Package ‘crlmm’

January 14, 2017

Type Package

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

Version 1.32.0

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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, parallel, graphics, limma, beanplot

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

methods-CNSetLM.R methods-eSet.R methods-SnpSuperSet.R
methods-PredictionRegion.R cnrna-functions.R cnset-accessors.R

LazyLoad yes

## Local Variables
## time-stamp-pattern ``/Date: %3a %3b %2d %02H:%02M:%02S %Z %:y\n\n## End

biocViews Microarray, Preprocessing, SNP, CopyNumberVariation

NeedsCompilation yes
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


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**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
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
calculateRBaf

Calculate log R ratios and B allele frequencies.

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 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(object, batch.name, chrom)

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)
**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`

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**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

<table>
<thead>
<tr>
<th>Object of class 'CNSet'</th>
</tr>
</thead>
<tbody>
<tr>
<td>cnSetExample</td>
</tr>
</tbody>
</table>

**Description**

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

**Usage**

```r
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**

```r
data(cnSetExample)
data(cnSetExample2)
```
**constructAffyCNSet**

Construct an object of class CNSet from Affymetrix cel files.

### Description

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

### Usage

```r
constructAffyCNSet(filenames, 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

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**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

```r
constructInf(sampleSheet = NULL, arrayNames = NULL, path = ".", arrayInfoColNames = list(barcode="SentrixBarcode_A", position="SentrixPosition_A"), highDensity = FALSE, sep = ":", fileExt = list(green = "Grn.idat", red = "Red.idat"), XY, cdfName, anno, genome, verbose = FALSE, batch = NULL, saveDate = TRUE)
```
constructInf

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) or 'nopackage' when an anno data.frame and genome supplied

anno data.frame containing SNP annotation information from manifest and additional columns 'isSnp', 'position', 'chromosome' and 'featureNames'. For use when cdfName='nopackage'

genome character string specifying which genome is used in annotation

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

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**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

```r
cA(object, ...) 
cB(object, ...) 
nuA(object) 
nuB(object) 
phiA(object) 
phiB(object) 
totalCopynumber(object,...) 
rawCopynumber(object,...)
```

Arguments

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>object</td>
<td>An object of class CNSet.</td>
</tr>
<tr>
<td>...</td>
<td>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.</td>
</tr>
</tbody>
</table>

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]

#### note, cb is NA at nonpolymorphic loci
#### 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)

#### markers 1-5, all samples

## all markers, samples 1-5

## End(Not run)
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

```r
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)
```

```r
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 \(\text{round}(-1000\times\log(2(1-p)))\), where p is the probability. The function \texttt{i2P} can be used to convert the integers back to the scale of probabilities.

Value

A \texttt{SnpSet} object.

- \texttt{calls} Genotype calls (1 - AA, 2 - AB, 3 - BB)
- \texttt{confs} Confidence scores \(\text{round}(-1000\times\log(2(1-p)))\)
- \texttt{SNPQC} SNP Quality Scores
- \texttt{batchQC} Batch Quality Score
- \texttt{params} Recalibrated parameters

References


See Also

- \texttt{i2p}, \texttt{snpCall}, \texttt{snpCallProbability}

Examples

```r
## 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)
c1 <- makeCluster(8, "SOCK")
registerDoSNOW(cl)
##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**

```r

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"),
                 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 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 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
Dec 22. PMID: 17189563.
Scharpf RB, Ruczinski I, Carvalho B, Doan B, Chakravarti A, and Irizarry RA, Biostatistics. Bio-
statistics, Epub July 2010.

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, genome=c("hg19", "hg18"))

Arguments

filenames  complete path to CEL files
cdfName    annotation package (see also validCdfNames)
batch      vector of class character denoting the batch for each sample in filenames.
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(filenames)
`genotype`

- `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)
- `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**


**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

## 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="SentrixBarcode_A", position="SentrixPosition_A"),
highDensity=FALSE, sep="_", fileExt=list(green="Grn.idat", red="Red.idat"), XY=NULL, anno,
gender=NULL, call.method="crlmm", trueCalls=NULL, cdfName, copynumber=TRUE, batch=NULL, saveDate=FALSE,
useTarget=TRUE, quantile.method="between", nopackage.norm="quantile", 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)
```r
crlmmIllumina(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"), XY=NULL, anno, call.method="crlmm", trueCalls=NULL, cdfName, copynumber=TRUE, batch=NULL, saveDate=FALSE, stripNorm=TRUE, useTarget=TRUE, quantile.method="between", nopackage.norm="quantile", 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**

- **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.
- **XY**: NChannelSet containing X and Y intensities.
- **anno**: data.frame containing SNP annotation information from manifest and additional columns 'isSnp', 'position', 'chromosome' and 'featureNames'. For use when cdfName='nopackage'
- **genome**: character string specifying which genome is used in annotation.
- **call.method**: character string specifying the genotype calling algorithm to use ('crlmm' or 'krlmm').
- **trueCalls**: matrix specifying known Genotype calls(can contain some NAs) for a subset of samples and features (1 - AA, 2 - AB, 3 - BB).
- **cdfName**: annotation package (see also validCdfNames) or 'nopackage' when combined with 'krlmm', an anno data.frame and genome.
- **copynumber**: 'logical.' Whether to store copy number intensities with SNP output.
- **batch**: character vector indicating the batch variable. Must be the same length as the number of samples. 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?
genotype.Illumina(Illumina)

quantile.method
  character string specifying the quantile normalization method to use (‘within’ or
  ‘between’ channels).

nopackage.norm
  character string specifying normalization to be used when cdfName=’nopackage’.
  Options are ’none’, ‘quantile’ (within channel, between array) and ’loess’.

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

genotype.Illumina (or equivalently crlmmIllumina) 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) has no effect on the nor-
malization 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 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 pro-
cess. 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).

In general, a chip specific annotation package is required to use the genotype.Illumina function.
If this is not available (newer chip types or custom chips often don’t have a chip-specific package
available on Bioconductor), consider using cdfName=’nopackage’ and specifying anno and genome,
which runs ‘krlmm’ on the samples available. Here anno is a data.frame read in from the relevant
chip-specific manifest, which must have additional columns ‘isSnp’ which is a logical that indicates
whether a probe is polymorphic or not, ‘position’, ‘chromosome’ and ‘featureNames’ that give the
location on the chromosome and SNP name.

Value

A SnpSuperSet instance.
genotype.Illumina

Author(s)
Matt Ritchie, Cynthia Liu, Zhiyin Dai

References

See Also
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 GenomeStudio's GenCall genotyping module
X Y = readGenCallOutput(c("HumanOmni2-5_4v1_FinalReport_83TUSCAN.csv","HumanOmni2-5_4v1_FinalReport_88CHB-JPT.csv", cdfName="humanomni25quadv1b", verbose=TRUE)
krllmmResult = genotype.Illumina(XY=XY, cdfName=ThiscdfName, call.method="krllmm", verbose=TRUE)

# example for 'krllmm' 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
krllmmResult = genotype.Illumina(XY=XY, cdfName=ThiscdfName, call.method="krllmm", trueCalls=hapmapCalls, verbose=TRUE)

## End(Not run)

---

genotypeAffy

Genotype Affymetrix CEL files

Description

Assign diallelic genotypes at polymorphic markers

Usage

genotypeAffy(cnSet, SNRMin = 5, recallMin = 10, recallRegMin = 1000, gender = NULL, badSNP = 0.7, returnParams = TRUE, verbose = TRUE)

Arguments

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

Details

Wrapper for krllmm 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 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, nopackage.norm="quantile", 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.
nopackage.norm  character string specifying normalization to be used when cdfName='nopackage'. Options are 'none', 'quantile' (within channel, between array) and 'quantileloess'.
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 '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.

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 'illuminacopynumber' 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

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

Description

Constructors for BafLrrSetList and OligoSetList objects.

Usage

```r
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

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

Description

These functions plot the M-values (log-ratios) versus S-values (average intensities) for given SNP/(s) or sample/(s) or beanplots for M-values from different samples.

Usage

plotSNPs(cnSet, row=1, offset=0, xlim=c(9,16), ylim=c(-5,5), verbose=FALSE)
plotSamples(cnSet, col=1, offset=0, xlim=c(9,16), ylim=c(-5,5), verbose=FALSE, sample=100000, seed=1, type="smoothScatter")

Arguments

- **cnSet**: An object of class CNSet
- **row**: scalar/vector of SNP indexes to plot
- **col**: scalar/vector of sample indexes to plot
- **offset**: numeric, offset to add to intensities in cnSet before log2-transforming to make log-ratios or average log-intensities
- **xlim**: the x limits of the plot
- **ylim**: the y limits of the plot
- **verbose**: 'logical.' Whether to print descriptive messages during processing
- **sample**: integer indicating the number of SNPs to sample for the plot
- **seed**: integer seed for the random number generator to sample the SNPs
- **type**: character vector specifying the type of sample plot (either 'smoothScatter' or 'beanplot')

Details

The `plotSNPs` and `plotSamples` functions plot the M and S values derived from the cnSet object.

Value

One or more M vs S plot for `plotSNPs` for a given SNP/(s) or either a smoothed scatter plot of M vs S or a beanplot of the M-values for a selected sample/(s) for `plotSamples`.

Author(s)

Matt Ritchie and Cynthia Liu

See Also

genotype.Illumina
Examples

```r
## Not run:
crlmmResult <- genotype.Illumina(sampleSheet=samples[1:10,], path=path,
   arrayInfoColNames=list(barcode=NULL,
   position="SentrixPosition"),
   saveDate=TRUE, cdfName="human370v1c")

par(mfrow=c(2,2))
plotSamples(crlmmResult, col=1:4)
plotSNPs(crlmmResult, row=1:4)

## End(Not run)
```

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

```r
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`
predictionRegion

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 diallelic genotype cluster medians. Denoting the background and slope by $\nu$ and $\phi$, respectively, the mean for the bivariate normal prediction region is given by

$$\mu_A = \nu_A + CA \times \phi_A$$

and

$$\mu_B = \nu_B + CB \times \phi_B$$

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"])

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")
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

```r
preprocessInf(cnSet, sampleSheet=NULL, arrayNames = NULL, ids = NULL,
               path = ".", arrayInfoColNames = list(barcode = "SentrixBarcode_A",
               position = "SentrixPosition_A"), highDensity = TRUE, sep = "\_", fileExt
               = list(green = "Grn.idat", red = "Red.idat"), XY, anno, 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 '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 object containing X and Y intensities.
- **anno**: data.frame containing SNP annotation information from manifest and additional columns 'isSnp', 'position', 'chromosome' and 'featureNames'. For use when cdfName='nopackage'
- **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

```r
## 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

```r
readGenCallOutput(filenames, path=".", cdfName, colnames=list("SampleID"="Sample ID", "SNPID"="SNP Name", "XRaw"="X Raw", "YRaw"="Y Raw"), type=list("SampleID"="character", "SNPID"="character", "XRaw"="integer", "YRaw"="integer"), verbose=FALSE)
```
readIdatFiles

Arguments

- filenames: '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 (e.g., 'human370v1c', 'human550v3b', 'human650v3a', 'human1mv1c', 'human370quadv3c', 'human610quadv1b', 'human660quadv1a', 'human1mduv3b', 'humanomni1quadv1b', 'humanomniexpress12v1b', 'humanomniexpress12v2p1h').
- 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


Examples

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

Description

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

Usage

```r
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


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, verbose = TRUE, seed = 1, cdfName, sns)

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

```r
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)

---

**snprmaAffy**

Quantile normalize intensities for SNPs

**Description**

Quantile normalize intensities for SNPs to a HapMap target reference distribution

**Usage**

```r
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.
**validCdfNames**

**Author(s)**
R.Scharpf

**See Also**

snprma

---

**validCdfNames**  
Supported annotation packages for crlmm genotyping

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

**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
Examples

library(oligoClasses)
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))
bsn <- 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))
bsn <- names(tab)[tab > 50]
sample.index <- which(batch(cnSetExample2))
np.index <- which(!isSnp(cnSetExample2))[1:10]
tax <- 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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