

Package ‘MinimumDistance’

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Title A Package for De Novo CNV Detection in Case-Parent Trios

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Description

Analysis of de novo copy number variants in trios from high-dimensional genotyping platforms.

License Artistic-2.0

Depends R (>= 3.5.0), VanillaICE (>= 1.47.1)

Imports methods, BiocGenerics, MatrixGenerics, Biobase, S4Vectors (>= 0.23.18), IRanges, GenomeInfoDb, GenomicRanges (>= 1.17.16), SummarizedExperiment (>= 1.15.4), oligoClasses, DNACopy, ff, foreach, matrixStats, lattice, data.table, grid, stats, utils

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Collate 'help.R' 'AllClasses.R' 'AllGenerics.R' 'coercion-methods.R' 'datasets.R' 'defunct.R' 'functions.R' 'generator-funs.R' 'lattice-methods.R' 'mad-methods.R' 'methods-AnnotatedDataFrame.R' 'methods-AssayData.R' 'methods-FileViews.R' 'methods-FilterParamMD.R' 'methods-ILimit.R' 'methods-MDRanges.R' 'methods-MinDistExperiment.R' 'methods-MinDistGRanges.R' 'methods-MinDistParam.R' 'methods-MinDistPosterior.R' 'methods-ParentOffspring.R' 'methods-ParentOffspringList.R' 'methods-Pedigree.R' 'methods-PennParam.R' 'methods-ShallowSimpleList.R' 'methods-SummarizedExperiment.R' 'methods-TrioSet.R' 'methods-TrioSetList.R' 'methods-ff_array.R' 'methods-grid.R' 'methods-list.R' 'methods-matrix.R' 'segment2-methods.R' 'utils.R' 'zzz.R'

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acf2 *Function for computing autocorrelations*

Description

By default, this function returns the lag-10 autocorrelations of a numeric vector and omits missing values.

Usage

```
acf2(  
  x,  
  lag.max = 10,  
  type = c("correlation", "covariance", "partial"),  
  plot = FALSE,  
  na.action = na.omit,  
  demean = TRUE,  
  ...  
)
```

Arguments

| | |
|-----------|--|
| x | a numeric vector |
| lag.max | see acf |
| type | see acf |
| plot | logical, as in acf |
| na.action | ignored. Missing values are automatically omitted. |
| demean | logical, as in acf |
| ... | additional arguments passed to acf |

See Also

[acf](#)

Examples

```
x <- rnorm(100)
x[5] <- NA
acf2(x)
```

calculateMindist *Deprecated function to calculate the minimum distance*

Description

The 'minimum distance' is the minimum signed absolute difference of the parental log R ratios and the offspring log R ratios. Specifically, let |O-F| denote the absolute difference in the log R ratios comparing offspring to father and |O-M| the absolute difference in the log R ratios comparing offspring to mother. The minimum distance at a marker is the signed minimum of |O-M| and |O-F|. After segmentation of the minimum distance, non-zero segments can indicate a de novo difference in the log R ratio of the offspring and either parent. For example, a positive minimum distance suggests that the log R ratio from the offspring is greater than the log R ratio of either parent.

Usage

```
calculateMindist(object, ...)

## S4 method for signature 'TrioSet'
calculateMindist(object, verbose = TRUE, ...)

## S4 method for signature 'TrioSetList'
calculateMindist(object)

## S4 method for signature 'list'
calculateMindist(object, outdir = ldPath(), ...)

## S4 method for signature 'arrayORff_array'
calculateMindist(object, outdir, center, ...)

## S4 method for signature 'matrix'
calculateMindist(object, ...)
```

Arguments

| | |
|---------|---|
| object | see showMethods("calculateMindist") |
| ... | Ignored |
| verbose | logical. Whether to display messages indicating progress. |
| outdir | character string indicating path to save output |
| center | ignored |

coerce *Coercion methods in MinimumDistance package*

Description

Coercion methods in MinimumDistance package

Coerces a TrioSetList to a TrioSet

Usage

```
as(from, to)
```

```
## S4 method for signature 'TrioSetList'  
stack(x, ...)
```

Arguments

| | |
|------|---------------------------|
| x | a TrioSetList |
| ... | ignored |
| from | see showMethods("coerce") |
| to | see showMethods("coerce") |

Value

a TrioSet

Defunct *Defunct functions/classes/methods in the MinimumDistance package*

Description

The function, class, or data object you asked is defunct.

denovoHemizygous *Filter the genomic intervals for denovo copy number states*

Description

This function filters the genomic intervals for denovo events.

Usage

```
denovoHemizygous(object, filters = FilterParamMD(state = "221"))
denovoHomozygous(object, filters = FilterParamMD(state = "220"))
denovo(object, filters = FilterParamMD(state = c("220", "221", "224")))
denovoDuplication(object, filters = FilterParamMD(state = "224"))

## S4 method for signature 'MinDistPosterior'
denovoHemizygous(object, filters = FilterParamMD(state = "221"))

## S4 method for signature 'MinDistPosterior'
denovoHomozygous(object, filters = FilterParamMD(state = "220"))

## S4 method for signature 'MinDistPosterior'
denovoDuplication(object, filters = FilterParamMD(state = "224"))

## S4 method for signature 'MinDistPosterior'
denovo(object, filters = FilterParamMD(state = c("220", "221", "224")))
```

Arguments

object see showMethods(denovo) for a list of defined methods
 filters an object of class FilterParamMD

Details

The function denovo filters genomic intervals for states '220', '221', and '224', corresponding to denovo homozygous deletion, denovo hemizygous deletion, and denovo duplication, respectively.

denovoHemizygous filters genomic intervals for state '221'.

denovoHomozygous filters genomic intervals for state '220'

See Also

FilterParamMD-class

DNACopyParam *Constructor for DNACopyParam class*

Description

Creates an instance of a parameter class for circular binary segmentation of the minimum distance and the log R ratios. Parameters in this object are passed to the segment function in the package DNACopy.

Usage

```
DNACopyParam(  
  alpha = 0.01,  
  min.width = 2L,  
  undo.splits = c("none", "prune", "sdundo"),  
  undo.SD = 3  
)
```

Arguments

| | |
|-------------|-----------------------------|
| alpha | see segment |
| min.width | see segment |
| undo.splits | see segment |
| undo.SD | see segment |

See Also

[segment](#)

Examples

```
segment_params <- DNACopyParam(alpha=0.01)  
params <- MinDistParam(dnacopy=segment_params)
```

exampleTrioSetList *An example TrioSetList object*

Description

A dataset containing log R ratios and B allele frequencies for two chromosomes, organized as a TrioSetList. Each element in the list class is a TrioSet object. Both TrioSetList and TrioSet classes are deprecated; the example data will be removed in a future release.

Format

a TrioSetList

| | |
|------------------|--|
| filterExperiment | <i>Methods for filtering MinDistExperiment objects</i> |
|------------------|--|

Description

Filter a `MinDistExperiment` object to exclude markers with missing values in the low-level summaries, exclude markers that lie in segments (`granges` argument) with small minimum distance values (unlikely to be de novo)

Usage

```
filterExperiment(object, granges, param)

## S4 method for signature 'MinDistExperiment,GRanges'
filterExperiment(object, granges, param)

## S4 method for signature 'MinDistExperiment,GRangesList'
filterExperiment(object, granges, param)

## S4 method for signature 'MinDistExperiment,MinDistGRanges'
filterExperiment(object, granges, param)
```

Arguments

| | |
|----------------------|---|
| <code>object</code> | A <code>MinDistExperiment</code> |
| <code>granges</code> | A <code>GRanges</code> , <code>GRangesList</code> , or <code>MinDistGRanges</code> object |
| <code>param</code> | a <code>MinDistParam</code> object |

Value

a `MinDistExperiment`

| | |
|---------------|---|
| FilterParamMD | <i>Parameters for filtering results from the segmentation and copy number inference</i> |
|---------------|---|

Description

A container for criteria used to filter the segmentation results post-hoc. Options including filtering on the posterior call, the posterior probability of the posterior call, the minimum number of markers spanned by the segment, the minimum width of the segment, and chromosome. Convenience functions are available for commonly used filters.

Usage

```
FilterParamMD(state = trioStateNames(), seqnames = paste0("chr", 1:22), ...)
```


Arguments

| | |
|----------|--|
| state | trio copy number states to select |
| seqnames | chromosome names to select |
| ... | additional arguments passed to FilterParam-class |

Examples

```
library(VanillaICE)
data(md_gr)
data(md_exp)
mdparam <- MinDistParam()
fit <- MAP2(md_exp, md_gr, mdparam)
## return all segments
segs(fit)

## Default filters
param <- FilterParamMD()
param
cnvFilter(fit, param)

param2 <- FilterParamMD(seqnames="chr22", probability=0.9, numberFeatures=10)
cnvFilter(fit, param2)
denovoHemizygous(fit)
```

FilterParamMD-class *A class for filtering genomic intervals called by MinimumDistance*

Description

Options for filtering include the number of markers spanned by a segment, the posterior probability of the maximum a posteriori estimate of the trio copy number state, and the trio copy number state.

Usage

```
## S4 method for signature 'FilterParamMD'
show(object)
```

Arguments

| | |
|--------|------------------------|
| object | a FilterParamMD object |
|--------|------------------------|

See Also

denovo

| | |
|------|--|
| mad2 | <i>Deprecated wrapper for computing the median absolute deviation of low-level summaries</i> |
|------|--|

Description

Deprecated wrapper for computing the median absolute deviation of low-level summaries

Usage

```
mad2(object, byrow = FALSE, ...)

## S4 method for signature 'list'
mad2(object, byrow, pedigree, ...)

## S4 method for signature 'TrioSetList'
mad2(object, byrow = FALSE, ...)

## S4 method for signature 'matrix'
mad2(object, byrow, pedigree, ...)

## S4 method for signature 'array'
mad2(object, byrow, pedigree, ...)
```

Arguments

| | |
|----------|--|
| object | see <code>showMethods("mad2")</code> |
| byrow | logical if TRUE, compute the median absolute deviation of the rows of a matrix |
| ... | additional arguments to <code>mad</code> |
| pedigree | an object of class <code>Pedigree</code> |

| | |
|-----|--|
| MAP | <i>Computes the maximum a posteriori trio copy number state for the segmented minimum distance</i> |
|-----|--|

Description

This functions is deprecated and will be defunct in a future release. The replacement function is `MAP2`.

Usage

```
MAP(
  object,
  ranges,
  id,
  TAUP = 1e+10,
  tauMAX = 1 - 5e-08,
  cnStates = c(-2, -0.4, 0, 0, 0.4, 1),
  pr.nonmendelian = 1.5e-06,
  mdThr = 0.9,
  ...
)
```

Arguments

| | |
|-----------------|---|
| object | see showMethods(MAP) |
| ranges | A GRanges object |
| id | character string for sample identifier |
| TAUP | scalar for transition probabilities |
| tauMAX | the maximum probability that the current state is the same as the previous state |
| cnStates | character vector for hidden Markov model state labels |
| pr.nonmendelian | numeric: the a priori probability of a non-Mendelian copy number alteration |
| mdThr | a length-one numeric vector. A minimum distance below this threshold in absolute value will not be evaluated for copy number alterations. |
| ... | Ignored. |

| | |
|------|--|
| MAP2 | <i>Computes maximum a posteriori estimate for the trio copy number state</i> |
|------|--|

Description

Computes maximum a posteriori estimate for the trio copy number state

Usage

```
MAP2(object, mdgr, param = MinDistParam(), ...)
```

S4 method for signature 'MinDistExperiment,MinDistGRanges'

```
MAP2(object, mdgr, param = MinDistParam(), ...)
```

S4 method for signature 'MinDistExperiment,GRangesList'

```
MAP2(object, mdgr, param = MinDistParam(), ...)
```

S4 method for signature 'MinDistExperiment,GRanges'

```
MAP2(object, mdgr, param = MinDistParam(), ...)
```

Arguments

| | |
|--------|---|
| object | An object of class MinDistExperiment |
| mdgr | An object of class MinDistGRanges, GRangesList, or GRanges. |
| param | An object of class MinDistParam. |
| ... | ignored |

Value

An object of class MinDistPosterior

Examples

```
library(oligoClasses)
library(VanillaICE)
## A MinDistExperiment object:
data(md_exp)
## Segmented data
data(md_gr)
e_param <- EmissionParam(temper=1, p_outlier=1/100)
param <- MinDistParam(thin=1L, emission=e_param)
## Not run:
md_g <- MAP2(md_exp, md_gr, param)

## End(Not run)
```

| | |
|----------|--|
| mdLegend | <i>Text summary of information encapsulated in a MDRanges object for a particular interval</i> |
|----------|--|

Description

Text summary of information encapsulated in a MDRanges object for a particular interval

Usage

```
mdLegend(g)
```

Arguments

| | |
|---|-------------------|
| g | a MDRanges object |
|---|-------------------|

| | |
|----------------|-------------------------|
| MDRanges-class | A GRanges-derived class |
|----------------|-------------------------|

Description

Contains maximum a posteriori estimates for each genomic interval

Usage

```
MDRanges(..., posteriors)
```

Arguments

| | |
|------------|---|
| ... | additional arguments to GRanges constructor |
| posteriors | a DataFrame |

Examples

```
MDRanges()
```

| | |
|--------|------------------------------|
| md_exp | An example MinDistExperiment |
|--------|------------------------------|

Description

This dataset contains log R ratios and B allele frequencies from a parent-offspring trio (three individuals). Only markers from chromosomes 7 and 22 are included in this object. The `MinDistExperiment` class extends `RangedSummarizedExperiment`, and so many of the methods defined for `RangedSummarizedExperiment` such as `findOverlaps` are available through inheritance.

Format

a `MinDistExperiment`

Examples

```
## Not run:
library(oligoClasses)
library(VanillaICE)
library(data.table)
library(BSgenome.Hsapiens.UCSC.hg18)
extdir <- system.file("extdata", package="VanillaICE")
features <- suppressWarnings(fread(file.path(extdir, "SNP_info.csv")))
fgr <- GRanges(paste0("chr", features$Chr), IRanges(features$Position, width=1),
              isSnp=features[["Intensity Only"]==0])
fgr <- SnpGRanges(fgr)
```

```

names(fgr) <- features[["Name"]]
sl <- seqlevels(BSgenome.Hsapiens.UCSC.hg18)
seqlevels(fgr) <- sl[sl %in% seqlevels(fgr)]
seqinfo(fgr) <- seqinfo(BSgenome.Hsapiens.UCSC.hg18)[seqlevels(fgr),]
fgr <- sort(fgr)
files <- list.files(extdir, full.names=TRUE, recursive=TRUE, pattern="FinalReport")
## parse files
parsedDir <- "ParsedFiles"
if(!file.exists(parsedDir)) dir.create(parsedDir)
views <- ArrayViews(rowRanges=fgr, sourcePaths=files, parsedPath=parsedDir)
dat <- fread(files[1])
select_columns <- match(c("SNP Name", "Allele1 - AB", "Allele2 - AB",
                          "Log R Ratio", "B Allele Freq"), names(dat))
index_genome <- match(names(fgr), dat[["SNP Name"]])
scan_params <- CopyNumScanParams(index_genome=index_genome, select=select_columns,
                                cnvar="Log R Ratio",
                                bafvar="B Allele Freq",
                                gtvar=c("Allele1 - AB", "Allele2 - AB"))
invisible(sapply(views, parseSourceFile, param=scan_params))
ped_hapmap <- ParentOffspring(id = "hapmap", father="12287_03",
                              mother="12287_02",
                              offspring="12287_01",
                              parsedPath=parsedPath(views))
ped_list <- ParentOffspringList(pedigrees=list(
  ParentOffspring(id = "hapmap", father="12287_03",
                  mother="12287_02",
                  offspring="12287_01",
                  parsedPath=parsedPath(views)),
  ParentOffspring(id = "cleft",
                  father="22169_03",
                  mother="22169_02",
                  offspring="22169_01",
                  parsedPath=parsedPath(views))))
sample_info <- read.csv(file.path(extdir, "sample_data.csv"), stringsAsFactors=FALSE)
ind_id <- setNames(gsub(" ", "", sample_info$IndividualID), sample_info$File)
colnames(views) <- ind_id[gsub(".csv", "", colnames(views))]
md_exp <- MinDistExperiment(views, pedigree=ped_list[[2]])
seqlevels(md_exp, pruning.mode="coarse") <- "chr22"
params <- MinDistParam()
md_gr <- segment2(md_exp, params)
save(md_exp, file=~ /Software/bridge/MinimumDistance/data/md_exp.rda")
save(md_gr, file=~ /Software/bridge/MinimumDistance/data/md_gr.rda")

## End(Not run)

```

Description

Prior to inferring de novo trio copy number states, the log R ratios are segmented independently for each individual in a `ParentOffspring` class. The segmentation results are recorded in separate `GRanges` objects for the parents. For segmentation of the offspring log R ratios and the minimum distance, the segments are stored in separate `GRangesList` objects. For convenience, these `GRanges`, `GRangesList`, and pedigree information are bound in a single container referred to as a `MinDistGRanges` object. The example `MinDistGRanges` object provided in this package was obtained from the segmentation of the data stored in the example `MinDistExperiment` object.

Format

a `MinDistGRanges` object

| | |
|---------|---|
| mindist | <i>Getter and setter for the minimum distance statistic</i> |
|---------|---|

Description

Getter and setter for the minimum distance statistic

Usage

```
mindist(object)
```

```
mindist(object) <- value
```

Arguments

| | |
|--------|---|
| object | see <code>showMethods("mindist")</code> |
| value | a matrix of the minimum distance |

| | |
|-------------------|--|
| MinDistExperiment | <i>Constructor for MinDistExperiment class</i> |
|-------------------|--|

Description

Constructor for `MinDistExperiment` class

Usage

```
MinDistExperiment(object = ArrayViews(), pedigree = ParentOffspring(), ...)
```

```
## S4 method for signature 'ArrayViews,ParentOffspring'
```

```
MinDistExperiment(object = ArrayViews(), pedigree = ParentOffspring(), ...)
```

Arguments

object see showMethods(MinDistExperiment)
 pedigree a ParentOffspring object
 ... ignored

Value

an object of class MinDistExperiment

MinDistExperiment-class

Class and methods for MinDistExperiment

Description

Class and methods for MinDistExperiment

Usage

```
## S4 method for signature 'MinDistExperiment'
show(object)

## S4 method for signature 'MinDistExperiment'
pedigree(object)

## S4 replacement method for signature 'MinDistExperiment'
pedigree(object) <- value

## S4 method for signature 'MinDistExperiment'
mindist(object)

## S4 replacement method for signature 'MinDistExperiment,ANY'
mindist(object) <- value

## S4 method for signature 'MinDistExperiment,ANY,ANY,ANY'
x[i, j, ..., drop = FALSE]

## S4 method for signature 'MinDistExperiment'
offspring(object)

## S4 method for signature 'MinDistExperiment'
father(object)

## S4 method for signature 'MinDistExperiment'
mother(object)
```



```
## S4 method for signature 'MinDistExperiment'
segment2(object, param = MinDistParam())

## S4 method for signature 'RangedSummarizedExperiment'
father(object)

## S4 method for signature 'RangedSummarizedExperiment'
mother(object)

## S4 method for signature 'RangedSummarizedExperiment'
offspring(object)
```

Arguments

| | |
|--------|--|
| object | a MinDistExperiment object |
| value | a ParentOffspring object |
| x | a MinDistExperiment object |
| i | a numeric-vector for indexing the rows (optional) |
| j | a numeric-vector for indexing the columns (optional) |
| ... | additional arguments propagated to subsetting methods for RangedSummarizedExperiment |
| drop | logical. Whether to simplify a one-row or one-column matrix to a vector. In most cases, this should always be FALSE. |
| param | a MinDistParam object |

Slots

| | |
|----------|--------------------------|
| mindist | a matrix |
| pedigree | a ParentOffspring object |

| | |
|----------------|---|
| MinDistGRanges | <i>Constructor for MinDistGRanges class</i> |
|----------------|---|

Description

The MinDistGRanges class contains the segmentation of the father, mother, offspring, and the minimum distance for each possible parent-offspring trio. For the parents, the segmentation results are expected to be in GRanges format. To accommodate multiple-offspring families, both the offspring segments and minimum distance segments should be of class GRangesList where the length of the list corresponds to the number of offspring.

Usage

```
MinDistGRanges(
  mindist = GRangesList(),
  offspring = GRangesList(),
  father = GRanges(),
  mother = GRanges(),
  pedigree = ParentOffspring()
)
```

Arguments

| | |
|-----------|--------------------------|
| mindist | a GRangesList object |
| offspring | a GRangesList object |
| father | a GRanges object |
| mother | a GRanges object |
| pedigree | a ParentOffspring object |

Examples

```
MinDistGRanges()
```

MinDistGRanges-class *A container for storing segmentation data for members in a ParentOffspring family*

Description

A container for storing segmentation data for members in a ParentOffspring family

Usage

```
## S4 method for signature 'MinDistGRanges'
names(x)

## S4 method for signature 'MinDistGRanges'
mindist(object)

## S4 replacement method for signature 'MinDistGRanges,GRangesList'
mindist(object) <- value

## S4 method for signature 'MinDistGRanges'
offspring(object)

## S4 method for signature 'MinDistGRanges'
mother(object)
```

```
## S4 method for signature 'MinDistGRanges'  
father(object)  
  
## S4 method for signature 'MinDistGRanges'  
pedigree(object)  
  
## S4 method for signature 'MinDistGRanges'  
show(object)  
  
## S4 method for signature 'GRangesList'  
offspring(object)
```

Arguments

| | |
|--------|-------------------------|
| x | a MinDistGRanges object |
| object | a MinDistGRanges object |
| value | a GRangesList object |

Slots

| | |
|-----------|--------------------------|
| mindist | a GRangesList object |
| offspring | a GRangesList object |
| father | a GRanges object |
| mother | a GRanges object |
| pedigree | a ParentOffspring object |

Examples

```
data(md_gr)  
offspring(md_gr)  
father(md_gr)  
mother(md_gr)  
mindist(md_gr)
```

MinDistParam

Constructor for MinDistParam class

Description

The MinDistParam class contains parameters used for the segmentation implemented in the DNACopy package, parameters extracted from the PennCNV HMM such as parent-offspring transmission probabilities (see citation below), and initial values / parameters for computing emission probabilities.

Usage

```
MinDistParam(
  nMAD = 0.75,
  dnacopy = DNACopyParam(),
  penncnv = PennParam(),
  emission = EmissionParam(),
  thin = 10L
)
```

Arguments

| | |
|----------|--|
| nMAD | a length-one numeric vector indicating the minimal number of median absolute deviations of the mean segmented minimum distance from zero. For non-zero segments (# median absolute deviations > nMAD), maximum a posteriori estimates of the parent-offspring copy number states are computed. Segments with minimum distance values near zero are not called as they are less likely to correspond to regions with de novo copy number alterations. |
| dnacopy | an object of class DNACopyParam. |
| penncnv | probabilities/parameters of the PennCNV hidden Markov model |
| emission | an object of class EmissionParam |
| thin | a length-one vector indicating whether to thin the data. This is primarily for internal use in conjunction with the filterExperiment function. |

See Also

[segment](#)

MinDistParam-class *Class and methods for parameters of minimum distance algorithm*

Description

Contains parameters used for circular binary segmentation (package DNACopy), parameters in the PennCNV hidden Markov model, and parameters used for computing emission probabilities.

Usage

```
## S4 method for signature 'MinDistParam'
nMAD(object)

## S4 replacement method for signature 'MinDistParam,numeric'
nMAD(object) <- value

## S4 method for signature 'MinDistParam'
show(object)

## S4 method for signature 'DNACopyParam'
show(object)
```

Arguments

object a MinDistParam object
 value a length-one numeric vector.

Slots

nMAD a length-one numeric vector
 dnacopy an object of class DNACopyParam
 penncnv an object of class PennParam
 emission an object of class EmissionParam
 thin a length-one non-negative integer

 MinDistPosterior-class

Container for the segmentation results from a MinDistExperiment

Description

MinDistPosterior is a GRangesList-derived container for the segmentation and maximum a posteriori trio copy number states.

Usage

```
## S4 method for signature 'MinDistPosterior,ANY,ANY,ANY'
x[i, j, ..., drop = FALSE]

## S4 method for signature 'MinDistPosterior'
show(object)
```

Arguments

x a MinDistPosterior object
 i an index for subsetting rows
 j an index for subsetting columns
 ... additional arguments passed to subsetting matrices
 drop logical – whether to coerce single-row matrices to vectors
 object a MinDistPosterior object

See Also

[denovo](#)

| | |
|-----------------|--|
| MinimumDistance | <i>De novo copy number alterations in parent-offspring trios</i> |
|-----------------|--|

| | |
|------|--|
| nMAD | <i>Setter and getter for number of median absolute deviations the mean minimum distance of a genomic interval is from zero</i> |
|------|--|

Description

Setter and getter for number of median absolute deviations the mean minimum distance of a genomic interval is from zero

Usage

```
nMAD(object)
```

```
nMAD(object) <- value
```

Arguments

| | |
|--------|-----------------------------|
| object | see showMethods("nMAD") |
| value | a length-one numeric vector |

| | |
|----------------|---|
| offspringNames | <i>Deprecated functions and methods</i> |
|----------------|---|

Description

These functions will be defunct in a future release.

Usage

```
offspringNames(object)
```

```
offspringNames(object) <- value
```

```
trios(object)
```

```
pedigree(object)
```

```
pedigree(object) <- value
```

Arguments

| | |
|--------|---|
| object | see showMethods("offspringNames") |
| value | a character vector of offspring identifiers |

ParentOffspring-class *Object containing the sample identifiers for members in a pedigree*

Description

Container for registering sample identifiers with membership in a pedigree. For representing multiple pedigrees, see [ParentOffspringList](#).

Accessor for the sample identifiers for the members in a pedigree

Usage

```
offspring(object)
```

```
mother(object)
```

```
father(object)
```

```
ParentOffspring(  
  id = character(),  
  father = character(),  
  mother = character(),  
  offspring = character(),  
  parsedPath = character()  
)
```

```
## S4 method for signature 'ParentOffspring'  
pedigreeName(object)
```

```
## S4 method for signature 'ParentOffspring'  
father(object)
```

```
## S4 method for signature 'ParentOffspring'  
mother(object)
```

```
## S4 method for signature 'ParentOffspring'  
offspring(object)
```

```
## S4 method for signature 'ParentOffspring'  
show(object)
```

```
## S4 method for signature 'ParentOffspring'  
names(x)
```

Arguments

object a ParentOffspring object

| | |
|------------|--|
| id | length-one character vector providing a family-level id |
| father | length-one character vector providing sample ids for father |
| mother | length-one character vector providing sample ids for mother |
| offspring | character vector providing sample ids for offspring (can have length greater than one if there is more than one offspring) |
| parsedPath | character vector providing path to low-level data |
| x | a ParentOffspring object |

Slots

| | |
|------------|--|
| id | length-one character vector providing a family-level id |
| father | length-one character vector providing sample ids for father |
| mother | length-one character vector providing sample ids for mother |
| offspring | character vector providing sample ids for offspring (can have length greater than one if there is more than one offspring) |
| parsedPath | character vector providing path to parsed files of the marker-level summaries |

See Also

ParentOffspringList-class

Examples

```
ParentOffspring()
```

ParentOffspringList-class

A list of ParentOffspring objects

Description

Each element of the list is an element of class [ParentOffspring](#).

Usage

```
ParentOffspringList(pedigrees = list(), id)

## S4 method for signature 'ParentOffspringList'
pedigreeName(object)

## S4 method for signature 'ParentOffspringList'
show(object)

## S4 method for signature 'ParentOffspringList,ANY,ANY'
x[[i, j, ..., drop = FALSE]]
```



```
## S4 method for signature 'ParentOffspringList,ANY,ANY,ANY'
x[i, j, ..., drop = FALSE]

## S4 method for signature 'ParentOffspringList'
length(x)
```

Arguments

| | |
|-----------|---|
| pedigrees | a list of ParentOffspring objects |
| id | identifier for a pedigree |
| object | a ParentOffspringList object |
| x | a ParentOffspringList object |
| i | a numeric vector for subsetting the list (optional) |
| j | ignored |
| ... | ignored |
| drop | ignored |

Slots

id a character vector of identifiers for the pedigrees. id must have the same length as pedigrees
 pedigrees A list of ParentOffspring objects.

Examples

```
ParentOffspringList()
```

Pedigree

Deprecated function for constructing an instance of class Pedigree

Description

This function is deprecated and will be removed in a future release.

Usage

```
Pedigree(
  pedigreeInfo,
  fatherIds = character(),
  motherIds = character(),
  offspringIds = character()
)
```

Arguments

| | |
|--------------|--|
| pedigreeInfo | a data.frame with column names 'F' (father), 'M' (mother), and 'O' (offspring). Elements of the data.frame are the sample names. |
| fatherIds | character vector of identifiers for the father |
| motherIds | character vector of identifiers for the mother |
| offspringIds | character vector of identifiers for the offspring |

Examples

```
Pedigree()
```

| | |
|----------------|---|
| Pedigree-class | <i>Deprecated class for storing pedigree data</i> |
|----------------|---|

Description

Deprecated class for storing pedigree data

Usage

```
## S4 method for signature 'Pedigree'
trios(object)

## S4 method for signature 'Pedigree'
offspringNames(object)

## S4 method for signature 'Pedigree'
show(object)

## S4 method for signature 'Pedigree,ANY,ANY,ANY'
x[i, j, ..., drop = FALSE]

## S4 method for signature 'Pedigree'
dim(x)
```

Arguments

| | |
|--------|--|
| object | a Pedigree object |
| x | a Pedigree object |
| i | a numeric vector for subsetting (optional) |
| j | ignored |
| ... | ignored |
| drop | ignored |

Slots

`trios` a data.frame with colnames 'F', 'M', and 'O' containing sample identifiers for the father (F), mother (M), and offspring (O).

`trioIndex` a data.frame

| | |
|--------------|--|
| pedigreeGrid | <i>Plot the log R ratios and BAFs on a grid given by precomputed viewports</i> |
|--------------|--|

Description

Plot the log R ratios and BAFs on a grid given by precomputed viewports

Usage

```
pedigreeGrid(g, vps, figs)
```

Arguments

`g` a MDRanges object

`vps` a list of viewports. See [pedigreeViewports](#).

`figs` a list of trellis objects created by the function [plotDenovo](#).

See Also

[plotDenovo pedigreeViewports](#)

Examples

```
library(VanillaICE)
require(grid)
##marker-level summaries
data(md_exp)
seqlevels(md_exp, pruning.mode="coarse") <- "chr22"
## segmentation results
data(md_gr)
posteriorCalls <- MAP2(md_exp, md_gr, MinDistParam())
g <- denovoHemizygous(posteriorCalls)
g
vps <- MinimumDistance:::pedigreeViewports()
param <- HmmTrellisParam()
p <- plotDenovo(md_exp, g[1], param)
p <- pedigreeGrid(g=g[1], vps=vps, figs=p)
leg <- mdLegend(g[1])
upViewport(0)
pushViewport(vps[["legend"]])
grid.text(leg, x=unit(0.02, "npc"), y=unit(0.95, "npc"), just=c("left", "top"),
          gp=gpar(cex=0.6, fontfamily="mono"))
```

```
##
## combine adjacent denovo hemizygous
##
g2 <- reduce(denovoHemizygous(posteriorCalls), min.gapwidth=500e3)
post <- MAP2(md_exp, g2)
g2 <- denovoHemizygous(post)
p <- plotDenovo(md_exp, g2, param)
p <- pedigreeGrid(g=g2, vps=vps, figs=p)
leg <- mdLegend(g2)
upViewport(0)
pushViewport(vps[["legend"]])
grid.text(leg, x=unit(0.02, "npc"), y=unit(0.95, "npc"), just=c("left", "top"),
          gp=gpar(cex=0.6, fontfamily="mono"))
```

| | |
|--------------|-----------------------------------|
| pedigreeName | <i>Accessor for pedigree name</i> |
|--------------|-----------------------------------|

Description

Accessor for pedigree name

Usage

```
pedigreeName(object)
```

Arguments

object a ParentOffspring or ParentOffspringList object

See Also

[ParentOffspring](#) [ParentOffspringList](#)

| | |
|-------------------|--|
| pedigreeViewports | <i>Default viewports for plotting log R ratios, BAFs, chromosome idiogram, and a legend for a case-parent trio</i> |
|-------------------|--|

Description

Default viewports for plotting log R ratios, BAFs, chromosome idiogram, and a legend for a case-parent trio

Usage

```
pedigreeViewports()
```

See Also

[plotDenovo pedigreeGrid](#)

Examples

```
vps <- pedigreeViewports()
```

| | |
|-----------|--|
| PennParam | <i>Constructor for class PennParam</i> |
|-----------|--|

Description

Parameters for the PennCNV Hidden Markov model

Usage

```
PennParam(
  states,
  referenceState = "222",
  prLessLikelyCN = 9e-04,
  prNonMendelian = 1.5e-06,
  prInitialStateNotDiploid = 4/5,
  prTransitionToNewState = 0.5,
  tauNM = 0.01
)

## S4 method for signature 'PennParam'
show(object)
```

Arguments

| | |
|--------------------------|--|
| states | character vector of possible trio states |
| referenceState | the reference (normal) trio copy number state (typically '222') |
| prLessLikelyCN | as defined in Wang et al. 2007, this is the probability of the less likely allele-specific copy numbers for the trio |
| prNonMendelian | the prior probability of a non-Mendelian copy number alteration |
| prInitialStateNotDiploid | initial probability for non-diploid states |
| prTransitionToNewState | probability of transitioning to a new state |
| tauNM | probability of transitioning from a Mendelian given previous event was non-Mendelian (and vice versa). |
| object | a PennParam object |

References

Wang et al., Genome Res. 2007 Nov;17(11):1665-74. PMID: 17921354

| | |
|------------|---|
| plotDenovo | <i>Plot marker-level summaries for a genomic interval of interest</i> |
|------------|---|

Description

Plot marker-level summaries for a genomic interval of interest

Usage

```
plotDenovo(object, g, param)

## S4 method for signature 'MinDistExperiment,MDRanges'
plotDenovo(object, g, param)
```

Arguments

| | |
|--------|-------------------------------|
| object | see showMethods("plotDenovo") |
| g | a MDRanges object |
| param | a HmmTrellisParam object |

| | |
|---------------------|--|
| range,ILimit-method | <i>compute the range of an ILimit instance</i> |
|---------------------|--|

Description

The range method for class ILimit is used internally in MinimumDistance.

Usage

```
## S4 method for signature 'ILimit'
range(x, ..., na.rm = FALSE)
```

Arguments

| | |
|-------|---|
| x | a ILimit object |
| ... | ignored |
| na.rm | logical. If TRUE, missing values are removed. |

segment2

A wrapper for DNACopy's segment function

Description

Methods for circular binary segmentation.

Usage

```
segment2(object, ...)

## S4 method for signature 'TrioSet'
segment2(object, md = NULL, segmentParents = TRUE, verbose = TRUE, ...)

## S4 method for signature 'matrix'
segment2(object, pos, chrom, id, featureNames, ...)

## S4 method for signature 'ff_matrix'
segment2(object, pos, chrom, id, featureNames, ...)

## S4 method for signature 'arrayORff_array'
segment2(
  object,
  pos,
  chrom,
  id,
  featureNames,
  segmentParents = TRUE,
  verbose = TRUE,
  ...
)
```

Arguments

| | |
|----------------|---|
| object | see showMethods{segment2} |
| ... | Additional arguments passed to DNACopy's segment. |
| md | a matrix of the minimum distance |
| segmentParents | logical. Whether to segment the log R ratios of the parents using circular binary segmentation. |
| verbose | logical. Whether to display messages that indicate progress. |
| pos | integer vector of physical position of markers in the genome |
| chrom | character or integer vector of chromosome names |
| id | character vector of trio identifiers for subsetting object |
| featureNames | character vector specifying marker names for subsetting object |

See Also

[segment](#)
[segment](#)

TrioSet *Deprecated constructor for TrioSet class*

Description

The TrioSet class has been deprecated and may be removed in a future release.

Usage

```
TrioSet(
  pedigreeData = Pedigree(),
  sample.sheet,
  row.names = NULL,
  lrr,
  baf,
  featureData,
  cdfname,
  drop = TRUE,
  mindist = NULL,
  genome = c("hg19", "hg18")
)
```

Arguments

| | |
|--------------|--|
| pedigreeData | an object of class Pedigree |
| sample.sheet | a data.frame containing metadata on the trios |
| row.names | a character vector providing row identifiers for the sample.sheet argument that match the names of the trios in the pedigreeData argument. |
| lrr | a matrix of log R ratios |
| baf | a matrix of B allele frequencies |
| featureData | a GenomeAnnotatedDataFrame object for the SNPs/nonpolymorphic markers |
| cdfname | character string indicating the annotation package used to extract physical position and chromosome of markers |
| drop | logical. When FALSE, the dimnames on the log R ratio and BAF arrays is set to NULL |
| mindist | can be either NULL or a matrix of the minimum distance |
| genome | character string providing the UCSC genome build |

Value

TrioSet

TrioSet-class *Deprecated class for storing low-level genomic data for trios*

Description

This class is deprecated and will be defunct in a future release.

Usage

```
## S4 method for signature 'TrioSet'
pedigree(object)

## S4 method for signature 'TrioSet'
show(object)

## S4 method for signature 'TrioSet'
mindist(object)

## S4 replacement method for signature 'TrioSet,matrix'
mindist(object) <- value

## S4 method for signature 'TrioSet'
dim(x)

## S4 method for signature 'TrioSet'
trios(object)

## S4 method for signature 'TrioSet,ANY,ANY,ANY'
x[i, j, ..., drop = FALSE]

## S4 method for signature 'TrioSet,GRanges'
MAP(
  object,
  ranges,
  transition_param = TransitionParam(),
  emission_param = EmissionParam(),
  mdThr = 0.9,
  ...
)

## S4 method for signature 'ff_array,ANY,ANY,ANY'
x[i, j, ..., drop = FALSE]
```

Arguments

| | |
|--------|------------------|
| object | a TrioSet object |
| value | a matrix |

| | |
|------------------|---|
| x | a TrioSet object |
| i | a numeric vector for subsetting rows (optional) |
| j | a numeric vector for subsetting trios (optional) |
| ... | additional arguments passed to subsetting methods for matrices and data frames |
| drop | logical. Whether to simplify matrices to numeric vectors. This should be left as FALSE. |
| ranges | a GRanges object |
| transition_param | an object of class TransitionParam |
| emission_param | an object of class EmissionParam |
| mdThr | the minimum absolute value of the minimum distance segment mean. Segments with means below mdThr in absolute value will not be called as they are unlikely to be de novo. |

Slots

| | |
|-----------------|---|
| fatherPhenoData | AnnotatedDataFrame containing covariates for the father |
| motherPhenoData | AnnotatedDataFrame containing covariates for the mother |
| pedigree | an object of class Pedigree |
| mindist | a numeric matrix of the minimum distance for each trio, or NULL |

TrioSetList

Constructor for TrioSetList class

Description

The TrioSetList class has been deprecated and may be removed in a future release. Use MinDistExperiment instead.

Usage

```
TrioSetList(
  chromosome = integer(),
  pedigreeData = Pedigree(),
  sample.sheet,
  row.names = NULL,
  lrr,
  baf,
  featureData,
  cdfname,
  ffname = "",
  genome
)
```

Arguments

| | |
|--------------|--|
| chromosome | integer vector of chromosome names |
| pedigreeData | a Pedigree object |
| sample.sheet | a data.frame containing sample covariates |
| row.names | a character vector |
| lrr | a matrix of log R ratios |
| baf | a matrix of B allele frequencies |
| featureData | a GenomeAnnotatedDataFrame |
| cdfname | a character string indicating the annotation package |
| ffname | prefix for ff-filenames |
| genome | character string indicating genome build |

TrioSetList-class *Deprecated class for storing low-level genomic data for trios*

Description

This class is deprecated and will be defunct in a future release.

Usage

```
## S4 method for signature 'TrioSetList,RangedSummarizedExperiment'
coerce(from, to)

## S4 method for signature 'TrioSetList'
pedigree(object)

## S4 method for signature 'TrioSetList'
trios(object)

## S4 method for signature 'TrioSetList'
offspringNames(object)

## S4 method for signature 'TrioSetList,ANY,ANY,ANY'
x[i, j, ..., drop = FALSE]

## S4 method for signature 'TrioSetList,ANY,ANY'
x[[i, j, ..., exact = TRUE]]

## S4 method for signature 'TrioSetList'
show(object)

## S4 method for signature 'TrioSetList'
length(x)
```

```

## S4 method for signature 'TrioSetList'
x$name

## S4 method for signature 'TrioSetList,GRanges'
MAP(
  object,
  ranges,
  id,
  TAUP = 1e+10,
  tauMAX = 1 - 5e-08,
  cnStates = c(-2, -0.4, 0, 0, 0.4, 1),
  pr.nonmendelian = 1.5e-06,
  mdThr = 0.9,
  ...
)

## S4 method for signature 'TrioSetList'
segment2(object, md = NULL, segmentParents = TRUE, verbose = TRUE, ...)

## S4 method for signature 'list'
segment2(
  object,
  pos,
  chrom,
  id = NULL,
  featureNames,
  segmentParents = TRUE,
  verbose = TRUE,
  genome,
  ...
)

```

Arguments

| | |
|--------|---|
| from | a TrioSetList |
| to | a RangedSummarizedExperiment |
| object | a TrioSetList object |
| x | a TrioSetList |
| i | a numeric vector for subsetting the chromosomes (optional) |
| j | a numeric vector for subsetting trios (optional) |
| ... | additional arguments passed to subsetting methods for matrices and data frames |
| drop | logical. Whether to simplify matrices to numeric vectors. This should be left as FALSE. |
| exact | ignored |
| name | character string of a variable name in the phenoData |

| | |
|-----------------|--|
| ranges | a GRanges object |
| id | a character vector of trio identifiers |
| TAUP | length-one numeric vector. Larger values decrease the probability of transitioning to an different state. |
| tauMAX | the maximum allowed transition probability |
| cnStates | a length-six numeric vector providing initial values for the mean copy number for each of the 6 states |
| pr.nonmendelian | a length-one numeric vector indicating the probability of a non-Mendelian copy number alteration in the offspring |
| mdThr | a length-one numeric vector indicating the minimum value of the mean minimum distance. Segments with absolute mean value less than mdThr are not called. |
| md | a list of minimum distance matrices. Length of list should be the same as the length of the TrioSetList object. |
| segmentParents | logical. Whether to segment the parental log R ratios. |
| verbose | logical. Whether to display messages indicating progress. |
| pos | a list of the genomic positions (integers) |
| chrom | list of chromosome names |
| featureNames | a list of the marker names |
| genome | a character vector indicating the UCSC genome build used for the annotation (i.e., 'hg18' or 'hg19'). |

Slots

fatherPhenoData AnnotatedDataFrame containing covariates for the father
 motherPhenoData AnnotatedDataFrame containing covariates for the mother
 pedigree an object of class Pedigree

TrioSetListLD

Deprecated TrioSetList constructor for large data

Description

The TrioSetListLD constructor uses ff objects to handle large datasets. This function is defunct. Use MinDistExperiment instead.

Usage

```
TrioSetListLD(
  path,
  fnames,
  ext = "",
  samplesheet,
  row.names,
  pedigreeData,
  featureData,
  annotationPkg,
  outdir = ldPath(),
  ffprefix = "",
  genome = c("hg19", "hg18")
)
```

Arguments

| | |
|---------------|---|
| path | Path to plain-text files containing log R ratios and B allele frequencies. Files should contain data for a single sample. |
| fnames | Character string providing filenames. |
| ext | Character string indicating whether the fnames has a file extension (e.g., ".txt") |
| samplesheet | (Optional) data.frame containing phenotypic / experimental covariates on the samples. Note that if samplesheet is provided, row.names must be specified. |
| row.names | Character vector indicating the sample id for each row in samplesheet. row.names should be unique and, ideally, correspond to fnames |
| pedigreeData | An object of class Pedigree. |
| featureData | A GenomeAnnotatedDataFrame |
| annotationPkg | Character string indicating the annotation package used to extract information on the features (chromosome, physical position, and whether the feature is polymorphic ('isSnp')). |
| outdir | Character string indicating the path for storing ff objects. Ignored if the ff package is not loaded. |
| ffprefix | Character string indicating the prefix used to name ff objects. Ignored if the ff package is not loaded. |
| genome | character string indicating UCSC genome build. Only "hg19" is allowed for annotation packages that support a single build. Supported builds for most platforms are "hg18" and "hg19". |

Value

A TrioSetList object

See Also

[TrioSetList](#)

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