Package ‘VanillaICE’

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Title A Hidden Markov Model for high throughput genotyping arrays

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acf2

Calculate lag 10 autocorrelation

Description

A wrapper for the function acf that returns the autocorrelation for the specified lag. Missing values are removed.

Usage

acf2(x, lag = 10, ...)

Arguments

x numeric vector
lag integer
... additional arguments to acf

See Also

acf

ArrayViews-class

ArrayViews class, constructor, and methods

Description

ArrayViews provides views to the low-level data – log R ratios, B allele frequencies, and genotypes that are stored in parsed files on disk, often scaled and coerced to an integer. Accessors to the low-level data are provided that extract the marker-level summaries from disk, rescaling when appropriate.
ArrayViews-class

Usage

ArrayViews(class = "ArrayViews", colData, rowRanges = GRanges(),
            sourcePaths = character(), scale = 1000, sample_ids,
            parsedPath = getwd(), lrrFiles = character(), bafFiles = character(),
            gtfFiles = character())

## S4 method for signature 'ArrayViews,ANY,ANY,ANY'

x[1, j, ..., drop = FALSE]

colnames(x) <- value

## S4 method for signature 'ArrayViews'

colnames(x, do.NULL = TRUE, prefix = "col")

## S4 method for signature 'ArrayViews'

x$name

## S4 replacement method for signature 'ArrayViews'

x$name <- value

## S4 method for signature 'ArrayViews'

show(object)

## S4 method for signature 'ArrayViews'

sapply(X, FUN, ..., simplify = TRUE,
       USE.NAMES = TRUE)

## S4 method for signature 'ArrayViews'

ncol(x)

## S4 method for signature 'ArrayViews'

nrow(x)

## S4 method for signature 'ArrayViews'

dim(x)

## S4 method for signature 'ArrayViews'

start(x)

Arguments

class character string
colData DataFrame
colRanges GRanges object
sourcePaths character string provide complete path to plain text source files (one file per
sample) containing log R ratios and B allele frequencies
scale log R ratios and B allele frequencies can be stored as integers on disk to increase
IO speed. If scale =1, the raw data is not transformed. If scale = 1000 (default),
the log R ratios and BAFs are multiplied by 1000 and coerced to an integer.
sample_ids character vector indicating how to name samples. Ignored if colData is specified.
parsedPath character vector indicating where parsed files should be saved
ArrayViews-class

- `lrrFiles` character vector of file names for storing log R ratios
- `bafFiles` character vector of file names for storing BAFs
- `gtFiles` character vector of file names for storing genotypes
- `x` a `ArrayViews` object
- `i` numeric vector or missing
- `j` numeric vector or missing
- `...` additional arguments to `FUN`
- `drop` ignored
- `value` a character-string vector
- `do.NULL` ignored
- `prefix` ignored
- `name` character string indicating name in `colData` slot of `ArrayViews` object
- `object` a `ArrayViews` object
- `X` a `ArrayViews` object
- `FUN` a function to apply to each column of `X`
- `simplify` logical indicating whether result should be simplified
- `USE.NAMES` whether the output should be a named vector

Slots

- `colData` A character string
- `rowRanges` A `DataFrame`. WARNING: The accessor for this slot is `rowRanges`, not `rowRanges`!
- `index` A `GRanges` object
- `sourcePaths` A character string providing complete path to source files (one file per sample) containing low-level summaries (Log R ratios, B allele frequencies, genotypes)
- `scale` A length-one numeric vector
- `parsedPath` A character string providing full path to where parsed files should be saved
- `lrrFiles` A character string providing full path to filenames for log R ratios
- `bafFiles` character vector of filenames for BAFs
- `gtFiles` character vector of filenames for genotypes

See Also

- `CopyNumScanParams`
- `parseSourceFile`

Examples

```r
ArrayViews()
## From unit test
require(BSgenome.Hsapiens.UCSC.hg18)
require(data.table)
extdir <- system.file("extdata", package="VanillaICE", mustWork=TRUE)
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"]
```
calculateEmission

bsgenome <- BSgenome.Hsapiens.UCSC.hg18
seqlevels(fgr) <- seqlevels(bsgenome)[seqlevels(bsgenome) %in% seqlevels(fgr)]
seqinfo(fgr) <- seqinfo(bsgenome)[seqlevels(fgr),]
fgr <- sort(fgr)
files <- list.files(extdir, full.names=TRUE, recursive=TRUE, pattern="FinalReport")
ids <- gsub(".rds", ",", gsub("FinalReport", "", basename(files)))
views <- ArrayViews(rowRanges=fgr,
                   sourcePaths=files,
                   sample_ids=ids)
lrrFile(views)
## view of first 10 markers and samples 3 and 5
views <- views[1:10, c(3,5)]

baumWelchUpdate

Function for updating parameters for emission probabilities

Description

This function is not meant to be called directly by the user. It is exported in the package NAMESPACE for internal use by other BioC packages.

Usage

baumWelchUpdate(param, assay_list)

Arguments

param A container for the HMM parameters
assay_list list of log R ratios and B allele frequencies

calculateEmission

Calculate the emission probabilities for the 6-state HMM

Description

Given the data and an object containing parameters for the HMM, this function computes emission probabilities. This function is not intended to be called by the user and is exported for internal use by other BioC packages.

Usage

calculateEmission(x, param = EmissionParam())

Arguments

x list of low-level data with two elements: a numeric vector of log R ratios and a numeric vector of B allele frequencies
param parameters for the 6-state HMM
**Value**

A matrix of emission probabilities. Column correspond to the HMM states and rows correspond to markers on the array (SNPs and nonpolymorphic markers)

**See Also**

baumWelchUpdate

---

**cnvFilter**

*Filter the HMM-derived genomic ranges for copy number variants*

**Description**

The HMM-derived genomic ranges are represented as a GRanges-derived object. `cnvFilter` returns a GRanges object using the filters stipulated in the `filters` argument.

**Usage**

```r
CNVFilter(object, filters = FilterParam())
cnvSegs(object, filters = FilterParam(state = c("1", "2", "5", "6")))
duplication(object, filters = FilterParam(state = c("5", "6")))
deletion(object, filters = FilterParam(state = c("1", "2")))
hemizygous(object, filters = FilterParam(state = "2"))
homozygous(object, filters = FilterParam(state = "1"))
```

## S4 method for signature 'HMM'

cnvSegs(object, filters = FilterParam(state =
  as.character(c(1, 2, 5, 6)))))

## S4 method for signature 'HMMList'

segs(object)

## S4 method for signature 'HMMList'

hemizygous(object)

## S4 method for signature 'HMMList'

homozygous(object)

## S4 method for signature 'HMMList'

duplication(object)

## S4 method for signature 'HMMList'

cnvSegs(object, filters = FilterParam(state =
  as.character(c(1, 2, 5, 6)))))

## S4 method for signature 'HMMList'

```
cn_means

A parameter class for computing Emission probabilities

description
Parameters for computing emission probabilities for a 6-state HMM, including starting values for the mean and standard deviations for log R ratios (assumed to be Gaussian) and B allele frequencies (truncated Gaussian), and initial state probabilities.

Usage

\[ \text{cn\_means}(\text{object}) \]

\[ \text{cn\_sds}(\text{object}) \]

\[ \text{baf\_means}(\text{object}) \]

\[ \text{baf\_sds}(\text{object}) \]

\[ \text{baf\_means}(\text{object}) \leftarrow \text{value} \]
baf_sds(object) <- value

cn_sds(object) <- value

cn_means(object) <- value

EmissionParam(cn_means = CN_MEANS(), cn_sds = CN_SDS(),
               baf_means = BAF_MEANS(), baf_sds = BAF_SDS(), initial = rep(1/6, 6),
               EMupdates = 5L, CN_range = c(-5, 3), temper = 1, p_outlier = 1/100,
               modelHomozygousRegions = FALSE)

EMupdates(object)

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

Arguments

object see showMethods("EMupdates")
value numeric vector
      cn_means numeric vector of starting values for log R ratio means (order is by copy number state)
      cn_sds numeric vector of starting values for log R ratio standard deviations (order is by copy number state)
      baf_means numeric vector of starting values for BAF means ordered. See example for details on how these are ordered.
      baf_sds numeric vector of starting values for BAF means ordered. See example for details on how these are ordered.
      initial numeric vector of intial state probabilities
      EMupdates number of EM updates
      CN_range the allowable range of log R ratios. Log R ratios outside this range are thresholded.
      temper Emission probabilities can be tempered by emit^temper. This is highly experimental.
      p_outlier probability that an observation is an outlier (assumed to be the same for all markers)
      modelHomozygousRegions logical. If FALSE (default), the emission probabilities for BAFs are modeled from a mixture of truncated normals and a Unif(0,1) where the mixture probabilities are given by the probability that the SNP is heterozygous. See Details below for a discussion of the implications.

Details

The log R ratios are assumed to be emitted from a normal distribution with a mean and standard deviation that depend on the latent copy number. Similarly, the BAFs are assumed to be emitted from a truncated normal distribution with a mean and standard deviation that depends on the latent number of B alleles relative to the total number of alleles (A+B).
Value

numeric vector

Details

When `modelHomozygousRegions` is FALSE (the default in versions >= 1.28.0), emission probabilities for B allele frequencies are calculated from a mixture of a truncated normal densities and a Unif(0,1) density with the mixture probabilities given by the probability that a SNP is homozygous. In particular, let \( p \) denote a 6 dimensional vector of density estimates from a truncated normal distribution for the latent genotypes ‘A’, ‘B’, ‘AB’, ‘AAB’, ‘ABB’, ‘AAAB’, and ‘ABBB’. The probability that a genotype is homozygous is estimated as

\[
prHom = (p["A"] + p["B"]) / \text{sum}(p)
\]

and the probability that the genotype is heterozygous (any latent genotype that is not ‘A’ or ‘B’) is given by

\[
prHet = 1 - prHom
\]

Since the density of a Unif(0,1) is 1, the 6-dimensional vector of emission probability at a SNP is given by

\[
emit = prHet * p + (1 - prHet)
\]

The above has the effect of minimizing the influence of BAFs near 0 and 1 on the state path estimated by the Viterbi algorithm. In particular, the emission probability at homozygous SNPs will be virtually the same for states 3 and 4, but at heterozygous SNPs the emission probability for state 3 will be an order of magnitude greater for state 3 (diploid) compared to state 4 (diploid region of homozygosity). The advantage of this parameterization are fewer false positive hemizygous deletion calls. [ Log R ratios tend to be more sensitive to technical sources of variation than the corresponding BAFs/ genotypes. Regions in which the log R ratios are low due to technical sources of variation will be less likely to be interpreted as evidence of copy number loss if heterozygous genotypes have more 'weight' in the emission estimates than homozygous genotypes. ] The trade-off is that only states estimated by the HMM are those with copy number alterations. In particular, copy-neutral regions of homozygosity will not be called.

By setting `modelHomozygousRegions = TRUE`, the emission probabilities at a SNP are given simply by the \( p \) vector described above and copy-neutral regions of homozygosity will be called.

Examples

```r
ep <- EmissionParam()
cn_means(ep)
ep <- EmissionParam()
ep_means(ep)
ep <- EmissionParam()
ep_sds(ep)
ep <- EmissionParam()
baf_means(ep)
baf_means(ep) <- baf_means(ep)
ep <- EmissionParam()
baf_sds(ep) <- baf_sds(ep)
```
CopyNumScanParams-class

Parameters for parsing source files containing SNP-array processed data, such as GenomeStudio files for the Illumina platform

Description

Raw SNP array processed files have headers and variable labels that may depend the software, how the output files was saved, the software version, and other factors. The purpose of this container is to collect the parameters relevant for reading in the source files for a particular project in a single container. This may require some experimentation as the example illustrates. The function fread in the data.table package greatly simplifies this process.

Usage

CopyNumScanParams(cnvar = "Log R Ratio", bafvar = "B Allele Freq", gtvar = c("Allele1 - AB", "Allele2 - AB"), index_genome = integer(), select = integer(), scale = 1000, row.names = 1L)

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

Arguments

cnvar          length-one character vector providing name of variable for log R ratios
bafvar         length-one character vector providing name of variable for B allele frequencies
gtvar          length-one character vector providing name of variable for genotype calls
index_genome   integer vector indicating which rows of the of the source files (e.g., GenomeStudio) to keep. By matching on a sorted GRanges object containing the feature annotation (see example), the information on the markers will also be sorted.
select         integer vector specifying indicating which columns of the source files to import (see examples)
scale          length-one numeric vector for rescaling the raw data and coercing to class integer. By default, the low-level data will be scaled and saved on disk as integers.
row.names      length-one numeric vector indicating which column the SNP names are in
object         a CopyNumScanParams object
doUpdate

Slots

  index_genome  an integer vector
  cnvar        the column label for the log R ratios
  bafvar       the column label for the B allele frequencies
  gtvar        the column label(s) for the genotypes
  scale        length-one numeric vector indicating how the low-level data should be scaled prior to saving on disk
  select       numeric vector indicating which columns to read
  row.names    length-one numeric vector indicating which column the SNP names are in

See Also

  ArrayViews parseSourceFile

Examples

  CopyNumScanParams() ## empty container

---

doUpdate

*Helper function to determine whether to update the HMM parameters via the Baum-Welch algorithm*

Description

This function is not intended to be called directly by the user, and is exported only for internal use by other BioC packages.

Usage

  doUpdate(param)

Arguments

  param  An object containing parameters for the HMM

See Also

  HmmParam
dropDuplicatedMapLocs

Drop markers on the same chromosome having the same genomic coordinates

Description

If there are multiple markers on the same chromosome with the same annotated position, only the first is kept.

Usage

dropDuplicatedMapLocs(object)

Arguments

object a container for which the methods seqnames and start are defined

Value

an object of the same class with duplicated genomic positions removed

Examples

data(snp_exp)
g <- rowRanges(snp_exp)
## duplicate the first row
g[length(g)] <- g[1]
rowRanges(snp_exp) <- g
snp_exp2 <- dropDuplicatedMapLocs(snp_exp)

dropSexChrom

Filter sex chromosomes

Description

Removes markers on chromosomes X and Y.

Usage

dropSexChrom(object)

Arguments

object an object for which the methods seqnames and rowRanges are defined.

Value

an object of the same class as the input
emission

Methods to set and get emission probabilities

Description

Get or set a matrix of emission probabilities. This function is exported primarily for internal use by other BioC packages.

Usage

emission(object)

emission(object) <- value

Arguments

object  see showMethods(emission)
value   a matrix of emission probabilities

Value

matrix

emissionParam

Accessor for parameters used to compute emission probabilities

Description

Parameters for computing emission probabilities include the starting values for the Baum Welch update and initial state probabilities.

Usage

emissionParam(object)

emissionParam(object) <- value

Arguments

object  an object of class EmissionParam
value   an object of class EmissionParam

Value

EmissionParam instance
Examples

```r
hparam <- HmmParam()
emissionParam(hparam)
ep <- EmissionParam()
 cn_means(ep) <- log2(c(.1/2, 1/2, 2/2, 2/2, 3/2, 4/2))
emissionParam(hparam) <- ep
```

Description

The maximum a posteriori estimate of the trio copy number state for each genomic range is represented in a GRanges-derived class. Ultimately, these ranges will be filtered based on the trio copy number state (e.g., de novo deletions), size, number of features (SNPs), or chromosome. FilterParam is a container for the parameters commonly used to filter the genomic ranges.

Usage

```r
FilterParam(probability = 0.99, numberFeatures = 10,
 seqnames = paste0("chr", c(1:22, "X", "Y")), state = as.character(1:6),
 width = 1L)
```

## S4 method for signature 'FilterParam'
probability(object)

## S4 method for signature 'FilterParam'
state(object)

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

Arguments

- `probability`: minimum probability for the call
- `numberFeatures`: minimum number of SNPs/nonpolymorphic features in a region
- `seqnames`: the seqnames (character string or Rle to keep)
- `state`: character: the HMM states to keep
- `width`: the minimum width of a region
- `object`: a FilterParam object

Slots

- `probability`: a length-one numeric vector indicating the minimum posterior probability for the called state. Genomic intervals with posterior probabilities below `probability` will be filtered.
- `numberFeatures`: a positive integer indicating the minimum number of features in a segment
- `seqnames`: a character vector of seqnames to select (i.e., ‘chr1’ for only those intervals on chromosome 1)
- `width`: positive integer indicating the minimal width of genomic intervals
- `state`: character string indicating which hidden Markov model states to select
See Also

cnvFilter cnvSegs hmm2

Examples

fp <- FilterParam()
width(fp)
numberFeatures(fp)
seqnames(fp)
## To select CNV segments for which
## - the CNV call has a 'posterior' probability of at least 0.95
## - the number of features is at least 10
## - the HMM states are 1 (homozygous deletion) or 2 (hemizygous deletion)
FilterParam(probability=0.95, numberFeatures=10, state=c("1", "2"))

description

Accessor for HMM filter parameters

Usage

filters(object)

Arguments

object see showMethods(filters)

description

Accessor for SNP genotypes

Usage

genotypes(object)

## S4 method for signature 'ArrayViews'
lrr(object)

## S4 method for signature 'ArrayViews'
baf(object)

## S4 method for signature 'ArrayViews'
genotypes(object)
getExampleSnpExperiment

Create an example SnpArrayExperiment from source files containing marker-level genomic data that are provided in this package

Usage

getExampleSnpExperiment(bsgenome)

Arguments

bsgenome a BSgenome object

Value

A SnpArrayExperiment

Examples

## Not run:
if(require("BSgenome.Hsapiens.UCSC.hg18")){
  genome <- BSgenome.Hsapiens.UCSC.hg18
  snp_exp <- getExampleSnpExperiment(genome)
}

## End(Not run)
getHmmParams  \hspace{1cm} \textit{Accessor for HMM model parameters}

\textbf{Description}

Accessor for HMM model parameters

\textbf{Usage}

\begin{verbatim}
getHmmParams(object)
\end{verbatim}

\textbf{Arguments}

\begin{itemize}
  \item \texttt{object} \hspace{1cm} see \texttt{showMethods(HmmParam)}
\end{itemize}

\textbf{Examples}

\begin{verbatim}
hmm_object <- HMM()
getHmmParams(hmm_object)
\end{verbatim}

\hspace{1cm}

\textbf{HMM-class}  \hspace{1cm} \textit{Container for the segmented data and the 6-state HMM model parameters}

\textbf{Description}

Container for the segmented data and the 6-state HMM model parameters

The constructor \texttt{HMM} creates and object of class \texttt{HMM}. Not typically called directly by the user.

\textbf{Usage}

\begin{verbatim}
HMM(granges = GRanges(), param = HmmParam(), posterior = matrix(),
    filters = FilterParam())
\end{verbatim}

\begin{verbatim}
## S4 method for signature 'HMM'
state(object)
\end{verbatim}

\begin{verbatim}
## S4 method for signature 'HMM'
show(object)
\end{verbatim}

\textbf{Arguments}

\begin{itemize}
  \item \texttt{granges} \hspace{1cm} a GRanges object
  \item \texttt{param} \hspace{1cm} a HmmParam object
  \item \texttt{posterior} \hspace{1cm} matrix of posterior probabilities
  \item \texttt{filters} \hspace{1cm} an object of class FilterParam
  \item \texttt{object} \hspace{1cm} a HMM object
**hmm2**

Slots

- granges: a GRanges object
- param: a HmmParam object
- posterior: a matrix of posterior probabilities
- filters: a FilterParam object

**See Also**

- hmm2

**Examples**

```r
data(snp_exp)
hmm_list <- hmm2(snp_exp[,1])
resultsFirstSample <- hmm_list[[1]]
resultsFirstSample
HMM()
```

---

**hmm2**  
*Fit a 6-state HMM to log R ratios and B allele frequencies estimated from SNP arrays*

**Description**

This function is intended for estimating the integer copy number from germline or DNA of clonal origin using a 6-state HMM. The states are homozygous deletion, hemizygous deletion, diploid copy number, diploid region of homozygosity, single copy gain, and two+ copy gain. Because heterozygous markers are more informative for copy number than homozygous markers and regions of homozygosity are common in normal genomes, we currently computed a weighted average of the BAF emission matrix with a uniform 0,1 distribution by the probability that the marker is heterozygous, thereby downweighting the contribution of homozygous SNPs to the likelihood. In addition to making the detection of copy-neutral regions of homozygosity less likely, it also helps prevent confusing hemizygous deletions with copy neutral regions of homozygosity – the former would be driven mostly by the log R ratios. This is experimental and subject to change.

**Usage**

```r
hmm2(object, emission_param = EmissionParam(),
      transition_param = TransitionParam(), ...)
```

```r
## S4 method for signature 'SnpArrayExperiment'
hmm2(object, emission_param = EmissionParam(),
      transition_param = TransitionParam(), ...)
```

```r
## S4 method for signature 'oligoSnpSet'
hmm2(object, emission_param = EmissionParam(),
      transition_param = TransitionParam(), ...)
```

```r
## S4 method for signature 'ArrayViews'
hmm2(object, emission_param = EmissionParam(),
      transition_param = TransitionParam(), tolerance = 2, verbose = FALSE,
      ...)
```
HMMList

Constructor for HMMList class

Description

The constructor function for the HMMList class. The constructor is useful for representing a list of HMM objects.

Arguments

object A SnpArrayExperiment
description: A SnpArrayExperiment object

emission_param A EmissionParam object
description: A EmissionParam object

transition_param A TransitionParam object
description: A TransitionParam object

tolerance length-one numeric vector. When the difference in the log-likelihood of the Viterbi state path between successive models (updated by Baum Welch) is less than the tolerance, no additional model updates are performed.

verbose logical. Whether to display messages indicating progress.

details

The hmm2 method allows parallelization across samples using the foreach paradigm. Parallelization is automatic when enabled via packages such as snow/doSNOW.

Examples

```r
tp <- TransitionParam()
TransitionParam(taup=1e12)
data(snp_exp)
emission_param <- EmissionParam(temper=1/2)
fit <- hmm2(snp_exp, emission_param)
unlist(fit)
cnvSegs(fit)
```

## There is too little data to infer cnv reliably in this trivial example.
## To illustrate filtering options on the results, we select
## CNVs for which
## - the CNV call has a posterior probability of at least 0.5
## - the number of features is 2 or more
## - the HMM states are 1 (homozygous deletion) or 2 (hemizygous deletion)
fp <- FilterParam(probability=0.5, numberFeatures=2, state=c("1", "2"))
cnvSegs(fit, fp)
```

## for parallelization
## Not run:
library(snow)
library(doSNOW)
cl <- makeCluster(2, type = "SOCK")
registerDoSNOW(cl)
fit <- hmm2(snp_exp, emission_param)
```

## End(Not run)
HMMList-class

Usage

HMMList(object)

Arguments

object a list. Each element of the list is in instance of the HMM class.

See Also

HMMList HMM hmm2

Description

Each element of the HMMList contains the genomic intervals of the HMM segmentation (GRanges-derived object), parameters from the Baum-Welch, and a FilterParam object.

Usage

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

## S4 method for signature 'HMMList'
unlist(x, recursive = TRUE, use.names = TRUE)

Arguments

object a HMMList object
x a HMMList object
recursive logical; currently ignored
use.names logical; currently ignored

Slots

.Data a list. Each element of the list should be a HMM object.

See Also

HMM

Examples

data(snp_exp)
fit <- hmm2(snp_exp)
class(fit)
identical(length(fit), ncol(snp_exp))
unlist(fit)
**HmmParam**

Constructor for *HmmParam* class

**Description**

Contains emission probabilities, parameters for emission probabilities, and transition probabilities required for computing the most likely state path via the Viterbi algorithm.

**Usage**

```r
HmmParam(emission = matrix(0, 0, 0), emission_param = EmissionParam(),
transition = rep(0.99, nrow(emission)),
chromosome = character(nrow(emission)), loglik = LogLik(),
viterbi = Viterbi(), compute_posteriors = TRUE, verbose = FALSE)
```

## S4 method for signature 'HmmParam'

```r
show(object)
```

## S4 method for signature 'HmmParam'

```r
nrow(x)
```

## S4 method for signature 'HmmParam'

```r
ncol(x)
```

**Arguments**

- **emission**
  - A matrix of emission probabilities
- **emission_param**
  - an object of class *EmissionParam*
- **transition**
  - vector of transition probabilities whose length is \( N-1 \), where \( N \) is the number of markers. User should provide the probability that the state at marker \( j \) is the same as the state at marker \( j-1 \). It is assumed that the probability of transitioning to state \( j \) from state \( j-1 \) is the same for all states \( \neq j-1 \).
- **chromosome**
  - character vector
- **loglik**
  - an object of class *LogLik*
- **viterbi**
  - an object of class *Viterbi*
- **compute_posteriors**
  - logical
- **verbose**
  - logical
- **object**
  - a *HmmParam* object
- **x**
  - a *HmmParam* object

**Examples**

```r
HmmParam()
```
hmmResults

Example output from the hidden markov model

Description

The results of a 6-state HMM fit to simulated copy number and genotype data.

Format

a GRanges object

HmmTrellisParam Constructor for HmmTrellisParam class

Description

Constructor for HmmTrellisParam class

Usage

HmmTrellisParam(ylimits = list(c(0, 1), c(-3, 1)), expandfun = function(g) {
  width(g) * 50 })

Arguments

ylimits length-two list of the y-axis limits for B allele frequencies and log R ratios, respectively
expandfun a function that takes a length-one GRanges object as an argument and computes a width relative to the width of the GRanges object

IdiogramParams Constructor for IdiogramParam objects

Description

Parameters for plotting idiograms

Usage

IdiogramParams(seqnames = character(), seqlengths = numeric(),
  unit = "kb", genome = "hg19", box = list(color = "blue", lwd = 1))

## S4 method for signature 'IdiogramParams,ANY'
plot(x, y, ...)
IdiogramParams-class

Arguments

- **seqnames**: length-one character vector providing chromosome name
- **seqlengths**: length-one numeric vector indicating size of chromosome
- **unit**: character string indicating unit for genomic position
- **genome**: character string indicating genome build
- **box**: a list of parameters for plotting the box around the part of the idiogram that is plotted
- **x**: an IdiogramParam object
- **y**: ignored
- **...**: ignored

Value

IdiogramParam object

Description

Parameter class for plotting idiograms

Usage

```r
## S4 method for signature 'IdiogramParams'
show(object)
```

Arguments

- **object**: an IdiogramParam object

Slots

- **seqnames**: length-one character vector providing chromosome name
- **seqlengths**: length-one numeric vector indicating size of chromosome
- **unit**: character string indicating unit for genomic position (default is ’kb’)
- **genome**: character string indicating genome build
- **box**: a list of parameters for plotting the box around the part of the idiogram that is plotted.
isHeterozygous

Examples

```r
if(require(BSgenome.Hsapiens.UCSC.hg18) && require(grid)){
  si <- seqinfo(BSgenome.Hsapiens.UCSC.hg18)
  iparam <- IdiogramParams(seqnames="chr1",
                           genome="hg18",
                           seqlengths=seqlengths(si)["chr1"],
                           box=list(xlim=c(20e6L, 25e6L), color="blue", lwd=2))

  iparam
  idiogram <- plot(iparam)
  vp <- viewport(x=0.05, y=0.8, width=unit(0.9, "npc"), height=unit(0.2, "npc"),
                 name="vp1", just=c("left", "bottom"))
  grid.newpage()
  pushViewport(vp)
  print(idiogram, vp=vp, newpage=FALSE)
}
```

isHeterozygous  
Assess whether genotype is heterozygous based on BAFs

Description

Assess whether genotype is heterozygous based on BAFs

Usage

```r
isHeterozygous(object, cutoff)
```

Arguments

- `object`: a SnpArrayExperiment or ArrayViews object containing BAFs, a matrix of BAFs, or a numeric vector of BAFs.
- `cutoff`: a length-two numeric vector providing the range of BAFs consistent with allelic heterozygosity.

Examples

```r
if(require("BSgenome.Hsapiens.UCSC.hg18")){
  bsgenome <- BSgenome.Hsapiens.UCSC.hg18
  snp_exp <- getExampleSnpExperiment(bsgenome)
}
```
\begin{verbatim}
is_het <- isHeterozygous(snp_exp[, 1], c(0.4, 0.6))
table(is_het)
\end{verbatim}

---

### LogLik

**Constructor for LogLik class**

**Description**

A container for the log likelihood of the Viterbi state path. Stores the log likelihood from successive updates of model parameters. When the difference between the log likelihoods at iteration i and i-1 is below the tolerance, no additional updates are performed.

**Usage**

\[
\text{LogLik}(\text{loglik} = \text{numeric()}, \text{tolerance} = 1L)
\]

**Arguments**

- `loglik`: length-one numeric vector for the log likelihood of the Viterbi state path
- `tolerance`: if the difference in the log-likelihood of the Viterbi state path after the Baum-Welch update is less than the specified tolerance, no additional Baum-Welch updates are required

**See Also**

`LogLik`

---

### LogLik-class

**Classes and methods for storing/getting log-likelihoods from Viterbi algorithm**

**Description**

Exported for internal use by other BioC packages

**Usage**

\[
\text{## S4 method for signature 'LogLik'}
\text{length}(x)
\]

\[
\text{## S4 method for signature 'LogLik'}
\text{show}(\text{object})
\]

**Arguments**

- `x`: object of class LogLik
- `object`: a LogLik object
slots

- `loglik` a numeric vector
- `tolerance` a numeric vector

See Also

- `LogLik`

Description

Accessors for objects of class ArrayViews

Usage

- `lrrFile(object)`
- `lrrFile(object) <- value`
- `bafFile(object)`
- `gtFile(object)`

Arguments

- `object` see `showMethods("lrrFile")`
- `value` a character vector of filenames for the log R ratios

Examples

```r
views <- ArrayViews(parsedPath=tempdir())
sourcePaths(views)
lrrFile(views)
bafFile(views)
gtFile(views)
```
matrixOrNULL

A class allowing matrix or NULL objects

Description

Exported for internal use by other BioC packages

NA_filter

Remove SNPs with NAs in any of the low-level estimates

Description

Remove SNPs with NAs in any of the low-level estimates

Usage

NA_filter(x, i)

Arguments

x

a container for SNP data (SnpArrayExperiment)

i

integer vector to subset

Value

An object of the same class

numberFeatures

The number of SNP/nonpolymorphic probes contained in a genomic interval

Description

The number of SNP/nonpolymorphic probes contained in a genomic interval

Usage

numberFeatures(object)

Arguments

object

see showMethods(numberFeatures)
parsedPath

**Description**

A character string indicating the complete path for storing parsed files.

**Usage**

```
parsedPath(object)
```

### S4 method for signature 'ArrayViews'
parsedPath(object)

**Arguments**

- **object**  
a `ArrayViews` object

**See Also**

`parseSourceFile`  
`ArrayViews`  
`CopyNumScanParams`

---

parseSourceFile

**Function for parsing GenomeStudio files**

**Description**

This function parses genome studio files, writing the low-level data for log R ratios, B allele frequencies, and genotypes to disk as integers (1 file per subject per data type).

**Usage**

```
parseSourceFile(object, param)
```

### S4 method for signature 'ArrayViews,CopyNumScanParams'
parseSourceFile(object, param)

**Arguments**

- **object**  
  An `ArrayViews` object
- **param**  
  An object of class `CopyNumScanParams`

**See Also**

`ArrayViews`  
`ArrayViews`  
`CopyNumScanParams`
Examples

```r
require(BSgenome.Hsapiens.UCSC.hg18)
bsgenome <- BSgenome.Hsapiens.UCSC.hg18
require(data.table)
extdir <- system.file("extdata", package="VanillaICE", mustWork=TRUE)
features <- suppressWarnings(fread(file.path(extdir, "SNP_info.csv")))
fr <- GRanges(paste0("chr", features$Chr), IRanges(features$Position, width=1),
isSnips=features["Intensity Only"] >= 0)
fr <- SnpGRanges(fr)
names(fr) <- features["Name"]
seqlevels(fr) <- seqlevels(bsgenome)[seqlevels(bsgenome) %in% seqlevels(fr)]
seqinfo(fr) <- seqinfo(bsgenome)[seqlevels(fr),]
fr <- sort(fr)
files <- list.files(extdir, full.names=TRUE, recursive=TRUE, pattern="FinalReport")
views <- ArrayViews(rowRanges=fr, sourcePaths=files, parsedPath=tempdir())
show(views)
## read the first file
dat <- fread(files[1])
## information to store on the markers
select <- match(c("SNP Name", "Allele1 - AB", "Allele2 - AB",
"Log R Ratio", "B Allele Freq"), names(dat))
## which rows to keep in the MAP file. By matching on the sorted GRanges object
## containing the feature annotation, the low-level data for the log R ratios/
## B allele frequencies will also be sorted
## index_genome <- match(names(fr), dat["SNP Name"])
## scan_params <- CopyNumScanParams(index_genome=index_genome, select=select)
## parse the source files
## parseSourceFile(views, scan_params)
list.files(parsedPath(views))
## Inspecting source data through accessors defined on the views object
## require(oligoClasses)
## log R ratios
r <- head(lrr(views))
## B allele frequencies
b <- head(baf(views))
g <- head(genotypes(views))
```

---

`probability` **Accessor for probability filter**

**Description**

Accessor for probability filter

**Usage**

`probability(object)`
**rescale**

**Arguments**

- object: a FilterParam object

---

**Description**

Rescale a numeric vector

**Usage**

```r
rescale(x, l, u)
```

**Arguments**

- `x`: numeric vector
- `l`: lower limit of rescaled `x`
- `u`: upper limit of rescaled `x`

---

**rowModes**

**Robust statistics for matrices**

**Description**

Compute the column-wide or row-wise mode of numeric matrices

Compute the median absolute deviation (MAD) for the rows of a matrix

**Usage**

```r
rowModes(x)
colModes(x)
rowMAD(x, ...)
```

**Arguments**

- `x`: matrix
- `...`: additional arguments to rowMedians

**Value**

numeric vector

**See Also**

- mad
- mad rowMedians
Examples

```r
X <- matrix(rnorm(100), 10, 10)
rowMAD(X)
```

---

**segs**  
*Accessor for the HMM segments*

---

**Description**

Accessor to obtain all segments from the HMM.

**Usage**

```r
segs(object)
```

**Arguments**

- `object` see `showMethods(segs)`

**Value**

a GRanges-derived object

---

**show, Viterbi-method**  
*Show method for objects of class Viterbi*

---

**Description**

Show method for objects of class Viterbi

**Usage**

```r
## S4 method for signature 'Viterbi'
show(object)
```

**Arguments**

- `object` a Viterbi object
snpArrayAssays

Create an assays object from log R ratios and B allele frequencies

Description
This function is exported primarily for internal use by other BioC packages.

Usage
snpArrayAssays(cn = new("matrix"), baf = new("matrix"), ...)

Arguments
- cn: matrix of log R ratios
- baf: matrix of B allele frequencies
- ...: additional matrices of the same dimension, such as SNP genotypes.

Examples

```r
data(snp_exp)
r <- lrr(snp_exp)
b <- baf(snp_exp)
sl <- snpArrayAssays(cn=r, baf=b)
```

SnpArrayExperiment-class

A RangedSummarizedExperiment-derived class of marker-level SNP array data for copy number inference

Description
A RangedSummarizedExperiment-derived class of marker-level SNP array data for copy number inference

Constructor for SnpArrayExperiment

Usage

```r
SnpArrayExperiment(cn, baf, rowRanges = GRanges(), colData = DataFrame(),
isSnp = logical(), ...)
```

## S4 method for signature 'missing'

```r
SnpArrayExperiment(cn, baf, rowRanges = GRanges(),
    colData = DataFrame(), isSnp = logical(), ...)
```

## S4 method for signature 'matrix'

```r
SnpArrayExperiment(cn, baf, rowRanges = GRanges(),
    colData = DataFrame(row.names = colnames(cn)), isSnp = logical(), ...)
```
SnpExperiment

Arguments

cn  matrix of copy number estimates (e.g., log R ratios)
baf  matrix of B allele frequencies
rowRanges  GRanges object for SNPs/nonpolymorphic markers
colData  DataFrame containing sample-level covariates
isSnp  logical vector indicating whether marker is a SNP
...  additional arguments passed to SummarizedExperiment() constructor function

Examples

## empty container
SnpArrayExperiment()

data(snp_exp) # example

SnpArrayExperiment(cn=lrr(snp_exp), baf=baf(snp_exp),
                    rowRanges=rowRanges(snp_exp))

SnpExperiment  Constructor for SnpArrayExperiment

Description

A single-argument generic function to construct a SnpArrayExperiment.

Usage

SnpExperiment(object)

## S4 method for signature 'ArrayViews'
SnpExperiment(object)

Arguments

object  see showMethods('SnpExperiment') for a list of supported objects

Examples

view <- ArrayViews()
SnpExperiment(view)
**SnpGRanges-class**

An extension to GRanges for representing SNPs

**Description**

An extension to GRanges for representing SNPs

Constructor for SnpGRanges class

**Usage**

SnpGRanges(object = GRanges(), isSnp, ...)

## S4 method for signature 'missing'

SnpGRanges(object, isSnp)

## S4 method for signature 'GRanges'

SnpGRanges(object, isSnp)

**Arguments**

- **object**
  - A GRanges object
- **isSnp**
  - A logical vector. Each genomic interval in the GRanges container corresponds to a marker on the genotyping array. isSnp is FALSE for nonpolymorphic markers such as those included on the Affymetrix 6.0 chips.
- **...**
  - ignored

**Slots**

- **elementMetadata**
  - a SnpDataFrame

**Examples**

SnpGRanges()

```
g <- GRanges("chr1", IRanges(15L, 15L))
SnpGRanges(g, isSnp=TRUE)
```

---

**snp_exp**

An example SnpArrayExperiment

---

**Description**

A container for low-level summaries used for downstream copy number estimation, including log R ratios, B allele frequencies, and genotypes

**Format**

- a SnpArrayExperiment object
sourcePaths

Accessor for file paths containing SNP-level summaries

Description

Files containing SNP-level summaries for log R ratios, B allele frequencies, and genotypes – one sample per subject – are required.

Usage

sourcePaths(object)

Arguments

object an ArrayViews object

Examples

sourcePaths(ArrayViews())

start,oligoSnpSet-method

Retrieve genomic location of SNPs

Description

Retrieve genomic location of SNPs

Usage

## S4 method for signature 'oligoSnpSet'
start(x)

Arguments

x a oligoSnpSet object
state,HmmGRanges-method

Accessor for copy number state

Description

Extract the copy number state for each genomic interval.

Usage

```r
## S4 method for signature 'HmmGRanges'
state(object)
```

Arguments

- `object` a HmmGRanges object

state-methods

Accessor for the Viterbi state path

Description

The states are represented as integers: 1=homozygous deletion, 2=hemizygous deletion, 3=diploid normal heterozygosity, 4=diploid region of homozygosity, 5=single copy gain, 6=two or more copy gain.

Usage

```r
## S4 method for signature 'Viterbi'
state(object)
```

Arguments

- `object` a Viterbi object

sweepMode

Sweep the modal log R ratio (by row or column) from a matrix of log R ratios

Description

This function simplifies the process of sweeping the modal log R ratio from the rows or columns of a SnpArrayExperiment object. It is most useful when a large number of samples (more than 10) are available and the dataset is a collection of germline samples. We assume that the samples are from a single batch and that the modal value will be a robust estimate of the mean log R ratio for diploid copy number. Variation in the modal estimates between markers is presumed to be attributable to probe effects (e.g., differences hybridization efficiency/PCR do to sequence composition). For sex chromosomes, one should apply this function separately to men and women and then recenter the resulting matrix according to the expected copy number.
Usage

sweepMode(x, MARGIN)

## S4 method for signature 'SnpArrayExperiment'
sweepMode(x, MARGIN)

Arguments

x see showMethods(sweepMode)
MARGIN integer indicating which margin (1=rows, 2=columns) to sweep the mode

Value

an object of the same class as x

Examples

data(snp_exp)
snp_exp_rowcentered <- sweepMode(snp_exp, 1)
snp_exp_colcentered <- sweepMode(snp_exp, 2)
x <- lrr(snp_exp)
x_rowcentered <- sweep(x, 1, rowModes(x))
all.equal(lrr(snp_exp_rowcentered), x_rowcentered)

threshold

Threshold numeric values

Description

Threshold numeric values according to user-specific limits. The thresholded values can also be jittered near the limits.

Usage

threshold(x, lim = c(-Inf, Inf), amount = 0)

Arguments

x numeric matrix or vector
lim limit at which to threshold entries in x
amount see jitter

See Also

jitter

Examples

x <- rnorm(1000, 0, 3)
y <- threshold(x, c(-5, 5))
range(y)
TransitionParam

*Constructor for TransitionParam class*

**Description**

Contains parameters for computing transition probabilities

**Usage**

```r
TransitionParam(taup = 1e+10, taumax = 1 - 5e+06)
```

```r
### S4 method for signature 'TransitionParam'
show(object)
```

**Arguments**

- `taup` length-one numeric vector
- `taumax` The maximum probability that the current state is the same as the preceding state. See details
- `object` a TransitionParam object

**Details**

Diagonal elements of the transition probability matrix are computed as $e^{-2d/taup}$, where $d$ is the distance between markers $i$ and $i-1$ and $taup$ is typically in the range of $1e10$. This probability is constrained to be no larger than $taumax$. The probabilities on the off-diagonal elements are the same and are subject to the constraint that the rows of the transition probability matrix sum to 1.

**Examples**

```r
TransitionParam()
```

```r
### higher values of taup make transitions between states less likely
TransitionParam(taup=1e12)
```

updateHmmParams

*Run the Baum-Welch algorithm to update HMM parameters*

**Description**

This function is not intended to be called directly by the user. It is exported in the package NAMESPACE for internal use by other BioC packages.

**Usage**

```r
updateHmmParams(object, emission_param = EmissionParam(),
    transition_param = TransitionParam())
```
Arguments

object a SnpArrayExperiment object
emission_param a EmissionParam object
transition_param a TransitionParam object

VanillaICE

A hidden markov model for detection of germline copy number variants from arrays

Description

A hidden markov model for detection of germline copy number variants from arrays

viewports

Default viewports for plotting CNV data with lattice-style graphics

Description

Default viewports for plotting CNV data with lattice-style graphics

Usage

viewports()

Value

list

See Also

xyplotList xygrid

Examples

vps <- viewports()
xyplotList

Lattice-style plots for granges and SnpArrayExperiment objects

Description

Data for the graphic is generated by a call to grangesData.

Usage

xyplotList(granges, se, param = HmmTrellisParam())

## S4 method for signature 'HmmGRanges,SnpArrayExperiment'
xyplotList(granges, se,
    param = HmmTrellisParam())

## S4 method for signature 'GRangesList,SnpArrayExperiment'
xyplotList(granges, se,
    param = HmmTrellisParam())

xygrid(trellis_plot, viewports, granges)

Arguments

granges     a HmmGRanges object
se          a SnpArrayExperiment
param       trellis parameters for plotting HMM
trellis_plot an object of class trellis
viewports   a list of viewports as provided by the viewports function

See Also

viewports

Examples

if(require("BSgenome.Hsapiens.UCSC.hg18")){
  bgencode <- BSgenome.Hsapiens.UCSC.hg18
  snp_exp <- getExampleSnpExperiment(bgencode)
  seqlevels(snp_exp, force=TRUE) <- "chr22"
  fit <- hmm2(snp_exp)
  g <- reduce(hemizygous(fit), min.gapwidth=500e3)
  trellis_param <- HmmTrellisParam()
  fig <- xyplotList(g, snp_exp, trellis_param)
  vps <- viewports()
  xygrid(fig[[1]], vps, g)
}
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