Package 'ADImpute'

February 1, 2026

Type Package

Title Adaptive Dropout Imputer (ADImpute)

Version 1.21.0

Description Single-cell RNA sequencing (scRNA-seq) methods are typically unable to quantify the expression levels of all genes in a cell, creating a need for the computational prediction of missing values ('dropout imputation'). Most existing dropout imputation methods are limited in the sense that they exclusively use the scRNA-seq dataset at hand and do not exploit external gene-gene relationship information. Here we propose two novel methods: a gene regulatory network-based approach using gene-gene relationships learnt from external data and a baseline approach corresponding to a sample-wide average. ADImpute can implement these novel methods and also combine them with existing imputation methods (currently supported: DrImpute, SAVER). ADImpute can learn the best performing method per gene and combine the results from different methods into an ensemble.

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Encoding UTF-8

LazyData true

Depends R (>= 4.0)

Imports checkmate, BiocParallel, data.table, DrImpute, kernlab, MASS, Matrix, methods, rsvd, S4Vectors, SAVER, SingleCellExperiment, stats, SummarizedExperiment, utils

Suggests BiocStyle, knitr, rmarkdown, testthat

biocViews GeneExpression, Network, Preprocessing, Sequencing, SingleCell, Transcriptomics

RoxygenNote 7.1.1

VignetteBuilder knitr

BugReports https://github.com/anacarolinaleote/ADImpute/issues

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

git_branch devel

git_last_commit 8a9fa73

git_last_commit_date 2025-10-29

Repository Bioconductor 3.23

Date/Publication 2026-02-01

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Contents

`ArrangeData` *Data trimming*

Description

`ArrangeData` finds common genes to the network and provided data and limits both datasets to these

Usage

```
ArrangeData(data, net.coef = NULL)
```

Arguments

`data`	matrix with entries equal to zero to be imputed (genes as rows and samples as columns)
`net.coef`	matrix; object containing network coefficients

Value

list; data matrix, network coefficients matrix and intercept for genes common between the data matrix and the network

---

`CenterData` *Data centering*

Description

`CenterData` centers expression of each gene at 0

Usage

```
CenterData(data)
```

Arguments

`data`	matrix of gene expression to be centered row-wise (genes as rows and samples as columns)

Value

list; row-wise centers and centered data

CheckArguments_Impute *Argument check to Impute()*

Description

CheckArguments_Impute checks whether the arguments passed to Impute are correct.

Usage

```
CheckArguments_Impute(data, method.choice, do, tr.length, labels,
cell.clusters, true.zero.thr, drop_thre)
```

Arguments

data	matrix; raw counts (genes as rows and samples as columns)
method.choice	character; best performing method in training data for each gene
do	character; choice of methods to be used for imputation. Currently supported methods are 'Baseline', 'DrImpute', 'Network', and 'Ensemble'. Defaults to 'Ensemble'. Not case-sensitive. Can include one or more methods. Non-supported methods will be ignored.
tr.length	matrix with at least 2 columns: 'hgnc_symbol' and 'transcript_length'
labels	character; vector specifying the cell type of each column of data
cell.clusters	integer; number of cell subpopulations
true.zero.thr	if set to NULL (default), no true zero estimation is performed. Set to numeric value between 0 and 1 for estimation. Value corresponds to the threshold used to determine true zeros: if the probability of dropout is lower than true.zero.thr, the imputed entries are set to zero.
drop_thre	numeric; between 0 and 1 specifying the threshold to determine dropout values

Value

NULL object

ChooseMethod *Method choice per gene*

Description

ChooseMethod determines the method for dropout imputation based on performance on each gene in training data

Usage

```
ChooseMethod(real, masked, imputed, write.to.file = TRUE)
```

Arguments

real	matrix; original gene expression data, i.e. before masking (genes as rows and samples as columns)
masked	matrix, logical indicating which entries were masked (genes as rows and samples as columns)
imputed	list; list of matrices with imputation results for all considered methods
write.to.file	logical; should the output be written to a file?

Details

The imputed values are compared to the real ones for every masked entry in real. The Mean Squared Error is computed for all masked entries per gene and the method with the best performance is chosen for each gene.

Value

character; best performing method in the training set for each gene

See Also

ComputeMSEGenewise

Combine *Combine imputation methods*

Description

Combine imputation methods

Usage

```
Combine(data, imputed, method.choice, write = FALSE)
```

Arguments

data	matrix with entries equal to zero to be imputed, already normalized (genes as rows and samples as columns)
imputed	list; list of matrices with imputation results for all considered methods
method.choice	named character; vector with the best performing method per gene
write	logical; should a file with the imputation results be written?

Details

Combines imputation results from all methods according to training results provided in method.choice

Value

matrix; imputation results combining the best performing method per gene

ComputeMSEGenewise *Computation of MSE per gene*

Description

ComputeMSEGenewise computes the MSE of dropout imputation for a given gene.

Usage

```
ComputeMSEGenewise(real, masked, imputed, baseline)
```

Arguments

real	numeric; vector of original expression of a given gene (before masking)
masked	logical; vector indicating which entries were masked for a given gene
imputed	matrix; imputation results for a given imputation method
baseline	logical; is this baseline imputation?

Value

MSE of all imputations indicated by masked

CreateArgCheck *Argument check*

Description

CreateArgCheck creates tests for argument correctness.

Usage

```
CreateArgCheck(missing = NULL, match = NULL, acceptable = NULL,
null = NULL)
```

Arguments

missing	named list; logical. Name corresponds to variable name, and corresponding entry to whether it was missing from the function call.
match	named list. Name corresponds to variable name, and corresponding entry to its value.
acceptable	named list. Name corresponds to variable name, and corresponding entry to its acceptable values.
null	named list; logical. Name corresponds to variable name, and corresponding entry to whether it was NULL in the function call.

Value

argument check object.

`CreateTrainData` *Preparation of training data for method evaluation*

Description

`CreateTrainingData` selects a subset of cells to use as training set and sets a portion (`mask`) of the non-zero entries in each row of the subset to zero

Usage

```
CreateTrainData(data, train.ratio = .7, train.only = TRUE, mask = .1,
write = FALSE)
```

Arguments

`data`	matrix; raw counts (genes as rows and samples as columns)
`train.ratio`	numeric; ratio of the samples to be used for training
`train.only`	logical; if TRUE define only a training dataset, if FALSE writes both training and validation sets (defaults to TRUE)
`mask`	numeric; ratio of total non-zero samples to be masked per gene (defaults to .1)
`write`	logical; should the output be written to a file?

Value

list with resulting matrix after subsetting and after masking

---

`DataCheck_Matrix` *Data check (matrix)*

Description

`DataCheck_Matrix` tests for potential format and storage issues with matrices. Helper function to ADImpute.

Usage

```
DataCheck_Matrix(data)
```

Arguments

`data`	data object to check

Value

data object with needed adjustments

DataCheck_Network *Data check (network)*

Description

DataCheck_Network tests for potential format and storage issues with the network coefficient matrix. Helper function to ADImpute.

Usage

```
DataCheck_Network(network)
```

Arguments

network	data object containing matrix coefficients

Value

network data object with needed adjustments

DataCheck_SingleCellExperiment *Data check (SingleCellExperiment)*

Description

DataCheck_SingleCellExperiment tests for existence of the appropriate assays in sce. Helper function to ADImpute.

Usage

```
DataCheck_SingleCellExperiment(sce, normalized = TRUE)
```

Arguments

sce	SingleCellExperiment; data for normalization or imputation
normalized	logical; is the data expected to be normalized?

Value

NULL object.

DataCheck_TrLength *Data check (transcript length)*

Description

DataCheck_TrLength tests for potential format and storage issues with the object encoding transcript length, for e.g. TPM normalization. Helper function to ADImpute.

Usage

```
DataCheck_TrLength(trlength)
```

Arguments

trlength	data object containing transcript length information

Value

transcript length object with needed adjustments

demo_data *Small dataset for example purposes*

Description

A small dataset to use on vignettes and examples (50 cells).

Usage

```
demo_data
```

Format

matrix; a subset of the Grun pancreas dataset, obtained with the scRNAseq R package, to use in the vignette and examples.

References

Grun D et al. (2016). De novo prediction of stem cell identity using single-cell transcriptome data. Cell Stem Cell 19(2), 266-277.

demo_net *Small regulatory network for example purposes*

Description

Subset of the Gene Regulatory Network used by ADImpute's Network imputation method.

Usage

```
demo_net
```

Format

matrix; subset of the Gene Regulatory Network installed along with ADImpute.

demo_sce *Small dataset for example purposes*

Description

A small dataset to use on vignettes and examples (50 cells).

Usage

```
demo_sce
```

Format

SingleCellExperiment; a subset of the Grun pancreas dataset, obtained with the `scRNAseq` R package, to use in the vignette and examples.

References

Grun D et al. (2016). De novo prediction of stem cell identity using single-cell transcriptome data. Cell Stem Cell 19(2), 266-277.

EvaluateMethods *Imputation method evaluation on training set*

Description

EvaluateMethods returns the best-performing imputation method for each gene in the dataset

Usage

```
EvaluateMethods(data, sce = NULL, do = c('Baseline', 'DrImpute',
'Network'), write = FALSE, train.ratio = .7, train.only = TRUE,
mask.ratio = .1, outdir = getwd(), scale = 1, pseudo.count = 1,
labels = NULL, cell.clusters = 2, drop_thre = NULL, type = 'count',
cores = BiocParallel::bpworkers(BPPARAM),
BPPARAM = BiocParallel::SnowParam(type = "SOCK"),
net.coef = ADImpute::network.coefficients, net.implementation = 'iteration',
tr.length = ADImpute::transcript_length, bulk = NULL, ...)
```

Arguments

data	matrix; normalized counts, not logged (genes as rows and samples as columns)
sce	SingleCellExperiment; normalized counts and associated metadata.
do	character; choice of methods to be used for imputation. Currently supported methods are 'Baseline', 'DrImpute' and 'Network'. Not case-sensitive. Can include one or more methods. Non- supported methods will be ignored.
write	logical; write intermediary and imputed objects to files?
train.ratio	numeric; ratio of samples to be used for training
train.only	logical; if TRUE define only a training dataset, if FALSE writes and returns both training and validation sets (defaults to TRUE)
mask.ratio	numeric; ratio of samples to be masked per gene
outdir	character; path to directory where output files are written. Defaults to working directory
scale	integer; scaling factor to divide all expression levels by (defaults to 1)
pseudo.count	integer; pseudo-count to be added to expression levels to avoid log(0) (defaults to 1)
labels	character; vector specifying the cell type of each column of data
cell.clusters	integer; number of cell subpopulations
drop_thre	numeric; between 0 and 1 specifying the threshold to determine dropout values
type	A character specifying the type of values in the expression matrix. Can be 'count' or 'TPM'
cores	integer; number of cores used for paralell computation
BPPARAM	parallel back-end to be used during parallel computation. See BiocParallelParam-class.

net.coef — matrix; network coefficients. Please provide if you don't want to use ADImpute's network model. Must contain one first column 'O' acconting for the intercept of the model and otherwise be an adjacency matrix with hgnc_symbols in rows and columns. Doesn't have to be squared. See `ADImpute::demo_net` for a small example.

net.implementation — character; either 'iteration', for an iterative solution, or 'pseudoinv', to use Moore-Penrose pseudo-inversion as a solution. 'pseudoinv' is not advised for big data.

tr.length — matrix with at least 2 columns: 'hgnc_symbol' and 'transcript_length'

bulk — vector of reference bulk RNA-seq, if available (average across samples)

... — additional parameters to pass to network-based imputation

Details

For each gene, a fraction (`mask.ratio`) of the quantified expression values are set to zero and imputed according to 3 different methods: scImpute, baseline (average gene expression across all cells) or a network-based method. The imputation error is computed for each of the values in the original dataset that was set to 0, for each method. The method resulting in a lowest imputation error for each gene is chosen.

Value

- if `sce` is provided: returns a SingleCellExperiment with the best performing method per gene stored as row-features. Access via `SingleCellExperiment::int_elementMetadata(sce)$ADImpute$methods`.
- if `sce` is not provided: returns a character with the best performing method in the training set for each gene

See Also

ImputeBaseline, ImputeDrImpute, ImputeNetwork

Examples

```
# Normalize demo data
norm_data <- NormalizeRPM(ADImpute::demo_data)
method_choice <- EvaluateMethods(norm_data, do = c('Baseline','DrImpute'),
cores = 2)
```

GetDropoutProbabilities *Get dropout probabilities*

Description

GetDropoutProbabilities computes dropout probabilities (probability of being a dropout that should be imputed rather than a true biological zero) using an adaptation of scImpute's approach

Usage

```
GetDropoutProbabilities(data, thre, cell.clusters, labels = NULL,
type = 'count', cores, BPPARAM, genelen = ADImpute::transcript_length)
```

Arguments

data	matrix; original data before imputation
thre	numeric; probability threshold to classify entries as biological zeros
cell.clusters	integer; number of cell subpopulations
labels	character; vector specifying the cell type of each column of data
type	A character specifying the type of values in the expression matrix. Can be 'count' or 'TPM'
cores	integer; number of cores used for paralell computation
BPPARAM	parallel back-end to be used during parallel computation. See BiocParallelParam-class.
genelen	matrix with at least 2 columns: 'hgnc_symbol' and 'transcript_length'

Details

This function follows scImpute's model to distinguish between true biological zeros and dropouts, and is based on adapted code from the scImpute R package.

Value

matrix with same dimensions as data containing the dropout probabilities for the corresponding entries

HandleBiologicalZeros *Get dropout probabilities*

Description

GetDropoutProbabilities computes dropout probabilities (probability of being a dropout that should be imputed rather than a true biological zero) using an adaptation of scImpute's approach

Usage

```
HandleBiologicalZeros(data, imputed, thre = 0.5, cell.clusters,
labels = NULL, type = 'count', cores = BiocParallel::bpworkers(BPPARAM),
BPPARAM = BiocParallel::SnowParam(type = "SOCK"),
genelen = ADImpute::transcript_length, prob.mat = NULL)
```

Arguments

data	matrix; original data before imputation
imputed	list; imputation results for considered methods
thre	numeric; between 0 and 1 specifying the threshold to determine dropout values
cell.clusters	integer; number of cell subpopulations
labels	character; vector specifying the cell type of each column of data
type	A character specifying the type of values in the expression matrix. Can be 'count' or 'TPM'
cores	integer; number of cores used for paralell computation
BPPARAM	parallel back-end to be used during parallel computation. See BiocParallelParam-class.
genelen	matrix with at least 2 columns: 'hgnc_symbol' and 'transcript_length'
prob.mat	matrix with same dimensions as data containing the dropout probabilities for the corresponding entries

Details

This function follows scImpute's model to distinguish between true biological zeros and dropouts, and is based on adapted code from the scImpute R package.

Value

list with 2 components: zerofiltered, a list equivalent to imputed but with entries of imputed likely biological zeros set back to zero, and dropoutprobabilities matrix with same dimensions as data containing the dropout probabilities for the corresponding entries

Impute *Dropout imputation using different methods*

Description

Impute performs dropout imputation on normalized data, based on the choice of imputation methods.

Usage

```
Impute(data, sce = NULL, do = 'Ensemble', write = FALSE,
outdir = getwd(), method.choice = NULL, scale = 1, pseudo.count = 1,
labels = NULL, cell.clusters = 2, drop_thre = NULL, type = 'count',
tr.length = ADImpute::transcript_length,
cores = BiocParallel::bpworkers(BPPARAM),
BPPARAM = BiocParallel::SnowParam(type = "SOCK"),
net.coef = ADImpute::network.coefficients, net.implementation = 'iteration',
bulk = NULL, true.zero.thr = NULL, prob.mat = NULL, ...)
```

Arguments

data	matrix; raw counts (genes as rows and samples as columns)
sce	SingleCellExperiment; normalized counts and associated metadata.
do	character; choice of methods to be used for imputation. Currently supported methods are 'Baseline', 'DrImpute', 'Network', and 'Ensemble'. Defaults to 'Ensemble'. Not case-sensitive. Can include one or more methods. Non-supported methods will be ignored.
write	logical; write intermediary and imputed objects to files?
outdir	character; path to directory where output files are written. Defaults to working directory
method.choice	character; best performing method in training data for each gene
scale	integer; scaling factor to divide all expression levels by (defaults to 1)
pseudo.count	integer; pseudo-count to be added to expression levels to avoid log(0) (defaults to 1)
labels	character; vector specifying the cell type of each column of data
cell.clusters	integer; number of cell subpopulations
drop_thre	numeric; between 0 and 1 specifying the threshold to determine dropout values
type	A character specifying the type of values in the expression matrix. Can be 'count' or 'TPM'
tr.length	matrix with at least 2 columns: 'hgnc_symbol' and 'transcript_length'
cores	integer; number of cores used for paralell computation
BPPARAM	parallel back-end to be used during parallel computation. See BiocParallelParam-class.

net.coef — matrix; network coefficients. Please provide if you don't want to use ADImpute's network model. Must contain one first column 'O' acconting for the intercept of the model and otherwise be an adjacency matrix with hgnc_symbols in rows and columns. Doesn't have to be squared. See `ADImpute::demo_net` for a small example.

net.implementation — character; either 'iteration', for an iterative solution, or 'pseudoinv', to use Moore-Penrose pseudo-inversion as a solution. 'pseudoinv' is not advised for big data.

bulk — vector of reference bulk RNA-seq, if available (average across samples)

true.zero.thr — if set to NULL (default), no true zero estimation is performed. Set to numeric value between 0 and 1 for estimation. Value corresponds to the threshold used to determine true zeros: if the probability of dropout is lower than `true.zero.thr`, the imputed entries are set to zero.

prob.mat — matrix of the same size as data, filled with the dropout probabilities for each gene in each cell

... — additional parameters to pass to network-based imputation

Details

Values that are 0 in `data` are imputed according to the best-performing methods indicated in `method.choice`. Currently supported methods are:

- `Baseline`: imputation with average expression across all cells in the dataset. See `ImputeBaseline`.
- Previously published approaches: `DrImpute` and `SAVER`.
- `Network`: leverages information from a gene regulatory network to predicted expression of genes that are not quantified based on quantified interacting genes, in the same cell. See `ImputeNetwork`.
- `Ensemble`: is based on results on a training subset of the data at hand, indicating which method best predicts the expression of each gene. These results are supplied via `method.choice`. Applies the imputation results of the best performing method to the zero entries of each gene.

If `'Ensemble'` is included in `do`, `method.choice` has to be provided (use output from `EvaluateMethods()`). `Impute` can create a directory `imputation` containing the imputation results of all methods in `do`. If `true.zero.thr` is set, dropout probabilities are computed using scImpute's framework. Expression values with dropout probabilities below `true.zero.thr` will be set back to 0 if imputed, as they likely correspond to true biological zeros (genes not expressed in cell) rather than technical dropouts (genes expressed but not captured). If `sce` is set, imputed values by the different methods are added as new assays to `sce`. Each assay corresponds to one imputation method. If `true.zero.thr` is set, only the values after filtering for biological zeros will be added. This is different from the output if `sce` is not set, where the original values before filtering and the dropout probability matrix are returned.

Value

- if `sce` is not set: returns a list of imputation results (normalized, log-transformed) for all selected methods in `do`. If `true.zero.thr` is defined, returns a list of 3 elements: 1) a list,

imputations, containing the direct imputation results from each method; 2) a list, zerofiltered, containing the results of imputation in imputations after setting biological zeros back to zero; 3) a matrix, dropoutprobabilities, containing the dropout probability matrix used to set biological zeros.

- if sce is set: returns a SingleCellExperiment with new assays, each corresponding to one of the imputation methods applied. If true.zero.thr is defined, the assays will contain the results after imputation and setting biological zeros back to zero.

See Also

EvaluateMethods, ImputeBaseline, ImputeDrImpute, ImputeNetwork, ImputeSAVER

Examples

```
# Normalize demo data
norm_data <- NormalizeRPM(demo_data)
# Impute with particular method(s)
imputed_data <- Impute(do = 'Network', data = norm_data[,1:10],
net.coef = ADImpute::demo_net)
imputed_data <- Impute(do = 'Network', data = norm_data[,1:10],
net.implementation = 'pseudoinv', net.coef = ADImpute::demo_net)
```

ImputeBaseline *Impute using average expression across all cells*

Description

ImputeBaseline imputes dropouts using gene averages across cells. Zero values are excluded from the mean computation.

Usage

```
ImputeBaseline(data, write = FALSE, ...)
```

Arguments

data	matrix with entries equal to zero to be imputed, normalized and log2-transformed (genes as rows and samples as columns)
write	logical; should a file with the imputation results be written?
...	additional arguments to saveRDS

Value

matrix; imputation results considering the average expression values of genes

ImputeDrImpute *Use DrImpute*

Description

ImputeDrImpute uses the DrImpute package for dropout imputation

Usage

```
ImputeDrImpute(data, write = FALSE)
```

Arguments

data	matrix with entries equal to zero to be imputed, normalized and log2-transformed (genes as rows and samples as columns)
write	logical; should a file with the imputation results be written?

Value

matrix; imputation results from DrImpute

See Also

DrImpute

ImputeNetParallel *Network-based parallel imputation*

Description

ImputeNetParallel implements network-based imputation in parallel

Usage

```
ImputeNetParallel(drop.mat, arranged, cores =
BiocParallel::bpworkers(BPPARAM), type = 'iteration', max.iter = 50,
BPPARAM = BiocParallel::SnowParam(type = "SOCK"))
#'
```

Arguments

drop.mat	matrix, logical; dropout entries in the data matrix (genes as rows and samples as columns)
arranged	list; output of ArrangeData
cores	integer; number of cores used for paralell computation
type	character; either 'iteration', for an iterative solution, or 'pseudoinv', to use Moore-Penrose pseudo-inversion as a solution.
max.iter	numeric; maximum number of iterations for network imputation. Set to -1 to remove limit (not recommended)
BPPARAM	parallel back-end to be used during parallel computation. See BiocParallelParam-class.

Value

matrix; imputation results incorporating network information

ImputeNetwork *Network-based imputation*

Description

Network-based imputation

Usage

```
ImputeNetwork(data, net.coef = NULL,
cores = BiocParallel::bpworkers(BPPARAM),
BPPARAM = BiocParallel::SnowParam(type = "SOCK"),
type = 'iteration', write = FALSE, ...)
```

Arguments

data	matrix with entries equal to zero to be imputed, normalized and log2-transformed (genes as rows and samples as columns)
net.coef	matrix; network coefficients.
cores	integer; number of cores to use
BPPARAM	parallel back-end to be used during parallel computation. See BiocParallelParam-class.
type	character; either 'iteration', for an iterative solution, or 'pseudoinv', to use Moore-Penrose pseudo-inversion as a solution.
write	logical; should a file with the imputation results be written?
...	additional arguments to ImputeNetParallel

Details

Imputes dropouts using a gene regulatory network trained on external data, as provided in `net.coef`. Dropout expression values are estimated from the expression of their predictor genes and the network coefficients.

Value

matrix; imputation results incorporating network information

See Also

`ImputeNetParallel`

`ImputeNPDropouts` *Helper function to PseudoInverseSolution_percell*

Description

`ImputeNPDropouts` computes the non-dropout- dependent solution of network imputation for each cell

Usage

```
ImputeNPDropouts(net, expr)
```

Arguments

`net`	matrix, logical; network coefficients for all dropout (to be imputed) genes that are predictive of the expression of other dropout genes
`expr`	numeric; vector of gene expression for all genes in the cell at hand

Value

vector; imputation results for the non-dropout-dependent genes

ImputePredictiveDropouts *Helper function to PseudoInverseSolution_percell*

Description

ImputePredictiveDropouts applies Moore-Penrose pseudo-inversion to compute the dropout-dependent solution of network imputation for each cell

Usage

```
ImputePredictiveDropouts(net, thr = 0.01, expr)
```

Arguments

net	matrix, logical; network coefficients for all dropout (to be imputed) genes that are predictive of the expression of other dropout genes
thr	numeric; tolerance threshold to detect zero singular values
expr	numeric; vector of gene expression for all genes in the cell at hand

Value

vector; imputation results for the dropout-dependent genes

ImputeSAVER *Use SAVER*

Description

ImputeSAVER uses the SAVER package for dropout imputation

Usage

```
ImputeSAVER(data, cores, try.mean = FALSE, write = FALSE)
```

Arguments

data	matrix with entries equal to zero to be imputed, normalized (genes as rows and samples as columns)
cores	integer; number of cores to use
try.mean	logical; whether to additionally use mean gene expression as prediction
write	logical; should a file with the imputation results be written?

Value

matrix; imputation results from SAVER

See Also

saver

MaskData *Masking of entries for performance evaluation*

Description

MaskData sets a portion (mask) of the non-zero entries of each row of data to zero

Usage

```
MaskData(data, write.to.file = FALSE, mask = .1)
```

Arguments

data	matrix; raw counts (genes as rows and samples as columns)
write.to.file	logical; should the output be written to a file?
mask	numeric; ratio of total non-zero samples to be masked per gene (defaults to .1)

Details

Sets a portion (mask) of the non-zero entries of each row of data to zero. Result is written to filename.

Value

matrix containing masked raw counts (genes as rows and samples as columns)

MaskerPerGene *Helper mask function*

Description

Helper mask function, per feature.

Usage

```
MaskerPerGene(x, rowmask)
```

Arguments

x	logical; data to mask
rowmask	numeric; number of samples to be masked per gene

Value

logical containing positions to mask

---

network.coefficients *Transcriptome wide gene regulatory network*

Description

Gene Regulatory Network used by ADImpute's Network imputation method. First column, 0, corresponds to the intercept of a gene- -specific predicion model. The remaining rows and columns correspond to the adjacency matrix of the inferred network, where rows are target genes and columns are predictors. Genes are identified by their hgnc_symbol.

Usage

```
network.coefficients
```

Format

dgCMatrix

NormalizeRPM *RPM normalization*

Description

NormalizeRPM performs RPM normalization, with possibility to log the result

Usage

```
NormalizeRPM(data, sce = NULL, log = FALSE, scale = 1,
pseudo.count = 1)
```

Arguments

data	matrix; raw data (genes as rows and samples as columns)
sce	SingleCellExperiment; raw data
log	logical; log RPMs?
scale	integer; scale factor to divide RPMs by
pseudo.count	numeric; if log = TRUE, value to add to RPMs in order to avoid taking log(0)

Value

matrix; library size normalized data

Examples

```
demo <- NormalizeRPM(ADImpute::demo_data)
```

`NormalizeTPM` *TPM normalization*

Description

`NormalizeTPM` performs TPM normalization, with possibility to log the result

Usage

```
NormalizeTPM(data, sce = NULL, tr_length = NULL, log = FALSE,
scale = 1, pseudo.count = 1)
```

Arguments

`data`	matrix; raw data (genes as rows and samples as columns)
`sce`	SingleCellExperiment; raw data
`tr_length`	data.frame with at least 2 columns: 'hgnc_symbol' and 'transcript_length'
`log`	logical; log TPMs?
`scale`	integer; scale factor to divide TPMs by
`pseudo.count`	numeric; if `log = T`, value to add to TPMs in order to avoid taking `log(0)`

Details

Gene length is estimated as the median of the lengths of all transcripts for each gene, as obtained from biomaRt. Genes for which length information cannot be found in biomaRt are dropped.

Value

matrix; normalized data (for transcript length and library size)

Examples

```
demo <- NormalizeTPM(ADImpute::demo_data)
```

PseudoInverseSolution_percell *Network-based parallel imputation - Moore-Penrose pseudoinversion*

Description

`PseudoInverseSolution_percell` applies Moore-Penrose pseudo-inversion to compute the solution of network imputation for each cell

Usage

```
PseudoInverseSolution_percell(expr, net, drop_ind, thr = 0.01)
```

Arguments

`expr`	numeric; expression vector for cell at hand
`net`	matrix; network coefficients
`drop_ind`	logical; dropout entries in the cell at hand
`thr`	numeric; tolerance threshold to detect zero singular values

Value

matrix; imputation results incorporating network information

ReadData *Data read*

Description

`ReadData` reads data from raw input file (.txt or .csv)

Usage

```
ReadData(path, ...)
```

Arguments

`path`	character; path to input file
`...`	additional arguments to `data.table::fread()`

Value

matrix; raw counts (genes as rows and samples as columns)

ReturnChoice *Wrapper for return of EvaluateMethods()*

Description

`ReturnChoice` Adjusts the output of `EvaluateMethods` to a character vector or a SingleCellExperiment object. Helper function to ADImpute.

Usage

```
ReturnChoice(sce, choice)
```

Arguments

`sce`	SingleCellExperiment; a SingleCellExperiment object if available; NULL otherwise
`choice`	character; best performing method in the training set for each gene

Value

- if `sce` is provided: returns a SingleCellExperiment with the best performing method per gene stored as row-features. Access via `SingleCellExperiment::int_elementMetadata(sce)$ADImpute$methods`.
- if `sce` is not provided: returns a character with the best performing method in the training set for each gene

ReturnOut *Wrapper for return of Impute()*

Description

`ReturnOut` Adjusts the output of `Impute` to a list of matrices or a SingleCellExperiment object. Helper function to ADImpute.

Usage

```
ReturnOut(result, sce)
```

Arguments

`result`	list; imputation result
`sce`	SingleCellExperiment; a SingleCellExperiment object if available; NULL otherwise

Value

imputation results. A SingleCellExperiment if `!is.null(sce)`, or a list with imputed results in matrix format otherwise.

SetBiologicalZeros *Set biological zeros*

Description

SetBiologicalZeros sets some of the entries back to zero after dropout imputation, as they likely correspond to true biological zeros (genes not expressed in given cell)

Usage

```
SetBiologicalZeros(imputation, drop_probs, thre = .2, was_zero)
```

Arguments

imputation	matrix; imputed values
drop_probs	matrix; dropout probabilities for each entry in imputation. 0 means certain biological zero, while 1 means certain dropout to be imputed
thre	numeric; probability threshold to classify entries as biological zeros
was_zero	matrix; logical matrix: was the corresponding entry of imputation originally a zero?

Details

Entries which were originally zero and have dropout probability below thre are considered biological zeros and, if they were imputed, are set back to 0.

Value

matrix containing likely biological zeros set back to 0.

SplitData *Selection of samples for training*

Description

SplitData selects a portion (ratio) of samples (columns in data) to be used as training set

Usage

```
SplitData(data, ratio = .7, write.to.file = FALSE, train.only = TRUE)
```

Arguments

data	matrix; raw counts (genes as rows and samples as columns)
ratio	numeric; ratio of the samples to be used for training
write.to.file	logical; should the output be written to a file?
train.only	logical; if TRUE define only a training dataset, if FALSE writes both training and validation sets (defaults to TRUE)

Details

Selects a portion (ratio) of samples (columns in data) to be used as training set and writes to file 'training_raw.txt'.

Value

matrix containing raw counts (genes as rows and samples as columns)

---

transcript_length *Table for transcript length calculations*

Description

A data.frame to be used for transcript length computations. May be necessary upon TPM normalization, or as input to scImpute. All data was retrieved from biomaRt.

Usage

```
transcript_length
```

Format

A data.frame with 2 columns:

hgnc_symbol Gene symbol identifier

transcript length Length of transcript

WriteCSV *Write csv file*

Description

WriteCSV writes data to a comma-delimited output file

Usage

```
WriteCSV(object, file)
```

Arguments

object	R object to write
file	character; path to output file

Value

Returns NULL

Examples

```
file <- tempfile()
WriteCSV(iris, file = file)
```

WriteTXT *Write txt file*

Description

WriteTXT writes data to a tab-delimited output file

Usage

```
WriteTXT(object, file)
```

Arguments

object	R object to write
file	character; path to output file

Value

Returns NULL

Examples

```
file <- tempfile()
WriteTXT(iris, file = file)
```

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