# Package 'VanillaICE'

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

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**Author** Robert Scharpf [aut, cre]

**Maintainer** Robert Scharpf <rscharpf@jhu.edu>

# 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