Package ‘qsmooth’

May 30, 2024

Title Smooth quantile normalization
Version 1.20.0
Imports SummarizedExperiment, utils, sva, stats, methods, graphics, Hmisc
Depends R (>= 4.0)
Suggests bodymapRat, quantro, knitr, rmarkdown, BiocStyle, testthat
VignetteBuilder knitr
RoxygenNote 7.1.1
Encoding UTF-8
License GPL-3

Description Smooth quantile normalization
is a generalization of quantile normalization,
which is average of the two types of assumptions
about the data generation process: quantile
normalization and quantile normalization between
groups.

biocViews Normalization, Preprocessing, MultipleComparison,
Microarray, Sequencing, RNASeq, BatchEffect
git_url https://git.bioconductor.org/packages/qsmooth
git_branch RELEASE_3_19
git_last_commit 5a2ec39
git_last_commit_date 2024-04-30
Repository Bioconductor 3.19

Date/Publication 2024-05-29

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### Description

This function applies a generalization of quantile normalization called smoothed quantile normalization. This function defines the `qsmooth` class and constructor.

### Usage

```r
qsmooth(object, group_factor, batch = NULL, norm_factors = NULL, window = 0.05)
```

### Arguments

- **object**: an object which is a matrix or `data.frame` with observations (e.g. probes or genes) on the rows and samples as the columns. Alternatively, a user can provide a `SummarizedExperiment` object and the `assay(object, "counts")` will be used as input for the `qsmooth` normalization.

- **group_factor**: a group level continuous or categorical covariate associated with each sample or column in the object. The order of the `group_factor` must match the order of the columns in `object`.

- **batch**: (Optional) batch covariate (multiple batches are not allowed). If batch covariate is provided, `Combat()` from `sva` is used prior to `qsmooth` normalization to remove batch effects. See `Combat()` for more details.

- **norm_factors**: optional normalization scaling factors.

- **window**: window size for running median which is a fraction of the number of rows in `object`. Default is 0.05.

### Details

Quantile normalization is one of the most widely used normalization tools for data analysis in genomics. Although it was originally developed for gene expression microarrays it is now used across many different high-throughput applications including RNAseq and ChIPseq. The methodology relies on the assumption that observed changes in the empirical distribution of samples are due to unwanted variability. Because the data is transformed to remove these differences it has the
potential to remove interesting biologically driven global variation. Therefore, applying quantile normalization, or other global normalization methods that rely on similar assumptions, may not be appropriate depending on the type and source of variation.

This function computes a weight at every quantile that compares the variability between groups relative to within groups. In one extreme quantile normalization is applied and in the other extreme quantile normalization within each biological condition is applied. The weight shrinks the group-level quantile normalized data towards the overall reference quantiles if variability between groups is sufficiently smaller than the variability within groups. See the vignette for more details.

Value

A object of the class qsmooth that contains a numeric vector of the qsmooth weights in the qsmoothWeights slot and a matrix of normalized values after applying smoothed quantile normalization in the qsmoothData slot.

Examples

dat <- cbind(matrix(rnorm(1000), nrow=100, ncol=10),
               matrix(rnorm(1000, .1, .7), nrow=100, ncol=10))
dat_qs <- qsmooth(object = dat,
                    group_factor = rep(c(0,1), each=10))
**qsmoothData**

*Generic function that returns the qsmooth normalized data*

**Description**

Given a qsmooth object, this function returns the qsmooth normalized data.

Accessors for the 'qsmoothData' slot of a qsmooth object.

**Usage**

```r
def qsmoothData(object)
```

```r
## S4 method for signature 'qsmooth'
def qsmoothData(object)
```

**Arguments**

object an object of class qsmooth.

**Value**

The normalized data after applying smoothed quantile normalization.

**Examples**

```r
dat <- cbind(matrix(rnorm(1000), nrow=100, ncol=10),
             matrix(rnorm(1000, .1, .7), nrow=100, ncol=10))
dat_qs <- qsmooth(object = dat,
                  group_factor = rep(c(0,1), each=10))
qsmoothData(dat_qs)
```

---

**qsmoothGC**

*qsmoothGC*

**Description**

This function applies smoothed quantile normalization separately for groups of features that are binned according to their GC-content.

**Usage**

```r
def qsmoothGC(object, group_factor, gc, nGroups = 50, round = TRUE, ...)
```
Arguments

object

an object which is a matrix or data.frame with observations (e.g. probes or genes) on the rows and samples as the columns. Alternatively, a user can provide a SummarizedExperiment object and the assay(object, "counts") will be used as input for the qsmooth normalization.

group_factor

a group level continuous or categorial covariate associated with each sample or column in the object. The order of the group_factor must match the order of the columns in object.

gc

GC-content of the features, ordered according to the features in object.

nGroups

The number of equally-sized bins used to group the GC-content values. Groups are created using Hmisc::cut2.

round

Should normalized values be rounded to integers?

... (Optional) Additional arguments passed to qsmooth.

Value

A matrix of normalized counts.

References


Examples

dat <- cbind(matrix(rnorm(1000), nrow=100, ncol=10), matrix(rnorm(1000, .1, .7), nrow=100, ncol=10))
gc <- runif(n=100, min=0.2, max=0.9)
dat_qs <- qsmoothGC(object = dat, gc = gc, group_factor = rep(c(0,1), each=10))

qsmoothPlotWeights

Plot weights from qsmooth function.

Description

This function plots a scatterplot showing the qsmoothWeights along the y-axis and the quantiles on the x-axis.
Usage

```r
qsmoothPlotWeights(
  object,
  xLab = "quantiles",
  yLab = "weights",
  mainLab = "qsmooth weights"
)
```

Arguments

- `object`: a qsmooth object from `qsmooth`
- `xLab`: label for x-axis. Default is "quantiles"
- `yLab`: label for y-axis. Default is "weights"
- `mainLab`: title of plot. Default is "qsmooth weights"

Value

A scatterplot will be created showing the `qsmoothWeights` along the y-axis and the quantiles on the x-axis.

Examples

```r
dat <- cbind(matrix(rnorm(1000), nrow=100, ncol=10),
             matrix(rnorm(1000, .1, .7), nrow=100, ncol=10))
dat_qs <- qsmooth(object = dat,
                   group_factor = rep(c(0,1), each=10))
qsmoothPlotWeights(dat_qs)
```

---

**qsmoothWeights**

Generic function that returns the qsmooth weights

Description

Given a qsmooth object, this function returns the qsmooth weights

Accessors for the `qsmoothWeights` slot of a qsmooth object.

Usage

```r
qsmoothWeights(object)
```

## S4 method for signature 'qsmooth'

```r
qsmoothWeights(object)
```

Arguments

- `object`: an object of class qsmooth.
The weights calculated for each feature after applying smoothed quantile normalization.

```r
dat <- cbind(matrix(rnorm(1000), nrow=100, ncol=10),
             matrix(rnorm(1000, .1, .7), nrow=100, ncol=10))
dat_qs <- qsmooth(object = dat,
                  group_factor = rep(c(0,1), each=10))
qusmoothWeights(dat_qs)
```

This function is a helper function that computes quantile statistics for the function `qsmooth`.

```r
qstats(object, group_factor, window = 0.05)
```

- **object**: an object which is a data frame or matrix with observations (e.g. probes or genes) on the rows and samples as the columns.
- **group_factor**: a group level continuous or categorial covariate associated with each sample or column in the `object`. The order of the `group_factor` must match the order of the columns in `object`.
- **window**: window size for running median which is a fraction of the number of rows in `object`. Default is 0.05.

- **Q**: sample quantiles
- **Qref**: reference quantile
- **Qhat**: linear model fit at each quantile
- **SST**: total sum of squares
- **SSB**: between sum of squares
- **SSE**: within sum of squares
- **roughWeights**: `SSE / SST`
- **smoothWeights**: smoothed weights computed using a running median with a given window size.
Examples

dat <- cbind(matrix(rnorm(1000), nrow=100, ncol=10),
             matrix(rnorm(1000, .1, .7), nrow=100, ncol=10))
qs <- qstats(object = dat,
             group_factor = rep(c(0,1), each=10),
             window = 0.05)
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