

Package ‘crlmm’

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Type Package

Title Genotype Calling (CRLMM) and Copy Number Analysis tool for Affymetrix SNP 5.0 and 6.0 and Illumina arrays.

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Description Faster implementation of CRLMM specific to SNP 5.0 and 6.0 arrays, as well as a copy number tool specific to 5.0, 6.0, and Illumina platforms

License Artistic-2.0

Depends R (>= 2.14.0), oligoClasses (>= 1.21.12), preprocessCore (>= 1.17.7)

LinkingTo preprocessCore (>= 1.17.7)

Imports methods, Biobase (>= 2.15.4), BiocGenerics, affyio (>= 1.23.2), illuminaio, ellipse, mvtnorm, splines, stats, SNPchip,utils, lattice, ff, foreach, RcppEigen (>= 0.3.1.2.1),matrixStats, VGAM

Suggests hapmapsnp6, genomewidesnp6Crlmm (>= 1.0.7), GGdata, snpStats,RUnit

Collate AllGenerics.R AllClasses.R methods-AssayData.R methods-CNSet.R methods-CNSetLM.R methods-eSet.R methods-SnpSuperSet.R methods-PredictionRegion.R cnrma-functions.R cnset-accessors.R crlmm-functions.R crlmmGT2.R crlmm-illumina.R krlmm.R snprma-functions.R utils.R zzz.R test_crlmm_package.R

LazyLoad yes

Local Variables

time-stamp-pattern ``8/Date: %3a %3b %2d %02H:%02M:%02S %Z %:y\{ }n"

End

biocViews Microarray, Preprocessing, SNP, CopyNumberVariation

R topics documented:

crlmm-package	2
ABpanel	3
AssayData-methods	4
batchStatisticAccessors	5
calculateRBaf	6
cnrmaAffy	7
CNSet-methods	8
cnSetExample	9
constructAffyCNSet	9
constructInf	10
copynumberAccessors	12
crlmm	13
crlmmCopynumber	16
crlmmIllumina	18
crlmmIlluminaV2	20
genotype	22
genotype.Illumina	25
genotypeAffy	28
genotypeInf	29
genotypes	31
ListClassConstructors	32
posteriorProbability	33
predictionRegion	34
PredictionRegion-class	35
preprocessInf	36
readGenCallOutput	38
readIdatFiles	39
snprma	40
snprmaAffy	42
validCdfNames	43
validCEL	43
xyplot	44
Index	46

crlmm-package

*Genotype Calling via CRLMM Algorithm***Description**

Faster implementation of CRLMM specific to SNP 5.0 and 6.0 arrays.

Details

Index:

crlmm-package	New implementation of the CRLMM Algorithm.
crlmm	Genotype SNP 5.0 or 6.0 samples.
calls	Accessor for genotype calls.
confs	Accessor for confidences.

The 'crlmm' package reimplements the CRLMM algorithm present in the 'oligo' package. This implementation primes for efficient genotyping of samples on SNP 5.0 and SNP 6.0 Affymetrix arrays.

To use this package, the user must have additional data packages: 'genomewidesnp5Crlmm' - SNP 5.0 arrays 'genomewidesnp6Crlmm' - SNP 6.0 arrays

Author(s)

Rafael A Irizarry Maintainer: Benilton S Carvalho <carvalho@bclab.org>

References

Carvalho BS, Louis TA, Irizarry RA. Quantifying uncertainty in genotype calls. *Bioinformatics*. 2010 Jan 15;26(2):242-9. Epub 2009 Nov 11.

ABpanel	<i>A panel function for plotting prediction regions and log-normalized intensities</i>
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Description

A panel function for plotting prediction regions and log-normalized intensities

Usage

```
ABpanel(x, y, predictRegion, copyNumber = 0:4, fill, ..., subscripts)
```

Arguments

x	log-normalized intensities for the A or B allele
y	log-normalized intensities for the A or B allele
predictRegion	A list. See predictionRegion.
copyNumber	Integer vector. Indicates which prediction regions are drawn.
fill	Character or integer vector for coloring the points. Only valid for certain point symbols. See points.
...	Additional arguments to panel.xyplot and lpolygon.
subscripts	See xyplot in the lattice package.

Value

Not applicable

Note

ABpanel can be passed as the argument to panel in the xyplot method for CNSet objects. See the examples in xyplot.

Author(s)

R. Scharpf

See Also

[xyplot](#), [panel.xyplot](#) [lpolygon](#)

AssayData-methods

Methods for class "AssayData" in crlmm

Description

The batchStatistics slot in a CNSet object is an instance of the AssayData slot. In general, the accessors for AssayData are called indirectly by the corresponding method for the CNSet class and not called directly by the user.

Methods

Ns signature(object="AssayData"): Accessor for genotype frequencies

corr signature(object="AssayData"): Accessor for the correlation of the log-transformed normalized intensities within the diallelic genotype clusters

mads signature(x="AssayData"): Accessor for the median absolute deviation of the normalized intensities within the diallelic genotype clusters

medians signature(object="AssayData"): Accessor for the posterior mean of the normalized intensity within the diallelic genotype clusters.

tau2 signature(object="AssayData"): Accessor for the median absolute deviation of the log-transformed intensities within the diallelic genotype clusters

See Also

[CNSet-class](#), [Ns](#), [tau2](#), [corr](#), [mads](#), [medians](#)

`batchStatisticAccessors`*Accessors for batch-specific summary statistics.*

Description

The summary statistics stored here are used by the tools for copy number estimation.

Usage

```
corr(object, ...)  
tau2(object, ...)  
mads(object, ...)  
medians(object, ...)  
Ns(object, ...)
```

Arguments

<code>object</code>	An object of class <code>CNSet</code> .
<code>...</code>	Ignored

Value

An array with dimension $R \times A \times G \times C$, or $R \times G \times C$.

`R`: number of markers `A`: number of alleles (2) `G`: number of biallelic genotypes (3) `C`: number of batches

`Ns` returns an array of genotype frequencies stratified by batch. Dimension $R \times G \times C$.

`corr` returns an array of within-genotype correlations (log2-scale) stratified by batch. Dimension $R \times G \times C$.

`medians` returns an array of the within-genotype medians (intensity-scale) stratified by batch and allele. Dimension $R \times A \times G \times C$.

`mads` returns an array of the within-genotype median absolute deviations (intensity-scale) stratified by batch and allele. Dimension is the same as for `medians`.

`tau2` returns an array of the squared within-genotype median absolute deviation on the log-scale. Only the `mads` for `AA` and `BB` genotypes are stored. Dimension is $R \times A \times G \times C$, where `G` is `AA` or `BB`. Note that the `mad` for allele `A/B` for subjects with genotype `BB/AA` is a robust estimate of the background variance, whereas the `mad` for allele `A/B` for subjects with genotype `AA/BB` is a robust estimate of the variance for copy number greater than 0 (we assume that on the log-scale the variance is roughly constant for `CA`, `CB` > 0).

See Also

[batchStatistics](#)

Examples

```

data(cnSetExample)
Ns(cnSetExample)[1:5, , ]
corr(cnSetExample)[1:5, , ]
meds <- medians(cnSetExample)
mads(cnSetExample)[1:5, , ]
tau2(cnSetExample)[1:5, , ]

```

calculateRBaf	<i>Calculate log R ratios and B allele frequencies.</i>
---------------	---

Description

Calculate log R ratios and B allele frequencies from a CNSet object

Usage

```
calculateRBaf(object, batch.name, chrom)
```

Arguments

object	A CNSet object.
batch.name	A character string indicating the batch. If missing, log R ratios and B allele frequencies are calculated for all batches in the object.
chrom	Integer indicating which chromosome to process. If missing, B allele frequencies and log R ratios are calculated for all autosomal chromosomes and chromosome X that are included in object.

Details

batch.name must be a value in batch(object). Currently, one must specify a single batch.name. If a character vector for batch.name is supplied, only the first is evaluated.

TODO: A description of how these values are calculated.

Value

A named list.

baf: Each element in the baf list is a matrix of B allele frequencies (one matrix for each chromosome).

lrr: Each element in the lrr list is a matrix of log R ratios (one matrix for each chromosome).

The log R ratios were scaled by a factor of 100 and stored as an integer. B allele frequencies were scaled by a factor of 1000 and stored as an integer.

Author(s)

Lynn Mireless

References

Peiffer et al., High-resolution genomic profiling of chromosomal aberrations using Infinium whole-genome genotyping (2006), Genome Research

Examples

```
data(cnSetExample)
baf.lrr <- suppressWarnings(calculateRBaf(cnSetExample, "SHELF"))
hist(baf.lrr[["baf"]][[1]]/1000, breaks=100)
hist(baf.lrr[["lrr"]][[1]]/100, breaks=100)
## Not run:
library(ff)
baf.lrr <- suppressWarnings(calculateRBaf(cnSetExample, "SHELF"))
class(baf.lrr[["baf"]][[1]]) ## ff_matrix
class(baf.lrr[["lrr"]][[1]]) ## ff_matrix

## End(Not run)
```

cnrmaAffy

quantile normalize nonpolymorphic markers

Description

Quantile normalize nonpolymorphic markers to hapmap reference distribution

Usage

```
cnrmaAffy(cnSet, seed = 1, verbose = TRUE)
```

Arguments

cnSet	Object of class CNSet
seed	Random number seed
verbose	Logical.

Value

Returns logical. Normalized intensities are written to the alleleA `ff_matrix` stored in the CNSet `assayData`.

Author(s)

R. Scharpf

See Also

[snprmaAffy](#)

Description

CNSet is a container defined in the oligoClasses package for storing normalized intensities for genotyping platforms, genotype calls, and parameters estimated for copy number. Accessors for data that an object of this class contains are largely defined in the package oligoClasses. CNSet methods that involve more complex calculations that are specific to the crlmm package, such as computing allele-specific copy number, are included in crlmm and described here.

Methods

as(from, "oligoSnpSet"): Method for coercing object from (class CNSet) to an object of class oligoSnpSet.

CA signature(object="CNSet"): calculates raw copy number for allele A

CB signature(object="CNSet"): calculates raw copy number for allele B

lines signature(x="CNSet"): plot ellipses (95th percentile) for prediction regions

totalCopynumber signature(object="CNSet"): calculates total raw copy number

rawCopynumber signature(object="CNSet"): same as totalCopynumber

nuA signature(object="CNSet"): estimate of mean background (intensity-scale) for allele A

nuB signature(object="CNSet"): estimate of mean background (intensity-scale) for allele A

phiA signature(object="CNSet"): estimate of slope coefficient (intensity-scale) for allele A

phiB signature(object="CNSet"): estimate of slope coefficient (intensity-scale) for allele B

Ns signature(object="CNSet"): genotype frequencies

corr signature(object="CNSet"): correlation of log-transformed normalized intensities within the genotype clusters

mads signature(x="CNSet"): ...

medians signature(object="CNSet"): ...

tau2 signature(object="CNSet"): ...

OligoSetList(object): constructs an object of class OligoSetList from object having class CNSet.

BafLrrSetList(object): constructs an object of class BafLrrSetList from object having class CNSet.

See Also

[CNSet-class](#), [CA](#), [CB](#), [totalCopynumber](#), [rawCopynumber](#)

cnSetExample	<i>Object of class 'CNSet'</i>
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Description

The data for the first 16 polymorphic markers in the HapMap analysis.

Usage

```
data(cnSetExample)
data(cnSetExample2)
```

Format

The data illustrates the CNSet-class, with assayData containing the quantile-normalized intensities for the A and B alleles, genotype calls and confidence scores.

Details

This object was created from the copynumber vignette in inst/scripts. A subset of markers was selected to keep the package size small.

Examples

```
data(cnSetExample)
data(cnSetExample2)
```

constructAffyCNSet	<i>Construct an object of class CNSet from Affymetrix cel files</i>
--------------------	---

Description

Construct a container for normalized intensities for Affymetrix cel files, referred to as a CNSet

Usage

```
constructAffyCNSet(filenamees, sns, cdfName, batch, verbose = TRUE, genome)
```

Arguments

filenames	Vector of cel file names.
sns	Sample identifiers. Defaults to basename(filenames).
cdfName	Character string indicating annotation package (e.g., "genomewidesnp6Crlmm")
batch	Vector of same length as filenames indicating batch.
verbose	Logical.
genome	Character string indicating UCSC genome build (hg18 or hg19 supported)

Value

An object of class CNSet

Author(s)

R. Scharpf

constructInf	<i>Instantiate an object of class CNSet for the Infinium platforms.</i>
--------------	---

Description

Instantiates an object of class CNSet for the Infinium platforms. Elements of assayData and batchStatistics will be ff objects. See details.

Usage

```
constructInf(sampleSheet = NULL, arrayNames = NULL, path = ".",
             arrayInfoColNames = list(barcode="SentrixBarcode_A", position="SentrixPosition_A"), highDensity =
             fileExt = list(green = "Grn.idat", red = "Red.idat"), XY, cdfName, verbose = FALSE, batch=NULL, save)
```

Arguments

sampleSheet	data.frame containing Illumina sample sheet information (for required columns, refer to BeadStudio Genotyping guide - Appendix A).
arrayNames	character vector containing names of arrays to be read in. If NULL, all arrays that can be found in the specified working directory will be read in.
path	character string specifying the location of files to be read by the function
arrayInfoColNames	(used when sampleSheet is specified) list containing elements 'barcode' which indicates column names in the sampleSheet which contains the arrayNumber/barcode number and 'position' which indicates the strip number. In older style sample sheets, this information is combined (usually in a column named 'SentrixPosition') and this should be specified as list(barcode=NULL, position="SentrixPosition").
highDensity	logical (used when sampleSheet is specified). If TRUE, array extensions '_A', '_B' in sampleSheet are replaced with 'R01C01', 'R01C02' etc.

sep	character string specifying separator used in .idat file names.
fileExt	list containing elements 'Green' and 'Red' which specify the .idat file extension for the Cy3 and Cy5 channels.
XY	an NChannelSet containing X and Y intensities.
cdfName	annotation package (see also validCdfNames)
verbose	'logical.' Whether to print descriptive messages during processing.
batch	batch variable. See details.
saveDate	'logical'. Should the dates from each .idat be saved with sample information?

Details

This function initializes a container for storing the normalized intensities for the A and B alleles at polymorphic loci and the normalized intensities for the 'A' allele at nonpolymorphic loci. CRLMM genotype calls and confidence scores are also stored in the assayData. This function does not do any preprocessing or genotyping – it only creates an object of the appropriate size. The initialized values will all be 'NA'.

The ff package provides infrastructure for accessing and writing data to disk instead of keeping data in memory. Each element of the assayData and batchStatistics slot are ff objects. ff objects in the R workspace contain pointers to several files with the '.ff' extension on disk. The location of where the data is stored on disk can be specified by use of the ldPath function. Users should not move or rename this directory. If only output files are stored in ldPath, one can either remove the entire directory prior to rerunning the analysis or all of the '.ff' files. Otherwise, one would accumulate a large number of '.ff' files on disk that are no longer in use.

We have adopted the ff package in order to reduce crlmm's memory footprint. The memory usage can be fine-tuned by the utilities ocSamples and ocProbesets provided in the oligoClasses package. In most instances, the user-level interface will be no different than accessing data from ordinary matrices in R. However, the differences in the underlying representation can become more noticeable for very large datasets in which the I/O for accessing data from the disk can be substantial.

Value

A CNSet object

Author(s)

R. Scharpf

See Also

[ldPath](#), [ocSamples](#), [ocProbesets](#), [CNSet-class](#), [preprocessInf](#), [genotypeInf](#)

Examples

```
## See the Illumina vignettes in inst/scripts of the
## source package for an example
```

copynumberAccessors *Accessors for allele-specific or total copy number*

Description

These methods can be applied after an object of class CNSet has been generated by the `cr1mmCopynumber` function.

Usage

```
CA(object, ...)
CB(object, ...)
nuA(object)
nuB(object)
phiA(object)
phiB(object)
totalCopynumber(object, ...)
rawCopynumber(object, ...)
```

Arguments

<code>object</code>	An object of class CNSet.
<code>...</code>	An additional argument named 'i' can be passed to subset the markers and an argument 'j' can be passed to subset the samples. Other arguments are ignored.

Details

At polymorphic markers, `nuA` and `nuB` provide the intercept coefficient (the estimated background intensity) for the A and B alleles, respectively. `phiA` and `phiB` provide the slope coefficients for the A and B alleles, respectively.

At nonpolymorphic markers, `nuB` and `phiB` are 'NA'.

These functions can be used to translate the normalized intensities to the copy number scale. Plotting the copy number estimates as a function of physical position can be used to guide downstream algorithms that smooth, as well as to assess possible mosaicism.

Value

`nu[A/B]` and `phi[A/B]` return matrices of the intercept and slope coefficients, respectively.

`CA` and `CB` return matrices of allele-specific copy number.

`totalCopynumber` (or `rawCopynumber`) returns a matrix of `CA+CB`.

Note

Subsetting the CNSet object before extracting copy number can be very inefficient when the data set is very large, particularly if using `ff` objects. The `[]` method will subset all of the assay data elements and all of the elements in the `LinearModelParameter` slot.

See Also

[crlmmCopynumber](#), [CNSet-class](#)

Examples

```
## Not run:
data(cnSetExample)
all(isCurrent(cnSetExample)) ## is the cnSet object current?

## -----
## calculating allele-specific copy number
## -----
## copy number for allele A, first 5 markers, first 2 samples
(ca <- CA(cnSetExample, i=1:5, j=1:2))
## copy number for allele B, first 5 markers, first 2 samples
(cb <- CB(cnSetExample, i=1:5, j=1:2))
## total copy number for first 5 markers, first 2 samples
(cn1 <- ca+cb)

## total copy number at first 5 nonpolymorphic loci
index <- which(!isSnp(cnSetExample))[1:5]
cn2 <- CA(cnSetExample, i=index, j=1:2)
## note, cb is NA at nonpolymorphic loci
(cb <- CB(cnSetExample, i=index, j=1:2))
## note, ca+cb will give NAs at nonpolymorphic loci
CA(cnSetExample, i=index, j=1:2) + cb
## A shortcut for total copy number
cn3 <- totalCopynumber(cnSetExample, i=1:5, j=1:2)
all.equal(cn3, cn1)
cn4 <- totalCopynumber(cnSetExample, i=index, j=1:2)
all.equal(cn4, cn2)

## markers 1-5, all samples
cn5 <- totalCopynumber(cnSetExample, i=1:5)
## all markers, samples 1-5
cn6 <- totalCopynumber(cnSetExample, j=1:2)

## End(Not run)
```

Description

This is a faster and more efficient implementation of the CRLMM algorithm, especially designed for Affymetrix SNP 5 and 6 arrays (to be soon extended to other platforms).

Usage

```

crlmm(filenamees, row.names=TRUE, col.names=TRUE,
       probs=c(1/3, 1/3, 1/3), DF=6, SNRMin=5,
       gender=NULL, save.it=FALSE, load.it=FALSE,
       intensityFile, mixtureSampleSize=10^5,
       eps=0.1, verbose=TRUE, cdfName, sns, recallMin=10,
       recallRegMin=1000, returnParams=FALSE, badSNP=0.7)
crlmm2(filenamees, row.names=TRUE, col.names=TRUE,
       probs=c(1/3, 1/3, 1/3), DF=6, SNRMin=5,
       gender=NULL, save.it=FALSE, load.it=FALSE,
       intensityFile, mixtureSampleSize=10^5,
       eps=0.1, verbose=TRUE, cdfName, sns, recallMin=10,
       recallRegMin=1000, returnParams=FALSE, badSNP=0.7)

```

Arguments

filenamees	'character' vector with CEL files to be genotyped.
row.names	'logical'. Use rownames - SNP names?
col.names	'logical'. Use colnames - Sample names?
probs	'numeric' vector with priors for AA, AB and BB.
DF	'integer' with number of degrees of freedom to use with t-distribution.
SNRMin	'numeric' scalar defining the minimum SNR used to filter out samples.
gender	'integer' vector, with same length as 'filenamees', defining sex. (1 - male; 2 - female)
save.it	'logical'. Save preprocessed data?
load.it	'logical'. Load preprocessed data to speed up analysis?
intensityFile	'character' with filename to be saved/loaded - preprocessed data.
mixtureSampleSize	Number of SNP's to be used with the mixture model.
eps	Minimum change for mixture model.
verbose	'logical'.
cdfName	'character' defining the CDF name to use ('GenomeWideSnp5', 'GenomeWideSnp6')
sns	'character' vector with sample names to be used.
recallMin	Minimum number of samples for recalibration.
recallRegMin	Minimum number of SNP's for regression.
returnParams	'logical'. Return recalibrated parameters.
badSNP	'numeric'. Threshold to flag as bad SNP (affects batchQC)

Details

'crlmm2' allows one to genotype very large datasets (via ff package) and also permits the use of clusters or multiple cores (via snow package) to speed up genotyping.

As noted above, the call probabilities are stored using an integer representation to reduce file size using the transformation $\text{round}(-1000 \cdot \log_2(1-p))$, where p is the probability. The function `i2P` can be used to convert the integers back to the scale of probabilities.

Value

A SnpSet object.

calls	Genotype calls (1 - AA, 2 - AB, 3 - BB)
confs	Confidence scores 'round(-1000*log2(1-p))'
SNPQC	SNP Quality Scores
batchQC	Batch Quality Score
params	Recalibrated parameters

References

Carvalho B, Bengtsson H, Speed TP, Irizarry RA. Exploration, normalization, and genotype calls of high-density oligonucleotide SNP array data. *Biostatistics*. 2007 Apr;8(2):485-99. Epub 2006 Dec 22. PMID: 17189563.

Carvalho BS, Louis TA, Irizarry RA. Quantifying uncertainty in genotype calls. *Bioinformatics*. 2010 Jan 15;26(2):242-9.

See Also

[i2p](#), [snpCall](#), [snpCallProbability](#)

Examples

```
## this can be slow
library(oligoClasses)
if (require(genomewidesnp6Crlmm) & require(hapmapsnp6)){
  path <- system.file("celFiles", package="hapmapsnp6")

  ## the filenames with full path...
  ## very useful when genotyping samples not in the working directory
  cels <- list.celfiles(path, full.names=TRUE)
  (crlmmOutput <- crlmm(cels))
  ## If gender is known, one should check that the assigned gender is
  ## correct, or pass the integer coding of gender as an argument to the
  ## crlmm function as done below
}

## Not run:
## HPC Example
library(ff)
library(snow)
library(crlmm)
## genotype 50K SNPs at a time
ocProbesets(50000)
## setup cluster - 8 cores on the machine
library(doSNOW)
cl <- makeCluster(8, "SOCK")
registerDoSNOW(cl)
##setCluster(8, "SOCK")
```

```

path <- system.file("celFiles", package="hapmapsnp6")
cels <- list.celfiles(path, full.names=TRUE)
crImmOutput <- crImm2(cels)

## End(Not run)

```

crImmCopynumber *Locus- and allele-specific estimation of copy number*

Description

Locus- and allele-specific estimation of copy number.

Usage

```

crImmCopynumber(object, MIN.SAMPLES=10, SNRMin = 5, MIN.OBS = 1,
  DF.PRIOR = 50, bias.adj = FALSE,
  prior.prob = rep(1/4, 4), seed = 1, verbose = TRUE,
  GT.CONF.THR = 0.80, MIN.NU = 2^3, MIN.PHI = 2^3,
  THR.NU.PHI = TRUE, type=c("SNP", "NP", "X.SNP", "X.NP"),
  fit.linearModel=TRUE)

```

Arguments

object	object of class CNSet.
MIN.SAMPLES	'Integer'. The minimum number of samples in a batch. Batches with fewer than MIN.SAMPLES are skipped. Therefore, samples in batches with fewer than MIN.SAMPLES have NA's for the allele-specific copy number and NA's for the linear model parameters.
SNRMin	Samples with low signal to noise ratios are excluded.
MIN.OBS	For a SNP with with fewer than MIN.OBS of a genotype in a given batch, the within-genotype median is imputed. The imputation is based on a regression using SNPs for which all three biallelic genotypes are observed. For example, assume at a given SNP genotypes AA and AB were observed and BB is an unobserved genotype. For SNPs in which all 3 genotypes were observed, we fit the model $E(\text{mean_BB}) = \beta_0 + \beta_1 * \text{mean_AA} + \beta_2 * \text{mean_AB}$, obtaining estimates; of β_0 , β_1 , and β_2 . The imputed mean at the SNP with unobserved BB is then $\hat{\beta}_0 + \hat{\beta}_1 * \text{mean_AA} + \hat{\beta}_2 * \text{mean_AB}$.
DF.PRIOR	The 2 x 2 covariance matrix of the background and signal variances is estimated from the data at each locus. This matrix is then smoothed towards a common matrix estimated from all of the loci. DF.PRIOR controls the amount of smoothing towards the common matrix, with higher values corresponding to greater smoothing. Currently, DF.PRIOR is not estimated from the data. Future versions may estimate DF.PRIOR empirically.

bias.adj	bias.adj is currently ignored (as well as the prior.prob argument). We plan to add this feature back to the crlmm package in the near future. This feature, when TRUE, updated initial estimates from the linear model after excluding samples with a low posterior probability of normal copy number. Excluding samples that have a low posterior probability can be helpful at loci in which a substantial fraction of the samples have a copy number alteration. For additional information, see Scharpf et al., 2010.
prior.prob	This argument is currently ignored. A numerical vector providing prior probabilities for copy number states corresponding to homozygous deletion, hemizygous deletion, normal copy number, and amplification, respectively.
seed	Seed for random number generation.
verbose	Logical.
GT.CONF.THR	Confidence threshold for genotype calls (0, 1). Calls with confidence scores below this threshold are not used to estimate the within-genotype medians. See Carvalho et al., 2007 for information regarding confidence scores of biallelic genotypes.
MIN.NU	numeric. Minimum value for background intensity. Ignored if THR.NU.PHI is FALSE.
MIN.PHI	numeric. Minimum value for slope. Ignored if THR.NU.PHI is FALSE.
THR.NU.PHI	If THR.NU.PHI is FALSE, MIN.NU and MIN.PHI are ignored. When TRUE, background (nu) and slope (phi) coefficients below MIN.NU and MIN.PHI are set to MIN.NU and MIN.PHI, respectively.
type	Character string vector that must be one or more of "SNP", "NP", "X.SNP", or "X.NP". Type refers to a set of markers. See details below
fit.linearModel	Logical. If TRUE, a linear model is fit to estimate the parameters for computing the absolute copy number. If FALSE, we compute the batch-specific, within-genotype median and MAD at polymorphic loci and the median and MAD at nonpolymorphic loci.

Details

We suggest a minimum of 10 samples per batch for using crlmmCopynumber. 50 or more samples per batch is preferred and will improve the estimates.

The functions crlmmCopynumberLD and crlmmCopynumber2 have been deprecated.

The argument type can be used to specify a subset of markers for which the copy number estimation algorithm is run. One or more of the following possible entries are valid: 'SNP', 'NP', 'X.SNP', and 'X.NP'.

'SNP' refers to autosomal SNPs.

'NP' refers to autosomal nonpolymorphic markers.

'X.SNP' refers to SNPs on chromosome X.

'X.NP' refers to autosomes on chromosome X.

However, users must run 'SNP' prior to running 'NP' and 'X.NP', or specify type = c(SNP, X.NP).

Value

The value returned by the `crlmmCopynumber` function depends on whether the data is stored in RAM or whether the data is stored on disk using the R package `ff` for reading / writing. If uncertain, the first line of the `show` method defined for `CNSet` objects prints whether the `assayData` elements are derived from the `ff` package in the first line. Specifically,

- if the elements of the `batchStatistics` slot in the `CNSet` object have the class `"ff_matrix"` or `"ffdf"`, then the `crlmmCopynumber` function updates the data stored on disk and returns the value `TRUE`.

- if the elements of the `batchStatistics` slot in the `CNSet` object have the class `'matrix'`, then the `crlmmCopynumber` function returns an object of class `CNSet` with the elements of `batchStatistics` updated.

Author(s)

R. Scharpf

References

Carvalho B, Bengtsson H, Speed TP, Irizarry RA. Exploration, normalization, and genotype calls of high-density oligonucleotide SNP array data. *Biostatistics*. 2007 Apr;8(2):485-99. Epub 2006 Dec 22. PMID: 17189563.

Carvalho BS, Louis TA, Irizarry RA. Quantifying uncertainty in genotype calls. *Bioinformatics*. 2010 Jan 15;26(2):242-9.

Scharpf RB, Ruczinski I, Carvalho B, Doan B, Chakravarti A, and Irizarry RA, *Biostatistics*. *Biostatistics*, Epub July 2010.

crlmmIllumina

Genotype Illumina Infinium II BeadChip data with CRLMM

Description

Implementation of the CRLMM algorithm for data from Illumina's Infinium II BeadChips.

Usage

```
crlmmIllumina(RG, XY, stripNorm=TRUE,
              useTarget=TRUE, row.names=TRUE, col.names=TRUE,
              probs=c(1/3, 1/3, 1/3), DF=6, SNRMin=5,
              gender=NULL, seed=1, mixtureSampleSize=10^5,
              eps=0.1, verbose=TRUE, cdfName, sns, recallMin=10,
              recallRegMin=1000, returnParams=FALSE, badSNP=0.7)
```

Arguments

RG	NChannelSet containing R and G bead intensities
XY	NChannelSet containing X and Y bead intensities
stripNorm	'logical'. Should the data be strip-level normalized?
useTarget	'logical' (only used when stripNorm=TRUE). Should the reference HapMap intensities be used in strip-level normalization?
row.names	'logical'. Use rownames - SNP names?
col.names	'logical'. Use colnames - Sample names?
probs	'numeric' vector with priors for AA, AB and BB.
DF	'integer' with number of degrees of freedom to use with t-distribution.
SNRMin	'numeric' scalar defining the minimum SNR used to filter out samples.
gender	'integer' vector, with same length as 'filenames', defining sex. (1 - male; 2 - female)
seed	'integer' scalar for random number generator (used to sample mixtureSampleSize SNPs for mixture model.
mixtureSampleSize	'integer'. The number of SNP's to be used when fitting the mixture model.
eps	Minimum change for mixture model.
verbose	'logical'.
cdfName	'character' defining the chip annotation (manifest) to use ('human370v1c', 'human550v3b', 'human650v3a', 'human1mv1c', 'human370quadv3c', 'human610quadv1b', 'human660quadv1a', 'human1mduov3b', 'humanomni1quadv1b', 'humanomniexpress12v1b', 'humancytosnp12v2p1h')
sns	'character' vector with sample names to be used.
recallMin	'integer'. Minimum number of samples for recalibration.
recallRegMin	'integer'. Minimum number of SNP's for regression.
returnParams	'logical'. Return recalibrated parameters.
badSNP	'numeric'. Threshold to flag as bad SNP (affects batchQC)

Details

Note: The user should specify either the RG or XY intensities, not both.

Value

A SnpSet object which contains

calls	Genotype calls (1 - AA, 2 - AB, 3 - BB)
callProbability	confidence scores 'round(-1000*log2(1-p))'

in the assayData slot and

SNPQC	SNP Quality Scores
batchQC	Batch Quality Scores

along with center and scale parameters when returnParams=TRUE in the featureData slot.

Author(s)

Matt Ritchie

References

Ritchie ME, Carvalho BS, Hetrick KN, Tavar`e S, Irizarry RA. R/Bioconductor software for Illumina's Infinium whole-genome genotyping BeadChips. *Bioinformatics*. 2009 Oct 1;25(19):2621-3.

Carvalho B, Bengtsson H, Speed TP, Irizarry RA. Exploration, normalization, and genotype calls of high-density oligonucleotide SNP array data. *Biostatistics*. 2007 Apr;8(2):485-99. Epub 2006 Dec 22. PMID: 17189563.

Carvalho BS, Louis TA, Irizarry RA. Quantifying uncertainty in genotype calls. *Bioinformatics*. 2010 Jan 15;26(2):242-9.

Examples

```
## crlmmOut = crlmmIllumina(RG)
```

crlmmIlluminaV2 *Read and Genotype Illumina Infinium II BeadChip data with CRLMM*

Description

Implementation of the CRLMM algorithm for data from Illumina's Infinium II BeadChips.

Usage

```
crlmmIlluminaV2(sampleSheet=NULL, arrayNames=NULL, ids=NULL, path=".",
  arrayInfoColNames=list(barcode="SentryBarcode_A", position="SentryPosition_A"),
  highDensity=FALSE, sep="_", fileExt=list(green="Grn.idat", red="Red.idat"),
  saveDate=FALSE, stripNorm=TRUE, useTarget=TRUE,
  row.names=TRUE, col.names=TRUE, probs=c(1/3, 1/3, 1/3),
  DF=6, SNRmin=5, gender=NULL, seed=1, mixtureSampleSize=10^5,
  eps=0.1, verbose=TRUE, cdfName, sns, recallMin=10,
  recallRegMin=1000, returnParams=FALSE, badSNP=.7)
```

Arguments

sampleSheet	data.frame containing Illumina sample sheet information (for required columns, refer to BeadStudio Genotyping guide - Appendix A).
arrayNames	character vector containing names of arrays to be read in. If NULL, all arrays that can be found in the specified working directory will be read in.
ids	vector containing ids of probes to be read in. If NULL all probes found on the first array are read in.
path	character string specifying the location of files to be read by the function

arrayInfoColNames	(used when sampleSheet is specified) list containing elements 'barcode' which indicates column names in the sampleSheet which contains the arrayNumber/barcode number and 'position' which indicates the strip number. In older style sample sheets, this information is combined (usually in a column named 'SentrixPosition') and this should be specified as list(barcode=NULL, position="SentrixPosition")
highDensity	logical (used when sampleSheet is specified). If TRUE, array extensions '_A', '_B' in sampleSheet are replaced with 'R01C01', 'R01C02' etc.
sep	character string specifying separator used in .idat file names.
fileExt	list containing elements 'Green' and 'Red' which specify the .idat file extension for the Cy3 and Cy5 channels.
saveDate	'logical'. Should the dates from each .idat be saved with sample information?
stripNorm	'logical'. Should the data be strip-level normalized?
useTarget	'logical' (only used when stripNorm=TRUE). Should the reference HapMap intensities be used in strip-level normalization?
row.names	'logical'. Use rownames - SNP names?
col.names	'logical'. Use colnames - Sample names?
probs	'numeric' vector with priors for AA, AB and BB.
DF	'integer' with number of degrees of freedom to use with t-distribution.
SNRMin	'numeric' scalar defining the minimum SNR used to filter out samples.
gender	'integer' vector, with same length as 'filenames', defining sex. (1 - male; 2 - female)
seed	'integer' scalar for random number generator (used to sample mixtureSampleSize SNPs for mixture model).
mixtureSampleSize	'integer'. The number of SNP's to be used when fitting the mixture model.
eps	Minimum change for mixture model.
verbose	'logical'.
cdfName	'character' defining the chip annotation (manifest) to use ('human370v1c', 'human550v3b', 'human650v3a', 'human1mv1c', 'human370quadv3c', 'human610quadv1b', 'human660quadv1a', 'human1mduov3b', 'humanomni1quadv1b', 'humanomniexpress12v1b', 'humancytosnp12v2p1h')
sns	'character' vector with sample names to be used.
recallMin	'integer'. Minimum number of samples for recalibration.
recallRegMin	'integer'. Minimum number of SNP's for regression.
returnParams	'logical'. Return recalibrated parameters.
badSNP	'numeric'. Threshold to flag as bad SNP (affects batchQC)

Details

This function combines the reading of data from idat files using readIdatFiles and genotyping to reduce memory usage.

Value

A SnpSet object which contains

calls Genotype calls (1 - AA, 2 - AB, 3 - BB)
 callProbability
 confidence scores `'round(-1000*log2(1-p))'`

in the assayData slot and

SNPQC SNP Quality Scores
 batchQC Batch Quality Scores

along with center and scale parameters when `returnParams=TRUE` in the featureData slot.

Author(s)

Matt Ritchie

References

Ritchie ME, Carvalho BS, Hetrick KN, Tavar'e S, Irizarry RA. R/Bioconductor software for Illumina's Infinium whole-genome genotyping BeadChips. *Bioinformatics*. 2009 Oct 1;25(19):2621-3.

Carvalho B, Bengtsson H, Speed TP, Irizarry RA. Exploration, normalization, and genotype calls of high-density oligonucleotide SNP array data. *Biostatistics*. 2007 Apr;8(2):485-99. Epub 2006 Dec 22. PMID: 17189563.

Carvalho BS, Louis TA, Irizarry RA. Quantifying uncertainty in genotype calls. *Bioinformatics*. 2010 Jan 15;26(2):242-9.

See Also

[crlmmIllumina](#)

Examples

```
## crlmmOut = crlmmIlluminaV2(samples,path=path,arrayInfoColNames=list(barcode="Chip",position="Section"),
##                               saveDate=TRUE,cdfName="human370v1c",returnParams=TRUE)
```

genotype

Preprocessing and genotyping of Affymetrix arrays.

Description

Preprocessing and genotyping of Affymetrix arrays.

Usage

```
genotype(filenamees, cdfName, batch, mixtureSampleSize = 10^5, eps = 0.1,
         verbose = TRUE, seed = 1, sns, probs = rep(1/3, 3),
         DF = 6, SNRMin = 5, recallMin = 10, recallRegMin = 1000,
         gender = NULL, returnParams = TRUE, badSNP = 0.7, genome=c("hg19", "hg18"))
```

Arguments

filenamees	complete path to CEL files
cdfName	annotation package (see also validCdfNames)
batch	vector of class character denoting the batch for each sample in filenamees. The batch vector must be the same length as the number of samples. See details.
mixtureSampleSize	Sample size to be use when fitting the mixture model.
eps	Stop criteria.
verbose	Logical. Whether to print descriptive messages during processing.
seed	Seed to be used when sampling. Useful for reproducibility
sns	The sample identifiers. If missing, the default sample names are basename(filenamees)
probs	'numeric' vector with priors for AA, AB and BB.
DF	'integer' with number of degrees of freedom to use with t-distribution.
SNRMin	'numeric' scalar defining the minimum SNR used to filter out samples.
recallMin	Minimum number of samples for recalibration.
recallRegMin	Minimum number of SNP's for regression.
gender	integer vector (male = 1, female =2) or missing, with same length as filenamees. If missing, the gender is predicted.
returnParams	'logical'. Return recalibrated parameters from crlmm.
badSNP	'numeric'. Threshold to flag as bad SNP (affects batchQC)
genome	character string indicating the UCSC genome build for the SNP annotation

Details

For large datasets it is important to utilize the large data support by installing and loading the ff package before calling the genotype function. In previous versions of the crlmm package, we used different functions for genotyping depending on whether the ff package is loaded, namely genotype and genotype2. The genotype function now handles both instances.

genotype is essentially a wrapper of the crlmm function for genotyping. Differences include (1) that the copy number probes (if present) are also quantile-normalized and (2) the class of object returned by this function, CNSet, is needed for subsequent copy number estimation. Note that the batch variable that must be passed to this function has no effect on the normalization or genotyping steps. Rather, batch is required in order to initialize a CNSet container with the appropriate dimensions and is used directly when estimating copy number.

Value

A SnpSuperSet instance.

Note

For large datasets, load the 'ff' package prior to genotyping – this will greatly reduce the RAM required for big jobs. See `ldPath` and `ocSamples`.

Author(s)

R. Scharpf

References

Carvalho B, Bengtsson H, Speed TP, Irizarry RA. Exploration, normalization, and genotype calls of high-density oligonucleotide SNP array data. *Biostatistics*. 2007 Apr;8(2):485-99. Epub 2006 Dec 22. PMID: 17189563.

Carvalho BS, Louis TA, Irizarry RA. Quantifying uncertainty in genotype calls. *Bioinformatics*. 2010 Jan 15;26(2):242-9.

See Also

[snprma](#), [crlmm](#), [ocSamples](#), [ldOpts](#), [batch](#), [crlmmCopynumber](#)

Examples

```
if (require(ff) & require(genomewidesnp6Crlmm) & require(hapmapsnp6)){
  ldPath(tempdir())
  path <- system.file("celFiles", package="hapmapsnp6")
  ## the filenames with full path...
  ## very useful when genotyping samples not in the working directory
  cels <- list.celfiles(path, full.names=TRUE)
  ## Note: one would need at least 10 CEL files for copy number estimation
  ## To use less RAM, specify a smaller argument to ocProbesets
  ocProbesets(50e3)
  batch <- rep("A", length(cels))
  (cnSet <- genotype(cels, cdfName="genomewidesnp6", batch=batch))

  ##Segment faults that occur with the above step can often be traced to a
  ##corrupt cel file. To check if any of the files are corrupt, try
  ##reading the files in one at a time:

  ## Not run:
  require(affyio)
  validCEL(cels)

  ## End(Not run)

  ## when gender is not specified (as in the above example), crlmm tries
  ## to predict the gender from SNPs on chromosome X
  cnSet$gender
```



```

## If gender is known, one should check that the assigned gender is
## correct. Alternatively, one can pass gender as an argument to the
## genotype function.
gender <- c("female", "female", "male")
gender[gender == "female"] <- 2
gender[gender == "male"] <- 1
dim(cnSet)
table(isSnp(cnSet))
}

```

genotype.Illumina *Preprocessing and genotyping of Illumina Infinium II arrays.*

Description

Preprocessing and genotyping of Illumina Infinium II arrays.

Usage

```

genotype.Illumina(sampleSheet=NULL, arrayNames=NULL, ids=NULL, path=".",
  arrayInfoColNames=list(barcode="SentrrixBarcode_A", position="SentrrixPosition_A"),
  highDensity=FALSE, sep="_", fileExt=list(green="Grn.idat", red="Red.idat"), XY=NULL,
  call.method="crlmm", trueCalls=NULL, cdfName, copynumber=TRUE, batch=NULL, saveDate=FALSE, stripN
  useTarget=TRUE, quantile.method="between", mixtureSampleSize=10^5, fitMixture=TRUE,
  eps=0.1, verbose = TRUE, seed = 1, sns, probs = rep(1/3, 3), DF = 6, SNRMin = 5,
  recallMin = 10, recallRegMin = 1000, gender = NULL, returnParams = TRUE, badSNP = 0.7)

```

Arguments

sampleSheet	data.frame containing Illumina sample sheet information (for required columns, refer to BeadStudio Genotyping guide - Appendix A).
arrayNames	character vector containing names of arrays to be read in. If NULL, all arrays that can be found in the specified working directory will be read in.
ids	vector containing ids of probes to be read in. If NULL all probes found on the first array are read in.
path	character string specifying the location of files to be read by the function
arrayInfoColNames	(used when sampleSheet is specified) list containing elements 'barcode' which indicates column names in the sampleSheet which contains the arrayNumber/barcode number and 'position' which indicates the strip number. In older style sample sheets, this information is combined (usually in a column named 'SentrrixPosition') and this should be specified as list(barcode=NULL, position="SentrrixPosition").
highDensity	logical (used when sampleSheet is specified). If TRUE, array extensions '_A', '_B' in sampleSheet are replaced with 'R01C01', 'R01C02' etc.
sep	character string specifying separator used in .idat file names.

<code>fileExt</code>	list containing elements 'Green' and 'Red' which specify the .idat file extension for the Cy3 and Cy5 channels.
<code>XY</code>	<code>NChannelSet</code> containing X and Y intensities.
<code>call.method</code>	character string specifying the genotype calling algorithm to use (' <code>cr1mm</code> ' or ' <code>kr1mm</code> ').
<code>trueCalls</code>	matrix specifying known Genotype calls(can contain some NAs) for a subset of samples and features (1 - AA, 2 - AB, 3 - BB).
<code>cdfName</code>	annotation package (see also <code>validCdfNames</code>)
<code>copynumber</code>	'logical.' Whether to store copy number intensities with SNP output.
<code>batch</code>	character vector indicating the batch variable. Must be the same length as the number of samples. See details.
<code>saveDate</code>	'logical'. Should the dates from each .idat be saved with sample information?
<code>stripNorm</code>	'logical'. Should the data be strip-level normalized?
<code>useTarget</code>	'logical' (only used when <code>stripNorm=TRUE</code>). Should the reference HapMap intensities be used in strip-level normalization?
<code>quantile.method</code>	character string specifying the quantile normalization method to use ('within' or 'between' channels).
<code>mixtureSampleSize</code>	Sample size to be use when fitting the mixture model.
<code>fitMixture</code>	'logical.' Whether to fit per-array mixture model.
<code>eps</code>	Stop criteria.
<code>verbose</code>	'logical.' Whether to print descriptive messages during processing.
<code>seed</code>	Seed to be used when sampling. Useful for reproducibility
<code>sns</code>	The sample identifiers. If missing, the default sample names are <code>basename(filenamees)</code>
<code>probs</code>	'numeric' vector with priors for AA, AB and BB.
<code>DF</code>	'integer' with number of degrees of freedom to use with t-distribution.
<code>SNRMin</code>	'numeric' scalar defining the minimum SNR used to filter out samples.
<code>recallMin</code>	Minimum number of samples for recalibration.
<code>recallRegMin</code>	Minimum number of SNP's for regression.
<code>gender</code>	integer vector (male = 1, female = 2) or missing, with same length as filenames. If missing, the gender is predicted.
<code>returnParams</code>	'logical'. Return recalibrated parameters from <code>cr1mm</code> .
<code>badSNP</code>	'numeric'. Threshold to flag as bad SNP (affects <code>batchQC</code>)

Details

For large datasets it is important to utilize the large data support by installing and loading the `ff` package before calling the `genotype` function. In previous versions of the `cr1mm` package, we used different functions for genotyping depending on whether the `ff` package is loaded, namely `genotype` and `genotype2`. The `genotype` function now handles both instances.

genotype.Illumina is a wrapper of the `crlmm` function for genotyping. Differences include (1) that the copy number probes (if present) are also quantile-normalized and (2) the class of object returned by this function, `CNSet`, is needed for subsequent copy number estimation. Note that the batch variable (a character string) that must be passed to this function has no effect on the normalization or genotyping steps. Rather, `batch` is required in order to initialize a `CNSet` container with the appropriate dimensions.

The new `'krlmm'` option is available for certain chip types. Optional argument `trueCalls` matrix contains known Genotype calls (1 - AA, 2 - AB, 3 - BB) for a subset of samples and features. This will be used to compute KRLMM coefficients by calling `vglm` function from VGAM package.

The `'krlmm'` method makes use of functions provided in `parallel` package to speed up the process. It by default initialises up to 8 clusters. This is configurable by setting up an option named `"krlmm.cores"`, e.g. `options("krlmm.cores" = 16)`.

Value

A `SnpSuperSet` instance.

Note

For large datasets, load the `'ff'` package prior to genotyping – this will greatly reduce the RAM required for big jobs. See `ldPath` and `ocSamples`. The function `genotype.Illumina` supports parallelization, as the (not run) example below indicates.

Author(s)

Matt Ritchie, Cynthia Liu, Zhiyin Dai

References

Ritchie ME, Carvalho BS, Hetrick KN, Tavaré S, Irizarry RA. R/Bioconductor software for Illumina's Infinium whole-genome genotyping BeadChips. *Bioinformatics*. 2009 Oct 1;25(19):2621-3.

Carvalho B, Bengtsson H, Speed TP, Irizarry RA. Exploration, normalization, and genotype calls of high-density oligonucleotide SNP array data. *Biostatistics*. 2007 Apr;8(2):485-99. Epub 2006 Dec 22. PMID: 17189563.

Carvalho BS, Louis TA, Irizarry RA. Quantifying uncertainty in genotype calls. *Bioinformatics*. 2010 Jan 15;26(2):242-9.

See Also

[crlmmIlluminaV2](#), [ocSamples](#), [ldOpts](#)

Examples

```
## Not run:
# example for crlmm option
library(ff)
library(crlmm)
## to enable parallelization, set to TRUE
if(FALSE){
```

```

library(snow)
library(doSNOW)
## with 10 workers
cl <- makeCluster(10, type="SOCK")
registerDoSNOW(cl)
}
## path to idat files
datadir <- "/thumper/ctsa/snpmicroarray/illumina/IDATS/370k"
## read in your samplesheet
samplesheet = read.csv(file.path(datadir, "HumanHap370Duo_Sample_Map.csv"), header=TRUE, as.is=TRUE)
samplesheet <- samplesheet[-c(28:46,61:75,78:79), ]
arrayNames <- file.path(datadir, unique(samplesheet[, "SentrixPosition"]))
arrayInfo <- list(barcode=NULL, position="SentrixPosition")
cnSet <- genotype.Illumina(sampleSheet=samplesheet,
  arrayNames=arrayNames,
  arrayInfoColNames=arrayInfo,
  cdfName="human370v1c",
  batch=rep("1", nrow(samplesheet)))

## End(Not run)
## Not run:
# example for krlmm option
library(crlmm)
library(ff)
# line below is an optional step for krlmm to initialise 16 workers
# options("krlmm.cores" = 16)
# read in raw X and Y intensities output by GenomeStudios GenCall genotyping module
XY = readGenCallOutput(c("HumanOmni2-5_4v1_FinalReport_83TUSCAN.csv", "HumanOmni2-5_4v1_FinalReport_88CHB-JPT.cs
cdfName="humanomni25quadv1b",
verbose=TRUE)
krlmmResult = genotype.Illumina(XY=XY,
  cdfName=ThiscdfName,
call.method="krlmm",
verbose=TRUE)

# example for krlmm option with known genotype call for some SNPs and samples
library(VGAM)
hapmapCalls = load("hapmapCalls.rda")
# hapmapCalls should have rownames and colnames corresponding to XY featureNames and sampleNames
krlmmResult = genotype.Illumina(XY=XY,
cdfName=ThiscdfName,
call.method="krlmm",
trueCalls=hapmapCalls,
verbose=TRUE)

## End(Not run)

```

Description

Assign diallelic genotypes at polymorphic markers

Usage

```
genotypeAffy(cnSet, SNRMin = 5, recallMin = 10, recallRegMin = 1000, gender = NULL, badSNP = 0.7, returnF
```

Arguments

cnSet	An object of class CNSet
SNRMin	See crlmm
recallMin	See crlmm
recallRegMin	See crlmm
gender	See crlmm
badSNP	See crlmm
returnParams	See crlmm
verbose	Logical.

Details

Wrapper for [crlmm](#) genotyping.

Value

Returns logical. SNP genotypes and confidence scores are written to `ff_matrix` objects.

Author(s)

R.Scharpf

See Also

[crlmm](#), [calls](#), [confs](#)

genotypeInf

Genotyping of Illumina Infinium II arrays.

Description

Genotyping of Illumina Infinium II arrays. This function provides CRLMM/KRLMM genotypes and confidence scores for the the polymorphic markers and is a required step prior to copy number estimation.

Usage

```
genotypeInf(cnSet, mixtureParams, probs = rep(1/3, 3), SNRMin = 5,
recallMin = 10, recallRegMin = 1000, verbose = TRUE, returnParams =
TRUE, badSNP = 0.7, gender = NULL, DF = 6, cdfName, call.method="crlmm",
trueCalls = NULL)
```

Arguments

cnSet	An object of class CNSet
mixtureParams	data.frame containing mixture model parameters needed for genotyping. The mixture model parameters are estimated from the preprocessInf function.
probs	'numeric' vector with priors for AA, AB and BB.
SNRMin	'numeric' scalar defining the minimum SNR used to filter out samples.
recallMin	Minimum number of samples for recalibration.
recallRegMin	Minimum number of SNP's for regression.
verbose	'logical.' Whether to print descriptive messages during processing.
returnParams	'logical'. Return recalibrated parameters from crlmm.
badSNP	'numeric'. Threshold to flag as bad SNP (affects batchQC)
gender	integer vector (male = 1, female =2) or missing, with same length as filenames. If missing, the gender is predicted.
DF	'integer' with number of degrees of freedom to use with t-distribution.
cdfName	character string indicating which annotation package to load.
call.method	character string specifying the genotype calling algorithm to use ('crlmm' or 'krlmm').
trueCalls	matrix specifying known Genotype calls for a subset of samples and features(1 - AA, 2 - AB, 3 - BB).

Details

The genotype calls and confidence scores are written to file using ff protocols for I/O. For the most part, the calls and confidence scores can be accessed as though the data is in memory through the methods snpCall and snpCallProbability, respectively.

The genotype calls are stored using an integer representation: 1 - AA, 2 - AB, 3 - BB. Similarly, the call probabilities are stored using an integer representation to reduce file size using the transformation $\text{round}(-1000 \cdot \log_2(1-p))$, where p is the probability. The function i2P can be used to convert the integers back to the scale of probabilities.

An optional trueCalls argument can be provided to KRLMM method which contains known genotype calls(can contain some NAs) for some samples and SNPs. This will used to compute KRLMM parameters by calling vglm function from VGAM package.

The KRLMM method makes use of functions provided in parallel package to speed up the process. It by default initialises up to 8 clusters. This is configurable by setting up an option named "krlmm.cores", e.g. options("krlmm.cores" = 16).

Value

Logical. If the genotyping is completed, the value 'TRUE' is returned. Note that assayData elements 'call' and 'callProbability' are updated on disk. Therefore, the genotypes and confidence scores can be retrieved using accessors for the CNSet class.

Author(s)

R. Scharpf

See Also

[crlmm](#), [snpCall](#), [snpCallProbability](#), [annotationPackages](#)

Examples

```
## See the illumina_copynumber vignette in inst/scripts of
## the source package
```

genotypes

The possible genotypes for an integer copy number.

Description

The possible genotypes for an integer copy number (0-4).

Usage

```
genotypes(copyNumber, is.snp=TRUE)
```

Arguments

copyNumber	Integer (0-4 allowed).
is.snp	Logical. If TRUE, possible genotypes for a polymorphic SNP is returned. If FALSE, only monomorphic genotypes returned.

Value

Character vector.

Author(s)

R. Scharpf

Examples

```
for(i in 0:4) print(genotypes(i))
for(i in 0:4) print(genotypes(i, FALSE))
```

ListClassConstructors *Methods for Function* BafLrrSetList in Package **crImm** ~~

Description

Constructors for BafLrrSetList and OligoSetList objects.

Usage

```
BafLrrSetList(object, ...)  
OligoSetList(object, ...)
```

Arguments

object	A CnSet object.
...	Additional arguments batch.name and chrom can be used to specify specific batches or chromosomes in the CnSet object.

Details

Constructs a BafLrrSetList object or a OligoSetList object from an object of class CnSet.

Value

A BafLrrSetList or OligoSetList

See Also

[BeadStudioSetList](#)

Examples

```
data(cnSetExample)  
oligoList <- OligoSetList(cnSetExample)  
## only contains 1 chromosome, so list only has one element  
dims(oligoList)  
brList <- BafLrrSetList(cnSetExample)  
dims(brList)
```

posteriorProbability *Calculate the posterior probability for integer copy numbers.*

Description

Calculate the posterior probability for integer copy numbers using the bivariate normal prediction regions.

Usage

```
posteriorProbability(object, predictRegion, copyNumber = 0:4, w)
```

Arguments

object	A CNSet object.
predictRegion	A list containing the bivariate normal prediction region for each of the possible genotypes.
copyNumber	Integer vector.
w	numeric vector of prior probabilities for each of the copy number states. Must be the same length as copyNumber and sum to 1.

Details

This is currently under development.

Value

An array (features x samples x copy number)

Note

This is under development. Use at your own risk.

Author(s)

R. Scharpf

See Also

[predictionRegion](#), [genotypes](#)

Examples

```

data(cnSetExample)
pr <- predictionRegion(cnSetExample, copyNumber=0:4)
pp <- posteriorProbability(cnSetExample, predictRegion=pr)
dim(pp)

## multiple batches
data(cnSetExample2)
pr <- predictionRegion(cnSetExample2, copyNumber=0:4)
pp <- posteriorProbability(cnSetExample2, predictRegion=pr)

```

predictionRegion *Prediction regions for integer copy number*

Description

Bivariate normal prediction regions for integer copy number. Copy numbers 0-4 allowed.

Usage

```
predictionRegion(object, copyNumber)
```

Arguments

object A CNSet object.
copyNumber Integer vector. 0-4 allowed.

Details

We fit a linear regression for each allele to the diallic genotype cluster medians. Denoting the background and slope by μ and ϕ , respectively, the mean for the bivariate normal prediction region is given by

$$\mu_A = \mu_A + CA * \phi_A$$

and

$$\mu_B = \mu_B + CB * \phi_B$$

The variance and correlation of the normalized intensities is estimated from the diallelic genotype clusters AA, AB, and BB on the log-scale. For copy number not equal to two, we assume that the variance is approximately the same for copy number not equal to 2.

Value

A list named by the genotype. 'NULL' refers to copy number zero, 'A' is a hemizygous deletion, etc. Each element is a list of the means (μ) and covariance (cov) for each marker stored as an array. For 'mu', the dimensions of the array are marker x allele (A or B) x batch. For 'cov', the dimensions of the array are marker x 3 (varA, cor, and varB) x batch.

Author(s)

R. Scharpf

References

Scharpf et al., 2011, Biostatistics.

See Also

[posteriorProbability](#), [genotypes](#)

Examples

```
data(cnSetExample)
pr <- predictionRegion(cnSetExample, copyNumber=0:4)
names(pr)
## bivariate normal prediction region for NULL genotype (homozygous deletion)
str(pr[["NULL"]])
```

PredictionRegion-class

Class "PredictionRegion"

Description

A container for bivariate normal prediction regions for SNP data and univariate prediction regions for nonpolymorphic markers.

Objects from the Class

Objects from the class are created from the predictionRegion function.

Slots

.Data: Object of class "list" ~~

Extends

Class "[list](#)", from data part. Class "[vector](#)", by class "list", distance 2. Class "[AssayData](#)", by class "list", distance 2. Class "[list_or_ffdf](#)", by class "list", distance 2. Class [vectorORfactor](#), by class "list", distance 3.

Methods

[signature(x = "PredictionRegion"): ... Prediction regions can be subset by markers.

Author(s)

R. Scharpf

See Also

[predictionRegion](#)

Examples

```
showClass("PredictionRegion")
```

```
preprocessInf
```

Preprocessing of Illumina Infinium II arrays.

Description

This function normalizes the intensities for the 'A' and 'B' alleles for a CNSet object and estimates mixture parameters used for subsequent genotyping. See details for how the normalized intensities are written to file. This step is required for subsequent genotyping and copy number estimation.

Usage

```
preprocessInf(cnSet, sampleSheet=NULL, arrayNames = NULL, ids = NULL,
path = ".", arrayInfoColNames = list(barcode = "SentryBarcode_A",
position = "SentryPosition_A"), highDensity = TRUE, sep = "_", fileExt
= list(green = "Grn.idat", red = "Red.idat"), XY, saveDate = TRUE, stripNorm
= TRUE, useTarget = TRUE, mixtureSampleSize = 10^5, fitMixture = TRUE,
quantile.method="between", eps = 0.1, verbose = TRUE, seed = 1, cdfName)
```

Arguments

cnSet	object of class CNSet
sampleSheet	data.frame containing Illumina sample sheet information (for required columns, refer to BeadStudio Genotyping guide - Appendix A).
arrayNames	character vector containing names of arrays to be read in. If NULL, all arrays that can be found in the specified working directory will be read in.
ids	vector containing ids of probes to be read in. If NULL all probes found on the first array are read in.
path	character string specifying the location of files to be read by the function
arrayInfoColNames	(used when sampleSheet is specified) list containing elements 'barcode' which indicates column names in the sampleSheet which contains the arrayNumber/barcode number and 'position' which indicates the strip number. In older style sample sheets, this information is combined (usually in a column named 'SentryPosition') and this should be specified as list(barcode=NULL, position="SentryPosition").
highDensity	logical (used when sampleSheet is specified). If TRUE, array extensions '_A', '_B' in sampleSheet are replaced with 'R01C01', 'R01C02' etc.
sep	character string specifying separator used in .idat file names.

fileExt	list containing elements 'Green' and 'Red' which specify the .idat file extension for the Cy3 and Cy5 channels.
XY	an NChannelSet object containing X and Y intensities.
saveDate	'logical'. Should the dates from each .idat be saved with sample information?
stripNorm	'logical'. Should the data be strip-level normalized?
useTarget	'logical' (only used when stripNorm=TRUE). Should the reference HapMap intensities be used in strip-level normalization?
mixtureSampleSize	Sample size to be use when fitting the mixture model.
fitMixture	'logical.' Whether to fit per-array mixture model.
quantile.method	character string specifying the quantile normalization method to use ('within' or 'between' channels).
eps	Stop criteria.
verbose	'logical.' Whether to print descriptive messages during processing.
seed	Seed to be used when sampling. Useful for reproducibility
cdfName	character string indicating which annotation package to load.

Details

The normalized intensities are written to disk using package `ff` protocols for writing/reading to disk. Note that the object `CNSet` containing the `ff` objects in the `assayData` slot will be updated after applying this function.

Value

A `ff_matrix` object containing parameters for fitting the mixture model. Note that while the `CNSet` object is not returned by this function, the object will be updated as the normalized intensities are written to disk. In particular, after applying this function the normalized intensities in the `alleleA` and `alleleB` elements of `assayData` are now available.

Author(s)

R. Scharpf

See Also

[CNSet-class](#), [A](#), [B](#), [constructInf](#), [genotypeInf](#), [annotationPackages](#)

Examples

```
## See the illumina_copynumber vignette in inst/scripts of
## the source package
```

readGenCallOutput *Read X and Y intensities from GenCall output*

Description

This function reads the raw X and Y intensities output by GenomeStudio's GenCall genotyping module in preparation for genotyping with crlmm.

Usage

```
readGenCallOutput(filename, path=".", cdfName, colnames=list("SampleID"="Sample ID", "SNPID"="SNP Na
                    type=list("SampleID"="character", "SNPID"="character", "XRaw"="integer", "YRaw"="integer
```

Arguments

filename	'character' string, or a vector of character string specifying the name of the file(s) to read in
path	'character' string specifying the location of file to be read by the function
cdfName	'character' defining the chip annotation (manifest) to use ('human370v1c', 'human550v3b', 'human650v3a', 'human1mv1c', 'human370quadv3c', 'human610quadv1b', 'human660quadv1a', 'human1mduov3b', 'humanomni1quadv1b', 'humanomniexpress12v1b', 'humancytosnp12v2p1h')
colnames	list containing elements 'SampleID', 'SNPID', 'XRaw' and 'YRaw', which specify the column names from in 'file' that pertain to these variables. The default should suffice in most situations.
type	list containing data types for the columns to be read in. The default should be fine in most situations.
verbose	'logical'. Should processing information be displayed as data is read in?

Details

This function returns an NChannelSet containing raw intensity data (X and Y) from GenCall final report file. It assumes the GenCall output is formatted to have samples listed one below the other, and that the columns 'X Raw' and 'Y Raw' are available in the file. The function crlmmillumina() can be run on the output of the readGenCallOutput function.

Value

NChannelSet containing X and Y bead intensities.

Author(s)

Cynthia Liu, Matt Ritchie, Zhiyin Dai

References

Ritchie ME, Carvalho BS, Hetrick KN, Tavar'e S, Irizarry RA. R/Bioconductor software for Illumina's Infinium whole-genome genotyping BeadChips. *Bioinformatics*. 2009 Oct 1;25(19):2621-3.

Examples

```
#XY = readGenCallOutput(file="Hap650Yv3_Final_Report.txt", cdfName="human650v3a")
#crlmmOut = crlmmIllumina(XY=XY)
```

readIdatFiles	<i>Reads Idat Files from Infinium II Illumina BeadChips</i>
---------------	---

Description

Reads intensity information for each bead type from .idat files of Infinium II genotyping BeadChips

Usage

```
readIdatFiles(sampleSheet=NULL, arrayNames=NULL, ids=NULL, path="",
              arrayInfoColNames=list(barcode="SentrixBarcode_A",
                                     position="SentrixPosition_A"),
              highDensity=FALSE, sep="_",
              fileExt=list(green="Grn.idat", red="Red.idat"),
              saveDate=FALSE, verbose=FALSE)
```

Arguments

sampleSheet	data.frame containing Illumina sample sheet information (for required columns, refer to BeadStudio Genotyping guide - Appendix A).
arrayNames	character vector containing names of arrays to be read in. If NULL, all arrays that can be found in the specified working directory will be read in.
ids	vector containing ids of probes to be read in. If NULL all probes found on the first array are read in.
path	character string specifying the location of files to be read by the function
arrayInfoColNames	(used when sampleSheet is specified) list containing elements 'barcode' which indicates column names in the sampleSheet which contains the arrayNumber/barcode number and 'position' which indicates the strip number. In older style sample sheets, this information is combined (usually in a column named 'SentrixPosition') and this should be specified as list(barcode=NULL, position="SentrixPosition").
highDensity	logical (used when sampleSheet is specified). If TRUE, array extensions '_A', '_B' in sampleSheet are replaced with 'R01C01', 'R01C02' etc.
sep	character string specifying separator used in .idat file names.
fileExt	list containing elements 'Green' and 'Red' which specify the .idat file extension for the Cy3 and Cy5 channels.
saveDate	logical. Should the dates from each .idat be saved with sample information?
verbose	logical. Should processing information be displayed as data is read in?

Details

The summarised Cy3 (G) and Cy5 (R) intensities (on the original scale) are read in from the .idat files.

Where available, a `sampleSheet` data.frame, in the same format as used by BeadStudio (columns 'Sample_ID', 'SentrixBarcode_A' and 'SentrixPosition_A' are required) which keeps track of sample information can be specified.

Thanks to Keith Baggerly who provided the code to read in the binary .idat files.

Value

NChannelSet with intensity data (R, G), and indicator for SNPs with 0 beads (zero) for each bead type.

Author(s)

Matt Ritchie

References

Ritchie ME, Carvalho BS, Hetrick KN, Tavar'e S, Irizarry RA. R/Bioconductor software for Illumina's Infinium whole-genome genotyping BeadChips. *Bioinformatics*. 2009 Oct 1;25(19):2621-3.

Examples

```
#RG = readIdatFiles()
```

snprma

Preprocessing tool for SNP arrays.

Description

SNPRMA will preprocess SNP chips. The preprocessing consists of quantile normalization to a known target distribution and summarization to the SNP-Allele level.

Usage

```
snprma(filenamees, mixtureSampleSize = 10^5, fitMixture = FALSE, eps = 0.1, verbose = TRUE, seed = 1, cdfn = "normal")
snprma2(filenamees, mixtureSampleSize = 10^5, fitMixture = FALSE, eps = 0.1, verbose = TRUE, seed = 1, cdfn = "normal")
```


Arguments

filenames	'character' vector with file names.
mixtureSampleSize	Sample size to be use when fitting the mixture model.
fitMixture	'logical'. Fit the mixture model?
eps	Stop criteria.
verbose	'logical'.
seed	Seed to be used when sampling.
cdfName	cdfName: 'GenomeWideSnp_5', 'GenomeWideSnp_6'
sns	Sample names.

Details

'snprma2' allows one to genotype very large datasets (via ff package) and also permits the use of clusters or multiple cores (via snow package) to speed up preprocessing.

Value

A	Summarized intensities for Allele A
B	Summarized intensities for Allele B
sns	Sample names
gns	SNP names
SNR	Signal-to-noise ratio
SKW	Skewness
mixtureParams	Parameters from mixture model
cdfName	Name of the CDF

Examples

```
if (require(genomewidesnp6Cr1mm) & require(hapmapsnp6) & require(oligoClasses)){
  path <- system.file("celFiles", package="hapmapsnp6")

  ## the filenames with full path...
  ## very useful when genotyping samples not in the working directory
  cels <- list.celfiles(path, full.names=TRUE)
  snprmaOutput <- snprma(cels)
  snprmaOutput[["A"]][1:10,]
  snprmaOutput[["B"]][1:10,]
}
## Not run:
## HPC Example
library(ff)
library(snow)
library(cr1mm)
## genotype 50K SNPs at a time
ocProbesets(50000)
```

```
## setup cluster - 8 cores on the machine
setCluster(8, "SOCK")

path <- system.file("celFiles", package="hapmapsnp6")
cels <- list.celfiles(path, full.names=TRUE)
snprmaOutput <- snprma2(cels)

## End(Not run)
```

snprmaAffy

Quantile normalize intensities for SNPs

Description

Quantile normalize intensities for SNPs to a HapMap target reference distribution

Usage

```
snprmaAffy(cnSet, mixtureSampleSize = 10^5, eps = 0.1, seed = 1, verbose = TRUE)
```

Arguments

cnSet	Object of class CNSet
mixtureSampleSize	Sample size to be use when fitting the mixture model.
eps	Stop criteria.
seed	Seed to be used when sampling.
verbose	Logical.

Value

Returns nothing. Normalized intensities are written to files.

Author(s)

R.Scharpf

See Also

[snprma](#)

validCdfNames	<i>Supported annotation packages for crlmm genotyping</i>
---------------	---

Description

Supported annotation packages for crlmm genotyping

Usage

```
validCdfNames()
```

Details

List of available annotation packages

Value

character vector

Author(s)

R.Scharpf

Examples

```
validCdfNames()
```

validCEL	<i>Reads cel files and return an error if a file is not read</i>
----------	--

Description

Reads cel files and return an error if a file is not read

Usage

```
validCEL(celfiles)  
celDates(celfiles)
```

Arguments

celfiles vector of cel file names to read

Value

Returns a message that cel files were successfully read, or an error if there were problems reading the cel files.

Author(s)

R. Scharpf

See Also

[read.celfile.header](#), [POSIXt](#), [read.celfile](#)

Examples

```
library(oligoClasses)
if(require(hapmapsnp6)){
  path <- system.file("celFiles", package="hapmapsnp6")
  cels <- list.celfiles(path, full.names=TRUE)
  validCEL(cels)
  celDates(cels)
}
```

xyplot

Plot prediction regions and normalized intensities.

Description

Plot prediction regions for integer copy number and normalized intensities.

Usage

```
xyplot(x, data, ...)
```

Arguments

x	A formula.
data	A CNSet object.
...	Additional arguments passed to xyplot function in lattice.

Value

A trellis object.

Author(s)

R. Scharpf

See Also

[xyplot](#), [ABpanel](#)

Index

- *Topic **IO**
 - readGenCallOutput, 38
 - readIdatFiles, 39
 - validCEL, 43
- *Topic **aplot**
 - ABpanel, 3
- *Topic **array**
 - posteriorProbability, 33
- *Topic **classes**
 - PredictionRegion-class, 35
- *Topic **classif**
 - cr1mm, 13
 - cr1mmIllumina, 18
 - cr1mmIlluminaV2, 20
 - genotype, 22
 - genotype.Illumina, 25
 - genotypeAffy, 28
 - genotypeInf, 29
 - snprma, 40
- *Topic **datasets**
 - cnSetExample, 9
- *Topic **distribution**
 - predictionRegion, 34
- *Topic **dplot**
 - xyplot, 44
- *Topic **hplot**
 - xyplot, 44
- *Topic **list**
 - calculateRBaf, 6
 - predictionRegion, 34
- *Topic **manip**
 - AssayData-methods, 4
 - batchStatisticAccessors, 5
 - constructAffyCNSet, 9
 - constructInf, 10
 - copynumberAccessors, 12
 - cr1mmCopynumber, 16
 - genotypes, 31
 - ListClassConstructors, 32
 - preprocessInf, 36
 - snprma, 40
 - validCdfNames, 43
- *Topic **methods**
 - calculateRBaf, 6
 - CNSet-methods, 8
- *Topic **package**
 - cr1mm-package, 2
- *Topic **robust**
 - cnrmaAffy, 7
 - snprmaAffy, 42
- [,PredictionRegion,ANY,ANY,ANY-method (PredictionRegion-class), 35
- A, 37
- ABpanel, 3, 44
- annotationPackages, 31, 37
- AssayData, 35
- AssayData-methods, 4
- B, 37
- BafLrrSetList (ListClassConstructors), 32
- BafLrrSetList, CNSet-method (CNSet-methods), 8
- batch, 24
- batchStatisticAccessors, 5
- batchStatistics, 5
- BeadStudioSetList, 32
- CA, 8
- CA (copynumberAccessors), 12
- CA, CNSet-method (CNSet-methods), 8
- calculateRBaf, 6
- calculateRBaf, CNSet-method (calculateRBaf), 6
- calls, 29
- CB, 8
- CB (copynumberAccessors), 12
- CB, CNSet-method (CNSet-methods), 8

- celDates (validCEL), 43
- cnrmaAffy, 7
- CNSet-methods, 8
- cnSetExample, 9
- cnSetExample2 (cnSetExample), 9
- coerce, CNSet, oligoSnpSet-method (CNSet-methods), 8
- confs, 29
- constructAffyCNSet, 9
- constructInf, 10, 37
- copynumberAccessors, 12
- corr, 4
- corr (batchStatisticAccessors), 5
- corr, AssayData-method (AssayData-methods), 4
- corr, CNSet-method (CNSet-methods), 8
- crlmm, 13, 24, 29, 31
- crlmm-package, 2
- crlmm2 (crlmm), 13
- crlmmCopynumber, 13, 16, 24
- crlmmCopynumber2 (crlmmCopynumber), 16
- crlmmCopynumberLD (crlmmCopynumber), 16
- crlmmIllumina, 18, 22
- crlmmIlluminaV2, 20, 27

- genotype, 22
- genotype.Illumina, 25
- genotype2 (genotype), 22
- genotypeAffy, 28
- genotypeInf, 11, 29, 37
- genotypeLD (genotype), 22
- genotypes, 31, 33, 35

- i2p, 15

- ldOpts, 24, 27
- ldPath, 11
- lines, CNSet-method (CNSet-methods), 8
- list, 35
- list_or_ffdf, 35
- ListClassConstructors, 32
- lpolygon, 4

- mads, 4
- mads (batchStatisticAccessors), 5
- mads, AssayData-method (AssayData-methods), 4
- mads, CNSet-method (CNSet-methods), 8
- medians, 4
- medians (batchStatisticAccessors), 5
- medians, AssayData-method (AssayData-methods), 4
- medians, CNSet-method (CNSet-methods), 8

- Ns, 4
- Ns (batchStatisticAccessors), 5
- Ns, AssayData-method (AssayData-methods), 4
- Ns, CNSet-method (CNSet-methods), 8
- nuA (copynumberAccessors), 12
- nuA, CNSet-method (CNSet-methods), 8
- nuB (copynumberAccessors), 12
- nuB, CNSet-method (CNSet-methods), 8

- ocProbesets, 11
- ocSamples, 11, 24, 27
- OligoSetList (ListClassConstructors), 32
- OligoSetList, CNSet-method (CNSet-methods), 8

- panel.xyplot, 4
- phiA (copynumberAccessors), 12
- phiA, CNSet-method (CNSet-methods), 8
- phiB (copynumberAccessors), 12
- phiB, CNSet-method (CNSet-methods), 8
- POSIXt, 44
- posteriorProbability, 33, 35
- posteriorProbability, CNSet-method (posteriorProbability), 33
- predictionRegion, 33, 34, 36
- predictionRegion, CNSet, integer-method (predictionRegion), 34
- PredictionRegion-class, 35
- preprocessInf, 11, 36

- rawCopynumber, 8
- rawCopynumber (copynumberAccessors), 12
- rawCopynumber, CNSet-method (CNSet-methods), 8
- read.celfile, 44
- read.celfile.header, 44
- readGenCallOutput, 38
- readIdatFiles, 39
- readIdatFiles2 (readIdatFiles), 39

- snpCall, 15, 31
- snpCallProbability, 15, 31
- snprma, 24, 40, 42

snprma2 (snprma), [40](#)
snprmaAffy, [7](#), [42](#)

tau2, [4](#)
tau2 (batchStatisticAccessors), [5](#)
tau2, AssayData-method
 (AssayData-methods), [4](#)
tau2, CNSet-method (CNSet-methods), [8](#)
totalCopynumber, [8](#)
totalCopynumber (copynumberAccessors),
 [12](#)
totalCopynumber, CNSet-method
 (CNSet-methods), [8](#)

validCdfNames, [43](#)
validCEL, [43](#)
vector, [35](#)

xyplot, [4](#), [44](#), [44](#)
xyplot, formula, CNSet-method (xyplot), [44](#)