Package ‘funtooNorm’

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Type Package

Title Normalization Procedure for Infinium HumanMethylation450 BeadChip Kit

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Description Provides a function to normalize Illumina Infinium Human Methylation 450 BeadChip (Illumina 450K), correcting for tissue and/or cell type.

License GPL-3

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      IlluminaHumanMethylation450kmanifest,
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funtooNorm-package

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Description

The funtooNorm Package provides a normalization method for data arising from the Illumina Infinium Human Methylation 450 BeadChip (Illumina 450K), including explicit considerations of differences between tissues or cell types. This method should only be used when the data set contains samples from multiple different tissues or cell types.

Details

Package: funtooNorm
Type: Package
License: GPL-3

Author(s)

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**agreement**

*Function to measure intra-replicate agreement for methylation data.*

**Description**

Function to measure intra-replicate agreement for methylation data.

**Usage**

`agreement(Beta, individualID)`

**Arguments**

- **Beta**: Matrix with beta-values, rows corresponding to probes, columns corresponding to samples.
- **individualID**: a vector where 2 replicates have the exact same value for two technical replicates. Order of samples should match the samples (columns) in Beta.

**Details**

We expect that the values returned by the agreement function after normalization by funtooNorm to be smaller than before.

**Value**

The average value of the square distance between replicates: a measure of agreement between replicates in methylation data.

**Examples**

`agreement(cbind(rnorm(n = 10), rnorm(n = 10), rnorm(n = 10)), c(1,1,1))`

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**fromGenStudFiles**

*Creates a S4 object of class ‘SampleSet’ from GenomeStudio files.*

**Description**

Creates a S4 object of class 'SampleSet' from GenomeStudio files.

**Usage**

`fromGenStudFiles(controlProbeFile, signalFile, cell_type)`
fromRGChannelSet

Arguments
controlProbeFile  The control probe file exported from GenomeStudio
signalFile        The signals exported from GenomeStudio samples must be in same order as the control probe File
cell_type         A vector of cell types, names must match control probes and signal files.

Value
An object of class 'SampleSet'.

Description
Creates a object of class SampleSet from the raw unprocessed data in RGChannelSet

Usage
fromRGChannelSet(myRGChannelSet)

Arguments
myRGChannelSet : RGChannelSet, from minfi package, should contain a cell_type vector in pData

Value
An object of class 'SampleSet'

Examples
require(minfiData)
pData(RGsetEx)$cell_type <- rep(c("type1","type2"),3)
mySampleSet=fromRGChannelSet(RGsetEx)
funtooNorm

The funtooNorm normalization function

Description
funtooNorm Returns the normalized signals to the SampleSet object

Usage
funtooNorm(object, type.fits = "PCR", ncmp = 4, force = FALSE,
sex = NULL)

## S4 method for signature 'SampleSet'
funtooNorm(object, type.fits = "PCR", ncmp = 4,
force = FALSE, sex = NULL)

Arguments
object Object of class SampleSet
type.fits Choice between "PCR" or "PLS" (default="PCR")
cmp Number of components included in the analysis (default=4)
force If set to TRUE, forces the normalization procedure to re-compute
sex Boolean vector if male. if NULL Beta values from ChrY are used for classification.

Details
This is a generic function which applies to autosomes and the X chromosome. Chromosome Y requires separate analysis as there are few probes on Y. We use a straightforward quantile normalization applied to males only.

Value
a S4 object of class SampleSet containing the normalized signal

Methods (by class)
• SampleSet: The funtooNorm normalization function

Examples
require(minfiData)
pData(RGsetEx)$cell_type <- rep(c("type1","type2"),3)
mySampleSet=fromRGChannelSet(RGsetEx)
mySampleSet=funtooNorm(mySampleSet)
### getGRanges

Build GRanges object of methylation probes

**Usage**

```r
getGRanges(object)
```

#### Arguments

- `object` Object of class SampleSet.

**Value**

A GRanges object of the positions of each cpg.

#### Methods (by class)

- `SampleSet` Build GRanges object of methylation probes

**Examples**

```r
require(minfiData)
pData(RGsetEx)$cell_type <- rep(c("type1","type2"),3)
mySampleSet=fromRGChannelSet(RGsetEx)
gr=getGRanges(mySampleSet)
```

---

### getNormBeta

Computes Beta values from normalized signals

**Description**

Computes Beta values from normalized signals

**Usage**

```r
getNormBeta(object, offset = 100)
```

#### Arguments

- `object` object
- `offset` offset = 100

#### Examples

```r
require(minfiData)
pData(RGsetEx)$cell_type <- rep(c("type1","type2"),3)
mySampleSet=fromRGChannelSet(RGsetEx)
gr=getGRanges(mySampleSet)
```
getNormM

Arguments

object of type SampleSet
offset default is 100 as Illumina standard

Value

a matrix containing beta after normalization value for each CpG position and each samples

Methods (by class)

- SampleSet: Computes Beta values from normalized signals

Examples

```r
require(minfiData)
pData(RGsetEx)$cell_type <- rep(c("type1","type2"),3)
mySampleSet=fromRGChannelSet(RGsetEx)
b=getNormBeta(funtooNorm(mySampleSet))
```

getNormM Computes M values, log2(Meth/Unmeth), from normalized signals

Description

Computes M values, log2(Meth/Unmeth), from normalized signals

Usage

getNormM(object)

```r
## S4 method for signature 'SampleSet'
getNormM(object)
```

Arguments

object An object of class SampleSet

Value

a matrix containing M values, log2(Meth/Unmeth), after normalization

Methods (by class)

- SampleSet: Computes M values, log2(Meth/Unmeth), from normalized signals
getRawBeta

Computes Beta value from raw signals

Description

Computes Beta value from raw signals

Usage

getRawBeta(object, offset = 100)

## S4 method for signature 'SampleSet'
getRawBeta(object, offset = 100)

Arguments

object object of class SampleSet
offset default is 100 as Illumina standard

Value

a matrix containing the raw beta value for each position and each samples

Methods (by class)

- SampleSet: Computes Beta value from raw signals

Examples

```r
require(minfiData)
pData(RGsetEx)$cell_type <- rep(c("type1","type2"),3)
mySampleSet=fromRGChannelSet(RGsetEx)
m=getNormM(funtooNorm(mySampleSet))
r=getRawBeta(mySampleSet)
```
**getSnpM**

*Computes M values after normalization of SNP data.*

**Description**

Computes M values after normalization of SNP data.

**Usage**

```r
getSnpM(object)
```

**Arguments**

- `object` of class `SampleSet`

**Value**

A matrix containing M values, log2(Meth/Unmeth), after normalization for SNP data.

**Methods (by class)**

- `SampleSet`: Computes M values, log2(Meth/Unmeth), for normalized SNP data

**Examples**

```r
require(minfiData)
pData(RGsetEx)$cell_type <- rep(c("type1","type2"),3)
mySampleSet=fromRGChannelSet(RGsetEx)
snp=getSnpM(funtooNorm(mySampleSet))
```

**plotValidationGraph**

*Plot of Validation Graph for determining number of components*

**Description**

Plots a series of graphs for each signal type, to determine the number of components to include in the normalization procedure.
SampleSet-class

Usage

plotValidationGraph(object, type.fits = "PCR", pdf.file = NULL)

## S4 method for signature 'SampleSet'
plotValidationGraph(object, type.fits = "PCR",
                      pdf.file = NULL)

Arguments

- object: of class SampleSet
- type.fits: can be "PCR" or "PLS" (default "PCR")
- pdf.file: if no file name is provided print pdf file plotValidationGraph.pdf in working directory.

Value

No value is returned. The function prints the plots to a pdf file.

Methods (by class)

- SampleSet: Plots a series of graphs for each signal type, to determine the number of components to include in the normalization procedure.

Examples

```r
require(minfiData)
pData(RGsetEx)$cell_type <- rep(c("type1","type2"),3)
mySampleSet=fromRGChannelSet(RGsetEx)
plotValidationGraph(mySampleSet)
```

SampleSet-class

S4 class object SampleSet

Description

SampleSet is an S4 class defined for the purpose of running the funtooNorm algorithm. They are lists containing signal data and different variables useful for funtooNorm. The data is separated into the 3 probes types, each having 2 channels (methylated and unmethylated ie : A and B) We then define then the 6 (2^3) labels: AIGrn BIGrn AIRed BIRed AII BII

Value

- a S4 object of class SampleSet
**show,SampleSet-method**

**Slots**

- **type**  Character: is 'minfi’ or 'GenomeStudio'
- **sampleNames**  character vector: contain the list of sample names in order used
- **sampleSize**  numeric: the number of samples
- **npos**  numeric: the number of positions in the ILLUMINA chip
- **annotation**  character: the annotation object from minfi package
- **cell_type**  factor: vector of the cell type for each sample as factors
- **qntllist**  numeric: vector of ordered quantiles
- **quantiles**  list: list of 6 quantiles tables for the 6 signal types
- **ctl.covmat**  matrix: covariance matrix for the model fit
- **signal**  list: list of the values for all 6 probe types.
- **names**  list: list of probes for each type
- **predmat**  list: list of the normalized values for all 6 probe types.

**Examples**

```r
showClass("SampleSet")
```

---

**Description**

Display informations about the SampleSet object

**Usage**

```r
## S4 method for signature 'SampleSet'
show(object)
```

**Arguments**

- **object**  an object of class SampleSet
- **...**  optional arguments passed to or from other methods.

**Value**

No value is returned. The function prints the summary of object of class SampleSet to screen

**Examples**

```r
require(minfiData)
pData(RGsetEx)$cell_type <- rep(c("type1","type2"),3)
mySampleSet=fromRGChannelSet(RGsetEx)
mySampleSet
```
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