

# Package ‘AllelicImbalance’

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**Type** Package

**Title** Investigates Allele Specific Expression

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**Author** Jesper R Gadin, Lasse Folkersen

**Maintainer** Jesper R Gadin <j.r.gadin@gmail.com>

**Description** Provides a framework for allelic specific expression investigation using RNA-seq data.

**License** GPL-3

**URL** <https://github.com/pappewaio/AllelicImbalance>

**BugReports** <https://github.com/pappewaio/AllelicImbalance/issues>

**Suggests** testthat, org.Hs.eg.db, TxDb.Hsapiens.UCSC.hg19.knownGene, SNPlocs.Hsapiens.dbSNP144.GRCh37, BiocStyle, knitr, rmarkdown

**Depends** R (>= 3.2.0), grid, GenomicRanges, SummarizedExperiment (>= 0.2.0), GenomicAlignments

**Imports** methods, BiocGenerics, AnnotationDbi, BSgenome, VariantAnnotation, Biostrings, S4Vectors (>= 0.9.25), IRanges, Rsamtools, GenomicFeatures, Gviz, lattice, latticeExtra, gridExtra, seqinr, GenomeInfoDb

**LazyData** TRUE

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**VignetteBuilder** knitr

**Collate** 'AllelicImbalance-package.R' 'initialize-methods.R'  
'ASEset-class.R' 'DetectedAI-class.R' 'GlobalAnalysis-class.R'  
'barplot-methods.R' 'locationplot-methods.R'  
'GvizTrack-methods.R' 'LinkVariantAlmlof-class.R'  
'RegionSummary-class.R' 'RiskVariant-class.R'  
'auxillary-functions-annotation.R'  
'auxillary-functions-visuals.R'  
'auxillary-methods-annotation.R'  
'auxillary-methods-summaries.R' 'auxillary-methods.R'  
'chisq.test-methods.R' 'binom.test-methods.R'  
'boxplot-methods.R' 'deprecations.R' 'detect-methods.R'

'filter-methods.R' 'histplot-methods.R' 'inference-methods.R'  
 'linkage-methods.R' 'list-methods.R' 'mapbias-methods.R'  
 'plot-methods.R' 'show-methods.R' 'simulation-methods.R'  
 'summary-methods.R' 'utils.R'

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## R topics documented:

AllelicImbalance-package	3
annotation-wrappers	4
annotationBarplot	6
ASEset-barplot	7
ASEset-class	9
ASEset-filters	14
ASEset-gbarplot	15
ASEset-glocationplot	16
ASEset-gviztrack	17
ASEset-locationplot	18
ASEset-scanForHeterozygotes	20
ASEset.old	21
ASEset.sim	22
ASEsetFromBam	22
barplot-lattice-support	23
binom.test	24
chisq.test	25
countAllelesFromBam	26
coverageMatrixListFromGAL	27
defaultMapBias	28
defaultPhase	29
detectAI	29
DetectedAI-class	31
DetectedAI-plot	32
DetectedAI-summary	34
fractionPlotDf	35
gba	36
genomatrix	37
genotype2phase	37
getAlleleCounts	38
getAlleleQuality	39
getAreaFromGeneNames	41
getDefaultMapBiasExpMean	42
getSnpIdFromLocation	43
GlobalAnalysis-class	44
GRvariants	45
histplot	45
implodeList.old	46
import-bam	47
import-bam-2	48
import-bcf	49
inferAlleles	50

inferAltAllele . . . . .	51
inferGenotypes . . . . .	52
initialize-ASEset . . . . .	53
initialize-DetectedAI . . . . .	55
initialize-GlobalAnalysis . . . . .	56
initialize-RiskVariant . . . . .	57
legendBarplot . . . . .	57
LinkVariantAlmlof-class . . . . .	58
LinkVariantAlmlof-plot . . . . .	59
lva . . . . .	60
lva.internal . . . . .	61
makeMaskedFasta . . . . .	63
mapBiasRef . . . . .	63
minCountFilt . . . . .	64
minFreqFilt . . . . .	65
multiAllelicFilt . . . . .	66
phase2genotype . . . . .	67
phaseArray2phaseMatrix . . . . .	68
phaseMatrix2Array . . . . .	69
randomRef . . . . .	70
reads . . . . .	71
refAllele . . . . .	71
regionSummary . . . . .	72
RegionSummary-class . . . . .	73
RiskVariant-class . . . . .	74
scanForHeterozygotes.old . . . . .	75
<b>Index</b>	<b>77</b>

---

AllelicImbalance-package

*A package meant to provide all basic functions for high-throughput allele specific expression analysis*

---

**Description**

Package AllelicImbalance has functions for importing, filtering and plotting high-throughput data to make an allele specific expression analysis. A major aim of this package is to provide functions to collect as much information as possible from regions of choice, and to be able to explore the allelic expression of that region in detail.

**Details**

Package: AllelicImbalance  
Type: Package  
Version: 1.2.0  
Date: 2014-08-24  
License: GPL-3

**Overview - standard procedure**

Start out creating a GRange object defining the region of interest. This can also be done using `getAreaFromGeneNames` providing gene names as arguments. Then use `BamImpGAList` to import reads from that region and find potential SNPs using `scanForHeterozygotes`. Then retrieve the allele counts of heterozygote sites by the function `getAlleleCount`. With this data create an ASEset. At this point all pre-requisites for a 'basic' allele specific expression analysis is available. Two ways to go on could be to apply `chisq.test` or `barplot` on this ASEset object.

**Author(s)**

Author: Jesper Robert Gadin Author: Lasse Folkersen  
 Maintainer: Jesper Robert Gadin <j.r.gadin@gmail.com>

**References**

Reference to published application note (work in progress)

**See Also**

- `code?ASEset`

---

annotation-wrappers    *AnnotationDb wrappers*

---

**Description**

These functions acts as wrappers to retrieve information from annotation database objects (`annotationDb` objects) or (`transcriptDb` objects)

**Usage**

```
getGenesFromAnnotation(OrgDb, GR, leftFlank = 0, rightFlank = 0,
  getUCSC = FALSE, verbose = FALSE)

getGenesVector(OrgDb, GR, leftFlank = 0, rightFlank = 0, verbose = FALSE)

getExonsFromAnnotation(TxDb, GR, leftFlank = 0, rightFlank = 0,
  verbose = FALSE)

getExonsVector(TxDb, GR, leftFlank = 0, rightFlank = 0, verbose = FALSE)

getTranscriptsFromAnnotation(TxDb, GR, leftFlank = 0, rightFlank = 0,
  verbose = FALSE)

getTranscriptsVector(TxDb, GR, leftFlank = 0, rightFlank = 0,
  verbose = FALSE)

getCDSFromAnnotation(TxDb, GR, leftFlank = 0, rightFlank = 0,
  verbose = FALSE)

getCDSVector(TxDb, GR, leftFlank = 0, rightFlank = 0, verbose = FALSE)
```

```
getAnnotationDataFrame(GR, strand = "+", annotationType = NULL,
  OrgDb = NULL, TxDb = NULL, verbose = FALSE)
```

### Arguments

OrgDb	An OrgDb object
GR	A GenomicRanges object with sample area
leftFlank	An integer specifying number of additional nucleotides around the SNPs for the leftFlank
rightFlank	An integer specifying number of additional nucleotides around the SNPs for the rightFlank
getUCSC	A logical indicating if UCSC transcript IDs should also be retrieved
verbose	A logical making the functions more talkative
TxDb	A transcriptDb object
strand	Two options, '+' or '-'
annotationType	select one or more from 'gene', 'exon', 'transcript', 'cds'.

### Details

These functions retrieve regional annotation from OrgDb or TxDb objects, when given GRanges objects.

### Value

GRanges object with ranges over the genes in the region.

The getGenesVector function will return a character vector where each element are gene symbols separated by comma

GRanges object with ranges over the exons in the region.

The getTranscriptsFromAnnotation function will return a GRanges object with ranges over the transcripts in the region.

The getCDSFromAnnotation function will return a GRanges object with ranges over the CDSFs in the region.

The getExonsVector function will return a character vector where each element are exons separated by comma

The getTranscriptsVector function will return a character vector where each element are transcripts separated by comma

The getCDSVector function will return a character vector where each element are CDSs separated by comma

The getAnnotationDataFrame function will return a data.frame with annotations. This function is used internally by i.e. the barplot-function

### Author(s)

Jesper R. Gadin, Lasse Folkersen

**Examples**

```

data(ASEset)
require(org.Hs.eg.db)
require(TxDb.Hsapiens.UCSC.hg19.knownGene)
OrgDb <- org.Hs.eg.db
TxDb <- TxDb.Hsapiens.UCSC.hg19.knownGene

#use for example BcfFiles as the source for SNPs of interest
GR <- rowRanges(ASEset)
#get annotation
g <- getGenesFromAnnotation(OrgDb,GR)
e <- getExonsFromAnnotation(TxDb,GR)
t <- getTranscriptsFromAnnotation(TxDb,GR)
c <- getCDSFromAnnotation(TxDb,GR)

```

---

annotationBarplot      *add annotation to AllelicImbalance barplot*

---

**Description**

adds a customizable annotation functionality for AllelicImbalance barplots.

**Usage**

```

annotationBarplot(strand, snp, lowerLeftCorner, annDfPlus, annDfMinus,
  cex = 0.7, ypos = 0, interspace = 1)

```

**Arguments**

strand	strand, "+", "-", "*" or "both"
snp	integer for the described snp
lowerLeftCorner	position of the plot to add legend to (default c(0,0))
annDfPlus	annotation dataframe plus strand
annDfMinus	annotation dataframe minus strand
cex	size of annotation text
ypos	relative y-axis position for the annotation text
interspace	space between each annotation block

**Details**

the function is preferably called from within the AllelicImbalance barplot method.

**Author(s)**

Jesper R. Gadin

**Examples**

```
#code placeholders
#< create a barplot without annotation >
#< add annotation >
```

---

ASEset-barplot

*barplot ASEset objects*


---

**Description**

Generates barplots for ASEset objects. Two levels of plotting detail are provided: a detailed barplot of read counts by allele useful for fewer samples and SNPs, and a less detailed barplot of the fraction of imbalance, useful for more samples and SNPs.

**Usage**

```
barplot(height, ...)
```

```
## S4 method for signature 'ASEset'
barplot(height, type = "count", sampleColour.top = NULL,
  sampleColour.bot = NULL, legend = TRUE, pValue = TRUE, strand = "*",
  testValue = NULL, testValue2 = NULL, OrgDb = NULL, TxDb = NULL,
  annotationType = c("gene", "exon", "transcript"), main = NULL,
  ylim = NULL, yaxis = TRUE, xaxis = FALSE, ylab = TRUE,
  ylab.text = NULL, xlab.text = "samples", xlab = TRUE,
  legend.colnames = "", las.ylab = 1, las.xlab = 2, cex.main = 1,
  cex.pValue = 0.7, cex.ylab = 0.7, cex.xlab = 0.7, cex.legend = 0.6,
  add = FALSE, lowerLeftCorner = c(0, 0), size = c(1, 1),
  addHorizontalLine = 0.5, add.frame = TRUE,
  filter.pValue.fraction = 0.99, legend.fill.size = 1,
  legend.interspace = 1, verbose = FALSE,
  top.fraction.criteria = "maxcount", cex.annotation = 0.7,
  ypos.annotation = 0, annotation.interspace = 1, ...)
```

**Arguments**

height	An ASEset object
...	for simpler generics when extending function
type	'count' or 'fraction'
sampleColour.top	User specified colours for top fraction
sampleColour.bot	User specified colours for bottom fraction
legend	Display legend
pValue	Display p-value
strand	four options, '+', '-', 'both' or '*'
testValue	if set, a matrix or vector with user p-values

testValue2	if set, a matrix or vector with user p-values
OrgDb	an OrgDb object which provides annotation
TxDb	a TxDb object which provides annotation
annotationType	select one or more from 'gene','exon','transcript','cds'.
main	text to use as main label
ylim	set plot y-axis limit
yaxis	wheter the y-axis is to be displayed or not
xaxis	wheter the x-axis is to be displayed or not
ylab	showing labels for the tic marks
ylab.text	ylab text
xlab.text	xlab text
xlab	showing labels for the tic marks
legend.colnames	gives colnames to the legend matrix
las.ylab	orientation of ylab text
las.xlab	orientation of xlab text
cex.main	set main label size (max 2)
cex.pValue	set pValue label size
cex.ylab	set ylab label size
cex.xlab	set xlab label size
cex.legend	set legend label size
add	boolean indicates if a new device should be started
lowerLeftCorner	integer that is only useful when add=TRUE
size	Used internally by locationplot. Rescales each small barplot window
addHorizontalLine	adds a horizontal line that marks the default fraction of 0.5 - 0.5
add.frame	boolean to give the new plot a frame or not
filter.pValue.fraction	numeric between 0 and 1 that filter away pValues where the main allele has this frequency.
legend.fill.size	size of the fill/boxes in the legend (default:NULL)
legend.interspace	set legend space between fills and text
verbose	Makes function more talkative
top.fraction.criteria	'maxcount', 'ref' or 'phase'
cex.annotation	size of annotation text
ypos.annotation	relative ypos for annotation text
annotation.interspace	space between annotation text



## Details

`filter.pValue.fraction` is intended to remove p-value annotation with very large difference in frequency, which could just be a sequencing mistake. This is to avoid p-values like  $1e-235$  or similar.

`sampleColourUser` specified colours, either given as named colours ('red', 'blue', etc) or as hexadecimal code. Can be either length 1 for all samples, or else of a length corresponding to the number of samples for individual colouring.

## Author(s)

Jesper R. Gadin, Lasse Folkersen

## See Also

- The [ASEset](#) class which the `barplot` function can be called up on.

## Examples

```
data(ASEset)
barplot(ASEset[1])
```

---

ASEset-class

*ASEset objects*

---

## Description

Object that holds allele counts, genomic positions and map-bias for a set of SNPs

## Usage

```
alleleCounts(x, strand = "*", return.class = "list")

## S4 method for signature 'ASEset'
alleleCounts(x, strand = "*", return.class = "list")

alleleCounts(x, ...) <- value

## S4 replacement method for signature 'ASEset'
alleleCounts(x, strand = "*", return.class = "array",
  ...) <- value

mapBias(x, ...)

## S4 method for signature 'ASEset'
mapBias(x, return.class = "list")

fraction(x, ...)

## S4 method for signature 'ASEset'
```

```
fraction(x, strand = "*",
        top.fraction.criteria = "maxcount", verbose = FALSE, ...)

arank(x, return.type = "names", return.class = "list", strand = "*", ...)

frequency(x, ...)

genotype(x, ...)

## S4 method for signature 'ASEset'
genotype(x, return.class = "matrix")

genotype(x) <- value

## S4 replacement method for signature 'ASEset'
genotype(x) <- value

countsPerSnp(x, ...)

## S4 method for signature 'ASEset'
countsPerSnp(x, return.class = "matrix",
             return.type = "mean", strand = "*")

countsPerSample(x, ...)

## S4 method for signature 'ASEset'
countsPerSample(x, return.class = "matrix",
                return.type = "mean", strand = "*")

phase(x, ...)

## S4 method for signature 'ASEset'
phase(x, return.class = "matrix")

phase(x) <- value

## S4 replacement method for signature 'ASEset'
phase(x) <- value

mapBias(x) <- value

## S4 replacement method for signature 'ASEset'
mapBias(x) <- value

refExist(x)

## S4 method for signature 'ASEset'
refExist(x)

ref(x)

## S4 method for signature 'ASEset'
```

```

ref(x)

ref(x) <- value

## S4 replacement method for signature 'ASEset,ANY'
ref(x) <- value

altExist(x)

## S4 method for signature 'ASEset'
altExist(x)

alt(x)

## S4 method for signature 'ASEset'
alt(x)

alt(x) <- value

## S4 replacement method for signature 'ASEset,ANY'
alt(x) <- value

aquals(x, ...)

## S4 method for signature 'ASEset'
aquals(x)

aquals(x) <- value

## S4 replacement method for signature 'ASEset'
aquals(x) <- value

maternalAllele(x, ...)

## S4 method for signature 'ASEset'
maternalAllele(x)

paternalAllele(x, ...)

## S4 method for signature 'ASEset'
paternalAllele(x)

```

### Arguments

x	ASEset object
strand	which strand of '+', '-' or '*'
return.class	return 'list' or 'array'
...	additional arguments
value	replacement variable
top.fraction.criteria	'maxcount', 'ref' or 'phase'

verbose            makes function more talkative  
 return.type        return 'names', rank or 'counts'

### Details

An ASEset object differs from a regular RangedSummarizedExperiment object in that the assays contains an array instead of matrix. This array has ranges on the rows, sampleNames on the columns and variants in the third dimension.

It is possible to use the commands `barplot` and `locationplot` on an ASEset object see more details in [barplot](#) and [locationplot](#).

Three different alleleCount options are available. The simplest one is the `*` option, and is for experiments where the strand information is not known e.g. non-stranded data. The unknown strand could also be for strand specific data when the aligner could not find any strand associated with the read, but this should normally not happen, and if it does probably having an extremely low mapping quality. Then there are an option too add plus and minus stranded data. When using this, it is essential to make sure that the RNA-seq experiment under analysis has in fact been created so that correct strand information was obtained. The most functions will by default have their strand argument set to `'*'`.

The phase information is stored by the convention of `'maternal chromosome|paternal chromosome'`, with 0 as reference allele and 1 as alternative allele. `'|'` when the phase is known and `'/'` when the phase is unknown. Internally the information will be stored as a three dimensional array, dim 1 for SNPs, dim 2 for Samples and dim 3 which is fixed and stores maternal chromosome, paternal chromosome and phased (1 equals TRUE).

### Value

An object of class ASEset containing location information and allele counts for a number of SNPs measured in a number of samples on various strand, as well as `mapBias` information. All data is stored in a manner similar to the [RangedSummarizedExperiment](#) class.

### Table

`table(...)`

Arguments:

`...` An ASEset object that contains the variants of interest

The generics for `table` does not easily allow more than one argument so in respect to the different strand options, `table` will return a SimpleList with length 3, one element for each strand.

### Frequency

`frequency(x, return.class = "list", strand = "*", threshold.count.sample = 15)`

Arguments:

`x` An ASEset object that contains the variants of interest

`x` `threshold.count.samples` if sample has fewer counts the function return NA.

### Constructor

`ASEsetFromCountList(rowRanges, countListNonStranded = NULL, countListPlus = NULL, countListMinus = NULL, countListUnknown = NULL, colData = NULL, mapBiasExpMean = array(), verbose=FALSE, ...)`

Arguments:

**rowRanges** A `GenomicRanges` object that contains the variants of interest

**countListNonStranded** A list where each entry is a matrix with allele counts as columns and sample counts as rows

**countListPlus** A list where each entry is a matrix with allele counts as columns and sample counts as rows

**countListMinus** A list where each entry is a matrix with allele counts as columns and sample counts as rows

**countListUnknown** A list where each entry is a matrix with allele counts as columns and sample counts as rows

**colData** A `DataFrame` object containing sample specific data

**mapBiasExpMean** A 3D array describing mapping bias. The SNPs are in the 1st dimension, samples in the 2nd dimension and variants in the 3rd dimension.

**verbose** Makes function more talkative

**...** arguments passed on to `SummarizedExperiment` constructor

**Author(s)**

Jesper R. Gadin, Lasse Folkersen

**See Also**

- [RangedSummarizedExperiment](#) objects.

**Examples**

```
#make example countList
set.seed(42)
countListPlus <- list()
snps <- c('snp1', 'snp2', 'snp3', 'snp4', 'snp5')
for(snp in snps){
  count<-matrix(rep(0,16),ncol=4,dimnames=list(
c('sample1', 'sample2', 'sample3', 'sample4'),
c('A', 'T', 'G', 'C')))
  #insert random counts in two of the alleles
  for(allele in sample(c('A', 'T', 'G', 'C'),2)){
count[,allele]<-as.integer(rnorm(4,mean=50,sd=10))
  }
  countListPlus[[snp]] <- count
}

#make example rowRanges
rowRanges <- GRanges(
  seqnames = Rle(c('chr1', 'chr2', 'chr1', 'chr3', 'chr1')),
  ranges = IRanges(1:5, width = 1, names = head(letters,5)),
  snp = paste('snp',1:5,sep='')
)

#make example colData
colData <- DataFrame(Treatment=c('ChIP', 'Input', 'Input', 'ChIP'),
  row.names=c('ind1', 'ind2', 'ind3', 'ind4'))
```

```

#make ASEset
a <- ASEsetFromCountList(rowRanges, countListPlus=countListPlus,
colData=colData)

#example phase matrix (simple form)
p1 <- matrix(sample(c(1,0),replace=TRUE, size=nrow(a)*ncol(a)),nrow=nrow(a), ncol(a))
p2 <- matrix(sample(c(1,0),replace=TRUE, size=nrow(a)*ncol(a)),nrow=nrow(a), ncol(a))
p <- matrix(paste(p1,sample(c("|","|","/"), size=nrow(a)*ncol(a), replace=TRUE), p2, sep=""),
nrow=nrow(a), ncol(a))

phase(a) <- p

#generate ASEset from array
snps <- 999
samples <-5
ar <-array(rep(unlist(lapply(1:snps,
function(x){(sample(c(TRUE,FALSE,TRUE,FALSE), size = 4))})), samples),
dim=c(4,snps,samples))
ar2 <- array(sample(50:300, 4*snps*samples,replace=TRUE), dim=c(4,snps,samples))
ar2[ar] <- 0
ar2 <- aperm(ar2, c(2, 3, 1))
dimnames(ar2) <- list(paste("snp",1:snps,sep=""),paste("sample",1:samples,sep=""),
c("A","C","G","T"))
gr <- GRanges(seqnames=c("chr2"), ranges=IRanges(start=1:dim(ar2)[1], width=1), strand="*")
a <- ASEsetFromArrays(gr, countsUnknown=ar2)

```

---

ASEset-filters

*genotype filter methods*


---

## Description

useful genotype filters

## Usage

```
hetFilt(x, ...)
```

```
## S4 method for signature 'ASEset'
hetFilt(x, source = "genotype", ...)
```

## Arguments

x	ASEset object
...	internal param
source	'genotype' or 'alleleCounts'

## Details

hetFilt returns TRUE if the samples is heterozygote, based on stored genotype information present in the phase data.

**Author(s)**

Jesper R. Gadin, Lasse Folkersen

**Examples**

```
#load example data
data(ASEset)
a <- ASEset

genotype(a) <- inferGenotypes(a)
hets <- hetFilt(a)
```

---

ASEset-gbarplot

*gbarplot ASEset objects*

---

**Description**

Generates gbarplots for ASEset objects. Two levels of plotting detail are provided: a detailed gbarplot of read counts by allele useful for fewer samples and SNPs, and a less detailed gbarplot of the fraction of imbalance, useful for more samples and SNPs.

**Usage**

```
gbarplot(x, type = "count", strand = "*", verbose = FALSE, ...)
```

**Arguments**

x	An ASEset object
type	'count' or 'fraction'
strand	four options, '+', '-', 'both' or '*'
verbose	Makes function more talkative
...	for simpler generics when extending function

**Details**

This function serves the same purpose as the normal barplot, but with trellis graphics using lattice, to be able to integrate well with Gviz track functionality.

**Author(s)**

Jesper R. Gadin

**See Also**

- The [ASEset](#) class which the gbarplot function can be called up on.
- The [barplot](#) non trellis barplot.

**Examples**

```
data(ASEset)
gbarplot(ASEset[1])
```

---

ASEset-glocationplot *glocationplot ASEset objects*

---

**Description**

plotting ASE effects over a specific genomic region using Gviz functionality

**Usage**

```
glocationplot(x, type = "fraction", strand = "*", BamGAL = NULL,
  GenomeAxisTrack = FALSE, trackNameDeAn = paste("deTrack", type),
  TxDb = NULL, sizes = NULL, add = FALSE, verbose = FALSE, ...)
```

**Arguments**

x	an ASEset object.
type	'fraction' or 'count'
strand	'+', '-', '*' or 'both'. This argument determines which strand is plotted. See <code>getAlleleCounts</code> for more information of choice of strand.
BamGAL	GAlignmentsList covering the same genomic region as the ASEset
GenomeAxisTrack	include an genomic axis track
trackNameDeAn	trackname for deAnnotation track
TxDb	a TxDb object which provides annotation
sizes	vector with the sum 1. Describes the size of the tracks
add	add to existing plot
verbose	if set to TRUE it makes function more talkative
...	arguments passed on to barplot function

**Details**

The `glocationplot` methods visualises the distribution of ASE over a larger region on one chromosome. It takes an ASEset object as well as additional information on plot type (see `gbarplot`), strand type (see `getAlleleCounts`), Annotation tracks are created from the Gviz package. It is obviously important to make sure that the genome build used is set correctly, e.g. 'hg19'.

`sizes` has to be of the same length as the number of tracks used.

**Author(s)**

Jesper R. Gadin



**See Also**

- The [ASEset](#) class which the `glocationplot` function can be called up on.

**Examples**

```
data(ASEset)
genome(ASEset) <- 'hg19'

glocationplot(ASEset, strand='+')

#for ASEsets with fewer SNPs the 'count' type plot is useful
glocationplot(ASEset, type='count', strand='+')
```

---

ASEset-gviztrack      *ASEset-gviztrack ASEset objects*

---

**Description**

plotting ASE effects over a specific genomic region

**Usage**

```
ASEDAnnotationTrack(x, GR = rowRanges(x), type = "fraction", strand = "*",
  trackName = paste("deTrack", type), verbose = TRUE, ...)
```

```
## S4 method for signature 'ASEset'
ASEDAnnotationTrack(x, GR = rowRanges(x),
  type = "fraction", strand = "*", trackName = paste("deTrack", type),
  verbose = TRUE, ...)
```

```
CoverageDataTrack(x, GR = rowRanges(x), BamList = NULL, strand = NULL,
  start = NULL, end = NULL, trackNameVec = NULL, meanCoverage = FALSE,
  verbose = TRUE, ...)
```

**Arguments**

<code>x</code>	an ASEset object.
<code>GR</code>	genomic range of plotting
<code>type</code>	'fraction' or 'count'
<code>strand</code>	'+', '-'. This argument determines which strand is plotted.
<code>trackName</code>	name of track (ASEDAnnotationTrack)
<code>verbose</code>	Setting <code>verbose=TRUE</code> gives details of procedure during function run
<code>...</code>	arguments passed on to <code>barplot</code> function
<code>BamList</code>	GAlignmentsList object of reads from the same genomic region as the ASEset
<code>start</code>	start position of reads to be plotted
<code>end</code>	end position of reads to be plotted
<code>trackNameVec</code>	names of tracks (CoverageDataTrack)
<code>meanCoverage</code>	mean of coverage over samples (CoverageGataTrack)

**Details**

For information of how to use these tracks in more ways, visit the Gviz package manual.

**Author(s)**

Jesper R. Gadin

**See Also**

- The [ASEset](#) class which the functions can be called up on.

**Examples**

```
data(ASEset)
x <- ASEset[,1:2]
r <- reads[1:2]
genome(x) <- 'hg19'
seqlevels(r) <- seqlevels(x)

GR <- GRanges(seqnames=seqlevels(x),
  ranges=IRanges(start=min(start(x)),end=max(end(x))),
  strand='+', genome=genome(x))

deTrack <- ASEAnnotationTrack(x, GR=GR, type='fraction',strand='+')
covTracks <- CoverageDataTrack(x,BamList=r,strand='+')

lst <- c(deTrack,covTracks)

sizes <- c(0.5,rep(0.5/length(covTracks),length(covTracks)))
#temporarily do not run this function
#plotTracks(lst, from=min(start(x)), to=max(end(x)),
#sizes=sizes, col.line = NULL, showId = FALSE, main='mainText',
#cex.main=1, title.width=1, type='histogram')
```

---

ASEset-locationplot    *locationplot ASEset objects*

---

**Description**

plotting ASE effects over a specific genomic region

**Usage**

```
locationplot(x, ...)

## S4 method for signature 'ASEset'
locationplot(x, type = "fraction", strand = "*",
  yaxis = TRUE, xaxis = FALSE, xlab = FALSE, ylab = TRUE,
  xlab.text = "", ylab.text = "", legend.colnames = "", size = c(0.8,
  1), main = NULL, pValue = FALSE, cex.main = 0.7, cex.ylab = 0.6,
```

```
cex.legend = 0.5, OrgDb = NULL, TxDb = NULL, verbose = TRUE,
top.fraction.criteria = "maxcount", allow.whole.chromosome = FALSE, ...)
```

### Arguments

x	an ASEset object.
...	arguments passed on to barplot function
type	'fraction' or 'count'
strand	'+', '-', '*' or 'both'. This argument determines which strand is plotted. See <code>getAlleleCounts</code> for more information on strand.
yaxis	whether the y-axis is to be displayed or not
xaxis	whether the x-axis is to be displayed or not
xlab	showing labels for the tic marks
ylab	showing labels for the tic marks
xlab.text	xlab text
ylab.text	ylab text
legend.colnames	gives colnames to the legend matrix
size	will give extra space in the margins of the inner plots
main	text to use as main label
pValue	Display p-value
cex.main	set main label size
cex.ylab	set ylab label size
cex.legend	set legend label size
OrgDb	an OrgDb object from which to plot a gene map. If given together with argument TxDb this will only be used to extract genesymbols.
TxDb	a TxDb object from which to plot an exon map.
verbose	Setting verbose=TRUE gives details of procedure during function run
top.fraction.criteria	'maxcount', 'ref' or 'phase'
allow.whole.chromosome	logical, overrides 200kb region limit, defaults to FALSE

### Details

The locationplot methods visualises how fractions are distributed over a larger region of genes on one chromosome. It takes an ASEset object as well as additional information on plot type (see [barplot](#)), strand type (see [getAlleleCounts](#)), colouring, as well as annotation. The annotation is taken either from the bioconductor OrgDb-sets, the TxDb sets or both. It is obviously important to make sure that the genome build used is the same as used in aligning the RNA-seq data.

### Author(s)

Jesper R. Gadin, Lasse Folkersen

### See Also

- The [ASEset](#) class which the locationplot function can be called up on.

**Examples**

```

data(ASEset)
locationplot(ASEset)

#SNPs are plotted in the order in which they are found.
#This can be sorted according to location as follows:
locationplot(ASEset[order(start(rowRanges(ASEset))),])

#for ASEsets with fewer SNPs the 'count' type plot is
# useful for detailed visualization.
locationplot(ASEset,type='count',strand='*')

```

---

```

ASEset-scanForHeterozygotes
      scanForHeterozygotes

```

---

**Description**

Identifies the positions of SNPs found in BamGR reads.

**Usage**

```

scanForHeterozygotes(BamList, ...)

## S4 method for signature 'GAlignmentsList'
scanForHeterozygotes(BamList,
  minimumReadsAtPos = 20, maximumMajorAlleleFrequency = 0.9,
  minimumMinorAlleleFrequency = 0.1, minimumBiAllelicFrequency = 0.9,
  verbose = TRUE, ...)

```

**Arguments**

BamList	A GAlignmentsList object
...	argument to pass on
minimumReadsAtPos	minimum number of reads required to call a SNP at a given position
maximumMajorAlleleFrequency	maximum frequency allowed for the most common allele. Setting this parameter lower will minimise the SNP calls resulting from technical read errors, at the cost of missing loci with potential strong ASE
minimumMinorAlleleFrequency	minimum frequency allowed for the second most common allele. Setting this parameter higher will minimise the SNP calls resulting from technical read errors, at the cost of missing loci with potential strong ASE
minimumBiAllelicFrequency	minimum frequency allowed for the first and second most common allele. Setting a Lower value for this parameter will minimise the identification of loci with three or more alleles in one sample. This is useful if sequencing errors are suspected to be common.

verbose            logical indicating if process information should be displayed

### Details

This function scans all reads stored in a `GAlignmentsList` for possible heterozygote positions. The user can balance the sensitivity of the search by modifying the `minimumReadsAtPos`, `maximumMajorAlleleFrequency` and `minimumBiAllelicFrequency` arguments.

### Value

`scanForHeterozygotes` returns a `GRanges` object with the SNPs for the `BamList` object that was used as input.

### Author(s)

Jesper R. Gadin, Lasse Folkersen

### See Also

- The [getAlleleCounts](#) which is a function that count the number of reads overlapping a site.

### Examples

```
data(reads)
s <- scanForHeterozygotes(reads, verbose=FALSE)
```

---

ASEset.old

*ASEset.old object*

---

### Description

old version of an ASEset which needs to be updated

### Author(s)

Jesper R. Gadin, Lasse Folkersen

### Examples

```
##load eample data (Not Run)
#data(ASEset.old)
```

---

 ASEset.sim

*ASEset.sim object*


---

### Description

ASEset with simulated data with SNPs within the first 200bp of chromosome 17, which is required to have example data for the refAllele function.

### Author(s)

Jesper R. Gadin, Lasse Folkersen

### Examples

```
##load eample data (Not Run)
#data(ASEset.sim)
```

---

 ASEsetFromBam

*ASEset from bam file*


---

### Description

count alleles and create an ASEset direct from bam file instead of reading into R first.

### Usage

```
ASEsetFromBam(gr, ...)

## S4 method for signature 'GRanges'
ASEsetFromBam(gr, pathToDir, PE = TRUE,
  flagsMinusStrand = c(83, 163), flagsPlusStrand = c(99, 147),
  strandUnknown = FALSE, ...)
```

### Arguments

<code>gr</code>	GenomicRanges of SNPs to create ASEset for
<code>...</code>	passed on to ASEsetFromBam function
<code>pathToDir</code>	Directory of bam files with index in same directory
<code>PE</code>	if paired end or not (default: TRUE)
<code>flagsMinusStrand</code>	flags that mark reads coming from minus strand
<code>flagsPlusStrand</code>	flags that mark reads coming from plus strand
<code>strandUnknown</code>	default: FALSE

**Details**

counts the alleles in a bam file based on GRanges positions.

**Author(s)**

Jesper R. Gadin

**Examples**

```
data(GRvariants)
gr <- GRvariants

##no execution at the moment
#pathToDir <- system.file('inst/extdata/ERP000101_subset', package='AllelicImbalance')
#a <- ASEsetFromBam(gr, pathToDir)
```

---

barplot-lattice-support

*lattice barplot inner functions for ASEset objects*

---

**Description**

Generates lattice barplots for ASEset objects. Two levels of plotting detail are provided: a detailed barplot of read counts by allele useful for fewer samples and SNPs, and a less detailed barplot of the fraction of imbalance, useful for more samples and SNPs.

**Usage**

```
barplotLatticeFraction(identifier, ...)
```

```
barplotLatticeCounts(identifier, ...)
```

**Arguments**

identifier,      the single snp name to plot  
...              used to pass on variables

**Details**

filter.pValue.fraction is intended to remove p-value annotation with very large difference in frequency, which could just be a sequencing mistake. This is to avoid p-values like 1e-235 or similar.

sampleColourUser specified colours, either given as named colours ('red', 'blue', etc) or as hexadecimal code. Can be either length 1 for all samples, or else of a length corresponding to the number of samples for individual colouring.

**Author(s)**

Jesper R. Gadin, Lasse Folkersen

**See Also**

- The [ASEset](#) class which the barplot function can be called up on.

**Examples**

```
a <- ASEset
name <- rownames(a)[1]

barplotLatticeFraction(identifier=name, x=a, astrand="+")
barplotLatticeCounts(identifier=name, x=a, astrand="+")
```

---

binom.test

*binomial test*

---

**Description**

Performs a binomial test on an ASEset object.

**Usage**

```
## S4 method for signature 'ASEset'
binom.test(x, n = "*")
```

**Arguments**

x	ASEset object
n	strand option

**Details**

the test can only be applied to one strand at the time.

**Value**

binom.test returns a matrix

**Author(s)**

Jesper R. Gadin, Lasse Folkersen

**See Also**

- The [chisq.test](#) which is another test that can be applied on an [ASEset](#) object.



## Examples

```
#load example data
data(ASEset)

#make a binomial test
binom.test(ASEset, '*')
```

---

chisq.test	<i>chi-square test</i>
------------	------------------------

---

## Description

Performs a `chisq.test` on an `ASEset` object.

## Usage

```
## S4 method for signature 'ASEset'
chisq.test(x, y = "")
```

## Arguments

x	ASEset object
y	strand option

## Details

The test is performed on one strand in an `ASEset` object.

## Value

`chisq.test` returns a matrix with the `chisq.test` P-value for each SNP and sample

## Author(s)

Jesper R. Gadin, Lasse Folkersen

## See Also

- The [binom.test](#) which is another test that can be applied on an [ASEset](#) object.

## Examples

```
#load example data
data(ASEset)

#make a chi-square test on default non-stranded strand
chisq.test(ASEset)
```

---

countAllelesFromBam    *alleleCounts from bam file*

---

### Description

count alleles before creating ASEse.

### Usage

```
countAllelesFromBam(gr, ...)

## S4 method for signature 'GRanges'
countAllelesFromBam(gr, pathToDir, flag = NULL,
  scanBamFlag = NULL, return.class = "array", verbose = TRUE, ...)
```

### Arguments

gr	GRanges that contains SNPs of interest
...	arguments to pass on
pathToDir	path to directory of bam files
flag	specify one flag to use as filter, default is no filtering. allowed flags are 99, 147, 83 and 163
scanBamFlag	set a custom flag to use as filter
return.class	type of class for the returned object
verbose	makes function more talkative

### Details

counts the alleles in a bam file based on GRanges positions.

Important excerpt from the details section of the internal applyPileups function: Regardless of 'param' values, the algorithm follows samtools by excluding reads flagged as unmapped, secondary, duplicate, or failing quality control.

### Author(s)

Jesper R. Gadin

### Examples

```
data(GRvariants)
gr <- GRvariants

##not run at the moment
#pathToDir <- system.file('inst/extdata/ERP000101_subset', package='AllelicImbalance')
#ar <- countAllelesFromBam(gr, pathToDir)
```

---

```
coverageMatrixListFromGAL
      coverage matrix of GAlignmentsList
```

---

## Description

Get coverage per nucleotide for reads covering a region

## Usage

```
coverageMatrixListFromGAL(BamList, ...)

## S4 method for signature 'GAlignmentsList'
coverageMatrixListFromGAL(BamList, strand = "*",
  ignore.empty.bam.row = TRUE)
```

## Arguments

BamList	GAlignmentsList containing reads over the region to calculate coverage
...	arguments to pass on
strand	strand has to be '+' or '-'
ignore.empty.bam.row	argument not in use atm

## Details

a convenience function to get the coverage from a list of reads stored in GAlignmentsList, and returns by default a list with one matrix, and information about the genomic start and stop positions.

## Author(s)

Jesper R. Gadin

## Examples

```
r <- reads
seqlevels(r) <- '17'
covMatList <- coverageMatrixListFromGAL(BamList=r, strand='+')
```

---

defaultMapBias	<i>Generate default mapbias from genotype</i>
----------------	---

---

### Description

Create mapbias array from genotype matrix requires genotype information

### Usage

```
defaultMapBias(x, ...)  
  
## S4 method for signature 'ASEset'  
defaultMapBias(x, return.class = "array")
```

### Arguments

x	ASEset object
...	internal arguments
return.class	"array" or "ASEset"

### Details

Default mapbias will be 0.5 for bi-allelic snps and 1 for homozygots. For genotypes with NA, 0.5 will be placed on all four alleles. Therefore tri-allelic can not be used atm. Genotype information has to be placed in the genotype(x) assay.

### Author(s)

Jesper R. Gadin, Lasse Folkersen

### Examples

```
#load example data  
data(ASEset.sim)  
  
fasta <- system.file('extdata/hg19.chr17.subset.fa', package='AllelicImbalance')  
refAllele(ASEset.sim, fasta=fasta)  
a <- refAllele(ASEset.sim, fasta=fasta)
```

---

defaultPhase	<i>defaultPhase</i>
--------------	---------------------

---

**Description**

used to populate the phase slot in an ASEset object

**Usage**

```
defaultPhase(i, ...)  
  
## S4 method for signature 'numeric'  
defaultPhase(i, j, ...)
```

**Arguments**

i	number of rows
...	arguments to forward to internal functions
j	number of columns

**Details**

will set everything to 0

**Author(s)**

Jesper R. Gadin, Lasse Folkersen

**Examples**

```
i <- 5  
j <- 10  
defaultPhase(i, j)
```

---

detectAI	<i>detectAI</i>
----------	-----------------

---

**Description**

detection of AllelicImbalance

**Usage**

```
detectAI(x, ...)

## S4 method for signature 'ASEset'
detectAI(x, return.class = "DetectedAI", strand = "*",
  threshold.frequency = 0, threshold.count.sample = 1,
  threshold.delta.frequency = 0, threshold.pvalue = 0.05,
  inferGenotype = FALSE, random.ref = FALSE, function.test = "binom.test",
  verbose = TRUE, gc = FALSE, biasMatrix = FALSE)
```

**Arguments**

x	ASEset
...	internal arguments
return.class	class to return (atm only class 'logical')
strand	strand to infer from
threshold.frequency	least fraction to classify (see details)
threshold.count.sample	least amount of counts to try to infer allele
threshold.delta.frequency	minimum of frequency difference from 0.5 (or mapbias adjusted value)
threshold.pvalue	pvalue over this number will be filtered out
inferGenotype	infer genotypes based on count data in ASEset object
random.ref	set the reference as random if you dont know. Affects interpretation of results.
function.test	At the moment the only available option is 'binomial.test'
verbose	makes function more talkative
gc	use garbage collection when possible to save space
biasMatrix	use biasMatrix in ASEset, or use default expected frequency of 0.5 for all sites

**Details**

threshold.frequency is the least fraction needed to classify as bi tri or quad allelic SNPs. If 'all' then all of bi tri and quad allelic SNPs will use the same threshold. Everything under the threshold will be regarded as noise. 'all' will return a matrix with snps as rows and uni bi tri and quad will be columns. For this function Anything that will return TRUE for tri-allelic will also return TRUE for uni and bi-allelic for the same SNP an Sample.

return.type 'ref' return only AI when reference allele is more expressed. 'alt' return only AI when alternative allele is more expressed or 'all' for both 'ref' and 'alt' alleles. Reference allele is the one present in the reference genome on the forward strand.

threshold.delta.frequency and function.test will use the value in mapBias(x) as expected value.

function.test will use the two most expressed alleles for testing. Make therefore sure there are no tri-allelic SNPs or somatic mutations among the SNPs in the ASEset.

inferGenotype(), set TRUE it should be used with as much samples as possible. If you split up the samples and run detectAI() on each sample separately, please make sure you have inferred the genotypes in before hand, alternatively used the genotypes detected by another variantCaller or chip-genotypes. Use ONLY biallelic genotypes.

**Author(s)**

Jesper R. Gadin

**Examples**

```
#load example data
data(ASEset)
a <- ASEset

dai <- detectAI(a)
```

---

DetectedAI-class	<i>DetectedAI class</i>
------------------	-------------------------

---

**Description**

Object that holds results from AI detection.

**Usage**

```
referenceFrequency(x, ...)

## S4 method for signature 'DetectedAI'
referenceFrequency(x, return.class = "array")

thresholdFrequency(x, ...)

## S4 method for signature 'DetectedAI'
thresholdFrequency(x, return.class = "array")

thresholdCountSample(x, ...)

## S4 method for signature 'DetectedAI'
thresholdCountSample(x, return.class = "array")

thresholdDeltaFrequency(x, ...)

## S4 method for signature 'DetectedAI'
thresholdDeltaFrequency(x, return.class = "array")

thresholdPvalue(x, ...)

## S4 method for signature 'DetectedAI'
thresholdPvalue(x, return.class = "array")
```

**Arguments**

x	ASEset object or list of ASEsets
...	pass arguments to internal functions
return.class	type of class returned eg. "list" or ""array".

**Details**

The DetectedAI-class contains

**Author(s)**

Jesper R. Gadin, Lasse Folkersen

**Examples**

```
data(ASEset)
a <- ASEset
dai <- detectAI(a)

#summary(gba)
#write.tables(dai)
```

---

DetectedAI-plot

*DetectedAI plot*

---

**Description**

plot functions for the DetectedAI-class

**Usage**

```
frequency_vs_threshold_variable_plot(x, ...)

## S4 method for signature 'DetectedAI'
frequency_vs_threshold_variable_plot(x,
  var = "threshold.count.sample", hetOverlay = TRUE,
  smoothscatter = FALSE)

detectedAI_vs_threshold_variable_plot(x, ...)

## S4 method for signature 'DetectedAI'
detectedAI_vs_threshold_variable_plot(x,
  var = "threshold.count.sample", summaryOverSamples = "sum",
  hetOverlay = TRUE, smoothscatter = FALSE)

reference_frequency_density_vs_threshold_variable_plot(x, ...)

## S4 method for signature 'DetectedAI'
reference_frequency_density_vs_threshold_variable_plot(x,
  var = "threshold.count.sample")

detectedAI_vs_threshold_variable_multigraph_plot(x, ...)

## S4 method for signature 'DetectedAI'
```



```

detectedAI_vs_threshold_variable_multigraph_plot(x,
  ncol = 2, ...)

frequency_vs_threshold_variable_multigraph_plot(x, ...)

## S4 method for signature 'DetectedAI'
frequency_vs_threshold_variable_multigraph_plot(x,
  ncol = 2, ...)

reference_frequency_density_vs_threshold_variable_multigraph_plot(x, ...)

## S4 method for signature 'DetectedAI'
reference_frequency_density_vs_threshold_variable_multigraph_plot(x,
  ncol = 2, ...)

```

### Arguments

x	detectedAI object
...	pass on variables internally
var	string, see details for available options
hetOverlay	logical, if TRUE show nr of het SNPs used to calculate the reference allele frequency mean
smoothscatter	boolean, smoothscatter over the means
summaryOverSamples	'mean' or 'sum'
ncol	nr of columns for multiplots

### Details

plot helper functions. The documentation will be improved before next release.

### Author(s)

Jesper R. Gadin, Lasse Folkersen

### Examples

```

#some example code here
#generate example
data(ASEset)
a <- ASEset
dai <- detectAI(a,
  threshold.count.sample=1:50,
  threshold.frequency=seq(0,0.5,by=0.01),
  threshold.delta.frequency=seq(0,0.5,by=0.01),
  threshold.pvalue=rev(seq(0.001,0.05, by=0.005))
)

frequency_vs_threshold_variable_plot(dai)
detectedAI_vs_threshold_variable_plot(dai)
detectedAI_vs_threshold_variable_multigraph_plot(dai)

```

```
frequency_vs_threshold_variable_multigraph_plot(dai)
```

---

DetectedAI-summary      *DetectedAI summary*

---

## Description

Summary helper functions for the DetectedAI-class

## Usage

```
frequency_vs_threshold_variable_summary(x, ...)  
  
## S4 method for signature 'DetectedAI'  
frequency_vs_threshold_variable_summary(x,  
  var = "threshold.count.sample", return.class = "matrix", ...)  
  
detectedAI_vs_threshold_variable_summary(x, ...)  
  
## S4 method for signature 'DetectedAI'  
detectedAI_vs_threshold_variable_summary(x,  
  var = "threshold.count.sample")  
  
usedSNPs_vs_threshold_variable_summary(x, ...)  
  
## S4 method for signature 'DetectedAI'  
usedSNPs_vs_threshold_variable_summary(x,  
  var = "threshold.count.sample")
```

## Arguments

x	detectedAI object
...	pass on variables internally
var	string, see details for available options
return.class	'matrix' or 'array'

## Details

Summary helper functions. The documentation will be improved before next release.

## Author(s)

Jesper R. Gadin, Lasse Folkersen

## Examples

```
#some example code here
#generate example
data(ASEset)
a <- ASEset
dai <- detectAI(a,
  threshold.count.sample=1:50,
  threshold.frequency=seq(0,0.5,by=0.01),
  threshold.delta.frequency=seq(0,0.5,by=0.01),
  threshold.pvalue=rev(seq(0.001,0.05, by=0.005))
)

frequency_vs_threshold_variable_summary(dai)
```

---

fractionPlotDf

*Plot Dataframe*

---

## Description

Summarizes information to ease creating plots

## Usage

```
fractionPlotDf(x, snp, strand = "*", top.fraction.criteria = "maxcount",
  ...)

## S4 method for signature 'ASEset'
fractionPlotDf(x, snp, strand = "*",
  top.fraction.criteria = "maxcount", ...)
```

## Arguments

x	ASEset
snp	rownames identifier for ASEset or row number
strand	'+', '-' or '*'
top.fraction.criteria	'maxcount', 'ref' or 'phase'
...	arguments to forward to internal functions

## Details

Main purpose is to reduce the amount of overall code and ease maintenance.

top.fraction.criteria can take three options, maxcount, ref and phase. The top allele will be every second row in the data frame, with start from row 2. The maxcount argument will put the allele with most reads on top of the bivariate fraction. Similarly the ref argument will put always the reference allele on top. The phase arguments puts the maternal phase always on top. The top.fraction.criteria for the ref or phase arguments requires that both ref and alt is set in mcols(ASEset).

**Author(s)**

Jesper R. Gadin, Lasse Folkersen

**Examples**

```
#test on example ASEset
data(ASEset)
a <- ASEset
df <- fractionPlotDf(a, 1, strand="+")
```

---

gba

*global analysis wrapper*

---

**Description**

A wrapper to make a global analysis based on paths for BAM, VCF and GFF files

**Usage**

```
gba(pathBam, ...)

## S4 method for signature 'character'
gba(pathBam, pathVcf, pathGFF = NULL, verbose)
```

**Arguments**

pathBam	path to bam file
...	arguments to pass on
pathVcf	path to vcf file
pathGFF	path to gff file
verbose	makes function more talkative

**Author(s)**

Jesper R. Gadin

**Examples**

```
#empty as function doesn't exist
```

---

genomatrix	<i>genomatrix object</i>
------------	--------------------------

---

**Description**

genomatrix is an example of a matrix with genotypes

**Author(s)**

Jesper R. Gadin, Lasse Folkersen

**Examples**

```
##load eample data (Not Run)
#data(genomatrix)
```

---

genotype2phase	<i>genotype2phase</i>
----------------	-----------------------

---

**Description**

used to convert the genomatrix from the visually friendly matrix to phase array.

**Usage**

```
genotype2phase(x, ...)

## S4 method for signature 'matrix'
genotype2phase(x, ref = NULL, return.class = "array",
  levels = c("A", "C", "G", "T"), ...)
```

**Arguments**

x	matrix see examples
...	pass on additional param
ref	reference alleles
return.class	'array' or 'list'
levels	vector of expected alleles

**Details**

To not introduce redundant information in the ASEset object, the genotype matrix is translated to a phase matrix, containing the same information. Does not allow tri-allelic or multi-allelic SNPs, and if present the multi-allelic SNPs will lose the least occurring genotype.

This function can handle indels, but if the reference allele is not provided, the rank matrix which is temporary created might use lots of memory, depending on the amount of indels among the genotypes. As conclusion, it is preferable to send in reference genome when converting to phase.

levels information is only important if the reference allele has to be guessed, and so if reference information is provided, the levels argument can be ignored.

**Author(s)**

Jesper R. Gadin, Lasse Folkersen

**Examples**

```
#load example data
data(genomatrix)
data(ASEset)
p <- genotype2phase(genomatrix, ref(ASEset))
```

---

getAlleleCounts	<i>snp count data</i>
-----------------	-----------------------

---

**Description**

Given the positions of known SNPs, this function returns allele counts from a BamGRL object

**Usage**

```
getAlleleCounts(BamList, ...)

## S4 method for signature 'GAlignmentsList'
getAlleleCounts(BamList, GRvariants, strand = "*",
  return.class = "list", verbose = TRUE, ...)
```

**Arguments**

BamList	A GAlignmentsList object or GRangesList object containing data imported from a bam file
...	parameters to pass on
GRvariants	A GRanges object that contains positions of SNPs to retrieve
strand	A length 1 character with value '+', '-', or '*'. This argument determines if getAlleleCounts will retrieve counts from all reads, or only from reads marked as '+', '-' or '*' (unknown), respectively.
return.class	'list' or 'array'
verbose	Setting verbose=TRUE makes function more talkative

**Details**

This function is used to retrieve the allele counts from specified positions in a set of RNA-seq reads. The BamList argument will typically have been created using the impBamGAL function on bam-files. The GRvariants is either a GRanges with user-specified locations or else it is generated through scanning the same bam-files as in BamList for heterozygote locations (e.g. using scanForHeterozygotes). The GRvariants will currently only accept locations having width=1, corresponding to bi-allelic SNPs. In the strand argument, specifying '\*' is the same as retrieving the sum count of '+' and '-' reads (and unknown strand reads in case these are found in the bam file). '\*' is the default behaviour and can be used when the RNA-seq experiments strand information is not available.

**Value**

getAlleleCounts returns a list of several data.frame objects, each storing the count data for one SNP.

**Author(s)**

Jesper R. Gadin, Lasse Folkersen

**See Also**

- The [scanForHeterozygotes](#) which is a function to find possible heterozygote sites in a [GAlignmentsList](#) object

**Examples**

```
#load example data
data(reads)
data(GRvariants)

#get counts at the three positions specified in GRvariants
alleleCount <- getAlleleCounts(BamList=reads,GRvariants,
strand='*')

#if the reads had contained stranded data, these two calls would
#have given the correct input objects for getAlleleCounts
alleleCountPlus <- getAlleleCounts(BamList=reads,GRvariants,
strand='+')
alleleCountMinus <- getAlleleCounts(BamList=reads,GRvariants,
strand='-')
```

---

getAlleleQuality      *snp quality data*

---

**Description**

Given the positions of known SNPs, this function returns allele quality from a BamGRL object

**Usage**

```
getAlleleQuality(BamList, ...)

## S4 method for signature 'GAlignmentsList'
getAlleleQuality(BamList, GRvariants,
  fastq.format = "illumina.1.8", return.class = "array", verbose = TRUE,
  ...)
```

**Arguments**

BamList	A GAlignmentsList object or GRangesList object containing data imported from a bam file
...	parameters to pass on
GRvariants	A GRanges object that contains positions of SNPs to retrieve.
fastq.format	default 'illumina.1.8'
return.class	'list' or 'array'
verbose	Setting verbose=TRUE makes function more talkative

**Details**

This function is used to retrieve the allele quality strings from specified positions in a set of RNA-seq reads. The BamList argument will typically have been created using the impBamGAL function on bam-files. The GRvariants is either a GRanges with user-specified locations or else it is generated through scanning the same bam-files as in BamList for heterozygote locations (e.g. using scanForHeterozygotes). The GRvariants will currently only accept locations having width=1, corresponding to bi-allelic SNPs. The strand type information will be kept in the returned object. If the strand is marked as unknown "\*", it will be forced to the "+" strand.

quality information is extracted from the BamList object, and requires the presence of mcols(BamList)[["qual"]] to contain quality sequences.

**Value**

getAlleleQuality returns a list of several data.frame objects, each storing the count data for one SNP.

**Author(s)**

Jesper R. Gadin, Lasse Folkersen

**Examples**

```
#load example data
data(reads)
data(GRvariants)

#get counts at the three positions specified in GRvariants
alleleQualityArray <- getAlleleQuality(BamList=reads,GRvariants)

#place in ASEset object
alleleCountsArray <- getAlleleCounts(BamList=reads,GRvariants,
                                     strand='*', return.class="array")

a <- ASEsetFromArrays(GRvariants, countsUnknown = alleleCountsArray)
aquals(a) <- alleleQualityArray
```



---

getAreaFromGeneNames *Get Gene Area*

---

### Description

Given a character vector with genesymbols and an OrgDb object, this function returns a GRanges giving the coordinates of the genes.

### Usage

```
getAreaFromGeneNames(genesymbols, ...)  
  
## S4 method for signature 'character'  
getAreaFromGeneNames(genesymbols, OrgDb, leftFlank = 0,  
  rightFlank = 0, na.rm = FALSE, verbose = TRUE)
```

### Arguments

genesymbols	A character vector that contains genesymbols of genes from which we wish to retrieve the coordinates
...	arguments to pass on
OrgDb	An OrgDb object containing gene annotation
leftFlank	A integer specifying number of additional nucleotides before the genes
rightFlank	A integer specifying number of additional nucleotides after the genes
na.rm	A boolean removing genes that returned NA from the annotation
verbose	Setting verbose=TRUE makes function more talkative

### Details

This function is a convenience function that can be used to determine which genomic coordinates to specify to e.g. `impBamGAL` when retrieving reads.

The function cannot handle genes that do not exist in the annotation. To remove these please set the `na.rm=TRUE`.

### Value

`getAreaFromGeneNames` returns a GRanges object with genomic coordinates around the specified genes

### Author(s)

Jesper R. Gadin, Lasse Folkersen

## Examples

```
#load example data
data(ASEset)

#get counts at the three positions specified in GRvariants
library(org.Hs.eg.db )
searchArea<-getAreaFromGeneNames(c('PAX8','TLR7'), org.Hs.eg.db)
```

---

```
getDefaultMapBiasExpMean
      Map Bias
```

---

## Description

an allele frequency array

## Usage

```
getDefaultMapBiasExpMean(alleleCountList, ...)

getDefaultMapBiasExpMean3D(alleleCountList, ...)

## S4 method for signature 'list'
getDefaultMapBiasExpMean(alleleCountList)

## S4 method for signature 'ANY'
getDefaultMapBiasExpMean3D(alleleCountList)
```

## Arguments

```
alleleCountList      A GRangesList object containing read information
...                  parameters to pass on
```

## Details

This function will assume there is no bias that comes from the mapping of reads, and therefore create a matrix with expected frequency of 0.5 for each allele.

## Value

getDefaultMapBiasExpMean returns a matrix with a default expected mean of 0.5 for every element.

## Author(s)

Jesper R. Gadin, Lasse Folkersen

## Examples

```
#load example data
data(ASEset)
#access SnpAflist
alleleCountList <- alleleCounts(ASEset)
#get default map bias exp mean
matExpMean <- getDefaultMapBiasExpMean(alleleCountList)
```

---

getSnpIdFromLocation *Get rsIDs from locations of SNP*

---

## Description

Given a GRanges object of SNPs and a SNPlocs annotation, this function attempts to replace the names of the GRanges object entries with rs-IDs.

## Usage

```
getSnpIdFromLocation(GR, ...)

## S4 method for signature 'GRanges'
getSnpIdFromLocation(GR, SNPloc, return.vector = FALSE,
  verbose = TRUE)
```

## Arguments

GR	A GRanges that contains positions of SNPs to look up
...	arguments to pass on
SNPloc	A SNPlocs object containing information on SNP locations (e.g. SNPlocs.Hsapiens.dbSNP.xxxxxx)
return.vector	Setting return.vector=TRUE returns vector with rsIds
verbose	Setting verbose=TRUE makes function more talkative

## Details

This function is used to try to identify the rs-IDs of SNPs in a GRanges object.

## Value

getSnpIdFromLocation returns the same GRanges object it was given with, but with updated with rs.id information.

## Author(s)

Jesper R. Gadin, Lasse Folkersen

## Examples

```
#load example data
data(ASEset)

#get counts at the three positions specified in GRvariants
if(require(SNPlocs.Hsapiens.dbSNP144.GRCh37)){
  updatedGRanges<-getSnpIdFromLocation(rowRanges(ASEset), SNPlocs.Hsapiens.dbSNP144.GRCh37)
  rowRanges(ASEset)<-updatedGRanges
}
```

---

GlobalAnalysis-class    *GlobalAnalysis class*

---

## Description

Object that holds results from a global AI analysis including reference bias estimations and AI detection.

## Arguments

x	ASEset object or list of ASEsets
TxDB	A transcriptDb object
...	pass arguments to internal functions

## Details

The GlobalAnalysis-class contains summaries and "pre-configured and pre-calculated lattice plots" needed to create an AI-report

## Value

An object of class GlobalAnalysis containing all data to make report.

## Author(s)

Jesper R. Gadin, Lasse Folkersen

## Examples

```
data(ASEset)
#a <- ASEset
#gba <- gba(a)

#report(gba)
#write.tables(gba)
#graphs(gba)
#as.list(gba)
```

---

GRvariants	<i>GRvariants object</i>
------------	--------------------------

---

**Description**

this data is a GRanges object that contains the ranges for three example SNPs.

**Author(s)**

Jesper R. Gadin, Lasse Folkersen

**See Also**

- The [reads](#) which is another example object

**Examples**

```
#load example data
data(GRvariants)
```

---

histplot	<i>histogram plots</i>
----------	------------------------

---

**Description**

uses base graphics hist plot

**Usage**

```
## S4 method for signature 'ASEset'
hist(x, strand = "*", type = "mean", log = 1, ...)
```

**Arguments**

x	ReferenceBias object or ASEset object
strand	'+', '-' or '*'
type	'mean' (only one option atm)
log	an integer to log each value (integer 10 for log10)
...	arguments to forward to interal boxplots function

**Details**

The histogram will show the density over frequencies for each sample

**Author(s)**

Jesper R. Gadin, Lasse Folkersen

**Examples**

```
##load example data

#data(ASEset)
#a <- ASEset
#hist(a)
```

---

`implodeList.old`*implode list of arguments into environment*

---

**Description**

apply on list of variables to be put in the local environment

**Usage**

```
implodeList.old(x)
```

**Arguments**

x                    list of variables

**Details**

help the propagation of e.g. graphical paramters

**Author(s)**

Jesper R. Gadin

**Examples**

```
lst <- list(hungry='yes', thirsty='no')
implodeList.old(lst)
#the check ls()
ls()
```

---

import-bam	<i>Import Bam</i>
------------	-------------------

---

## Description

Imports a specified genomic region from a bam file using a GRanges object as search area.

## Usage

```
impBamGAL(UserDir, ...)

## S4 method for signature 'character'
impBamGAL(UserDir, searchArea, files = NULL,
           XStag = FALSE, verbose = TRUE, ...)
```

## Arguments

UserDir	The relative or full path of folder containing bam files.
...	arguments to pass on
searchArea	A GenomicRanges object that contains the regions of interest
files	use character vector to specify one or more files to import. The default imports all bam files from the directory.
XStag	Setting XStag=TRUE stores the strand specific information in the mcols slot 'XS'
verbose	makes the function more talkative.

## Details

If the sequence data is strand-specific you may want to set XStag=TRUE. The strand specific information has then to be stored in the meta columns with column name 'XS'. If the aligner did not set the XS-tag and the data is strand-specific it is still possible to infer the strand from the bit flags after importing the reads to R. Depending on the strand-specific protocol different combinations of the flags will have to be used. For illumina fr-secondstrand, 83 and 163 are minus strand reads and 99 and 147 are plus strand reads.

## Author(s)

Jesper R. Gadin, Lasse Folkersen

## Examples

```
#Declare searchArea
searchArea <- GRanges(seqnames=c('17'), ranges=IRanges(79478301,79478361))

#Relative or full path
pathToFiles <- system.file('extdata/ERP000101_subset', package='AllelicImbalance')

#all files in directory
reads <- impBamGAL(pathToFiles,searchArea,verbose=FALSE)
#specified files in directory
reads <- impBamGAL(pathToFiles,searchArea,
```

```
files=c("ERR009160.bam", "ERR009167.bam"), verbose=FALSE)
```

---

import-bam-2

*Import Bam-2*


---

## Description

Imports bla bal bal a specified genomic region from a bam file using a GenomicRanges object as search area.

## Usage

```
impBamGRL.old(UserDir, searchArea, verbose = TRUE)
```

## Arguments

UserDir	The relative or full path of folder containing bam files.
searchArea	A GenomicRanges object that contains the regions of interest
verbose	Setting verbose=TRUE gives details of procedure during function run.

## Details

These functions are right on tahea wrappers to import bam files into R and store them into either GRanges, GAlignments or GappedAlignmentpairs objects.

It is recommended to use the impBamGAL() which takes information of gaps into account. It is also possible to use the other variants as well, but then pre-filtering becomes important keys to understand because gapped, intron-spanning reads will cause problems. This is because the GRanges objects can not handle if gaps are present and will then give a wrong result when calculating the allele (SNP) count table.

## Value

impBamGRL returns a GRangesList object containing the RNA-seq reads in the region defined by the searchArea argument. impBamGAL returns a list with GAlignments objects containing the RNA-seq reads in the region defined by the searchArea argument. funImpBamGAPL returns a list with GappedAlignmentPairs object containing the RNA-seq reads in the region defined by the searchArea argument.

## Author(s)

Jesper R. Gadin, Lasse Folkersen

## Examples

```
#Declare searchArea
searchArea <- GRanges(seqnames=c('17'), ranges=IRanges(79478301,79478361))

#Relative or full path
pathToFiles <- system.file('extdata/ERP000101_subset', package='AllelicImbalance')
```



---

import-bcf	<i>Import Bcf Selection</i>
------------	-----------------------------

---

**Description**

Imports a selection of a bcf file or files specified by a GenomicRanges object as search area.

**Usage**

```
impBcfGRL(UserDir, ...)

## S4 method for signature 'character'
impBcfGRL(UserDir, searchArea = NULL, verbose = TRUE,
  ...)

impBcfGR(UserDir, ...)

## S4 method for signature 'character'
impBcfGR(UserDir, searchArea = NULL, verbose = TRUE,
  ...)
```

**Arguments**

UserDir	The relative or full path of folder containing bam files.
...	parameters to pass on
searchArea	A GenomicRanges object that contains the regions of interest
verbose	Setting verbose=TRUE gives details of the procedure during function run.

**Details**

A wrapper to import bcf files into R in the form of GenomicRanges objects.

**Value**

BcfImpGRL returns a GRangesList object. BcfImpGR returns one GRanges object of all unique entries from one or more bcf files.

**Note**

Make sure there is a complementary index file \*.bcf.bci for each bcf file in UserDir. If there is not, then the functions impBcfGRL and impBcfGR will try to create them.

**Author(s)**

Jesper R. Gadin, Lasse Folkersen

**See Also**

- The `impBamGRL` for importing bam files
- The [getAlleleCounts](#) for how to get allele(SNP) counts
- The [scanForHeterozygotes](#) for how to find possible heterozygote positions

**Examples**

```
#Declare searchArea
searchArea <- GRanges(seqnames=c('17'), ranges=IRanges(79478301,79478361))

#Relative or full path
pathToFiles <- system.file('extdata/ERP000101_subset', package='AllelicImbalance')

#import
reads <- impBcfGRL(pathToFiles, searchArea, verbose=FALSE)
```

---

inferAlleles	<i>inference of SNPs of ASEset</i>
--------------	------------------------------------

---

**Description**

inference of SNPs

**Usage**

```
inferAlleles(x, strand = "*", return.type = "bi", threshold.frequency = 0,
  threshold.count.sample = 1, inferOver = "eachSample", allow.NA = FALSE)
```

**Arguments**

x	ASEset
strand	strand to infer from
return.type	'uni' 'bi' 'tri' 'quad' 'all'
threshold.frequency	least fraction to classify (see details)
threshold.count.sample	least amount of counts to try to infer allele
inferOver	'eachSample' or 'allSamples'
allow.NA	treat NA as zero when TRUE

**Details**

threshold.frequency is the least fraction needed to classify as bi tri or quad allelic SNPs. If 'all' then all of bi tri and quad allelic SNPs will use the same threshold. Everything under the threshold will be regarded as noise. 'all' will return a matrix with snps as rows and uni bi tri and quad will be columns. For this function Anything that will return TRUE for tri-allelic will also return TRUE for uni and bi-allelic for the same SNP an Sample.

**Author(s)**

Jesper R. Gadin

**Examples**

```
data(ASEset)
i <- inferAlleles(ASEset)
```

---

inferAltAllele	<i>inferAltAllele</i>
----------------	-----------------------

---

**Description**

inference of the alternate allele based on count data

**Arguments**

x	matrix see examples
return.class	class of returned object
allele.source	'arank'
verbose	make function more talkative
...	arguments to forward to internal functions

**Details**

The inference essentially ranks all alleles and the most expressed allele not declared as reference will be inferred as the alternative allele. At the moment only inference of bi-allelic alternative alleles are available.

**Author(s)**

Jesper R. Gadin, Lasse Folkersen

**Examples**

```
#load data
data(ASEset)

alt <- inferAltAllele(ASEset)
```

---

inferGenotypes	<i>inference of genotypes from ASEset count data</i>
----------------	--

---

### Description

inference of genotypes

### Usage

```
inferGenotypes(x, strand = "*", return.class = "matrix",  
  return.allele.allowed = "bi", threshold.frequency = 0,  
  threshold.count.sample = 1)
```

### Arguments

x	ASEset
strand	strand to infer from
return.class	'matrix' or 'vector'
return.allele.allowed	vector with 'bi' 'tri' or 'quad'. 'uni' Always gets returned
threshold.frequency	least fraction to classify (see details)
threshold.count.sample	least amount of counts to try to infer allele

### Details

Often necessary information to link AI to SNPs outside coding region

### Author(s)

Jesper R. Gadin

### Examples

```
data(ASEset)  
g <- inferGenotypes(ASEset)
```

---

<code>initialize-ASEset</code>	<i>Initialize ASEset</i>
--------------------------------	--------------------------

---

## Description

Functions to construct ASEset objects

## Usage

```
ASEsetFromCountList(rowRanges, countListUnknown = NULL,
  countListPlus = NULL, countListMinus = NULL, colData = NULL,
  mapBiasExpMean = NULL, phase = NULL, aquals = NULL, verbose = FALSE,
  ...)
```

```
ASEsetFromArrays(rowRanges, countsUnknown = NULL, countsPlus = NULL,
  countsMinus = NULL, colData = NULL, mapBiasExpMean = NULL,
  phase = NULL, genotype = NULL, aquals = NULL, verbose = FALSE, ...)
```

## Arguments

<code>rowRanges</code>	A <code>GenomicRanges</code> object that contains the variants of interest
<code>countListUnknown</code>	A list where each entry is a matrix with allele counts as columns and sample counts as rows
<code>countListPlus</code>	A list where each entry is a matrix with allele counts as columns and sample counts as rows
<code>countListMinus</code>	A list where each entry is a matrix with allele counts as columns and sample counts as rows
<code>colData</code>	A <code>DataFrame</code> object containing sample specific data
<code>mapBiasExpMean</code>	A 3D array where the SNPs are in the 1st dimension, samples in the 2nd dimension and variants in the 3rd dimension.
<code>phase</code>	A matrix or an array containing phase information.
<code>aquals</code>	A 4-D array containing the count information, see details
<code>verbose</code>	Makes function more talkative
<code>...</code>	arguments passed on to <code>SummarizedExperiment</code> constructor
<code>countsUnknown</code>	An array containing the count information
<code>countsPlus</code>	An array containing the count information
<code>countsMinus</code>	An array containing the count information
<code>genotype</code>	matrix

## Details

The resulting ASEset object is based on the `RangedSummarizedExperiment` class, and will therefore inherit the same accessors and ranges operations.

If both `countListPlus` and `countListMinus` are given they will be used to calculate `countListUnknown`, which is the sum of the plus and minus strands.

countListPlus, countListMinus and countListUnknown are i.e. the outputs from the getAlleleCounts function.

aquals is new for the devel branch and will be changed slightly before the release to include better granularity.

### Value

ASEsetFromCountList returns an ASEset object.

### Note

ASEsetFromCountList requires the same input data as a RangedSummarizedExperiment, but with minimum one assay for the allele counts.

### Author(s)

Jesper R. Gadin, Lasse Folkersen

### See Also

- [RangedSummarizedExperiment](#) objects.

### Examples

```
#make example alleleCountListPlus
set.seed(42)
countListPlus <- list()
snps <- c('snp1', 'snp2', 'snp3', 'snp4', 'snp5')
for(snp in snps){
  count<-matrix(rep(0,16),ncol=4,dimnames=list(
    c('sample1', 'sample2', 'sample3', 'sample4'),
    c('A', 'T', 'G', 'C')))
  #insert random counts in two of the alleles
  for(allele in sample(c('A', 'T', 'G', 'C'),2)){
    count[,allele]<-as.integer(rnorm(4,mean=50,sd=10))
  }
  countListPlus[[snp]] <- count
}

#make example alleleCountListMinus
countListMinus <- list()
snps <- c('snp1', 'snp2', 'snp3', 'snp4', 'snp5')
for(snp in snps){
  count<-matrix(rep(0,16),ncol=4,dimnames=list(
    c('sample1', 'sample2', 'sample3', 'sample4'),
    c('A', 'T', 'G', 'C')))
  #insert random counts in two of the alleles
  for(allele in sample(c('A', 'T', 'G', 'C'),2)){
    count[,allele]<-as.integer(rnorm(4,mean=50,sd=10))
  }
  countListMinus[[snp]] <- count
}

#make example rowRanges
```

```

rowRanges <- GRanges(
  seqnames = Rle(c('chr1', 'chr2', 'chr1', 'chr3', 'chr1')),
    ranges = IRanges(1:5, width = 1, names = head(letters,5)),
    snp = paste('snp',1:5,sep='')
)
#make example colData
colData <- DataFrame(Treatment=c('ChIP', 'Input','Input','ChIP'),
  row.names=c('ind1','ind2','ind3','ind4'))

#make ASEset
a <- ASEsetFromCountList(rowRanges, countListPlus=countListPlus,
  countListMinus=countListMinus, colData=colData)

```

---

initialize-DetectedAI *Initialize DetectedAI*

---

## Description

Functions to construct DetectedAI objects

## Usage

```

DetectedAIFromArray(x = "ASEset", strand = "*",
  reference.frequency = NULL, threshold.frequency = NULL,
  threshold.count.sample = NULL, threshold.delta.frequency = NULL,
  threshold.pvalue = NULL, threshold.frequency.names = NULL,
  threshold.count.sample.names = NULL,
  threshold.delta.frequency.names = NULL, threshold.pvalue.names = NULL,
  ...)

```

## Arguments

x	ASEset
strand	set strand to detectAI over "+","-","*"
reference.frequency	frequencies of reference alleles based allele counts
threshold.frequency	logical array for frequency thresholds
threshold.count.sample	logical array for per sample allele count thresholds
threshold.delta.frequency	logical array for delta frequency thresholds.
threshold.pvalue	logical array for pvalue thresholds (max 1, min 0)
threshold.frequency.names	character vector
threshold.count.sample.names	character vector
threshold.delta.frequency.names	character vector

```
threshold.pvalue.names  
                        character vector  
...                    internal arguments
```

**Details**

produces a class container for reference bias calculations

**Author(s)**

Jesper R. Gadin, Lasse Folkersen

**Examples**

```
data(ASEset)  
a <- ASEset  
dai <- detectAI(a)
```

---

```
initialize-GlobalAnalysis  
                        Initialize GlobalAnalysis
```

---

**Description**

Functions to construct GlobalAnalysis objects

**Usage**

```
GAnalysis(x = "ASEset", ...)
```

**Arguments**

```
x                    ASEset  
...                 internal arguments
```

**Details**

produces a class container for a global analysis

**Author(s)**

Jesper R. Gadin, Lasse Folkersen

**Examples**

```
data(ASEset)  
a <- ASEset  
# gba <- gba(a)
```



---

initialize-RiskVariant  
*Initialize RiskVariant*

---

**Description**

Functions to construct RiskVariant objects

**Usage**

```
RiskVariantFromGRangesAndPhaseArray(x, phase, ...)
```

**Arguments**

x	GRanges object for the SNPs
phase	array with phaseinfo
...	internal arguments

**Details**

produces a class container for reference bias calculations

**Author(s)**

Jesper R. Gadin, Lasse Folkersen

**Examples**

```
data(ASEset)
#p <- getPhaseFromSomewhere
#rv <- RiskVariantFromGRangesAndPhaseArray(x=GRvariants, phase=p)
```

---

legendBarplot *add legend to AllelicImbalance barplot*

---

**Description**

adds a very customizable legend function for AllelicImbalance barplots.

**Usage**

```
legendBarplot(lowerLeftCorner, size, rownames, colnames, boxsize = 1,
  boxspace = 1, fgCol, bgCol, ylegendPos = 1, xlegendPos = 0.96,
  cex = 1)
```

**Arguments**

lowerLeftCorner	position of the plot to add legend to (default c(0,0))
size	scale the plot, default is 1
rownames	rownames in legend
colnames	colnames in legend
boxsize	size of each box fill
boxspace	space inbetween the box fill
fgCol	color for allele1
bgCol	color for allele2
ylegendPos	placement of the legend within the plot for y
xlegendPos	placement of the legend within the plot for x
cex	size of legend text

**Details**

the function is preferably called from within the AllelicImbalance barplot method.

**Author(s)**

Jesper R. Gadin

**Examples**

```
#code placeholders
#< create a barplot with legend >
#< add legend >
```

---

LinkVariantAlmlof-class

*LinkVariantAlmlof class*

---

**Description**

Object that holds results from AI detection.

**Usage**

```
pvalue(x, ...)
```

```
## S4 method for signature 'LinkVariantAlmlof'
pvalue(x)
```

**Arguments**

x	LinkVariantAlmlof object
...	pass arguments to internal functions

**Details**

The LinkVariantAlmlof-class contains

**Author(s)**

Jesper R. Gadin, Lasse Folkersen

**Examples**

```
#some code
```

---

LinkVariantAlmlof-plot

*plot LinkVariantAlmlof objects*

---

**Description**

plot an object of type LinkVariantAlmlof

**Usage**

```
plot(x, y, ...)
```

```
## S4 method for signature 'LinkVariantAlmlof,ANY'
```

```
plot(x, y, ...)
```

**Arguments**

x	LinkVariantAlmlof object
y	not used
...	pass on arguments to internal methods

**Author(s)**

Jesper R. Gadin, Lasse Folkersen

**Examples**

```
data(ASEset)
a <- ASEset
# Add phase
set.seed(1)
p1 <- matrix(sample(c(1,0),replace=TRUE, size=nrow(a)*ncol(a)),nrow=nrow(a), ncol(a))
p2 <- matrix(sample(c(1,0),replace=TRUE, size=nrow(a)*ncol(a)),nrow=nrow(a), ncol(a))
p <- matrix(paste(p1,sample(c("|", "|", "/"), size=nrow(a)*ncol(a), replace=TRUE), p2, sep=""),
nrow=nrow(a), ncol(a))

phase(a) <- p
```

```

#add alternative allele information
mcols(a)[["alt"]] <- inferAltAllele(a)

#init risk variants
p.ar <- phaseMatrix2Array(p)
rv <- RiskVariantFromGRangesAndPhaseArray(x=GRvariants, phase=p.ar)

#colnames has to be samea and same order in ASEset and RiskVariant
colnames(a) <- colnames(rv)

# in this example each and every snp in the ASEset defines a region
r1 <- granges(a)

# in this example two overlapping subsets of snps in the ASEset defines the region
r2 <- split(granges(a)[c(1,2,2,3)],c(1,1,2,2))

# link variant almlf (lva)
lv1 <- lva(a, rv, r1)
lv2 <- lva(a, rv, r2)
plot(lv2[1])

```

---

lva

*lva*


---

## Description

make an almlf regression for arrays

## Usage

```
lva(x, ...)
```

```
## S4 method for signature 'ASEset'
lva(x, rv, region, settings = list(),
    return.class = "LinkVariantAlmlf", verbose = FALSE, ...)
```

## Arguments

x	ASEset object with phase and 'ref'/'alt' allele information
...	arguments to forward to internal functions
rv	RiskVariant object with phase and 'ref'/'alt' allele information
region	RiskVariant object with phase and alternative allele information
settings	RiskVariant object with phase and alternative allele information
return.class	'LinkVariantAlmlf' (more options in future)
verbose	logical, if set TRUE, then function will be more talkative

## Details

internal method that takes one array with results from regionSummary and one matrix with group information for each risk SNP (based on phase)

**Author(s)**

Jesper R. Gadin, Lasse Folkersen

**Examples**

```

data(ASEset)
a <- ASEset
# Add phase
set.seed(1)
p1 <- matrix(sample(c(1,0),replace=TRUE, size=nrow(a)*ncol(a)),nrow=nrow(a), ncol(a))
p2 <- matrix(sample(c(1,0),replace=TRUE, size=nrow(a)*ncol(a)),nrow=nrow(a), ncol(a))
p <- matrix(paste(p1,sample(c("|","|","/"), size=nrow(a)*ncol(a), replace=TRUE), p2, sep=""),
nrow=nrow(a), ncol(a))

phase(a) <- p

#add alternative allele information
mcols(a)[["alt"]] <- inferAltAllele(a)

#init risk variants
p.ar <- phaseMatrix2Array(p)
rv <- RiskVariantFromGRangesAndPhaseArray(x=GRvariants, phase=p.ar)

#colnames has to be samea and same order in ASEset and RiskVariant
colnames(a) <- colnames(rv)

# in this example each and every snp in the ASEset defines a region
r1 <- granges(a)

#use GRangesList to merge and use regions defined by each element of the
#GRangesList
r1b <- GRangesList(r1)
r1c <- GRangesList(r1, r1)

# in this example two overlapping subsets of snps in the ASEset defines the region
r2 <- split(granges(a)[c(1,2,2,3)],c(1,1,2,2))

# link variant almlf (lva)
lva(a, rv, r1)
lva(a, rv, r1b)
lva(a, rv, r1c)
lva(a, rv, r2)

```

---

lva.internal

*lva.internal*


---

**Description**

make an almlf regression for arrays (internal function)

**Usage**

```
lva.internal(x, ...)

## S4 method for signature 'array'
lva.internal(x, grp, element = 3, ...)
```

**Arguments**

x	regionSummary array phased for maternal allele
...	arguments to forward to internal functions
grp	group 1-3 (1 for 0:0, 2 for 1:0 or 0:1, and 3 for 1:1)
element	which column in x contains the values to use with lm.

**Details**

internal method that takes one array with results from regionSummary and one matrix with group information for each risk SNP (based on phase). Input and output objects can change format slightly in future.

**Author(s)**

Jesper R. Gadin, Lasse Folkersen

**Examples**

```
data(ASEset)
a <- ASEset
# Add phase
set.seed(1)
p1 <- matrix(sample(c(1,0),replace=TRUE, size=nrow(a)*ncol(a)),nrow=nrow(a), ncol(a))
p2 <- matrix(sample(c(1,0),replace=TRUE, size=nrow(a)*ncol(a)),nrow=nrow(a), ncol(a))
p <- matrix(paste(p1,sample(c("|","|","/"), size=nrow(a)*ncol(a), replace=TRUE), p2, sep=""),
nrow=nrow(a), ncol(a))

phase(a) <- p

#add alternative allele information
mcols(a)[["alt"]] <- inferAltAllele(a)

# in this example two overlapping subsets of snps in the ASEset defines the region
region <- split(granges(a)[c(1,2,2,3)], c(1,1,2,2))
rs <- regionSummary(a, region, return.class="array", return.meta=FALSE)

# use (change to generated riskSNP phase later)
phs <- array(c(phase(a,return.class="array")[1,,c(1, 2)],
  phase(a,return.class="array")[2,,c(1, 2)]), dim=c(20,2,2))
grp <- matrix(2, nrow=dim(phs)[1], ncol=dim(phs)[2])
grp[(phs[,,1] == 0) & (phs[,,2] == 0)] <- 1
grp[(phs[,,1] == 1) & (phs[,,2] == 1)] <- 3
#only use mean.fr at the moment, which is col 3
lva.internal(assays(rs)[["rs1"]], grp, 3)
```

---

makeMaskedFasta	<i>makes masked fasta reference</i>
-----------------	-------------------------------------

---

### Description

Replaces all selected positions in a fasta file with the character N

### Usage

```
makeMaskedFasta(fastaIn, ...)  
  
## S4 method for signature 'character'  
makeMaskedFasta(fastaIn, fastaOut, posToReplace,  
  splitOnSeqlevels = TRUE, verbose = TRUE)
```

### Arguments

fastaIn	character string of the path for the fasta file to be used
...	arguments to pass on
fastaOut	character string of the path for the masked fasta file (no extension)
posToReplace	GRanges object with the genomic ranges to replace
splitOnSeqlevels	write on file for each seqlevel to save memory
verbose	makes function more talkative

### Author(s)

Jesper R. Gadin

### Examples

```
data(ASEset.sim)  
gr <- rowRanges(ASEset.sim)  
fastaIn <- system.file('extdata/hg19.chr17.subset.fa', package='AllelicImbalance')  
makeMaskedFasta(fastaIn=fastaIn, fastaOut="fastaOut",posToReplace=gr)
```

---

mapBiasRef	<i>mapBias for reference allele</i>
------------	-------------------------------------

---

### Description

Create a matrix of bias for the reference allele

**Usage**

```
mapBiasRef(x, ...)

## S4 method for signature 'ASEset'
mapBiasRef(x)
```

**Arguments**

```
x          ASEset object
...        internal arguments
```

**Details**

select the expected frequency for the reference allele

**Author(s)**

Jesper R. Gadin, Lasse Folkersen

**Examples**

```
#load example data
data(ASEset)
a <- ASEset

mat <- mapBiasRef(a)
```

---

minCountFilt

*minCountFilt methods*


---

**Description**

filter on minCountFilt snps

**Usage**

```
minCountFilt(x, ...)

## S4 method for signature 'ASEset'
minCountFilt(x, strand = "*", threshold.counts = 1,
  sum = "all", replace.with = "zero", return.class = "ASEset")
```

**Arguments**

```
x          ASEset object
...        internal param
strand     strand to infer from
threshold.counts
            cutoff for read counts (see details)
```



```

sum          'each' or 'all'
replace.with only option 'zero'
return.class 'ASEset', 'array' or 'matrix'

```

### Details

Description info here

### Author(s)

Jesper R. Gadin, Lasse Folkersen

### Examples

```

#load example data
data(ASEset)
a <- ASEset

minCountFilt(a)

```

---

minFreqFilt	<i>minFreqFilt methods</i>
-------------	----------------------------

---

### Description

filter on minFreqFilt snps

### Usage

```

minFreqFilt(x, ...)

## S4 method for signature 'ASEset'
minFreqFilt(x, strand = "*", threshold.frequency = 0.1,
  replace.with = "zero", return.class = "ASEset", sum = "all")

```

### Arguments

```

x          ASEset object
...        internal param
strand     strand to infer from
threshold.frequency
            least fraction to classify (see details)
replace.with only option 'zero'
return.class 'ASEset', 'array' or 'matrix'
sum         'each' or 'all'

```

### Details

Description info here

**Author(s)**

Jesper R. Gadin, Lasse Folkersen

**Examples**

```
#load example data
data(ASEset)
a <- ASEset

minFreqFilt(a)
```

---

multiAllelicFilt      *multi-allelic filter methods*

---

**Description**

filter on multiallelic snps

**Usage**

```
multiAllelicFilt(x, ...)

## S4 method for signature 'ASEset'
multiAllelicFilt(x, strand = "*",
  threshold.count.sample = 10, threshold.frequency = 0.1,
  filterOver = "eachSample")
```

**Arguments**

x	ASEset object
...	internal param
strand	strand to infer from
threshold.count.sample	least amount of counts to try to infer allele
threshold.frequency	least fraction to classify (see details)
filterOver	'eachSample' or 'allSamples'

**Details**

based on the allele counts for all four variants A, T, G and C and returns true if there is counts enough suggesting a third or more alleles. The sensitivity can be specified using 'threshold.count.sample' and 'threshold.frequency'.

**Author(s)**

Jesper R. Gadin, Lasse Folkersen

## Examples

```
#load example data
data(ASEset)
a <- ASEset

multiAllelicFilt(a)
```

---

phase2genotype	<i>phase2genotype</i>
----------------	-----------------------

---

## Description

Convert the phase from the internally stored phase, ref and alt information

## Usage

```
phase2genotype(x, ...)

## S4 method for signature 'array'
phase2genotype(x, ref, alt, return.class = "matrix", ...)
```

## Arguments

x	array see examples
...	pass on additional param
ref	reference allele vector
alt	alternative allele vector
return.class	'matrix' or 'array'

## Details

To not introduce redundant information in the ASEset object, the genotype matrix is accessed from the phase matrix, which together with ref and alt allele information contains the same information(not taken into account three-allelic or more SNPs).

The genotype matrix retrieved from an ASEset object can differ from the genotype matrix stored in the object if reference and alternative alleles were not used or has changed since the phase genotype matrix was stored. Basically, it is preferable to provide reference and alternative information when storing the genotype matrix.

If possible, it is better to not use a genotype matrix, but instead relying completely on storing a phase matrix(or array) together with reference and alternative allele information.

## Author(s)

Jesper R. Gadin, Lasse Folkersen

**Examples**

```
#load example data
data(ASEset)
data(genomatrix)
p <- genotype2phase(genomatrix, ref(ASEset), return.class="array")
ref <- ref(ASEset)
alt <- inferAltAllele(ASEset)

gt <- phase2genotype(p, ref, alt, return.class="matrix")
```

---

```
phaseArray2phaseMatrix
phaseArray2phaseMatrix
```

---

**Description**

used to convert the phase from the visually friendly matrix to array.

**Usage**

```
phaseArray2phaseMatrix(x, ...)

## S4 method for signature 'array'
phaseArray2phaseMatrix(x, ...)
```

**Arguments**

x	array see examples
...	arguments to forward to internal functions

**Details**

A more effective way of store the phase data in the ASEset object

**Author(s)**

Jesper R. Gadin, Lasse Folkersen

**Examples**

```
#load data
data(ASEset)
a <- ASEset

#example phase matrix
p1 <- matrix(sample(c(1,0),replace=TRUE, size=nrow(a)*ncol(a)),nrow=nrow(a), ncol(a))
p2 <- matrix(sample(c(1,0),replace=TRUE, size=nrow(a)*ncol(a)),nrow=nrow(a), ncol(a))
p <- matrix(paste(p1,sample(c("|","|","/"), size=nrow(a)*ncol(a), replace=TRUE), p2, sep=""),
nrow=nrow(a), ncol(a))
```

```
ar <- phaseMatrix2Array(p)

#Convert back
mat <- phaseArray2phaseMatrix(ar)
```

---

phaseMatrix2Array      *phaseMatrix2Array*

---

## Description

used to convert the phase from the visually friendly matrix to array.

## Usage

```
phaseMatrix2Array(x, ...)

## S4 method for signature 'matrix'
phaseMatrix2Array(x, dimnames = NULL, ...)
```

## Arguments

x	matrix see examples
...	arguments to forward to internal functions
dimnames	list with dimnames

## Details

A more effective way of store the phase data in the ASEset object

## Author(s)

Jesper R. Gadin, Lasse Folkersen

## Examples

```
#load data
data(ASEset)
a <- ASEset

#example phase matrix
p1 <- matrix(sample(c(1,0),replace=TRUE, size=nrow(a)*ncol(a)),nrow=nrow(a), ncol(a))
p2 <- matrix(sample(c(1,0),replace=TRUE, size=nrow(a)*ncol(a)),nrow=nrow(a), ncol(a))
p <- matrix(paste(p1,sample(c("|",",","/"), size=nrow(a)*ncol(a), replace=TRUE), p2, sep=""),
nrow=nrow(a), ncol(a))

ar <- phaseMatrix2Array(p)
```

---

randomRef	<i>Random ref allele from genotype</i>
-----------	--

---

### Description

Create a vector of random reference alleles

### Usage

```
randomRef(x, ...)  
  
## S4 method for signature 'ASEset'  
randomRef(x, source = "alleleCounts", ...)
```

### Arguments

x	ASEset object
...	internal arguments
source	'alleleCounts'

### Details

Randomly shuffles which of the two alleles for each genotype that is indicated as reference allele, based on either allele count information or previous ref and alt alleles.

When the source is 'alleleCounts', the two most expressed alleles are taken as reference and alternative allele.

### Author(s)

Jesper R. Gadin, Lasse Folkersen

### Examples

```
#load example data  
data(ASEset.sim)  
a <- ASEset.sim  
  
ref(a) <- randomRef(a, source = 'alleleCounts')
```

---

reads	<i>reads object</i>
-------	---------------------

---

**Description**

This data set corresponds to the BAM-file data import illustrated in the vignette. The data set consists of a chromosome 17 region from 20 RNA-seq experiments of HapMap samples.

**Author(s)**

Jesper R. Gadin, Lasse Folkersen

**References**

Montgomery SB et al. Transcriptome genetics using second generation sequencing in a Caucasian population. Nature. 2010 Apr 1;464(7289):773-7.

**See Also**

- The [GRvariants](#) which is another example object

**Examples**

```
##load eample data (Not Run)
#data(reads)
```

---

refAllele	<i>Reference allele</i>
-----------	-------------------------

---

**Description**

Extract the allele based on SNP location from the reference fasta file

**Usage**

```
refAllele(x, fasta)
```

**Arguments**

x	ASEset object
fasta	path to fasta file, index should be located in the same folder

**Details**

The alleles will be placed in the rowRanges() meta column 'ref'

**Author(s)**

Jesper R. Gadin, Lasse Folkersen

**Examples**

```
#load example data
data(ASEset.sim)

fasta <- system.file('extdata/hg19.chr17.subset.fa', package='AllelicImbalance')
a <- refAllele(ASEset.sim,fasta=fasta)
```

---

regionSummary	<i>regionSummary</i>
---------------	----------------------

---

**Description**

Gives a summary of AI-consistency for a transcript

**Usage**

```
regionSummary(x, ...)

## S4 method for signature 'ASEset'
regionSummary(x, region, strand = "*",
  return.class = "RegionSummary", ...)
```

**Arguments**

x	ASEset object
...	arguments to forward to internal functions
region	to summarize over, the object can be a GRanges, GRangesList
strand	can be "+", "-" or "*"
return.class	"array" or "list".

**Details**

From a given set of e.g. transcripts exon ranges the function will return a summary for the sum of all exons. Phase information, reference and alternative allele is required.

A limitation comes to the strand-specificness. At the moment it is not possible to call over more than one strand type using the strands in region. This will be improved before going to release.

to calculate the direction and binomial p-values of AI the mapbias stored in the ASEset is used. see `?mapBias`.

**Author(s)**

Jesper R. Gadin, Lasse Folkersen



**Examples**

```

data(ASEset)
a <- ASEset
# Add phase
set.seed(1)
p1 <- matrix(sample(c(1,0),replace=TRUE, size=nrow(a)*ncol(a)),nrow=nrow(a), ncol(a))
p2 <- matrix(sample(c(1,0),replace=TRUE, size=nrow(a)*ncol(a)),nrow=nrow(a), ncol(a))
p <- matrix(paste(p1,sample(c("|","|","/"), size=nrow(a)*ncol(a), replace=TRUE), p2, sep=""),
nrow=nrow(a), ncol(a))

phase(a) <- p

#add alternative allele information
mcols(a)[["alt"]] <- inferAltAllele(a)

# in this example each and all snps in the ASEset defines the region
region <- granges(a)
t <- regionSummary(a, region)

# in this example two overlapping subsets of snps in the ASEset defines the region
region <- split(granges(a)[c(1,2,2,3)],c(1,1,2,2))
t <- regionSummary(a, region)

```

---

RegionSummary-class     *RegionSummary class*

---

**Description**

Object that holds results from the regionSummary method

**Usage**

```

sumnames(x, ...)

## S4 method for signature 'RegionSummary'
sumnames(x)

basic(x, ...)

## S4 method for signature 'RegionSummary'
basic(x)

```

**Arguments**

x                    RegionSummary object  
...                    pass arguments to internal functions

**Details**

The RegionSummary-class objects contains summaries for specified regions

**Author(s)**

Jesper R. Gadin, Lasse Folkersen

**Examples**

```
#some code
```

---

RiskVariant-class	<i>RiskVariant class</i>
-------------------	--------------------------

---

**Description**

Object that holds results from AI detection.

**Usage**

```
## S4 method for signature 'RiskVariant'
ref(x)

## S4 replacement method for signature 'RiskVariant,ANY'
ref(x) <- value

## S4 method for signature 'RiskVariant'
alt(x)

## S4 replacement method for signature 'RiskVariant,ANY'
alt(x) <- value

## S4 method for signature 'RiskVariant'
phase(x, return.class = "matrix")

## S4 replacement method for signature 'RiskVariant'
phase(x) <- value
```

**Arguments**

x	RiskVariant object or list of RiskVariants
value	argument used for replacement
return.class	type of class returned eg. "list" or "array".
...	pass arguments to internal functions

**Details**

The RiskVariant-class contains

**Author(s)**

Jesper R. Gadin, Lasse Folkersen

## Examples

```
#some code
```

---

```
scanForHeterozygotes.old  
    scanForHeterozygotes-old
```

---

## Description

Identifies the positions of SNPs found in BamGR reads.

## Usage

```
scanForHeterozygotes.old(BamList, minimumReadsAtPos = 20,  
    maximumMajorAlleleFrequency = 0.9, minimumBiAllelicFrequency = 0.9,  
    maxReads = 15000, verbose = TRUE)
```

## Arguments

BamList	A GAlignmentsList object
minimumReadsAtPos	minimum number of reads required to call a SNP at a given position
maximumMajorAlleleFrequency	maximum frequency allowed for the most common allele. Setting this parameter lower will minimise the SNP calls resulting from technical read errors, at the cost of missing loci with potential strong ASE
minimumBiAllelicFrequency	minimum frequency allowed for the first and second most common allele. Setting a Lower value for this parameter will minimise the identification of loci with three or more alleles in one sample. This is useful if sequencing errors are suspected to be common.
maxReads	max number of reads of one list-element allowed
verbose	logical indicating if process information should be displayed

## Details

This function scans all reads stored in a GAlignmentsList for possible heterozygote positions. The user can balance the sensitivity of the search by modifying the minimumReadsAtPos, maximumMajorAlleleFrequency and minimumBiAllelicFrequency arguments.

## Value

scanForHeterozygotes.old returns a GRanges object with the SNPs for the BamList object that was used as input.

## Author(s)

Jesper R. Gadin, Lasse Folkersen

**See Also**

- The [getAlleleCounts](#) which is a function that count the number of reads overlapping a site.

**Examples**

```
data(reads)
s <- scanForHeterozygotes.old(reads, verbose=FALSE)
```

# Index

- \*Topic **ASEDAnnotationTrack**
  - ASEset-gviztrack, 17
- \*Topic **ASEsetFromCountList**
  - initialize-ASEset, 53
- \*Topic **ASEset**
  - ASEset-class, 9
  - ASEsetFromBam, 22
  - DetectedAI-class, 31
  - GlobalAnalysis-class, 44
  - initialize-ASEset, 53
- \*Topic **CDS**
  - annotation-wrappers, 4
- \*Topic **CoverageDataTrack**
  - ASEset-gviztrack, 17
- \*Topic **LinkVariantAlmlof**
  - LinkVariantAlmlof-class, 58
- \*Topic **RegionSummary**
  - RegionSummary-class, 73
- \*Topic **RiskVariant**
  - RiskVariant-class, 74
- \*Topic **SNP**
  - ASEset-scanForHeterozygotes, 20
  - getAlleleCounts, 38
  - getSnpIdFromLocation, 43
  - scanForHeterozygotes.old, 75
- \*Topic **allelecount**
  - countAllelesFromBam, 26
- \*Topic **allele**
  - getAlleleQuality, 39
- \*Topic **annotation**
  - annotation-wrappers, 4
  - annotationBarplot, 6
- \*Topic **bam**
  - import-bam, 47
  - import-bam-2, 48
- \*Topic **barplot**
  - annotationBarplot, 6
  - ASEset-barplot, 7
  - barplot-lattice-support, 23
  - legendBarplot, 57
- \*Topic **bcf**
  - import-bcf, 49
- \*Topic **bias**
  - getDefaultMapBiasExpMean, 42
  - initialize-DetectedAI, 55
  - initialize-RiskVariant, 57
- \*Topic **binomial**
  - binom.test, 24
- \*Topic **chi-square**
  - chisq.test, 25
- \*Topic **class**
  - ASEset-class, 9
  - DetectedAI-class, 31
  - GlobalAnalysis-class, 44
  - LinkVariantAlmlof-class, 58
  - RegionSummary-class, 73
  - RiskVariant-class, 74
- \*Topic **counting**
  - countAllelesFromBam, 26
- \*Topic **count**
  - getAlleleCounts, 38
- \*Topic **coverage**
  - coverageMatrixListFromGAL, 27
- \*Topic **data**
  - ASEset.old, 21
  - ASEset.sim, 22
  - genomatrix, 37
  - GRvariants, 45
  - reads, 71
- \*Topic **detection**
  - detectAI, 29
- \*Topic **example**
  - ASEset.old, 21
  - ASEset.sim, 22
  - GRvariants, 45
  - reads, 71
- \*Topic **exons**
  - annotation-wrappers, 4
- \*Topic **fasta**
  - makeMaskedFasta, 63
- \*Topic **filter**
  - ASEset-filters, 14
  - minCountFilt, 64
  - minFreqFilt, 65
  - multiAllelicFilt, 66
- \*Topic **gbarplot**

- ASEset-gbarplot, 15
  - \*Topic **genes**
    - annotation-wrappers, 4
    - getAreaFromGeneNames, 41
  - \*Topic **genotype**
    - genomatrix, 37
  - \*Topic **global**
    - gba, 36
    - initialize-GlobalAnalysis, 56
  - \*Topic **glocationplot**
    - ASEset-glocationplot, 16
  - \*Topic **heterozygote**
    - ASEset-scanForHeterozygotes, 20
    - scanForHeterozygotes.old, 75
  - \*Topic **hist**
    - histplot, 45
  - \*Topic **implode**
    - implodeList.old, 46
  - \*Topic **import**
    - import-bam, 47
    - import-bam-2, 48
    - import-bcf, 49
  - \*Topic **infer**
    - inferAlleles, 50
    - inferGenotypes, 52
  - \*Topic **legend**
    - legendBarplot, 57
  - \*Topic **list**
    - DetectedAI-plot, 32
    - DetectedAI-summary, 34
  - \*Topic **locationplot**
    - ASEset-locationplot, 18
  - \*Topic **locations**
    - getAreaFromGeneNames, 41
  - \*Topic **mapbias**
    - defaultMapBias, 28
    - initialize-DetectedAI, 55
    - initialize-RiskVariant, 57
    - mapBiasRef, 63
    - randomRef, 70
    - refAllele, 71
  - \*Topic **mapping**
    - getDefaultMapBiasExpMean, 42
  - \*Topic **masked**
    - makeMaskedFasta, 63
  - \*Topic **object**
    - ASEset.old, 21
    - ASEset.sim, 22
    - GRvariants, 45
    - reads, 71
  - \*Topic **package**
    - AllelicImbalance-package, 3
  - \*Topic **phase**
    - defaultPhase, 29
    - fractionPlotDf, 35
    - genotype2phase, 37
    - inferAltAllele, 51
    - lva, 60
    - lva.internal, 61
    - phase2genotype, 67
    - phaseArray2phaseMatrix, 68
    - phaseMatrix2Array, 69
  - \*Topic **plotDf**
    - fractionPlotDf, 35
  - \*Topic **plot**
    - histplot, 45
    - LinkVariantAlmlof-plot, 59
  - \*Topic **quality**
    - getAlleleQuality, 39
  - \*Topic **refBias**
    - initialize-DetectedAI, 55
    - initialize-RiskVariant, 57
  - \*Topic **reference**
    - makeMaskedFasta, 63
    - refAllele, 71
  - \*Topic **rs-id**
    - getSnpIdFromLocation, 43
  - \*Topic **scan**
    - ASEset-scanForHeterozygotes, 20
    - scanForHeterozygotes.old, 75
  - \*Topic **summary**
    - regionSummary, 72
  - \*Topic **test**
    - binom.test, 24
    - chisq.test, 25
  - \*Topic **transcripts**
    - annotation-wrappers, 4
  - \*Topic **wrapper**
    - gba, 36
- alleleCounts (ASEset-class), 9
  - alleleCounts, ASEset-method (ASEset-class), 9
  - alleleCounts<- (ASEset-class), 9
  - alleleCounts<- , ASEset-method (ASEset-class), 9
  - AllelicImbalance (AllelicImbalance-package), 3
  - AllelicImbalance-package, 3
  - alt (ASEset-class), 9
  - alt, ASEset-method (ASEset-class), 9
  - alt, RiskVariant-method (RiskVariant-class), 74
  - alt<- (ASEset-class), 9

alt<- ,ASEset,ANY-method (ASEset-class),  
     9  
 alt<- ,RiskVariant,ANY-method  
     (RiskVariant-class), 74  
 altExist (ASEset-class), 9  
 altExist,ASEset-method (ASEset-class), 9  
 annotation-wrappers, 4  
 annotationBarplot, 6  
 aquals (ASEset-class), 9  
 aquals,ASEset-method (ASEset-class), 9  
 aquals<- (ASEset-class), 9  
 aquals<- ,ASEset-method (ASEset-class), 9  
 arank (ASEset-class), 9  
 arank,ASEset-method (ASEset-class), 9  
 ASEDAnnotationTrack (ASEset-gviztrack),  
     17  
 ASEDAnnotationTrack,ASEset-method  
     (ASEset-gviztrack), 17  
 ASEset, 9, 15, 17–19, 24, 25  
 ASEset (ASEset-class), 9  
 ASEset-barplot, 7  
 ASEset-class, 9  
 ASEset-filters, 14  
 ASEset-gbarplot, 15  
 ASEset-glocationplot, 16  
 ASEset-gviztrack, 17  
 ASEset-locationplot, 18  
 ASEset-scanForHeterozygotes, 20  
 ASEset.old, 21  
 ASEset.sim, 22  
 ASEsetFromArrays (initialize-ASEset), 53  
 ASEsetFromBam, 22  
 ASEsetFromBam,GRanges-method  
     (ASEsetFromBam), 22  
 ASEsetFromCountList  
     (initialize-ASEset), 53  
  
 barplot, 4, 12, 15, 19  
 barplot (ASEset-barplot), 7  
 barplot,ASEset-method (ASEset-barplot),  
     7  
 barplot-lattice-support, 23  
 barplotLatticeCounts  
     (barplot-lattice-support), 23  
 barplotLatticeFraction  
     (barplot-lattice-support), 23  
 basic (RegionSummary-class), 73  
 basic,RegionSummary-method  
     (RegionSummary-class), 73  
 binom.test, 24, 25  
 binom.test,ASEset-method (binom.test),  
     24

chisq.test, 4, 24, 25  
 chisq.test,ASEset-method (chisq.test),  
     25  
 countAllelesFromBam, 26  
 countAllelesFromBam,GRanges-method  
     (countAllelesFromBam), 26  
 countsPerSample (ASEset-class), 9  
 countsPerSample,ASEset-method  
     (ASEset-class), 9  
 countsPerSnp (ASEset-class), 9  
 countsPerSnp,ASEset-method  
     (ASEset-class), 9  
 CoverageDataTrack (ASEset-gviztrack), 17  
 CoverageDataTrack,ASEset-method  
     (ASEset-gviztrack), 17  
 coverageMatrixListFromGAL, 27  
 coverageMatrixListFromGAL,GAlignmentsList-method  
     (coverageMatrixListFromGAL), 27  
  
 defaultMapBias, 28  
 defaultMapBias,ASEset-method  
     (defaultMapBias), 28  
 defaultPhase, 29  
 defaultPhase,numeric-method  
     (defaultPhase), 29  
 detectAI, 29  
 detectAI,ASEset-method (detectAI), 29  
 DetectedAI (DetectedAI-class), 31  
 DetectedAI-class, 31  
 DetectedAI-method (DetectedAI-class), 31  
 DetectedAI-plot, 32  
 DetectedAI-summary, 34  
 detectedAI\_vs\_threshold\_variable\_multigraph\_plot  
     (DetectedAI-plot), 32  
 detectedAI\_vs\_threshold\_variable\_multigraph\_plot,DetectedAI-method  
     (DetectedAI-plot), 32  
 detectedAI\_vs\_threshold\_variable\_plot  
     (DetectedAI-plot), 32  
 detectedAI\_vs\_threshold\_variable\_plot,DetectedAI-method  
     (DetectedAI-plot), 32  
 detectedAI\_vs\_threshold\_variable\_summary  
     (DetectedAI-summary), 34  
 detectedAI\_vs\_threshold\_variable\_summary,DetectedAI-method  
     (DetectedAI-summary), 34  
 DetectedAIFromArray  
     (initialize-DetectedAI), 55  
  
 fraction (ASEset-class), 9  
 fraction,ASEset-method (ASEset-class), 9  
 fractionPlotDf, 35  
 fractionPlotDf,ASEset-method  
     (fractionPlotDf), 35  
 frequency (ASEset-class), 9

- frequency, ASEset-method (ASEset-class), 9  
 frequency\_vs\_threshold\_variable\_multigraph\_plot (DetectedAI-plot), 32  
 frequency\_vs\_threshold\_variable\_multigraph\_plot (DetectedAI-plot), 32  
 frequency\_vs\_threshold\_variable\_plot (DetectedAI-plot), 32  
 frequency\_vs\_threshold\_variable\_plot, DetectedAI-class (DetectedAI-plot), 32  
 frequency\_vs\_threshold\_variable\_plot, DetectedAI-method (DetectedAI-plot), 32  
 frequency\_vs\_threshold\_variable\_summary (DetectedAI-summary), 34  
 frequency\_vs\_threshold\_variable\_summary, DetectedAI-method (DetectedAI-summary), 34  
  
 GAlignmentsList, 39  
 GAnalysis (initialize-GlobalAnalysis), 56  
 gba, 36  
 gba, character-method (gba), 36  
 gbarplot, 16  
 gbarplot (ASEset-gbarplot), 15  
 gbarplot, ASEset-method (ASEset-gbarplot), 15  
 genomatrix, 37  
 genotype (ASEset-class), 9  
 genotype, ASEset-method (ASEset-class), 9  
 genotype2phase, 37  
 genotype2phase, matrix-method (genotype2phase), 37  
 genotype<- (ASEset-class), 9  
 genotype<-, ASEset-method (ASEset-class), 9  
 getAlleleCounts, 16, 19, 21, 38, 49, 76  
 getAlleleCounts, GAlignmentsList-method (getAlleleCounts), 38  
 getAlleleQuality, 39  
 getAlleleQuality, GAlignmentsList-method (getAlleleQuality), 39  
 getAnnotationDataFrame (annotation-wrappers), 4  
 getAreaFromGeneNames, 41  
 getAreaFromGeneNames, character-method (getAreaFromGeneNames), 41  
 getCDSFromAnnotation (annotation-wrappers), 4  
 getCDSVector (annotation-wrappers), 4  
 getDefaultMapBiasExpMean, 42  
 getDefaultMapBiasExpMean, ANY-method (getDefaultMapBiasExpMean), 42  
 getDefaultMapBiasExpMean, list-method (getDefaultMapBiasExpMean), 42  
 getDefaultMapBiasExpMean3D (getDefaultMapBiasExpMean), 42  
 getDefaultMapBiasExpMean3D, ANY-method (getDefaultMapBiasExpMean), 42  
 getExonsFromAnnotation (annotation-wrappers), 4  
 getClassVector (annotation-wrappers), 4  
 getGenesFromAnnotation (annotation-wrappers), 4  
 getGenesVector (annotation-wrappers), 4  
 getSnidFromLocation, 43  
 getSnidFromLocation, GRanges-method (getSnidFromLocation), 43  
 getTranscriptsFromAnnotation (annotation-wrappers), 4  
 getTranscriptsVector (annotation-wrappers), 4  
 GlobalAnalysis (GlobalAnalysis-class), 44  
 GlobalAnalysis-class, 44  
 GlobalAnalysis-method (GlobalAnalysis-class), 44  
 glocationplot (ASEset-glocationplot), 16  
 glocationplot, ASEset-method (ASEset-glocationplot), 16  
 GRvariants, 45, 71  
  
 hetFilt (ASEset-filters), 14  
 hetFilt, ASEset-method (ASEset-filters), 14  
 hist (histplot), 45  
 hist, ASEset-method (histplot), 45  
 hist, ReferenceBias-method (histplot), 45  
 histplot, 45  
  
 impBamGAL (import-bam), 47  
 impBamGAL, character-method (import-bam), 47  
 impBamGRL (import-bam-2), 48  
 impBcfGR (import-bcf), 49  
 impBcfGR, character-method (import-bcf), 49  
 impBcfGRL (import-bcf), 49  
 impBcfGRL, character-method (import-bcf), 49  
 implodeList.old, 46  
 import-bam, 47  
 import-bam-2, 48  
 import-bcf, 49  
 inferAlleles, 50



- inferAlleles, ASEset-method  
(inferAlleles), 50
- inferAltAllele, 51
- inferAltAllele, ASEset-method  
(inferAltAllele), 51
- inferGenotypes, 52
- inferGenotypes, ASEset-method  
(inferGenotypes), 52
- initialize-ASEset, 53
- initialize-DetectedAI, 55
- initialize-GlobalAnalysis, 56
- initialize-RiskVariant, 57
- legendBarplot, 57
- LinkVariantAlmlof  
(LinkVariantAlmlof-class), 58
- LinkVariantAlmlof-class, 58
- LinkVariantAlmlof-method  
(LinkVariantAlmlof-class), 58
- LinkVariantAlmlof-plot, 59
- locationplot, 12
- locationplot (ASEset-locationplot), 18
- locationplot, ASEset-method  
(ASEset-locationplot), 18
- lva, 60
- lva, array-method (lva), 60
- lva, ASEset-method (lva), 60
- lva.internal, 61
- lva.internal, array-method  
(lva.internal), 61
- makeMaskedFasta, 63
- makeMaskedFasta, character-method  
(makeMaskedFasta), 63
- mapBias (ASEset-class), 9
- mapBias, ASEset-method (ASEset-class), 9
- mapBias<- (ASEset-class), 9
- mapBias<-, ASEset-method (ASEset-class),  
9
- mapBiasRef, 63
- mapBiasRef, ASEset-method (mapBiasRef),  
63
- maternalAllele (ASEset-class), 9
- maternalAllele, ASEset-method  
(ASEset-class), 9
- minCountFilt, 64
- minCountFilt, ASEset-method  
(minCountFilt), 64
- minFreqFilt, 65
- minFreqFilt (minFreqFilt), 65
- minFreqFilt, ASEset-method  
(minFreqFilt), 65
- multiAllelicFilt, 66
- multiAllelicFilt, ASEset-method  
(multiAllelicFilt), 66
- paternalAllele (ASEset-class), 9
- paternalAllele, ASEset-method  
(ASEset-class), 9
- phase (ASEset-class), 9
- phase, ASEset-method (ASEset-class), 9
- phase, RiskVariant-method  
(RiskVariant-class), 74
- phase2genotype, 67
- phase2genotype, array-method  
(phase2genotype), 67
- phase<- (ASEset-class), 9
- phase<-, ASEset-method (ASEset-class), 9
- phase<-, RiskVariant-method  
(RiskVariant-class), 74
- phaseArray2phaseMatrix, 68
- phaseArray2phaseMatrix, array-method  
(phaseArray2phaseMatrix), 68
- phaseMatrix2Array, 69
- phaseMatrix2Array, matrix-method  
(phaseMatrix2Array), 69
- plot (LinkVariantAlmlof-plot), 59
- plot, LinkVariantAlmlof, ANY-method  
(LinkVariantAlmlof-plot), 59
- plot, LinkVariantAlmlof-method  
(LinkVariantAlmlof-plot), 59
- pvalue (LinkVariantAlmlof-class), 58
- pvalue, LinkVariantAlmlof-method  
(LinkVariantAlmlof-class), 58
- randomRef, 70
- randomRef, ASEset-method (randomRef), 70
- RangedSummarizedExperiment, 12, 13, 54
- reads, 45, 71
- ref (ASEset-class), 9
- ref, ASEset-method (ASEset-class), 9
- ref, RiskVariant-method  
(RiskVariant-class), 74
- ref<- (ASEset-class), 9
- ref<-, ASEset, ANY-method (ASEset-class),  
9
- ref<-, RiskVariant, ANY-method  
(RiskVariant-class), 74
- refAllele, 71
- refAllele, ASEset-method (refAllele), 71
- reference\_frequency\_density\_vs\_threshold\_variable\_multi  
(DetectedAI-plot), 32
- reference\_frequency\_density\_vs\_threshold\_variable\_multi  
(DetectedAI-plot), 32
- reference\_frequency\_density\_vs\_threshold\_variable\_plot  
(DetectedAI-plot), 32

- reference\_frequency\_density\_vs\_threshold\_variable, DetectedAI-method (DetectedAI-plot), [32](#)
- referenceFrequency (DetectedAI-class), [31](#)
- referenceFrequency, DetectedAI-method (DetectedAI-class), [31](#)
- refExist (ASEset-class), [9](#)
- refExist, ASEset-method (ASEset-class), [9](#)
- RegionSummary (RegionSummary-class), [73](#)
- regionSummary, [72](#)
- regionSummary, ASEset-method (regionSummary), [72](#)
- regionSummary, numeric-method (regionSummary), [72](#)
- RegionSummary-class, [73](#)
- RegionSummary-method (RegionSummary-class), [73](#)
- RiskVariant (RiskVariant-class), [74](#)
- RiskVariant-class, [74](#)
- RiskVariant-method (RiskVariant-class), [74](#)
- RiskVariantFromGRangesAndPhaseArray (initialize-RiskVariant), [57](#)
  
- scanForHeterozygotes, [39](#), [49](#)
- scanForHeterozygotes (ASEset-scanForHeterozygotes), [20](#)
- scanForHeterozygotes, ASEset-method (ASEset-scanForHeterozygotes), [20](#)
- scanForHeterozygotes, GAlignmentsList-method (ASEset-scanForHeterozygotes), [20](#)
- scanForHeterozygotes.old, [75](#)
- sumnames (RegionSummary-class), [73](#)
- sumnames, RegionSummary-method (RegionSummary-class), [73](#)
  
- thresholdCountSample (DetectedAI-class), [31](#)
- thresholdCountSample, DetectedAI-method (DetectedAI-class), [31](#)
- thresholdDeltaFrequency (DetectedAI-class), [31](#)
- thresholdDeltaFrequency, DetectedAI-method (DetectedAI-class), [31](#)
- thresholdFrequency (DetectedAI-class), [31](#)
- thresholdFrequency, DetectedAI-method (DetectedAI-class), [31](#)
- thresholdPvalue (DetectedAI-class), [31](#)
  
- thresholdPvalue, DetectedAI-method (DetectedAI-class), [31](#)
- usedSNPs\_vs\_threshold\_variable\_summary (DetectedAI-summary), [34](#)
- usedSNPs\_vs\_threshold\_variable\_summary, DetectedAI-method (DetectedAI-summary), [34](#)