crlmm

March 24, 2012

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

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]()

`CNSet-methods`   *crlmm methods for class "CNSet"*

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

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"): ...

See Also

CNSet-class, CA, CB, totalCopynumber, rawCopynumber

PredictionRegion-class

Class '"PredictionRegion"'

Description

A container for bivariate normal prediction regions for SNP data and univarite 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")
```

---

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

object   An object of class CNSet.

...   Ignored

Value

An array with dimension R x A x G x C, or R x G x 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 x G x C.

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

medians returns an array of the within-genotype medians (intensity-scale) stratified by batch and allele. Dimension R x A x G x 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 x A x G x 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 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 rougly 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 *Calculate log R ratios and B allele frequencies.*

Description

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

Usage

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

Arguments

object   A `CNSet` object.

batch.name   A character string. See details.

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 list.

`baf`: A matrix of B allele frequencies.

`lrr`: A matrix of log R ratios.

Author(s)

Lynn Mireless

References

Reference for BAFs, LRRs.

Examples

```
data(cnSetExample)
baf.lrr <- calculateRBaf(cnSetExample, "SHELF")
hist(baf.lrr[["baf"]], breaks=100)
hist(baf.lrr[["lrr"]], breaks=100)
```

---

celDates *Extract dates from the cel file header*

Description

Extract dates from the cel file header.

Usage

```
celDates(celfiles)
```

Arguments

celfiles   CEL file names. Must specify the complete path.

Value

date-time class POSIXt

Author(s)

R. Scharpf

See Also

read.celfile.header, *POSIXt*

---

cnSetExample *Object of class 'CNSet'*

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. New slots that specific to copy number estimation are batch and batchStatistics.

Details

This object was created from the copynumber vignette in inst/scripts.

Examples

```
data(cnSetExample)
## --------------------------------------------------
## accessors for the feature-level info
## --------------------------------------------------
chromosome(cnSetExample)[1:5]
position(cnSetExample)[1:5]
isSnp(cnSetExample)[1:5]
table(isSnp(cnSetExample))
## --------------------------------------------------
## sample-level statistics computed by crlmm
## --------------------------------------------------
varLabels(cnSetExample)
## accessors for sample-level statistics
## The signal to noise ratio (SNR)
cnSetExample$SNR[]
## the skew
cnSetExample$SKW[]
## the gender (gender is imputed unless specified in the call to crlmm)
table(cnSetExample$gender[])  ## 1=male, 2=female
## --------------------------------------------------
## batchStatistics
## -------------------------------------------------- estimate of
## intercept from linear model
dim(nu(cnSetExample, "A"))
## background for the A allele in the 2 batches for the
## first 5 markers
nu(cnSetExample, "A")[1:5, ]
## background for the B allele in the 2 batches for the
## first 5 markers
nu(cnSetExample, "B")[1:5, ]
## the slope
phi(cnSetExample, "A")[1:5, ]

## --------------------------------------------------
## calculating allele-specific copy number
## --------------------------------------------------
(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))
index <- which(!isSnp(cnSetExample))[1:5]
cn2 <- CA(cnSetExample, i=index, j=1:2)
## note, cb is 0 at nonpolymorphic loci
CB(cnSetExample, i=index, j=1:2)
## A shortcut for total copy number
cn3 <- totalCopynumber(cnSetExample, i=1:5, j=1:2)
all.equal(cn3, ca+cb)
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 1-2
cn6 <- totalCopynumber(cnSetExample, j=1:2)
```

| constructInf | *Instantiate an object of class CNSet for the Infinium platforms.* |

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 = ".", arrayInfoColName
```

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.
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_copynumber.Rnw vignette 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 `crlmmCopynumber` function.

Usage

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

Arguments

object	An object of class `CNSet`.
...	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 tranlate 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

```
## Version 1.6* of crlmm used CNSetLM objects.
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)
```

---

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.

---

crlmm *Genotype oligonucleotide arrays with CRLMM*

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(filenames, 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(filenames, 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

`filenames`	'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 'filenames', 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 'round(-1000*log2(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
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))
  invisible(open(crlmmOutput$gender))
  stopifnot(all(crlmmOutput$gender[] == c(2,2,1)))
  invisible(close(crlmmOutput$gender))

  ## 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
  gender <- c("female", "female", "male")
  gender[gender == "female"] <- 2
  gender[gender == "male"] <- 1

}

## 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
setCluster(8, "SOCK")
```

```
path <- system.file("celFiles", package="hapmapsnp6")
cels <- list.celfiles(path, full.names=TRUE)
crlmmOutput <- crlmm2(cels)


## End(Not run)
```

---

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

Description

Locus- and allele-specific estimation of copy number.

Usage

```
crlmmCopynumber(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"))
```

Arguments

object	object of class `CNSet`.
MIN.SAMPLES	'Integer'. The minimum number of samples in a batch. Bathes 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 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(mean_BB) = beta0 + beta1*mean_AA + beta2*mean_AB, obtaining estimates; of beta0, beta1, and beta2. The imputed mean at the SNP with unobserved BB is then beta0hat + beta1hat * mean_AA of beta2hat * 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 theshold 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

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' referers 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 `batchStaticts` 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.

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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="SentrixBarcode_A", position="SentrixPositi
      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",pos
##                               saveDate=TRUE,cdfName="human370v1c",returnParams=TRUE)
```

---

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="SentrixBarcode_A", position="SentrixPositi
       highDensity=FALSE, sep="_", fileExt=list(green="Grn.idat", red="Red.idat")
       cdfName, copynumber=TRUE, batch, saveDate=TRUE, stripNorm=TRUE, useTarget=
       mixtureSampleSize=10^5, fitMixture=TRUE, eps =0.1, verbose = TRUE, seed =
       sns, probs = rep(1/3, 3), DF = 6, SNRMin = 5, recallMin = 10, recallRegMin
       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 '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.
cdfName	annotation package (see also validCdfNames)

`copynumber`	'logical.' Whether to store copy number intensities with SNP output.
`batch`	batch variable. See details.
`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.
`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(filenames)`
`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 filenames. If missing, the gender is predicted.
`returnParams`	'logical'. Return recalibrated parameters from crlmm.
`badSNP`	'numeric'. Threshold to flag as bad SNP (affects batchQC)

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.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 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.

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)

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

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

Examples

```
##
```

---

genotype	*Preprocessing and genotyping of Affymetrix arrays.*

Description

Preprocessing and genotyping of Affymetrix arrays.

Usage

```
genotype(filenames, 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)
```

Arguments

filenames	complete path to CEL files
cdfName	annotation package (see also `validCdfNames`)
batch	batch variable. 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(filenames)`
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 filenames. If missing, the gender is predicted.
returnParams	'logical'. Return recalibrated parameters from crlmm.
badSNP	'numeric'. Threshold to flag as bad SNP (affects batchQC)

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 useed 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.

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)){

  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 <- as.factor(rep("A", length(cels)))
  (cnSet <- genotype(cels, cdfName="genomewidesnp6", batch=batch))

  ## 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))
  ## Not run:
        ##-------------------------------------------------------------------------------
        ##
  ## Genotype Imputation
        ##
        ##-------------------------------------------------------------------------------
     if(require("ff")){
  path <- system.file("celFiles", package="hapmapsnp6")
  cels <- list.celfiles(path, full.names=TRUE)
  gtSet <- genotype(cels, batch=rep(1L,3))

        gt1 <- calls(crlmmOutput)
        gt2 <- calls(gtSet)[isSnp(gtSet), ]
        gt2 <- gt2[match(rownames(gt2), rownames(gt1)), ]
  stopifnot(all.equal(gt1, gt2))

  XIndex <- which(chromosome(gtSet)==23 & isSnp(gtSet))
  YIndex <- which(chromosome(gtSet)==24 & isSnp(gtSet))
  A.X <- log2(A(gtSet)[XIndex,,drop=FALSE])
  B.X <- log2(B(gtSet)[XIndex,,drop=FALSE])
  meds.X <- apply(A.X+B.X, 2, median)/2
  A.Y <- log2(A(gtSet)[YIndex,,drop=FALSE])
  B.Y <- log2(B(gtSet)[YIndex,,drop=FALSE])
  meds.Y <- apply(A.Y+B.Y, 2, median)/2
  R <- meds.X - meds.Y
  SNR <- gtSet$SNR[]
  SNRMin <- 5
  gender <- kmeans(R, c(min(R[SNR[]>SNRMin]), max(R[SNR[]>SNRMin])))[["cluster"]]
  plot(seq_along(R), R, pch=21, bg=c("royalblue", "red")[gender],
       xlim=c(0, 4), xaxt='n', xlab="sample index")
  legend("topright", fill=c("royalblue", "red"), legend=c("male", "female"))
  delete(A(gtSet))
  delete(B(gtSet))
  delete(calls(gtSet))
  delete(assayDataElement(gtSet, "snpCallProbability"))
  ff.filenames <- list.files(".", pattern=".ff")
  unlink(ff.filename)
     } ## end if(require("ff"))

## End(Not run)
}
```

---

genotypeInf *Genotyping of Illumina Infinium II arrays.*

Description

Genotyping of Illumina Infinium II arrays. This function provides CRLMM 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 = 1
```

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.

Details

The CRLMM 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 'round(-1000*log2(1-p))', where p is the probability. The function `i2P` can be used to convert the integers back to the scale of probabilities.

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

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))
```

```
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 nu and phi, respectively, the mean for the bivariate normal prediction region is given by

mu_A = nu_A + CA * phi_A

and

mu_B nu_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 (mu) 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"]])
```

---

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 = "."
```

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 '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?
mixtureSampleSize	
	Sample size to be use when fitting the mixture model.

fitMixture	'logical.' Whether to fit per-array mixture model.
eps	Stop criteria.
verbose	'logical.' Whether to print descriptive messages during processing.
seed	Seed to be used when sampling. Useful for reproducibility

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`

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(file, path=".", cdfName, colnames=list("SampleID"="Sample ID",
                type=list("SampleID"="character", "SNPID"="character", "XRaw"=
```

Arguments

`file`	'character' string specifying the name of the file 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', 'humanom-niexpress12v1b', '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 and 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

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

`readIDAT`	*Low-level function to read idat files*

Description

Reads intensity information for each bead type from a single .idat file from Infinium II platforms. This is a low-level function which `readIdatFiles` is a wrapper to

Usage

```
readIDAT(idatFile)
```

Arguments

idatFile   character string specifying idat file to be read in

Details

This function returns a list containing summarised intensities and other information extracted from a single .idat file.

The `readIdatFiles` function makes use of `readIDAT` to read the paired Cy3 and Cy5 idats from one or more arrays.

Thanks to Keith Baggerly who providing this code.

Value

list which includes item `Quants` which contains average intensity (`Mean`), number of beads (`NBeads`) and a measure of variability (`SD`) for each bead type on the array.

Author(s)

Keith Baggerly, with modifications by 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

```
#idatdata = readIDAT("4019585367_A_Grn.idat")
#names(idatdata
#idatdata$Quants[1:5,]
```

---

readIdatFiles   *Reads Idat Files from Infinium II Illumina BeadChips*

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 orginal 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(filenames, mixtureSampleSize = 10^5, fitMixture = FALSE, eps = 0.1, verbo
snprma2(filenames, mixtureSampleSize = 10^5, fitMixture = FALSE, eps = 0.1, verb
```

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(genomewidesnp6Crlmm) & 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(crlmm)
## 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)
```

---

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

Examples

```
data(cnSetExample2)
table(batch(cnSetExample2))
sample.index <- which(batch(cnSetExample2) == "CUPID")
## A single SNP
pr <- predictionRegion(cnSetExample2[1:4, sample.index], copyNumber=0:4)
gt <- calls(cnSetExample2[1:4, sample.index])
lim <- c(6,13)
xyplot(B~A|snpid, data=cnSetExample2[1:4, sample.index],
       predictRegion=pr,
       panel=ABpanel,
       pch=21,
       fill=c("red", "blue", "green3")[gt],
       xlim=lim, ylim=lim)

## multiple SNPs, prediction regions for 3 batches
## Not run:
tab <- table(batch(cnSetExample2))
bns <- names(tab)[tab > 50]
sample.index <- which(batch(cnSetExample2)
pr <- predictionRegion(cnSetExample2[1:10, sample.index], copyNumber=0:4)
gt <- as.integer(calls(cnSetExample2[1:10, sample.index]))
xyplot(B~A|snpid, data=cnSetExample2[1:10, sample.index],
       predictRegion=pr,
       panel=ABpanel,
       pch=21,
       fill=c("red", "blue", "green3")[gt],
       xlim=c(6,12), ylim=c(6,12))

## nonpolymorphic markers
data(cnSetExample2)
tab <- table(batch(cnSetExample2))
bns <- names(tab)[tab > 50]
sample.index <- which(batch(cnSetExample2)
np.index <- which(!isSnp(cnSetExample2))[1:10]
taus <- tau2(cnSetExample)[np.index, , , ]
pr <- predictionRegion(cnSetExample2[np.index, sample.index],
       copyNumber=0:4)
pp <- posteriorProbability(cnSetExample2[np.index, sample.index],
   predictRegion=pr,
   copyNumber=0:4)

## End(Not run)
```

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