Package 'VanillaICE'

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Title A Hidden Markov Model for high throughput genotyping arrays

Description
Hidden Markov Models for characterizing chromosomal alteration in high throughput SNP arrays.

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Contents

acf2 . . . 3
ArrayViews-class . . . 4
baumWelchUpdate . . . 7
calculateEmission . . . 7
cnvFilter . . . 8
cn_means . . . 9
CopyNumScanParams-class . . . 12
doUpdate . . . 14
dropDuplicatedMapLocs . . . 14
dropSexChrom . . . 15
emission . . . 15
emissionParam . . . 16
FilterParam-class . . . 16
filters . . . 18
genotypes . . . 18
getExampleSnpExperiment . . . 19
getHmmParams . . . 20
HMM-class . . . 20
hmm2 . . . 21
HMMList . . . 23
HMMList-class . . . 24
HmmParam . . . 25
hmmResults . . . 26
HmmTrellisParam . . . 26
IdiogramParams . . . 27
IdiogramParams-class . . . 28
isHeterozygous . . . 29
LogLik . . . 29
LogLik-class . . . 30
lrrFile . . . 31
matrixOrNULL . . . 32
NA_filter . . . 32
numberFeatures . . . 32
parsedPath . . . 33
parseSourceFile . . . 33
probability . . . 34
rescale . . . 35
rowModes . . . 35
segs . . . 36
show,Viterbi-method . . . 36

snpArrayAssays 37
SnpArrayExperiment-class 37
SnpExperiment 38
SnpGRanges-class 39
snp_exp 40
sourcePaths 40
start,oligoSnpSet-method 41
state,HmmGRanges-method 41
state-methods 42
sweepMode 42
threshold 43
TransitionParam 44
updateHmmParams 44
VanillaICE 45
viewports 45
xyplotList 46

Index **47**

`acf2` *Calculate lag10 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.

Usage

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

## S4 method for signature 'ArrayViews,ANY,ANY,ANY'
x[i, 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
rowRanges	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 multipled 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
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 simplied
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` character vector of filenames for log R ratios

`bafFiles` character vector of filenames for BAFs

`gtFiles` character vector of filenames for genotypes

See Also

`CopyNumScanParams` `parseSourceFile`

Examples

```
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"]]
  bsgenome <- BSgenome.Hsapiens.UCSC.hg18
 seqlevels(fgr, pruning.mode="coarse") <- 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

```
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'
cnvFilter(object, filters = FilterParam())

## S4 method for signature 'HmmGRanges'
cnvSegs(object, filters = FilterParam(state = as.character(c(1, 2, 5, 6))))
```

Arguments

object	see showMethods(cnvFilter)
filters	a FilterParam object

See Also

FilterParam

Examples

```
data(snp_exp)
fit <- hmm2(snp_exp)
segs(fit) ## all intervals
cnvSegs(fit)
filter_param <- FilterParam(probability=0.95, numberFeatures=10, state=c("1", "2"))
cnvSegs(fit, filter_param)
filter_param <- FilterParam(probability=0.5, numberFeatures=2, state=c("1", "2"))
cnvSegs(fit, filter_param)
hemizygous(fit)
homozygous(fit)
duplication(fit)
```

---

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.

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

Usage

```
cn_means(object)

cn_sds(object)

baf_means(object)

baf_sds(object)

baf_means(object) <- 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 frequences 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

$$prHom = (p["A"] + p["B"])/sum(p)$$

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 homozgous 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

```
ep <- EmissionParam()
cn_means(ep)
ep <- EmissionParam()
cn_sds(ep)
ep <- EmissionParam()
baf_means(ep)
ep <- EmissionParam()
baf_sds(ep)
ep <- EmissionParam()
baf_means(ep) <- baf_means(ep)
ep <- EmissionParam()
baf_sds(ep) <- baf_sds(ep)
ep <- EmissionParam()
cn_sds(ep) <- cn_sds(ep)
ep <- EmissionParam()
cn_means(ep) <- cn_means(ep)
ep <- EmissionParam()
show(ep)
cn_means(ep)
cn_sds(ep)
baf_means(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

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 co-ordinates*

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

```
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
```

FilterParam-class *Container for the common criteria used to filtering genomic ranges*

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., denovo deletions), size, number of features (SNPs), or chromosome. FilterParam is a container for the parameters commmonly used to filter the genomic ranges.

Usage

```
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	minumum probability for the call
numberFeatures	minumum 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 widht 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"))
```

`filters` *Accessor for HMM filter parameters*

Description

Accessor for HMM filter parameters

Usage

```
filters(object)
```

Arguments

`object`	see `showMethods(filters)`

`genotypes` *Accessor for SNP genotypes*

Description

Extract SNP genotypes. Genotypes are assumed to be represented as integers: 1=AA, 2=AB, 3=BB.

Usage

```
genotypes(object)

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

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

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

```
## S4 method for signature 'SnpArrayExperiment'
baf(object)

## S4 method for signature 'SnpArrayExperiment'
copyNumber(object)

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

## S4 method for signature 'SnpArrayExperiment'
genotypes(object)
```

Arguments

object	see showMethods("genotypes")

See Also

copyNumber

---

getExampleSnpExperiment

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

---

Description

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` *Accessor for HMM model parameters*

Description

Accessor for HMM model parameters

Usage

```
getHmmParams(object)
```

Arguments

`object`	see `showMethods(HmmParam)`

Examples

```
hmm_object <- HMM()
getHmmParams(hmm_object)
```

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

Description

The contructor `HMM` creates and object of class `HMM`. Not typically called directly by the user.

Usage

```
HMM(
  granges = GRanges(),
  param = HmmParam(),
  posterior = matrix(),
  filters = FilterParam()
)
```

```
## S4 method for signature 'HMM'
state(object)

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

Arguments

granges	a GRanges object
param	a HmmParam object
posterior	matrix of posterior probabilities
filters	an object of class FilterParam
object	a HMM object

Slots

granges a GRanges object

param a HmmParam object

posterior a matrix of posterior probabilities

filters a FilterParam object

See Also

hmm2

Examples

```
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 homozgosity 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 homozgosity 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

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

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

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

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

Arguments

object	A SnpArrayExperiment
emission_param	A EmissionParam object
transition_param	A TransitionParam object
...	currently ignored
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

```
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 *Constructor for* HMMList *class*

Description

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

Usage

```
HMMList(object)
```

Arguments

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

See Also

HMMList HMM hmm2

HMMList-class *Class, constructor, and methods for representing HMM results from multiple samples*

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

```
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'
show(object)

## S4 method for signature 'HmmParam'
nrow(x)

## S4 method for signature 'HmmParam'
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 != state_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

```
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, ...)
```

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

IdiogramParams-class *Paramater class for plotting idiograms*

Description

Paramater class for plotting idiograms

Usage

```
## 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.

Examples

```
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

```
isHeterozygous(object, cutoff)

## S4 method for signature 'ArrayViews'
isHeterozygous(object, cutoff)

## S4 method for signature 'SnpArrayExperiment'
isHeterozygous(object, cutoff)

## S4 method for signature 'numeric'
isHeterozygous(object, cutoff)

## S4 method for signature 'matrix'
isHeterozygous(object, cutoff)
```

Arguments

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

Examples

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

LogLik *Constructor for LogLik class*

Description

A container for the log likelihood of the Viterbi state path. Stores the log likelihood from succesive 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

```
LogLik(loglik = numeric(), 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

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

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

Arguments

x	object of class LogLik
object	a LogLik object

Slots

loglik a numeric vector

tolerance a numeric vector

See Also

LogLik

lrrFile *Accessors for objects of class ArrayViews*

Description

Accessors for objects of class ArrayViews

Usage

```
lrrFile(object)

lrrFile(object) <- value

bafFile(object)

gtFile(object)

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

## S4 replacement method for signature 'ArrayViews'
lrrFile(object) <- value

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

## S4 method for signature 'ArrayViews'
gtFile(object)
```

Arguments

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

Examples

```
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 *Complete path to directory for keeping parsed files*

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

ArrayViews

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

```
  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")))
  fgr <- GRanges(paste0("chr", features$Chr), IRanges(features$Position, width=1),
                 isSnp=features[["Intensity Only"]]==0)
  fgr <- SnpGRanges(fgr)
  names(fgr) <- features[["Name"]]
  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")
  views <- ArrayViews(rowRanges=fgr, sourcePaths=files, parsedPath=tempdir())
  show(views)

## read the first file
dat <- fread(files[1], skip="[Data]")
## 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(fgr), 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)
```

Arguments

object	a FilterParam object

---

rescale *Rescale a numeric vector*

Description

Rescale a numeric vector

Usage

```
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

Usage

```
rowModes(x)

colModes(x)

rowMAD(x, ...)
```

Arguments

x	matrix
...	additional arguments to rowMedians

Value

numeric vector

See Also

mad

mad rowMedians

Examples

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

---

segs *Accessor for the HMM segments*

Description

Accessor to obtain all segments from the HMM.

Usage

```
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

```
## 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

```
data(snp_exp, package="VanillaICE")
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

Constructor for SnpArrayExperiment

Usage

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

## S4 method for signature 'missing'
```

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

## S4 method for signature 'matrix'
SnpArrayExperiment(
  cn,
  baf,
  rowRanges = GRanges(),
  colData = DataFrame(row.names = colnames(cn)),
  isSnp = logical(),
  ...
)
```

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
library(VanillaICE)
data(snp_exp, package="VanillaICE") # example

se <- 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

```
## 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

```
## 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

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

## 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^-2*d/taup, where d is the distance between markers i and i-1 and taup is typically in the range of 1xe10. 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

```
TransitionParam()
## 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

```
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*

---

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")){
  bsgenome <- BSgenome.Hsapiens.UCSC.hg18
  snp_exp <- getExampleSnpExperiment(bsgenome)
  seqlevels(snp_exp, pruning.mode="coarse") <- "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)
}
```

Index

∗ **EmissionParam-methods**
    cn_means, 9
∗ **datasets**
    hmmResults, 26
    snp_exp, 40
∗ **manip**
    rescale, 35
'[',ArrayViews,ANY-method *(*ArrayViews-class*)*, 4
[,ArrayViews,ANY,ANY,ANY-method *(*ArrayViews-class*)*, 4
[,ArrayViews,ANY-method *(*ArrayViews-class*)*, 4
$,ArrayViews-method *(*ArrayViews-class*)*, 4
$<-,ArrayViews-method *(*ArrayViews-class*)*, 4

acf, *3*
acf2, 3
ArrayViews, *13*, *33*
ArrayViews *(*ArrayViews-class*)*, 4
ArrayViews,numeric,numeric-method *(*ArrayViews-class*)*, 4
ArrayViews-class, 4

baf,ArrayViews-method *(*genotypes*)*, 18
baf,SnpArrayExperiment-method *(*genotypes*)*, 18
baf_means *(*cn_means*)*, 9
baf_means,ArrayViews-method *(*ArrayViews-class*)*, 4
baf_means,EmissionParam-method *(*cn_means*)*, 9
baf_means,HmmParam-method *(*cn_means*)*, 9
baf_means<- *(*cn_means*)*, 9
baf_means<-,EmissionParam,numeric-method *(*cn_means*)*, 9
baf_sds *(*cn_means*)*, 9
baf_sds,EmissionParam-method *(*cn_means*)*, 9
baf_sds,HmmParam-method *(*cn_means*)*, 9
baf_sds<- *(*cn_means*)*, 9
baf_sds<-,EmissionParam,numeric-method *(*cn_means*)*, 9
bafFile *(*lrrFile*)*, 31
bafFile,ArrayViews-method *(*lrrFile*)*, 31
baumWelchUpdate, 7

calculateEmission, 7
calculateEmission,list-method *(*calculateEmission*)*, 7
calculateEmission,numeric-method *(*calculateEmission*)*, 7
calculateEmission,RangedSummarizedExperiment-method *(*calculateEmission*)*, 7
cn_means, 9
cn_means,EmissionParam-method *(*cn_means*)*, 9
cn_means,HmmParam-method *(*cn_means*)*, 9
cn_means<- *(*cn_means*)*, 9
cn_means<-,EmissionParam,numeric-method *(*cn_means*)*, 9
cn_sds *(*cn_means*)*, 9
cn_sds,EmissionParam-method *(*cn_means*)*, 9
cn_sds,HmmParam-method *(*cn_means*)*, 9
cn_sds<- *(*cn_means*)*, 9
cn_sds<-,EmissionParam,numeric-method *(*cn_means*)*, 9
cnvFilter, 8, *17*
cnvFilter,GRanges-method *(*cnvFilter*)*, 8
cnvFilter,HMM-method *(*cnvFilter*)*, 8
cnvFilter,HMMList-method *(*cnvFilter*)*, 8
cnvSegs, *17*
cnvSegs *(*cnvFilter*)*, 8
cnvSegs,HMM-method *(*cnvFilter*)*, 8
cnvSegs,HmmGRanges-method *(*cnvFilter*)*, 8
cnvSegs,HMMList-method *(*cnvFilter*)*, 8

colModes (rowModes), 35
colnames (ArrayViews-class), 4
colnames,ArrayViews-method (ArrayViews-class), 4
colnames<- (ArrayViews-class), 4
colnames<-,ArrayViews,character-method (ArrayViews-class), 4
copyNumber,SnpArrayExperiment-method (genotypes), 18
CopyNumScanParams, *6*, *33*
CopyNumScanParams (CopyNumScanParams-class), 12
CopyNumScanParams-class, 12

deletion (cnvFilter), 8
deletion,HMM-method (cnvFilter), 8
dim,ArrayViews-method (ArrayViews-class), 4
doUpdate, 14
dropDuplicatedMapLocs, 14
dropSexChrom, 15
duplication (cnvFilter), 8
duplication,HMM-method (cnvFilter), 8
duplication,HMMList-method (cnvFilter), 8

emission, 15
emission,HmmParam-method (emission), 15
emission<- (emission), 15
emission<-,HMM-method (emission), 15
emission<-,HmmParam-method (emission), 15
EmissionParam, *16*, *22*, *45*
EmissionParam (cn_means), 9
emissionParam, 16
emissionParam,HMM-method (emissionParam), 16
emissionParam,HmmGRanges-method (emissionParam), 16
emissionParam,HmmParam-method (emissionParam), 16
EmissionParam,missing-method (cn_means), 9
EmissionParam,numeric-method (cn_means), 9
emissionParam<- (emissionParam), 16
emissionParam<-,HmmGRanges,EmissionParam-method (emissionParam), 16
emissionParam<-,HmmParam,EmissionParam-method (emissionParam), 16
EMupdates (cn_means), 9
EMupdates,EmissionParam-method (cn_means), 9
EMupdates,HmmParam-method (cn_means), 9

FilterParam, *9*
FilterParam (FilterParam-class), 16
FilterParam-class, 16
filters, 18
filters,HMM-method (filters), 18
filters,HmmParam-method (filters), 18
fread, *12*

genotypes, 18
genotypes,ArrayViews-method (genotypes), 18
genotypes,SnpArrayExperiment-method (genotypes), 18
getExampleSnpExperiment, 19
getHmmParams, 20
getHmmParams,HMM-method (getHmmParams), 20
getHmmParams,HmmParam-method (getHmmParams), 20
GRanges, *16*
gtFile (lrrFile), 31
gtFile,ArrayViews-method (lrrFile), 31

hemizygous (cnvFilter), 8
hemizygous,HMM-method (cnvFilter), 8
hemizygous,HMMList-method (cnvFilter), 8
HMM, *24*
HMM (HMM-class), 20
HMM-class, 20
hmm2, *17*, *21*, 21, *24*
hmm2,ArrayViews-method (hmm2), 21
hmm2,oligoSnpSet-method (hmm2), 21
hmm2,SnpArrayExperiment-method (hmm2), 21
HMMList, 23, *24*
HMMList-class, 24
HmmParam, *14*, 25
HmmParam,matrix-method (HmmParam), 25
HmmParam,missing-method (HmmParam), 25
hmmResults, 26
HmmTrellisParam, 26
homozygous (cnvFilter), 8

homozygous,HMM-method (cnvFilter), 8
homozygous,HMMList-method (cnvFilter), 8

IdiogramParams, 27
IdiogramParams-class, 28
isHeterozygous, 29
isHeterozygous,ArrayViews-method (isHeterozygous), 29
isHeterozygous,matrix-method (isHeterozygous), 29
isHeterozygous,numeric-method (isHeterozygous), 29
isHeterozygous,SnpArrayExperiment-method (isHeterozygous), 29

jitter, *43*

length,LogLik-method (LogLik-class), 30
LogLik, 29, *30*
LogLik-class, 30
lrr,ArrayViews-method (genotypes), 18
lrr,SnpArrayExperiment-method (genotypes), 18
lrrFile, 31
lrrFile,ArrayViews-method (lrrFile), 31
lrrFile<- (lrrFile), 31
lrrFile<-,ArrayViews-method (lrrFile), 31

mad, *36*
matrixOrNULL, 32
matrixOrNULL-class (matrixOrNULL), 32

NA_filter, 32
NA_filter,character-method (NA_filter), 32
NA_filter,list-method (NA_filter), 32
NA_filter,numeric-method (NA_filter), 32
NA_filter,oligoSnpSet-method (NA_filter), 32
NA_filter,SnpArrayExperiment-method (NA_filter), 32
ncol,ArrayViews-method (ArrayViews-class), 4
ncol,HmmParam-method (HmmParam), 25
nrow,ArrayViews-method (ArrayViews-class), 4
nrow,HmmParam-method (HmmParam), 25
numberFeatures, 32
numberFeatures,FilterParam-method (numberFeatures), 32
numberFeatures,HMM-method (numberFeatures), 32
numberFeatures,HmmGRanges-method (numberFeatures), 32

parsedPath, 33
parsedPath,ArrayViews-method (parsedPath), 33
parseSourceFile, *6*, *13*, *33*, 33
parseSourceFile,ArrayViews,CopyNumScanParams-method (parseSourceFile), 33
plot,IdiogramParams,ANY-method (IdiogramParams), 27
plot,IdiogramParams-method (IdiogramParams), 27
probability, 34
probability,FilterParam-method (FilterParam-class), 16

rescale, 35
rowMAD (rowModes), 35
rowMedians, *36*
rowModes, 35

sapply,ArrayViews-method (ArrayViews-class), 4
segs, 36
segs,HMM-method (segs), 36
segs,HMMList-method (cnvFilter), 8
show,ArrayViews-method (ArrayViews-class), 4
show,CopyNumScanParams-method (CopyNumScanParams-class), 12
show,EmissionParam-method (cn_means), 9
show,FilterParam-method (FilterParam-class), 16
show,HMM-method (HMM-class), 20
show,HMMList-method (HMMList-class), 24
show,HmmParam-method (HmmParam), 25
show,IdiogramParams-method (IdiogramParams-class), 28
show,LogLik-method (LogLik-class), 30
show,TransitionParam-method (TransitionParam), 44
show,Viterbi-method, 36
snp_exp, 40
snpArrayAssays, 37

SnpArrayExperiment, *19*, *22*, *32*, *45*
SnpArrayExperiment (SnpArrayExperiment-class), 37
SnpArrayExperiment,matrix-method (SnpArrayExperiment-class), 37
SnpArrayExperiment,missing-method (SnpArrayExperiment-class), 37
SnpArrayExperiment-class, 37
SnpExperiment, 38
SnpExperiment,ArrayViews-method (SnpExperiment), 38
SnpGRanges (SnpGRanges-class), 39
SnpGRanges,GRanges-method (SnpGRanges-class), 39
SnpGRanges,missing-method (SnpGRanges-class), 39
SnpGRanges-class, 39
sourcePaths, 40
sourcePaths,ArrayViews-method (sourcePaths), 40
start,ArrayViews-method (ArrayViews-class), 4
start,oligoSnpSet-method, 41
state,FilterParam-method (FilterParam-class), 16
state,HMM-method (HMM-class), 20
state,HmmGRanges-method, 41
state,Viterbi-method (state-methods), 42
state-methods, 42
sweepMode, 42
sweepMode,SnpArrayExperiment-method (sweepMode), 42

threshold, 43
TransitionParam, *22*, 44, *45*
TransitionParam,missing-method (TransitionParam), 44
TransitionParam,numeric-method (TransitionParam), 44

unlist,HMMList-method (HMMList-class), 24
updateHmmParams, 44

VanillaICE, 45
viewports, 45, *46*

xygrid, *45*
xygrid (xyplotList), 46
xyplotList, *45*, 46
xyplotList,GRangesList,SnpArrayExperiment-method (xyplotList), 46
xyplotList,HmmGRanges,SnpArrayExperiment-method (xyplotList), 46