Package 'qsvaR'

April 10, 2023

Title Generate Quality Surrogate Variable Analysis for Degradation
Correction

Version 1.2.0

Date 2022-04-01

Description The qsvaR package contains functions for removing the effect of
degration in rna-seq data from postmortem brain tissue. The package is
equipped to help users generate principal components associated with
degradation. The components can be used in differential expression analysis
to remove the effects of degradation.

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URL https://github.com/LieberInstitute/qsvaR

BugReports https://support.bioconductor.org/t/qsvaR

biocViews Software, WorkflowStep, Normalization, BiologicalQuestion,
DifferentialExpression, Sequencing, Coverage

Encoding UTF-8

Roxygen list(markdown = TRUE)

RoxygenNote 7.1.2

Suggests BiocFileCache, BiocStyle, covr, knitr, limma, RefManageR,
rmarkdown, sessioninfo, testthat (>= 3.0.0)

Config/testthat/edition 3

Imports sva, stats, ggplot2, methods

Depends R (>= 4.2), SummarizedExperiment

LazyData true

VignetteBuilder knitr

git_url https://git.bioconductor.org/packages/qsvaR

git_branch RELEASE_3_16

git_last_commit cb5aee3

git_last_commit_date 2022-11-01

Date/Publication 2023-04-10

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R topics documented:

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covComb_tx_deg   *RSE object of RNA-seq data that serves as output for degradation*
                               analysis

Description

This data was generated from an experiment using degraded RNA-seq samples post-mortem brain
tissue. The transcripts included are the result of the qsva expanded framework study and will be
used to remove the effect of degradation in bulk RNA-seq data.

Format

A RangedSummarizedExperiment-class

See Also

getPCs k_qsvs getDegTx

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degradation_tstats *Degradation time t-statistics*

Description

These t-statistics are derived from the same data that was used for [covComb_tx_deg](). They are the results from main model where we determined the relationship with degradation time adjusting for the brain region (so parallel degradation effects across brain regions). They are used for plotting in DEqual().

Format

A data.frame() with the t statistics for degradation time. The rownames() are the GENCODE transcript IDs.

See Also

[DEqual]()

DEqual *Differential expression quality (DEqual) plot*

Description

A DEqual plot compares the effect of RNA degradation from an independent degradation experiment on the y axis to the effect of the outcome of interest. They were orignally described by Jaffe et al, PNAS, 2017 <https://doi.org/10.1073/pnas.1617384114>. Other DEqual versions are included in Collado-Torres et al, Neuron, 2019 <https://doi.org/10.1016/j.neuron.2019.05.013>. This function compares your t-statistics of interest computed on transcripts against the t-statistics from degradation time adjusting for the six brain regions from degradation experiment data used for determining covComb_tx_deg.

Usage

```
DEqual(DE)
```

Arguments

DE   a data.frame() with one column containing the t-statistics from Differential Expression, typically generated with limma::topTable(). The rownames(DE) should be transcript GENCODE IDs.

Value

a ggplot object of the DE t-statistic vs the DE statistic from degradation

Examples

```
## Random differential expression t-statistics for the same transcripts
## we have degradation t-statistics for in `degradation_tstats`.
set.seed(101)
random_de <- data.frame(
    t = rt(nrow(degradation_tstats), 5),
    row.names = sample(
        rownames(degradation_tstats),
        nrow(degradation_tstats)
    )
)

## Create the DEqual plot
DEqual(random_de)
```

---

getDegTx   *Obtain expression matrix for degraded transcripts*

Description

This function is used to obtain a [RangedSummarizedExperiment-class](#) of transcripts and their expression values #' These transcripts are selected based on a prior study of RNA degradation in postmortem brain tissues. This object can later be used to obtain the principle components necessary to remove the effect of degradation in differential expression.

Usage

```
getDegTx(
  rse_tx,
  type = "cell_component",
  sig_transcripts = select_transcripts(type),
  assayname = "tpm"
)
```

Arguments

rse_tx   A [RangedSummarizedExperiment-class](#) object containing the transcript data desired to be studied.

type   A character(1) specifying the transcripts set type. These were determined by Joshua M. Stolz et al, 2022. Here the names "cell_component", "top1500", and "standard" refer to models that were determined to be effective in removing degradation effects. The "standard" model involves taking the union of the top 1000 transcripts associated with degradation from the interaction model and the main effect model. The "top1500" model is the same as the "standard model except the union of the top 1500 genes associated with degradation is selected. The most effective of our models, "cell_component", involved deconvolution of the degradation matrix to determine the proportion of cell types within our

studied tissue. These proportions were then added to our model.matrix() and the union of the top 1000 transcripts in the interaction model, the main effect model, and the cell proportions model were used to generate this model of qSVs.

sig_transcripts
A list of transcripts determined to have degradation signal in the qsva expanded paper.

assayname   character string specifying the name of the assay desired in rse_tx

Value

A [RangedSummarizedExperiment-class](#) object.

Examples

```
getDegTx(covComb_tx_deg)
stopifnot(mean(rowMeans(assays(covComb_tx_deg)$tpm)) > 1)
```

---

getPCs   *PCs from transcripts*

Description

This function returns the pcs from the obtained RangedSummarizedExperiment object of selected transcripts

Usage

```
getPCs(rse_tx, assayname = "tpm")
```

Arguments

rse_tx   Ranged Summarizeed Experiment with only trancsripts selected for qsva

assayname   character string specifying the name of the assay desired in rse_tx

Value

prcomp object generated by taking the pcs of degraded transcripts

Examples

```
getPCs(covComb_tx_deg, "tpm")
```

---

get_qsvs   *Generate matrix of qsvs*

Description

Using the pcs and the k number of components be included, we generate the qsva matrix.

Usage

```
get_qsvs(qsvPCs, k)
```

Arguments

qsvPCs   prcomp object generated by taking the pcs of degraded transcripts

k   number of qsvs to be included.

Value

matrix with k principal components for each sample.

Examples

```
qsv <- list(x = matrix(seq_len(9), ncol = 3))
get_qsvs(qsv, 2)
```

---

k_qsvs   *Apply num.sv algorithm to determine the number of pcs to be included*

Description

Apply num.sv algorithm to determine the number of pcs to be included

Usage

```
k_qsvs(rse_tx, mod, assayname)
```

Arguments

rse_tx   A [RangedSummarizedExperiment-class](#) object containing the transcript data desired to be studied.

mod   Model Matrix with necessary variables the you would model for in differential expression

assayname   character string specifying the name of the assay desired in rse_tx

Value

integer representing number of pcs to be included

Examples

```
mod <- model.matrix(~ mitoRate + Region + rRNA_rate + totalAssignedGene + RIN,
    data = colData(covComb_tx_deg)
)
k_qsvs(covComb_tx_deg, mod, "tpm")
```

---

qSVA   *A wrapper function used to perform qSVA in one step.*

Description

A wrapper function used to perform qSVA in one step.

Usage

```
qSVA(
  rse_tx,
  type = "cell_component",
  sig_transcripts = select_transcripts(type),
  mod,
  assayname
)
```

Arguments

rse_tx	A [RangedSummarizedExperiment-class](#) object containing the transcript data desired to be studied.
type	a character string specifying which model you would like to use when selecting a degradation matrix.
sig_transcripts	
	A list of transcripts determined to have degradation signal in the qsva expanded paper.
mod	Model Matrix with necessary variables the you would model for in differential expression
assayname	character string specifying the name of the assay desired in rse_tx

Value

matrix with k principal components for each sample

Examples

```
mod <- model.matrix(~ mitoRate + Region + rRNA_rate + totalAssignedGene + RIN,
    data = colData(covComb_tx_deg)
)
qSVA(rse_tx = covComb_tx_deg, type = "cell_component", mod = mod, assayname = "tpm")
```

---

select_transcripts   *Select transcripts associated with degradation*

Description

Helper function to select which experimental model will be used to generate the qSVs.

Usage

```
select_transcripts(type = c("cell_component", "top1500", "standard"))
```

Arguments

type   A `character(1)` specifying the transcripts set type. These were determined
                    by Joshua M. Stolz et al, 2022. Here the names "cell_component", "top1500",
                    and "standard" refer to models that were determined to be effective in removing
                    degradation effects. The "standard" model involves taking the union of the top
                    1000 transcripts associated with degradation from the interaction model and the
                    main effect model. The "top1500" model is the same as the "standard model
                    except the union of the top 1500 genes associated with degradation is selected.
                    The most effective of our models, "cell_component", involved deconvolution
                    of the degradation matrix to determine the proportion of cell types within our
                    studied tissue. These proportions were then added to our `model.matrix()` and
                    the union of the top 1000 transcripts in the interaction model, the main effect
                    model, and the cell proportions model were used to generate this model of qSVs.

Value

A `character()` with the transcript IDs.

Examples

```
## Default set of transcripts associated with degradation
sig_transcripts <- select_transcripts()
length(sig_transcripts)
head(sig_transcripts)

## Example where match.arg() auto-completes
select_transcripts("top")
```

---

transcripts *Transcripts for Degradation Models*

Description

An object storing three lists of transcripts each corresponding to a model used in the degradation experiment. These were determined by Joshua M. Stolz et al, 2022. Here the names "cell_component", "top1500", and "standard" refer to models that were determined to be effective in removing degradation effects. The "standard" model involves taking the union of the top 1000 transcripts associated with degradation from the interaction model and the main effect model. The "top1500" model is the same as the "standard" model except the union of the top 1500 genes associated with degradation is selected. The most effective of our models, "cell_component", involved deconvolution of the degradation matrix to determine the proportion of cell types within our studied tissue. These proportions were then added to our model.matrix() and the union of the top 1000 transcripts in the interaction model, the main effect model, and the cell proportions model were used to generate this model of qSVs.

Usage

```
transcripts
```

Format

A list() with character strings containing the transcripts selected by each model. Each string is a GENCODE transcript IDs.

See Also

select_transcripts

Index