected foldchange for copy number 3 or 4. Default = 0.5.
lowerThreshold	Negative real value that sets the cut-off for copy number losses. All CNV calling values below this value will be called as "loss". The value should be set close to the log2 of the expected foldchange for copy number 1 or 0. Default = -0.9.
minWidth	Positive integer that is exactly the parameter "min.width" of the "segment" function of "DNAcopy". minWidth is the minimum number of segments a CNV should span. Default = 3.
segAlgorithm	Which segmentation algorithm should be used. If set to "DNAcopy" circular binary segmentation is performed. Any other value will initiate the use of our fast segmentation algorithm. Default = "fast".
minReadCount	If all samples are below this value the algorithm will return the prior knowledge. This prevents that the algorithm from being applied to segments with very low coverage. Default=5.
useMedian	Whether "median" instead of "mean" of a segment should be used for the CNV call. Default=FALSE.
returnPosterior	Flag that decides whether the posterior probabilities should be returned. The posterior probabilities have a dimension of samples times copy number states times genomic regions and therefore consume a lot of memory. Default=FALSE.
...	Additional parameters will be passed to the "DNAcopy" or the standard segmentation algorithm.

Value

An instance of "CNVDetectionResult".

Author(s)

Guenter Klambauer <klambauer@bioinf.jku.at>

Examples

```
data(cn.mops)
cn.mops(XRanges)
```

CNVDetectionResult-class

Class "CNVDetectionResult"

Description

S4 class for storing results of a CNV detection method.

Slots

The following slots are defined for [CNVDetectionResult](#) objects:

gr The segments in which the reads are counted. GRanges object.

normalizedData The normalized data.

localAssessments The data to which the segmentation algorithm is applied. These can be z-Scores, ratios, log-ratios or I/NI calls.

individualCall The CNV call that the method provides for a specific sample

iniCall The CNV call that the method provides a specific segment.

posteriorProbs The posterior probabilities for different copy numbers.

cnvs The detected CNVs.

cnvr The detected CNV regions.

segmentation The segmentation of the reference sequence (sample-wise).

integerCopyNumber The most probable integer copy number.

sampleNames The sample names.

params The parameters with which the method was run.

Methods

gr signature(object = "CNVDetectionResult"): ...

cnvr signature(object = "CNVDetectionResult"): ...

cnvs signature(object = "CNVDetectionResult"): ...

individualCall signature(object = "CNVDetectionResult"): ...

iniCall signature(object = "CNVDetectionResult"): ...

integerCopyNumber signature(object = "CNVDetectionResult"): ...

localAssessments signature(object = "CNVDetectionResult"): ...

normalizedData signature(object = "CNVDetectionResult"): ...

params signature(object = "CNVDetectionResult"): ...

```
plot signature(x = "CNVDetectionResult", y = "missing"): ...  
posteriorProbs signature(object = "CNVDetectionResult"): ...  
sampleNames signature(object = "CNVDetectionResult"): ...  
segmentation signature(object = "CNVDetectionResult"): ...  
segplot signature(object = "CNVDetectionResult"): ...  
show signature(object = "CNVDetectionResult"): ...  
calcIntegerCopyNumbers signature(object = "CNVDetectionResult"): ...
```

Author(s)

Guenter Klambauer <klambauer@bioinf.jku.at>

Examples

```
showClass("CNVDetectionResult")
```

cnvr

This generic function returns CNV regions of a CNV detection method stored in an instance of [CNVDetectionResult-class](#).

Description

This generic function returns CNV regions of a CNV detection method stored in an instance of [CNVDetectionResult-class](#).

Arguments

object An instance of "CNVDetectionResult"

Value

cnvr returns a returns a "GRanges" object containing the CNV regions.

Author(s)

Guenter Klambauer <klambauer@bioinf.jku.at>

Examples

```
data(cn.mops)  
r <- cn.mops(X[1:100,1:5])  
cnvr(r)
```

CNVRanges

Genomic locations and indices of the simulated CNVs.

Description

This data set gives the starts, ends, and the integer copy number of the simulated CNVs in the data set [XRanges](#) object.

Usage

CNVRanges

Format

A GRanges object with 20 rows and 40 value columns across 1 space.

Source

<http://www.bioinf.jku.at/cnmops/cnmops.html>.

References

Guenter Klambauer, Karin Schwarzbauer, Andreas Mayr, Djork-Arne Clevert, Andreas Mitterecker, Ulrich Bodenhofer, Sepp Hochreiter. *cn.MOPS: mixture of Poissons for discovering copy number variations in next generation sequencing data with a low false discovery rate*. Nucleic Acids Research 2012 40(9); doi:10.1093/nar/gks003.

cnvs

This generic function returns CNVs of a CNV detection method stored in an instance of [CNVDetectionResult-class](#).

Description

This generic function returns CNVs of a CNV detection method stored in an instance of [CNVDetectionResult-class](#).

Arguments

object An instance of "CNVDetectionResult"

Value

cnvs returns a returns a "GRanges" object containing the CNVs.

Author(s)

Guenter Klambauer <klambauer@bioinf.jku.at>

Examples

```
data(cn.mops)
r <- cn.mops(X[1:100,1:5])
cnvs(r)
```

exomecn.mops

Copy number detection in exome sequencing data.

Description

Performs the cn.mops algorithm for copy number detection in NGS data with parameters adjusted to exome sequencing data.

Usage

```
exomecn.mops(input,
  I = c(0.025, 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4),
  classes = c("CN0", "CN1", "CN2", "CN3", "CN4", "CN5", "CN6", "CN7", "CN8"),
  priorImpact = 10, cyc = 20, parallel = 0,
  normType = "poisson", normQu = 0.25, norm = TRUE,
  upperThreshold = 0.5, lowerThreshold = -0.8,
  minWidth = 5, segAlgorithm = "fast", minReadCount = 1,
  useMedian = FALSE, returnPosterior = FALSE, ...)
```

Arguments

input	Either an instance of "GRanges" or a raw data matrix, where columns are interpreted as samples and rows as genomic regions. An entry is the read count of a sample in the genomic region.
I	Vector positive real values that contain the expected fold change of the copy number classes. Length of this vector must be equal to the length of the "classes" parameter vector. For human copy number polymorphisms we suggest to use the default $I = c(0.025, 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4)$.
classes	Vector of characters of the same length as the parameter vector "I". One vector element must be named "CN2". The names reflect the labels of the copy number classes. Default = $c("CN0", "CN1", "CN2", "CN3", "CN4", "CN5", "CN6", "CN7", "CN8")$.
priorImpact	Positive real value that reflects how strong the prior assumption affects the result. The higher the value the more samples will be assumed to have copy number 2. Default = 10.
cyc	Positive integer that sets the number of cycles for the algorithm. Usually after less than 15 cycles convergence is reached. Default = 20.
parallel	How many cores are used for the computation. If set to zero than no parallelization is applied. The package "snow" has to be installed for this option. Default = 0.

normType	Mode of the normalization technique. Possible values are "mean", "min", "median", "quant", "poisson" and "mode". Read counts will be scaled sample-wise. Default = "poisson".
normQu	Real value between 0 and 1. If the "normType" parameter is set to "quant" then this parameter sets the quantile that is used for the normalization. Default = 0.25.
norm	Logical that indicates whether normalization should be applied or not. Default = TRUE.
upperThreshold	Positive real value that sets the cut-off for copy number gains. All CNV calling values above this value will be called as "gain". The value should be set close to the log2 of the expected foldchange for copy number 3 or 4. Default = 0.55.
lowerThreshold	Negative real value that sets the cut-off for copy number losses. All CNV calling values below this value will be called as "loss". The value should be set close to the log2 of the expected foldchange for copy number 1 or 0. Default = -0.8.
minWidth	Positive integer that is exactly the parameter "min.width" of the "segment" function of "DNAcopy". minWidth is the minimum number of segments a CNV should span. Default = 5.
segAlgorithm	Which segmentation algorithm should be used. If set to "DNAcopy" circular binary segmentation is performed. Any other value will initiate the use of our fast segmentation algorithm. Default = "fast".
minReadCount	If all samples are below this value the algorithm will return the prior knowledge. This prevents that the algorithm from being applied to segments with very low coverage. Default=1.
useMedian	Whether "median" instead of "mean" of a segment should be used for the CNV call. Default=FALSE.
returnPosterior	Flag that decides whether the posterior probabilities should be returned. The posterior probabilities have a dimension of samples times copy number states times genomic regions and therefore consume a lot of memory. Default=FALSE.
...	Additional parameters will be passed to the "DNAcopy" or the standard segmentation algorithm.

Value

An instance of "CNVDetectionResult".

Author(s)

Guenter Klambauer <klambauer@bioinf.jku.at>

Examples

```
data(cn.mops)
exomecn.mops(exomeCounts)
```

`exomeCounts`*Read counts from exome sequencing for CNV detection*

Description

This data set gives the read counts on chromosome 22 (hg19) of 22 samples in 3785 exons. The rows correspond to targeted regions or exons and columns to samples. An entry is the number of reads that map to the specific segment, i.e. targeted region or exon, of the sample. The GRanges object contains the information of the genomic location. The read counts were generated from freely available exome sequencing data of the 1000Genomes Project.

Usage`exomeCounts`**Format**

A GRanges object of 3785 rows and 22 columns.

Source

<http://www.bioinf.jku.at/software/cnmops/cnmops.html>.

References

Guenter Klambauer, Karin Schwarzbauer, Andreas Mayr, Djork-Arne Clevert, Andreas Mitterecker, Ulrich Bodenhofer, Sepp Hochreiter. *cn.MOPS: mixture of Poissons for discovering copy number variations in next generation sequencing data with a low false discovery rate*. Nucleic Acids Research 2012 40(9); doi:10.1093/nar/gks003.

The 1000 Genomes Project Consortium. *A map of human genome variation from population-scale sequencing*. Nature 2010 467(1061-1073); doi:10.1038/nature09534.

`getReadCountsFromBAM`*Calculation of read counts from BAM files.*

Description

Generates the read counts from BAM Files. These counts are necessary for CNV detection methods based on depth of coverage information. Note that the function is much faster, if the BAM files have an index file. The index file is assumed to be in the same folder and have an identical file name except that ".bai" is appended.

This function can also be run in a parallel version.

Usage

```
getReadCountsFromBAM(BAMFiles, sampleNames, refSeqName,
  WL, mode, parallel = 0)
```

Arguments

BAMFiles	BAMFiles
sampleNames	The corresponding sample names to the BAM Files.
refSeqName	Name of the reference sequence that should be analyzed. The name must appear in the header of the BAM file. If it is not given the function will select the first reference sequence that appears in the header of the BAM files.
WL	Windowlength. Length of the initial segmentation of the genome in basepairs. Should be chosen such that on the average 100 reads are contained in each segment. If not given, cn.mops will try to find an appropriate window length.
mode	Possible values are "paired" and "unpaired", whether the mapping algorithm was using a "paired" or "unpaired" strategy.
parallel	The number of parallel processes to be used for this function. Default=0.

Value

An instance of "GRanges", that contains the breakpoints of the initial segments and the raw read counts that were extracted from the BAM files. This object can be used as input for cn.mops and other CNV detection methods.

Author(s)

Guenter Klambauer <klambauer@bioinf.jku.at>

Examples

```
BAMFiles <- list.files(system.file("extdata", package="cn.mops"), pattern=".bam$",
  full.names=TRUE)
bamDataRanges <- getReadCountsFromBAM(BAMFiles,
  sampleNames=paste("Sample", 1:3), WL=5000, mode="unpaired")
```

```
getSegmentReadCountsFromBAM
```

Calculation of read counts from BAM files for predefined segments.

Description

Generates the read counts from BAM Files for predefined segments. This is the appropriate choice for exome sequencing data, where the bait regions, target regions or exons are the predefined segments. These counts are necessary for CNV detection methods based on depth of coverage information. Note that the function is much faster, if the BAM files have an index file. The index file is assumed to be in the same folder and have an identical file name except that ".bai" is appended.

This function can also be run in a parallel version.

Usage

```
getSegmentReadCountsFromBAM(BAMFiles, GR, sampleNames,
  mode, parallel = 0, BAIFiles = NULL)
```

Arguments

BAMFiles	BAMFiles
sampleNames	The corresponding sample names to the BAM Files.
GR	A genomic ranges object that contains the genomic coordinates of the segments.
mode	Possible values are "paired" and "unpaired", whether the mapping algorithm was using a "paired" or "unpaired" strategy.
parallel	The number of parallel processes to be used for this function. Default=0.
BAIFiles	The names of the BAI files that belong to the BAM files. The vector has to be in the same order as the vector BAMFiles. If the BAI files have the same name as the BAM files, only with ".bai" attached, this parameter needs not be set. (Default = NULL).

Value

An instance of "GRanges", that contains the breakpoints of the initial segments and the raw read counts that were extracted from the BAM files. This object can be used as input for `cn.mops` and other CNV detection methods.

Author(s)

Guenter Klambauer <klambauer@bioinf.jku.at>

Examples

```
BAMFiles <- list.files(system.file("extdata", package="cn.mops"),pattern=".bam$",
  full.names=TRUE)
gr <- GRanges(c("20","20"),IRanges(c(60000,70000),c(70000,80000)))
bamDataRanges <- getSegmentReadCountsFromBAM(BAMFiles,GR=gr,mode="unpaired")
```

gr *This generic function returns the genomic ranges of a CNV detection method stored in an instance of [CNVDetectionResult-class](#).*

Description

This generic function returns the genomic ranges of a CNV detection method stored in an instance of [CNVDetectionResult-class](#).

Arguments

object An instance of "CNVDetectionResult".

Value

normalizedData returns a "GRanges" object containing the normalized data.

Author(s)

Guenter Klambauer <klambauer@bioinf.jku.at>

Examples

```
data(cn.mops)
r <- cn.mops(X[1:100,1:5])
gr(r)
```

haplocn.mops

Copy number detection in NGS data of haploid samples.

Description

Performs the cn.mops algorithm for copy number detection in NGS data adjusted to haploid genomes. It is assumed that the normal state is copy number 1. This is an experimental method at the moment.

Usage

```
haplocn.mops(input, I = c(0.025, 1, 2, 3, 4, 5, 6, 7, 8),
  classes = c("CN0", "CN1", "CN2", "CN3", "CN4", "CN5", "CN6", "CN7", "CN8"),
  priorImpact = 1, cyc = 20, parallel = 0,
  normType = "poisson", normQu = 0.25, norm = TRUE,
  upperThreshold = 0.6, lowerThreshold = -0.9,
  minWidth = 3, segAlgorithm = "fast", minReadCount = 1,
  returnPosterior = FALSE, ...)
```

Arguments

input	Either an instance of "GRanges" or a raw data matrix, where columns are interpreted as samples and rows as genomic regions. An entry is the read count of a sample in the genomic region.
I	Vector positive real values that contain the expected fold change of the copy number classes. Length of this vector must be equal to the length of the "classes" parameter vector. For copy number polymorphisms in haploid organisms we suggest to use the default $I = c(0.025, 1, 2, 3, 4, 5, 6, 7, 8)$.
classes	Vector of characters of the same length as the parameter vector "I". One vector element must be named "CN1". The names reflect the labels of the copy number classes. Default = $c("CN0", "CN1", "CN2", "CN3", "CN4", "CN5", "CN6", "CN7", "CN8")$.
priorImpact	Positive real value that reflects how strong the prior assumption affects the result. The higher the value the more samples will be assumed to have copy number 1. Default = 1.

cyc	Positive integer that sets the number of cycles for the algorithm. Usually after less than 15 cycles convergence is reached. Default = 20.
parallel	How many cores are used for the computation. If set to zero than no parallelization is applied. The package "snow" has to be installed for this option. Default = 0.
normType	Mode of the normalization technique. Possible values are "mean", "min", "median", "quant", "poisson" and "mode". Read counts will be scaled sample-wise. Default = "poisson".
normQu	Real value between 0 and 1. If the "normType" parameter is set to "quant" then this parameter sets the quantile that is used for the normalization. Default = 0.25.
norm	Logical that indicates whether normalization should be applied or not. Default = TRUE.
upperThreshold	Positive real value that sets the cut-off for copy number gains. All CNV calling values above this value will be called as "gain". The value should be set close to the log2 of the expected foldchange for copy number 3 or 4. Default = 0.5.
lowerThreshold	Negative real value that sets the cut-off for copy number losses. All CNV calling values below this value will be called as "loss". The value should be set close to the log2 of the expected foldchange for copy number 1 or 0. Default = -0.9.
minWidth	Positive integer that is exactly the parameter "min.width" of the "segment" function of "DNAcopy". minWidth is the minimum number of segments a CNV should span. Default = 4.
segAlgorithm	Which segmentation algorithm should be used. If set to "DNAcopy" circular binary segmentation is performed. Any other value will initiate the use of our fast segmentation algorithm. Default = "fast".
minReadCount	If all samples are below this value the algorithm will return the prior knowledge. This prevents that the algorithm from being applied to segments with very low coverage.
...	Additional parameters will be passed to the "DNAcopy" or the standard segmentation algorithm.
returnPosterior	Flag that decides whether the posterior probabilities should be returned. The posterior probabilities have a dimension of samples times copy number states times genomic regions and therefore consume a lot of memory. Default=FALSE.

Value

An instance of "CNVDetectionResult".

Author(s)

Guenter Klambauer <klambauer@bioinf.jku.at>

Examples

```
data(cn.mops)
haplocln.mops(XRanges[1:200, ])
```

individualCall	<i>This generic function returns the individual calls of a CNV detection method stored in an instance of CNVDetectionResult-class.</i>
----------------	--

Description

This generic function returns the individual calls of a CNV detection method stored in an instance of [CNVDetectionResult-class](#).

Arguments

object An instance of "CNVDetectionResult"

Value

individualCalls returns a "GRanges" object containing the individual calls.

Author(s)

Guenter Klambauer <klambauer@bioinf.jku.at>

Examples

```
data(cn.mops)
r <- cn.mops(X[1:100,1:5])
individualCall(r)
```

iniCall	<i>This generic function returns the informative/non-informative call of a CNV detection method stored in an instance of CNVDetectionResult-class. The I/NI call is a measure for a genomic segment across all samples, whether this segment is a CNV region (informative) or a normal genomic region (non-informative).</i>
---------	--

Description

This generic function returns the informative/non-informative call of a CNV detection method stored in an instance of [CNVDetectionResult-class](#). The I/NI call is a measure for a genomic segment across all samples, whether this segment is a CNV region (informative) or a normal genomic region (non-informative).

Arguments

object An instance of "CNVDetectionResult"

Value

iniCall returns a "GRanges" object containing the individual calls.

Author(s)

Guenter Klambauer <klambauer@bioinf.jku.at>

Examples

```
data(cn.mops)
r <- cn.mops(X[1:100,1:5])
iniCall(r)
```

integerCopyNumber	<i>This generic function returns the integer copy numbers of a CNV detection method stored in an instance of CNVDetectionResult-class.</i>
-------------------	--

Description

This generic function returns the integer copy numbers of a CNV detection method stored in an instance of [CNVDetectionResult-class](#).

Arguments

object An instance of "CNVDetectionResult"

Value

integerCopyNumber returns a returns a "GRanges" object containing the integer copy numbers.

Author(s)

Guenter Klambauer <klambauer@bioinf.jku.at>

Examples

```
data(cn.mops)
r <- cn.mops(X[1:100,1:5])
integerCopyNumber(r)
```

localAssessments	<i>This generic function returns the local assessments, i.e. signed individual informative/non-informative calls, of a CNV detection method stored in an instance of <code>CNVDetectionResult</code>-class. For other CNV detection methods this can be (log-) ratios or z-scores.</i>
------------------	--

Description

This generic function returns the local assessments, i.e. signed individual informative/non-informative calls, of a CNV detection method stored in an instance of `CNVDetectionResult`-class. For other CNV detection methods this can be (log-) ratios or z-scores.

Arguments

object	An instance of "CNVDetectionResult"
--------	-------------------------------------

Value

localAssessments returns a "GRanges" object containing the local assessments.

Author(s)

Guenter Klambauer <klambauer@bioinf.jku.at>

Examples

```
data(cn.mops)
r <- cn.mops(X[1:100,1:5])
localAssessments(r)
```

makeRobustCNVR	<i>Calculates robust CNV regions.</i>
----------------	---------------------------------------

Description

This generic function calculates robust CNV regions by segmenting the I/NI call per genomic region.

Arguments

object	An instance of "CNVDetectionResult"
robust	Robustness parameter. The higher the value, the more samples are required to have a CNV that confirms the CNV region. Setting this parameter to 0 restores the original CNV regions. (Default=0.5)
minWidth	The minimum length measured in genomic regions a CNV region has to span in order to be called. A parameter of the segmentation algorithm. (Default=4).

Details

cn.mops usually reports a CNV region if at least one individual has a CNV in this region. For some applications it is useful to find more common CNV regions, i.e., regions in which more than one sample has a CNV. The I/NI call measures both signal strength and how many sample show an abnormal copy number, therefore segmentation of the I/NI call can provide robust CNV regions.

Value

makeRobustCNVR returns a "CNVDetectionResult" object containing new values in the slot "cnvr".

Author(s)

Guenter Klambauer <klambauer@bioinf.jku.at>

Examples

```
data(cn.mops)
r <- cn.mops(X[1:100,1:5])
rr <- calcIntegerCopyNumbers(makeRobustCNVR(r,robust=0.1,minWidth=3))
```

normalizeChromosomes *Normalization of NGS data. Normalize quantitative NGS data in order to make counts comparable over samples, i.e., correcting for different library sizes or coverages. Scales each samples' reads such that the coverage is even for all samples after normalization.*

Description

Normalization of NGS data.

Normalize quantitative NGS data in order to make counts comparable over samples, i.e., correcting for different library sizes or coverages. Scales each samples' reads such that the coverage is even for all samples after normalization.

Usage

```
normalizeChromosomes(X, chr, normType = "median",
  qu = 0.75, ploidy)
```

Arguments

X	Matrix of positive real values, where columns are interpreted as samples and rows as genomic regions. An entry is the read count of a sample in the genomic region. Alternatively this can be a GRanges object containing the read counts as values.
chr	Character vector that has as many elements as "X" has rows. The vector assigns each genomic segment to a reference sequence (chromosome).

normType	Type of the normalization technique. Each samples' read counts are scaled such that the total number of reads is equal after normalization. By this parameter one can decide to which coverage (i.e. total reads) the read counts should be normalized. Possible choices are the minimal coverage ("min"), the mean or median coverage ("mean", "median") or any quantile ("quant"). If this parameter is set to the value "mode", the read counts are scaled such that each samples' most frequent value (the "mode") is equal after normalization. Possible values are "mean", "min", "median", "quant", and "mode". Default = "median".
qu	Real value between 0 and 1 that determines the quantile to be used for normalization (see above). Default = 0.75.
ploidy	An integer value for each sample or each column in the read count matrix. At least two samples must have a ploidy of 2. Default = "missing".

Value

A data matrix of normalized read counts with the same dimensions as the input matrix X.

Author(s)

Guenter Klambauer <klambauer@bioinf.jku.at>

Examples

```
data(cn.mops)
X.norm <- normalizeChromosomes(X)
```

normalizedData	<i>This generic function returns the normalized data of a CNV detection method stored in an instance of CNVDetectionResult-class.</i>
----------------	---

Description

This generic function returns the normalized data of a CNV detection method stored in an instance of [CNVDetectionResult-class](#).

Arguments

object An instance of "CNVDetectionResult".

Value

normalizedData returns a "GRanges" object containing the normalized data.

Author(s)

Guenter Klambauer <klambauer@bioinf.jku.at>

Examples

```
data(cn.mops)
r <- cn.mops(X[1:100,1:5])
normalizedData(r)
```

normalizeGenome	<i>Normalization of NGS data</i>
-----------------	----------------------------------

Description

Normalize quantitative NGS data in order to make counts comparable over samples. Scales each samples' reads such that the coverage is even for all samples after normalization.

Usage

```
normalizeGenome(X, normType = "poisson", qu = 0.25,
               ploidy)
```

Arguments

X	Matrix of positive real values, where columns are interpreted as samples and rows as genomic regions. An entry is the read count of a sample in the genomic region. Alternatively this can be a GRanges object containing the read counts as values.
normType	normType Type of the normalization technique. Each samples' read counts are scaled such that the total number of reads is equal after normalization. By this parameter one can decide to which coverage (i.e. total reads) the read counts should be normalized. Possible choices are the minimal coverage ("min"), the mean or median coverage ("mean", "median") or any quantile ("quant"). If this parameter is set to the value "mode", the read counts are scaled such that each samples' most frequent value (the "mode") is equal after normalization. If the parameter is set to "poisson" the values are scaled such that the distribution is (rowwise) close to a Poisson distribution. Possible values are "mean", "min", "median", "quant", "poisson", and "mode". Default = "poisson".
qu	Real value between 0 and 1. Default = 0.25.
ploidy	An integer value for each sample or each column in the read count matrix. At least two samples must have a ploidy of 2. Default = "missing".

Value

A data matrix of normalized read counts with the same dimensions as the input matrix X.

Author(s)

Guenter Klambauer <klambauer@bioinf.jku.at>

Examples

```
data(cn.mops)
X.norm <- normalizeGenome(X)
```

params	<i>This generic function returns the parameters of a CNV detection method stored in an instance of CNVDetectionResult-class.</i>
--------	--

Description

This generic function returns the parameters of a CNV detection method stored in an instance of [CNVDetectionResult-class](#).

Arguments

object An instance of "CNVDetectionResult"

Value

params returns a returns a "GRanges" object containing the parameters.

Author(s)

Guenter Klambauer <klambauer@bioinf.jku.at>

Examples

```
data(cn.mops)
r <- cn.mops(X[1:100,1:5])
params(r)
```

plot	<i>Plots a CNVDetectionResult</i>
------	-----------------------------------

Description

Plots read counts, call values and CNV calls in an identified CNV region.

Usage

```
## S4 method for signature CNVDetectionResult,missing
plot(x,
      which,margin=c(10,10),toFile=FALSE)
```

Arguments

x	An instance of "CNVDetectionResult"
which	The index of the CNV region to be plotted.
margin	Vector of two positive integers that states how many segments left and right of the CNV region should be included in the plot. Default = c(10,10).
toFile	Logical value whether the output should be plotted to a file. Default = FALSE.

Value

Generates a CNV calling plot.

Author(s)

Guenther Klambauer <klambauer@bioinf.jku.at>

posteriorProbs	<i>This generic function returns the posterior probabilities of a CNV detection method stored in an instance of CNVDetectionResult-class. The posterior probabilities are represented as a three dimensional array, where the three dimensions are segment, copy number and individual.</i>
----------------	---

Description

This generic function returns the posterior probabilities of a CNV detection method stored in an instance of [CNVDetectionResult-class](#). The posterior probabilities are represented as a three dimensional array, where the three dimensions are segment, copy number and individual.

Arguments

object	An instance of "CNVDetectionResult"
--------	-------------------------------------

Value

posteriorProbs returns a three dimensional array.

Author(s)

Guenther Klambauer <klambauer@bioinf.jku.at>

Examples

```
data(cn.mops)
r <- cn.mops(X[1:100,1:5])
posteriorProbs(r)
```

referencecn.mops	<i>Copy number detection in NGS data with in a control versus cases setting.</i>
------------------	--

Description

This function performs the an alternative version of the cn.mops algorithm adapted to a setting of control versus cases

Usage

```
referencecn.mops(cases, controls,
  I = c(0.025, 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 8, 16, 32, 64),
  classes = paste("CN", c(0:8, 16, 32, 64, 128), sep = ""),
  priorImpact = 1, cyc = 20, parallel = 0,
  normType = "mode", normQu = 0.25, norm = 1,
  upperThreshold = 0.5, lowerThreshold = -0.9,
  minWidth = 4, segAlgorithm = "DNACopy",
  minReadCount = 1, verbose=1, returnPosterior = FALSE, ...)
```

Arguments

cases	Either an instance of "GRanges" or a raw data matrix, where columns are interpreted as samples and rows as genomic regions. An entry is the read count of a sample in the genomic region.
controls	Either an instance of "GRanges" or a raw data matrix, where columns are interpreted as samples and rows as genomic regions. An entry is the read count of a sample in the genomic region.
I	Vector positive real values that contain the expected fold change of the copy number classes. Length of this vector must be equal to the length of the "classes" parameter vector. For human copy number polymorphisms we suggest to use the default <code>I = c(0.025,0.5,1,1.5,2,2.5,3,3.5,4,8,16,32,64)</code> .
classes	Vector of characters of the same length as the parameter vector "I". One vector element must be named "CN2". The names reflect the labels of the copy number classes. Default = <code>paste("CN",c(0:8,16,32,64,128),sep="")</code> .
priorImpact	Positive real value that reflects how strong the prior assumption affects the result. The higher the value the more samples will be assumed to have copy number 2. Default = 1.
cyc	Positive integer that sets the number of cycles for the algorithm. Usually after less than 15 cycles convergence is reached. Default = 20.
parallel	How many cores are used for the computation. If set to zero than no parallelization is applied. The package "snow" has to be installed for this option. Default = 0.
normType	Mode of the normalization technique. Possible values are "mean", "min", "median", "quant", "poisson" and "mode". Read counts will be scaled sample-wise. Default = "mode".

normQu	Real value between 0 and 1. If the "normType" parameter is set to "quant" then this parameter sets the quantile that is used for the normalization. Default = 0.25.
norm	The normalization strategy to be used. If set to 0 the read counts are not normalized and cn.mops does not model different coverages. If set to 1 the read counts are normalized. If set to 2 the read counts are not normalized and cn.mops models different coverages. (Default=1).
upperThreshold	Positive real value that sets the cut-off for copy number gains. All CNV calling values above this value will be called as "gain". The value should be set close to the log2 of the expected foldchange for copy number 3 or 4. Default = 0.5.
lowerThreshold	Negative real value that sets the cut-off for copy number losses. All CNV calling values below this value will be called as "loss". The value should be set close to the log2 of the expected foldchange for copy number 1 or 0. Default = -0.9.
minWidth	Positive integer that is exactly the parameter "min.width" of the "segment" function of "DNAcopy". minWidth is the minimum number of segments a CNV should span. Default = 3.
segAlgorithm	Which segmentation algorithm should be used. If set to "DNAcopy" circular binary segmentation is performed. Any other value will initiate the use of our fast segmentation algorithm. Default = "DNAcopy".
minReadCount	If all samples are below this value the algorithm will return the prior knowledge. This prevents that the algorithm from being applied to segments with very low coverage. Default=1.
verbose	Flag that decides whether referencecn.mops gives status messages. Default=1.
returnPosterior	Flag that decides whether the posterior probabilities should be returned. The posterior probabilities have a dimension of samples times copy number states times genomic regions and therefore consume a lot of memory. Default=FALSE.
...	Additional parameters will be passed to the "DNAcopy" or the standard segmentation algorithm.

Value

An instance of "CNVDetectionResult".

Author(s)

Guenter Klambauer <klambauer@bioinf.jku.at>

Examples

```
data(cn.mops)
referencecn.mops(X[1:200, ],rowMedians(X[1:200, ]))
```

sampleNames	<i>This generic function returns the sample names of a CNV detection method stored in an instance of CNVDetectionResult-class.</i>
-------------	--

Description

This generic function returns the sample names of a CNV detection method stored in an instance of [CNVDetectionResult-class](#).

Arguments

object An instance of "CNVDetectionResult"

Value

sampleNames returns a returns a "GRanges" object containing the parameters.

Author(s)

Guenter Klambauer <klambauer@bioinf.jku.at>

Examples

```
data(cn.mops)
r <- cn.mops(X[1:100,1:5])
sampleNames(r)
```

segment	<i>Fast segmentation of CNV calls.</i>
---------	--

Description

Performs a fast segmentation algorithm based on the cyber t test and the t statistics. This is a special version for log-ratios or I/NI calls that are assumed to be centered around 0. For segmentation of data with different characteristics you can a) subtract the mean/median/mode from your data or b) use the more general version of this algorithm in the R Bioconductor package "fastseg".

Usage

```
segment(x, alpha = 0.05, segMedianT = NULL, minSeg = 3,
        eps = 0, delta = 20, maxInt = 40, cyberWeight = 50)
```

Arguments

x	Values to be segmented.
alpha	Real value between 0 and 1 is interpreted as the percentage of total points that are considered as initial breakpoints. An integer greater than 1 is interpreted as number of initial breakpoints. Default = 0.05.
segMedianT	Vector of length 2. Thresholds on the segment's median. Segments' medians above the first element are considered as gains and below the second value as losses. If set to NULL the segmentation algorithm tries to determine the thresholds itself. If set to 0 the gain and loss segments are not merged. (Default = NULL).
minSeg	Minimum length of segments. Default = 3.
eps	Real value greater or equal zero. A breakpoint is only possible between to consecutive values of x that have a distance of at least "eps". Default = 0.
delta	Positive integer. A parameter to make the segmentation more efficient. If the statistics of a breakpoint lowers while extending the window, the algorithm extends the windows by "delta" more points until it stops. Default = 20.
maxInt	The maximum length of a segment left of the breakpoint and right of the breakpoint that is considered. Default = 40.
cyberWeight	The "nu" parameter of the cyber t-test. Default = 50.

Value

A data frame containing the segments.

Author(s)

Guenter Klambauer <klambauer@bioinf.jku.at>

Examples

```
x <- rnorm(n=500,sd=0.5)
x[150:200] <- rnorm(n=51,mean=3,sd=0.5)
segment(x)
```

segmentation	<i>This generic function returns segmentation of a CNV detection method stored in an instance of CNVDetectionResult-class.</i>
--------------	--

Description

This generic function returns segmentation of a CNV detection method stored in an instance of [CNVDetectionResult-class](#).

Arguments

object	An instance of "CNVDetectionResult"
--------	-------------------------------------

Value

segmentation returns a "GRanges" object containing the segmentation.

Author(s)

Guenter Klambauer <klambauer@bioinf.jku.at>

Examples

```
data(cn.mops)
r <- cn.mops(X[1:100,1:5])
segmentation(r)
```

segplot

Visualization of a CNV detection result.

Description

Plots the log normalized read counts and the detected segments as a segmentation plot.

Arguments

r	An instance of "CNVDetectionResult"
mainCN	The name of the main copy number. That is "CN2" for diploid individuals. For haplo.cn.mops this should be set to "CN1".
sampleIdx	The index of the samples to be plotted. (Default = missing)
seqnames	The names of the reference sequence (chromosomes) to be plotted. (Default = missing)
segStat	Whether the segment line should display the mean or the median of a segments calls. (Default = "mean").
plot.type	the type of plot. (Default = "s").
altcol	logical flag to indicate if chromosomes should be plotted in alternating colors in the whole genome plot. (Default = TRUE).
sbyc.layout	layout settings for the multiframe grid layout for the 'samplebychrom' type. It should be specified as a vector of two integers which are the number of rows and columns. The default values are chosen based on the number of chromosomes to produce a near square graph. For normal genome it is 4x6 (24 chromosomes) plotted by rows. (Default = NULL).
cbys.layout	layout settings for the multiframe grid layout for the 'chrombysample' type. As above it should be specified as number of rows and columns and the default chosen based on the number of samples. (Default = NULL).
cbys.nchrom	the number of chromosomes per page in the layout. (Default = 1).
include.means	logical flag to indicate whether segment means are to be drawn. (Default = TRUE).

zeroline	logical flag to indicate whether a horizontal line at y=0 is to be drawn. (Default = TRUE).
pt.pch	the plotting character used for plotting the log-ratio values. (Default = ".")
pt.cex	the size of plotting character used for the log-ratio values (Default = 3).
pt.cols	the color list for the points. The colors alternate between chromosomes. (Default = c("green", "black").)
segcol	the color of the lines indicating the segment means. (Default = "red").
z1col	the color of the zeroline. (Default = "grey").
ylim	this argument is present to override the default limits which is the range of symmetrized log-ratios. (Default = NULL).
lwd	line weight of lines for segment mean and zeroline. (Default = 3).
...	other arguments which will be passed to plot commands.

Value

Generates a segmentation plot.

Author(s)

Guenter Klambauer <klambauer@bioinf.jku.at>

Examples

```
data(cn.mops)
r <- cn.mops(X[1:200, ])
segplot(r, sampleIdx=1)
```

show

Displays the result object of a copy number detection method.

Description

Displays method for S4 class [CNVDetectionResult](#)

Usage

```
## S4 method for signature CNVDetectionResult
show(object)
```

Arguments

object An instance of a "CNVDetectionResult".

Value

Displays the result object of a CNV detection method.

Author(s)

Guenter Klambauer <klambauer@bioinf.jku.at>

singlecn.mops	<i>Copy number detection in NGS data with in a setting in which only one sample is available</i>
---------------	--

Description

This function performs the an alternative version of the cn.mops algorithm adapted to a setting of a single sample.

Usage

```
singlecn.mops(x,
  I = c(0.025, 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4),
  classes = c("CN0", "CN1", "CN2", "CN3", "CN4", "CN5", "CN6", "CN7", "CN8"),
  priorImpact = 1, cyc = 20, parallel = 0,
  normType = "poisson", normQu = 0.25, norm = 1,
  upperThreshold = 0.5, lowerThreshold = -0.9,
  minWidth = 3, segAlgorithm = "fast", minReadCount = 1,
  returnPosterior = FALSE, ...)
```

Arguments

x	Either an instance of "GRanges" or a raw data matrix with one column or a vector of read counts. An entry is the read count of the sample in the genomic region.
I	Vector positive real values that contain the expected fold change of the copy number classes. Length of this vector must be equal to the length of the "classes" parameter vector. For human copy number polymorphisms we suggest to use the default I = c(0.025,0.5,1,1.5,2,2.5,3,3.5,4).
classes	Vector of characters of the same length as the parameter vector "I". One vector element must be named "CN2". The names reflect the labels of the copy number classes. Default = c("CN0","CN1","CN2","CN3","CN4","CN5","CN6","CN7","CN8").
priorImpact	Positive real value that reflects how strong the prior assumption affects the result. The higher the value the more samples will be assumed to have copy number 2. Default = 1.
cyc	Positive integer that sets the number of cycles for the algorithm. Usually after less than 15 cycles convergence is reached. Default = 20.
parallel	How many cores are used for the computation. If set to zero than no parallelization is applied. The package "snow" has to be installed for this option. Default = 0.

normType	Mode of the normalization technique. Possible values are "mean", "min", "median", "quant", "poisson" and "mode". Read counts will be scaled sample-wise. Default = "poisson".
normQu	Real value between 0 and 1. If the "normType" parameter is set to "quant" then this parameter sets the quantile that is used for the normalization. Default = 0.25.
norm	The normalization strategy to be used. If set to 0 the read counts are not normalized and cn.mops does not model different coverages. If set to 1 the read counts are normalized. If set to 2 the read counts are not normalized and cn.mops models different coverages. (Default=1).
upperThreshold	Positive real value that sets the cut-off for copy number gains. All CNV calling values above this value will be called as "gain". The value should be set close to the log2 of the expected foldchange for copy number 3 or 4. Default = 0.5.
lowerThreshold	Negative real value that sets the cut-off for copy number losses. All CNV calling values below this value will be called as "loss". The value should be set close to the log2 of the expected foldchange for copy number 1 or 0. Default = -0.9.
minWidth	Positive integer that is exactly the parameter "min.width" of the "segment" function of "DNAcopy". minWidth is the minimum number of segments a CNV should span. Default = 3.
segAlgorithm	Which segmentation algorithm should be used. If set to "DNAcopy" circular binary segmentation is performed. Any other value will initiate the use of our fast segmentation algorithm. Default = "fast".
minReadCount	If all samples are below this value the algorithm will return the prior knowledge. This prevents that the algorithm from being applied to segments with very low coverage. Default=1.
returnPosterior	Flag that decides whether the posterior probabilities should be returned. The posterior probabilities have a dimension of samples times copy number states times genomic regions and therefore consume a lot of memory. Default=FALSE.
...	Additional parameters will be passed to the "DNAcopy" or the standard segmentation algorithm.

Value

An instance of "CNVDetectionResult".

Author(s)

Guenter Klambauer <klambauer@bioinf.jku.at>

Examples

```
data(cn.mops)
singlecn.mops(XRanges[,1])
```

X *A simulated data set for CNV detection from NGS data.*

Description

This data set gives the read counts of 40 samples in 5000 genomic locations. The rows correspond to genomic segments of 25kbp length and the columns to samples. An entry is the number of reads that map to the specific segment of the sample. The rownames contain the information of the genomic location - they are in the format `refseqname_startposition_endposition`. The simulated data contains CNVs given in the `CNVRanges` object. It was generated using distributions of read counts as they appear in real sequencing experiments. CNVs were implanted under the assumption that the expected read count is linear dependent on the copy number (e.g. in a certain genomic we expect λ reads for copy number 2, then we expect $2 \cdot \lambda$ reads for copy number 4).

Usage

X

Format

A data matrix of 5000 rows and 40 columns.

Source

<http://www.bioinf.jku.at/software/cnmops/cnmops.html>.

References

Guenter Klambauer, Karin Schwarzbauer, Andreas Mayr, Djork-Arne Clevert, Andreas Mitterecker, Ulrich Bodenhofer, Sepp Hochreiter. *cn.MOPS: mixture of Poissons for discovering copy number variations in next generation sequencing data with a low false discovery rate*. *Nucleic Acids Research* 2012 40(9); doi:10.1093/nar/gks003.

XRanges *A simulated data set for CNV detection from NGS data.*

Description

This data set gives the read counts of 40 samples in 5000 genomic locations. The rows correspond to genomic segments of 25kbp length and the columns to samples. An entry is the number of reads that map to the specific segment of the sample. The "GRanges" object contains the name of the reference sequence, start and end position of the genomic segments. The simulated data contains CNVs given in the `CNVRanges` object. It was generated using distributions of read counts as they appear in real sequencing experiments. CNVs were implanted under the assumption that the expected read count is linear dependent on the copy number (e.g. in a certain genomic we expect λ reads for copy number 2, then we expect $2 \cdot \lambda$ reads for copy number 4).

Usage

`XRanges`

Format

A GRanges object with 5000 rows and 40 value columns across 1 space.

Source

<http://www.bioinf.jku.at/software/cnmops/cnmops.html>.

References

Guenter Klambauer, Karin Schwarzbauer, Andreas Mayr, Djork-Arne Clevert, Andreas Mitterecker, Ulrich Bodenhofer, Sepp Hochreiter. *cn.MOPS: mixture of Poissons for discovering copy number variations in next generation sequencing data with a low false discovery rate*. Nucleic Acids Research 2012 40(9); doi:10.1093/nar/gks003.

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