Package 'MOSim'

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Title Multi-Omics Simulation (MOSim)

Version 2.4.0

Description MOSim package simulates multi-omic experiments that mimic regulatory mechanisms within the cell, allowing flexible experimental design including time course and multiple groups.

Encoding UTF-8

Depends R (>= 4.2.0)

License GPL-3

LazyData false

biocViews Software, TimeCourse, ExperimentalDesign, RNASeq

BugReports https://github.com/ConesaLab/MOSim/issues

URL https://github.com/ConesaLab/MOSim

Imports HiddenMarkov, zoo, IRanges, S4Vectors, dplyr, ggplot2, lazyeval, matrixStats, methods, rlang, stringi, stringr, scran, Seurat, Signac, edgeR, Rcpp

Suggests testthat, knitr, rmarkdown, codetools, BiocStyle, stats, utils, purrr, scales, tibble, tidyr, Biobase, scater, SingleCellExperiment, decor, markdown, Rsamtools, igraph, leiden, bluster

Collate 'AllClass.R' 'AllGeneric.R' 'Simulator.R' 'SimulatorRegion.R' 'ChIP-seq.R' 'DNase-seq.R' 'MOSim-package.R' 'functions.R' 'Simulation.R' 'MOSim.R' 'RNA-seq.R' 'data.R' 'simulate_WGBS_functions.R' 'methyl-seq.R' 'miRNA-seq.R' 'sc_MOSim.R' 'sc_coexpression.R' 'sparsim_functions.R' 'zzz.R'

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Description

Multiomics simulation package.

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See Also

Useful links:

- https://github.com/ConesaLab/MOSim
- Report bugs at https://github.com/ConesaLab/MOSim/issues

associationList

Data to showcase scRNA and scATAC-seq association

Description

Data to showcase scRNA and scATAC-seq association

Usage

```
data("associationList")
```

Format

A dataframe with two columns and rows according to gene/feature relationships

Peak_ID ATAC chromosomic positions associated to genes

Gene_ID RNA genes associated to peaks

@source Created in-house to serve as an example

4 check_patterns

Description

Helper function to calculate mean expression per celltype

Usage

```
calculate_mean_per_list_df(df, named_lists)
```

Arguments

df dataframe of expression where columns are cells named_lists list of which cells belong to each celltype

Examples

```
rna <- data.frame(c1 = c(1.5, 15.5, 3.5, 20.5), c2 = c(2, 15, 4, 20), c3 = c(10, 1, 12, 13), c4 = c(11, 1, 13, 14)) cell_types <- list("ct1" = c(1,2), "ct2" = c(3, 4)) calculate_mean_per_list_df(rna, cell_types)
```

check_patterns

check_patterns

Description

Function to check if the TRUE FALSE patterns have at least two rows that are opposite, we need this to be able to generate repressor regulators

Usage

```
check_patterns(patterns)
```

Arguments

patterns

tibble of TRUE FALSE values

Value

list of indices where the rows are opposite

discretize 5

Examples

discretize

Discretize ChIP-Seq counts to simulate a binary dataset

Description

Discretize ChIP-Seq counts to simulate a binary dataset

Usage

```
discretize(df, omic)
```

Arguments

df A MOSimulated object

omic Character string of the omic to transform into binary data

Value

A regulator dataframe of 0 and 1

```
omic_list <- c("RNA-seq", "ChIP-seq")
rnaseq_simulation <- mosim(omics = omic_list,
    omicsOptions = c(omicSim("ChIP-seq", totalFeatures = 2500)))
rnaseq_simulated <- omicResults(rnaseq_simulation, omic_list)
discrete_ChIP <- discretize(rnaseq_simulated, "ChIP-seq")</pre>
```

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experimentalDesign

Retrieves the experimental design

Description

Retrieves the experimental design

Usage

```
experimentalDesign(simulation)
```

Arguments

simulation

A MOSimulation object

Value

A data frame containing the experimental design used to simulate the data.

Examples

```
omic_list <- c("RNA-seq")
rnaseq_simulation <- mosim(omics = omic_list)
# This will be a data frame with RNA-seq counts
design_matrix <- experimentalDesign(rnaseq_simulation)</pre>
```

is.declared

Check if a variable is declared.

Description

Check if a variable is declared.

Usage

```
is.declared(object, key = NULL)
```

Arguments

object

Variable name to check

key

Optional key to check inside object.

Value

TRUE or FALSE indicating if the variable is initialized & non-empty.

Description

This function generates a dataframe containing the information of the relationship between ATAC and RNA, based on the cluster groups, and then tells the order the genes and peaks should be in the simulated dataframe of the group

Usage

```
make_association_dataframe(
   group,
   genereggroup,
   numtotalgenes,
   numtotalpeaks,
   minFC,
   maxFC
)
```

Arguments

group Group from which we are generating the association dataframe

genereggroup list of elements to generate the association dataframe such as clusters of each

omic, indices of opposite clusters, which genes are activated, repressed, behav-

ior of the features etc.

numtotalgenes total number of genes numtotalpeaks total number of peaks

minFC FC below which is downregulated

maxFC FC above which is upregulated

Value

a dataframe with all the information the user needs about each gene and the order of gene and peak names to rename them in the simulated datasets of the group

```
make_cluster_patterns make_cluster_patterns
```

Description

Function to make the tibble with cluster combinations for the gene expression patterns along the cells This function is a slightly modified copy of the 'make_cluster_patterns' function from the 'Acorde' package (v1.0.0), originally developed by Arzalluz-Luque A, Salguero P, Tarazona S, Conesa A. (2022). acorde unravels functionally interpretable networks of isoform co-usage from single cell data. Nature communications 1828. DOI: 10.1038/s41467-022-29497-w. The original package is licensed under the GPL-3 license.

Usage

```
make_cluster_patterns(numcells = 4, clusters = 8)
```

Arguments

numcells Number of different celltypes we are simulating

clusters OPTIONAL. Number of co-expression patterns the user wants to simulate

Value

A tibble with number of columns equal to number of celltypes, rows according to the number of TRUE/FALSE combinations corresponding to the gene expression patterns along the cells

Examples

```
match_gene_regulator match_gene_regulator
```

Description

Helper function to make the most similar profiles possible between gene and regulator

Usage

```
match_gene_regulator(rna, atac, cell_types, associationList)
```

Arguments

rna dataframe of RNA expression

atac dataframe of ATAC expression

cell_types list of which cells belong to each celltype

associationList

dataframe of two columns, Gene_ID and Peak_ID

Examples

Description

```
match_gene_regulator_cluster
```

Usage

```
match_gene_regulator_cluster(rna, atac, cell_types, associationMatrix)
```

Arguments

```
rna rna expression dataframe

atac atac expression dataframe

cell_types list of which cells belong to each celltype

associationMatrix

matrix of related genes and peaks
```

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Examples

mosim

mosim

Description

Performs a multiomic simulation by chaining two actions: 1) Creating the "MOSimulation" class with the provided params. 2) Calling "simulate" method on the initialized object.

Usage

```
mosim(
  omics,
  omicsOptions,
  diffGenes,
  numberReps,
  numberGroups,
  times,
  depth,
  profileProbs,
  minMaxFC,
  TFtoGene
)
```

Arguments

omics

Character vector containing the names of the omics to simulate, which can be "RNA-seq", "miRNA-seq", "DNase-seq", "ChIP-seq" or "Methyl-seq" (e.g. c("RNA-seq", "miRNA-seq")). It can also be a list with the omic names as names and their options as values, but we recommend to use the argument omic-Sim to provide the options to simulated each omic.

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omicsOptions

List containing the options to simulate each omic. We recommend to apply the helper method omicSim to create this list in a friendly way, and the function omicData to provide custom data (see the related sections for more information). Each omic may have different configuration parameters, but the common ones are:

simuData/idToGene Seed sample and association tables for regulatory omics. The helper function omicData should be used to provide this information (see the following section).

regulatorEffect For regulatory omics. List containing the percentage of effect types (repressor, activator or no effect) over the total number of regulators. See vignette for more information.

totalFeatures Number of features to simulate. By default, the total number of features in the seed dataset.

depth Sequencing depth in millions of reads. If not provided, it takes the global parameter passed to mosim function.

replicateParams List with parameters *a* and *b* for adjusting the variability in the generation of replicates using the negative binomial. See vignette for more information.

diffGenes Number of differentially expressed genes to simulate, given in percentage (0 -

1) or in absolute number (> 1). By default 0.15

numberReps Number of replicates per experimetal condition (and time point, if time series

are to be generated). By default 3.

numberGroups Number of experimental groups or conditions to simulate.

times Vector of time points to consider in the experimental design.

depth Sequencing depth in millions of reads.

profileProbs Numeric vector with the probabilities to assign each of the patterns. Defaults to

0.2 for each.

minMaxFC Numeric vector of length 2 with minimum and maximum fold-change for dif-

ferentially expressed features, respectively.

TFtoGene A logical value indicating if default transcription factors data should be used

(TRUE) or not (FALSE), or a 3 column data frame containing custom associa-

tions. By default FALSE.

Value

Instance of class "MOSimulation" containing the multiomic simulation data.

```
moSimulation <- mosim(
   omics = c("RNA-seq"),
   numberReps = 3,
   times = c(0, 2, 6, 12, 24)
)
# Retrieve simulated count matrix for RNA-seq</pre>
```

dataRNAseq <- omicResults(moSimulation, "RNA-seq")</pre>

MOSimulation-class

This class manages the global simulation process, like associating genes with gene classes, regulatory programs and other settings. Finally it will initialize the simulators with their options that will use the previously generated settings to simulate the data.

Description

This class manages the global simulation process, like associating genes with gene classes, regulatory programs and other settings. Finally it will initialize the simulators with their options that will use the previously generated settings to simulate the data.

Slots

simulators Vector containing either S4 initialized classes of simulators or a list with the class name as keys, and its options as value, see example.

totalGenes A number with the total number of genes including not expressed. Overwritten if a genome reference is provided. Currently not used as we force to provide real data.

diffGenes A number with the total number of differential genes (if value > 1) or % or total genes (if value < 1).

numberReps Number of replicates of the experiment.

numberGroups Number of samples considered on the experiment.

times Numeric vector containing the measured times. If numberGroups < 2, the number of times must be at least 2.

geneNames Read only. List containing the IDs of the genes. Overwrited by the genome reference if provided. Currently not used as we force to provide real data.

simSettings List of settings that overrides initializing the configuration of the simulation by passing a previously generated list. This could be used to tweak by hand the assigned profiles, genes, regulatory programs, etc.

noiseFunction Noise function to apply when simulating counts. Must accept the parameter 'n' and return a vector of the same length. Defaults to 'rnorm'

profiles Named list containing the patterns with their coefficients.

profileProbs Numeric vector with the probabilities to assign each of the patterns. Defaults to 0.2 for each.

noiseParams Default noise parameters to be used with noise function.

depth Default depth to simulate.

TFtoGene Boolean (for default data) or 3 column data frame containing Symbol-TFGene-LinkedGene minMaxQuantile Numeric vector of length 2 indicating the quantiles to use in order to retrieve the absolute minimum and maximum value that a differentially expressed feature can have.

minMaxFC Numeric vector of length 2 indicating the minimum and maximum fold-change that a differentially expressed feature can have.

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MOSimulator-class

Virtual class containing common methods and slots for child classes.

Description

Virtual class containing common methods and slots for child classes.

Slots

name Name of the simulator to be used in messages.

data Data frame containing the initial sample to be used, with the features IDs as rownames and only one column named "Counts".

regulator Boolean flag to indicate if the omic is a regulator or not.

regulatorEffect Possible regulation effects of the omic (enhancer, repressor or both).

idToGene Data frame with the association table between genes and other features. The structure must be 2 columns, one named "ID" and the other "Gene".

min Minimum value allowed in the omic.

max Maximum value allowed in the omic.

depth Sequencing depth to simulate.

depthRound Number of decimal places to round when adjusting depth.

depthAdjust Boolean indicating whether to adjust by sequencing depth or not.

totalFeatures Number of features to simulate. This will replace the data with a subset.

noiseFunction Noise function to apply when simulating counts. Must accept the parameter 'n' and return a vector of the same length. Defaults to 'rnorm'

increment Read-only. Minimum value to increase when simulating counts.

simData Contains the final simulated data.

pregenerated Indicates if the child class will generate the simulated data instead of the general process.

randData Auxiliary vector containing the original count data in random order with other adjustments.

noiseParams Noise parameters to be used with noise function.

roundDigits Number of digits to round the simulated count values.

minMaxQuantile Numeric vector of length 2 indicating the quantiles to use in order to retrieve the absolute minimum and maximum value that a differentially expressed feature can have.

minMaxFC Numeric vector of length 2 indicating the minimum and maximum fold-change that a differentially expressed feature can have.

minMaxDist Named list containing different minimum and maximum constraints values calculated at the beginning of the simulation process.

replicateParams Named list containing the parameters a and b to be used in the replicates generation process, see the vignette for more info.

MOSimulatorRegion-class

Virtual class containing general methods for simulators based on regions of the chromosomes, like DNase-seq, ChIP-seq or Methyl-seq

Description

Virtual class containing general methods for simulators based on regions of the chromosomes, like DNase-seq, ChIP-seq or Methyl-seq

Class to simulate RNA-seq data

Class to simulate transcription factor data

Class to simulate miRNA-seq

Class to simulate ChIP-seq data

Class to simulate DNase-seq data

Class to simulate Methyl-seq data.

Slots

locs Vector containing the list of locations of the sites.

locsName Type of the site to simulate, only for debug.

splitChar Character symbol used to split identifiers in chr/start/end

nCpG numeric. Number of CpG sites to simulate.

pSuccessMethReg numeric. Probability of success in methylated region.

pSuccessDemethReg numeric. Probability of success in non methylated region

errorMethReg numeric. Error rate in methylated region

errorDemethReg numeric. Error rate in methylated region

nReadsMethReg numeric. Mean number of reads in methylated region.

nReadsDemethReg numeric. Mean number of reads in non methylated regions.

 $phase \ Diff\ numeric.\ Phase\ difference\ in\ the\ differentially\ methylated\ regions\ between\ two\ samples$

balanceHypoHyper numeric. Balance of hypo/hyper methylation

ratesHMMMatrix numeric. Matrix of values that describes the exponential decay functions that define the distances between CpG values.

distType character. Distribution used to generate replicates:

transitionSize numeric.

PhiMeth matrix. Transition matrix for CpG locations.

PhiDemeth matrix. <Not used>

typesLocation numeric. <Not used>

returnValue character. Selected column:

betaThreshold numeric. Beta threshold value used to calculate M values.

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omicData

Set customized data for an omic.

Description

Set customized data for an omic.

Usage

```
omicData(omic, data = NULL, associationList = NULL)
```

Arguments

omic The name of the omic to provide data.

data Data frame with the omic identifiers as row names and just one column named

Counts containing numeric values used as initial sample for the simulation.

associationList

Only for regulatory omics, a data frame with 2 columns, the first called containing the regulator ID and the second called Gene with the gene identifier.

Value

Initialized simulation object with the given data.

```
# Take a subset of the included dataset for illustration
# purposes. We could also load it from a csv file or RData,
# as long as we transform it to have 1 column named "Counts"
# and the identifiers as row names.
data(sampleData)
custom_rnaseq <- head(sampleData$SimRNAseq$data, 100)</pre>
# In this case, 'custom_rnaseq' is a data frame with
# the structure:
head(custom_rnaseq)
                      Counts
## ENSMUSG00000000001
## ENSMUSG00000000003
## ENSMUSG00000000028
                        4644
## ENSMUSG00000000031
                           8
## ENSMUSG0000000037
                           0
## ENSMUSG00000000049
                           0
# The helper 'omicData' returns an object with our custom data.
rnaseq_customdata <- omicData("RNA-seq", data = custom_rnaseq)</pre>
```

16 omicResults

omicResults	Retrieves the simulated data.

Description

Retrieves the simulated data.

Usage

```
omicResults(simulation, omics = NULL, format = "data.frame")
```

Arguments

simulation A MOSimulation object.

omics List of the omics to retrieve the simulated data.

format Type of object to use for returning the results

Value

A list containing an element for every omic specifiec, with the simulation data in the format indicated, or a numeric matrix with simulated data if the omic name is directly provided.

```
omic_list <- c("RNA-seq")</pre>
rnaseq_simulation <- mosim(omics = omic_list)</pre>
#' # This will be a data frame with RNA-seq counts
rnaseq_simulated <- omicResults(rnaseq_simulation, "RNA-seq")</pre>
                     Group1.Time0.Rep1 Group1.Time0.Rep2 Group1.Time0.Rep3 ...
# ENSMUSG00000073155
                                   4539
                                                      5374
                                                                         5808 ...
# ENSMUSG00000026251
                                     0
                                                       0
                                                                            0 ...
# ENSMUSG00000040472
                                   2742
                                                      2714
                                                                         2912 ...
# ENSMUSG00000021598
                                   5256
                                                      4640
                                                                         5130 ...
# ENSMUSG00000032348
                                                       348
                                                                         492 ...
                                    421
                                                                           9 ...
# ENSMUSG00000097226
                                     16
                                                        14
                                                                           0 ...
# ENSMUSG00000027857
                                      0
                                                         0
# ENSMUSG00000032081
                                      1
                                                         0
                                                                            0 ...
                                                                          965 ...
# ENSMUSG00000097164
                                    794
                                                       822
# ENSMUSG00000097871
                                                                            0 ...
```

omicSettings 17

omicSettings Retrieves the settings used in a simulation
--

Description

Retrieves the settings used in a simulation

Usage

```
omicSettings(
  simulation,
  omics = NULL,
  association = FALSE,
  reverse = FALSE,
  only.linked = FALSE,
  prefix = FALSE,
  include.lagged = TRUE
)
```

Arguments

simulation	A MOSimulation object.
omics	List of omics to retrieve the settings.
association	A boolean indicating if the association must also be returned for the regulators.
reverse	A boolean, swap the column order in the association list in case we want to use the output directly and the program requires a different ordering.
only.linked	Return only the interactions that have an effect.
prefix	Logical indicating if the name of the omic should prefix the name of the regulator.
include.lagged	Logical indicating if interactions with transitory profile and different minimum/maximum time point between gene and regulator should be included or not.

Value

A list containing a data frame with the settings used to simulate each of the indicated omics. If association is TRUE, it will be a list with 3 keys: 'associations', 'settings' and 'regulators', with the first two keys being a list containing the information for the selected omics and the last one a global data frame giving the merged information.

```
omic_list <- c("RNA-seq", "miRNA-seq")
multi_simulation <- mosim(omics = omic_list)

# This will be a data frame with RNA-seq settings (DE flag, profiles)
rnaseq_settings <- omicSettings(multi_simulation, "RNA-seq")</pre>
```

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```
# This will be a list containing all the simulated omics (RNA-seq
# and DNase-seq in this case)
all_settings <- omicSettings(multi_simulation)</pre>
```

omicSim

Set the simulation settings for an omic.

Description

Set the simulation settings for an omic.

Usage

```
omicSim(omic, depth = NULL, totalFeatures = NULL, regulatorEffect = NULL)
```

Arguments

omic Name of the omic to set the settings.

depth Sequencing depth in millions of counts. If not provided will take the global

parameter passed to mosim function.

totalFeatures Limit the number of features to simulate. By default include all present in the

dataset.

regulatorEffect

only for regulatory omics. Associative list containing the percentage of effects over the total number of regulator, including repressor, association and no effect

(NE).

Value

A list with the appropriate structure to be given as options in mosim function.

plotProfile 19

plotProfile	Generate a plot of a feature's profile for one or two omics.

Description

Generate a plot of a feature's profile for one or two omics.

Usage

```
plotProfile(simulation, omics, featureIDS, drawReps = FALSE, groups = NULL)
```

Arguments

simulation	A MOSimulation object
omics	Character vector of the omics to simulate.
featureIDS	List containing the feature to show per omic. Must have the omics as the list names and the features as values.
drawReps	Logical to enable/disable the representation of the replicates inside the plot.
groups	Character vector indicating the groups to plot in the form "GroupX" (i.e. Group1)

Value

A ggplot2 object.

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random_unif_interval

random_unif_interval Function to call the C code This function is a copy of the 'random_unif_interval' function from the 'SPARSim' package (v0.9.5), originally developed by Giacomo Baruzzo, Ilaria Patuzzi, Barbara Di Camillo (2020). The original package is licensed under the GPL-3 license.

Description

random_unif_interval Function to call the C code This function is a copy of the 'random_unif_interval' function from the 'SPARSim' package (v0.9.5), originally developed by Giacomo Baruzzo, Ilaria Patuzzi, Barbara Di Camillo (2020). The original package is licensed under the GPL-3 license.

Usage

```
random_unif_interval(size, max_val)
```

Arguments

size from sparsim max_val from sparsim

sampleData

Default data

Description

Dataset with base counts and id-gene tables.

Usage

```
data("sampleData")
```

Format

An object of class list of length 6.

Details

List with 6 elements:

SimRNAseq data Dataframe with base counts with gene id as rownames.

geneLength Length of every gene.

SimChIPseq data Dataframe with base counts with regions as rownames.

idToGene Dataframe with region as "ID" column and gene name on "Gene" column.

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SimDNaseseq data Dataframe with base counts with regions as rownames.

idToGene Dataframe with region as "ID" column and gene name on "Gene" column.

SimMiRNAseq data Dataframe with base counts with miRNA id as rownames.

idToGene Dataframe with miRNA as "ID" column and gene name on "Gene" column.

SimMethylseq idToGene Dataframe with region as "ID" column and gene name on "Gene" col-

CpGisland Dataframe of CpG to be used as initialization data, located on "Region" column

scatac

Data to test scMOSim

Description

Data to test scMOSim

Usage

```
data("scatac")
```

Format

A seurat Object, subset from seuratData with ATAC

assays ATAC expression values

meta.data annotations of celltypes

@source https://github.com/satijalab/seurat-data, we took 11 cells from each of 4 celltypes

scrna

Data to test scMOSim

Description

Data to test scMOSim

Usage

```
data("scrna")
```

sc_mosim

Format

A seurat Object, subset from seuratData with RNA

```
assays RNA expression values
```

meta.data annotations of celltypes

@source https://github.com/satijalab/seurat-data, we took 11 cells from each of 4 celltypes This is how: dat <- pbmcMultiome.SeuratData::pbmc.rna dat <- subset(x = dat, subset = seurat_annotations "cDC", "Memory B", "Treg")) unique_cell_types <- unique(datATmeta.data\$seurat_annotations) extracted_cells <- list() cellnames <- c() for (cell_type in unique_cell_types) type_cells <- subset(dat, subset = seurat_annotations counts <- as.matrix(type_cellsATassays[["RNA"]]ATcounts) extracted_cells[[cell_type]] <- counts[, 1:10] cellnames <- append(cellnames, replicate(11, cell_type))

```
scrna <- Reduce(cbind, extracted_cells)</pre>
```

sc_mosim

sc mosim

Description

Performs multiomic simulation of single cell datasets

Usage

```
sc_mosim(
 omics,
  cellTypes,
 numberReps = 1,
 numberGroups = 1,
 diffGenes = NULL,
 minFC = 0.25,
 maxFC = 4,
 numberCells = NULL,
 mean = NULL,
  sd = NULL,
  noiseRep = 0.1,
  noiseGroup = 0.5,
  regulatorEffect = NULL,
  associationList = NULL,
  feature_no = 8000,
  clusters = 3,
  cluster_size = NULL,
 TF = FALSE,
  TFdf = NULL
)
```

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Arguments

omics named list containing the omic to simulate as names, which can be "scRNA-seq"

or "scATAC-seq".

cellTypes list where the i-th element of the list contains the column indices for i-th exper-

imental conditions. List must be a named list.

numberReps OPTIONAL. Number of replicates per group numberGroups OPTIONAL. number of different groups

diffGenes OPTIONAL. If number groups > 1, Percentage DE genes to simulate. List of

vectors (one per group to compare to group 1) where the vector contains absolute number of genes for Up and Down ex: c(250, 500) or a percentage for up, down

ex: c(0.2, 0.2). The rest will be NE

minFC OPTIONAL. Threshold of FC below which are downregulated, by default 0.25

maxFC OPTIONAL. Threshold of FC above which are upregulated, by default 4

numberCells OPTIONAL. Vector of numbers. The numbers correspond to the number of cells

the user wants to simulate per each cell type. The length of the vector must be

the same as length of cellTypes.

mean OPTIONAL. Vector of numbers of mean depth per each cell type. Must be

specified just if numberCells is specified. The length of the vector must be the

same as length of cellTypes.

sd OPTIONAL. Vector of numbers of standard deviation per each cell type. Must

be specified just if numberCells is specified. The length of the vector must be

the same as length of cellTypes.

noiseRep OPTIONAL. Number indicating the desired standard deviation between biolog-

ical replicates.

noiseGroup OPTIONAL. Number indicating the desired standard deviation between treat-

ment groups

regulatorEffect

OPTIONAL. To simulate relationship scRNA-scATAC, list of vectors (one per group) where the vector contains absolute number of regulators for Activator and repressor ex: c(150, 200) or a percentage for Activator and repressor ex: c(0.2, 0.1). The rest will be NE. If not provided, no table of association between

scRNA and scATAC is outputted.

association List

REQUIRED A 2 columns dataframe reporting peak ids related to gene names.

If user doesnt have one, load from package data("associationList")

feature_no OPTIONAL. If only scRNA-seq to simulate or scRNA and scATAC but no reg-

ulatory constraints, total number of features to be distributed between the coex-

pression clusters.

clusters OPTIONAL. Number of co-expression patterns the user wants to simulate

cluster_size OPTIONAL. It may be inputted by the user. Recommended: by default, its the

number of features divided by the number of patterns to generate.

TF OPTIONAL default is FALSE, if true, extract TF dataframe

TFdf OPTIONAL, default is NULL. If an association matrix of TF and Target_gene

is given the TF expression values are extracted. If no data.frame is given, using

the association of human TF from https://tflink.net/

24 sc_omicData

Value

a list of Seurat object, one per each omic.

Examples

```
omic_list <- sc_omicData(list("scRNA-seq"))
cell_types <- list('Treg' = c(1:10),'cDC' = c(11:20),'CD4_TEM' = c(21:30),
'Memory_B' = c(31:40))
sim <- sc_mosim(omic_list, cell_types)</pre>
```

sc_omicData

sc_omicData

Description

Checks if the user defined data is in the correct format, or loads the default multiomics pbmc dataset, a subset from SeuratData package

Usage

```
sc_omicData(omics_types, data = NULL)
```

Arguments

omics_types A list of strings which can be either "scRNA-seq" or "scATAC-seq"

data A user input matrix with genes (peaks in case of scATAC-seq) as rows and cells

as columns. By default, it loads the example data. If a user input matrix is

included, cell columns must be sorted by cell t ype.

Value

a named list with omics type as name and the count matrix as value

```
# Simulate from PBMC
omicsList <- sc_omicData(list("scRNA-seq", "scATAC-seq"))</pre>
```

sc_omicResults 25

sc_omicResults

sc_omicResults

Description

```
sc\_omicResults
```

Usage

```
sc_omicResults(sim)
```

Arguments

sim

a simulated object from sc_mosim function

Value

list of seurat objects with simulated data

Examples

```
cell_types <- list('Treg' = c(1:10),'cDC' = c(11:20),'CD4_TEM' = c(21:30),
'Memory_B' = c(31:40))
omicsList <- sc_omicData(list("scRNA-seq"))
sim <- sc_mosim(omicsList, cell_types)
res <- sc_omicResults(sim)</pre>
```

sc_omicSettings

sc_omicSettings

Description

```
sc_omicSettings
```

Usage

```
sc_omicSettings(sim, TF = FALSE)
```

Arguments

sim a simulated object from sc_mosim function

TF OPTIONAL default is FALSE, if true, extract TF association matrix

Value

list of Association matrices explaining the effects of each regulator to each gene

26 sc_param_estimation

Examples

```
 cell\_types <- list('Treg' = c(1:10), 'cDC' = c(11:20), 'CD4\_TEM' = c(21:30), 'Memory\_B' = c(31:40)) \\ omicsList <- sc\_omicData(list("scRNA-seq")) \\ sim <- sc\_mosim(omicsList, cell\_types) \\ res <- sc\_omicSettings(sim)
```

sc_param_estimation sc_param_estimation

Description

Evaluate the users parameters for single cell simulation and use SPARSim to simulate the main dataset. Internal function

Usage

```
sc_param_estimation(
  omics,
  cellTypes,
  diffGenes = list(c(0.2, 0.2)),
  minFC = 0.25,
  maxFC = 4,
  numberCells = NULL,
  mean = NULL,
  sd = NULL,
  noiseGroup = 0.5,
  group = 1,
  genereggroup
)
```

Arguments

omics	named list containing the omics to simulate as names, which can be "scRNA-seq" or "scATAC-seq".
cellTypes	list where the i-th element of the list contains the column indices for i-th cell type. List must be a named list.
diffGenes	If number groups $>$ 1, Percentage DE genes to simulate. List of vectors (one per group to compare to group 1) where the vector contains absolute number of genes for Up and Down ex: c(250, 500) or a percentage for up, down ex: c(0.2, 0.2). The rest will be NE
minFC	Threshold of FC below which are downregulated, by default 0.25
maxFC	Threshold of FC above which are upregulated, by default 4
numberCells	vector of numbers. The numbers correspond to the number of cells the user wants to simulate per each cell type. The length of the vector must be the same

as length of cellTypes.

shuffle_group_matrix 27

mean	vector of numbers of	f mean depth per each cell type.	Must be specified just if
		. 6 1	

numberCells is specified.

sd vector of numbers of standard deviation per each cell type. Must be specified

just if numberCells is specified.

noiseGroup OPTIONAL. Number indicating the desired standard deviation between treat-

ment groups

group Group for which to estimate parameters

genereggroup List with information of genes, clusters and regulators that must be related to

each other

Value

a list of Seurat object, one per each omic.

a named list with simulation parameters for each omics as values.

Examples

```
omicsList <- sc_omicData(list("scRNA-seq"))
cell_types <- list('Treg' = c(1:10),'cDC' = c(11:20),'CD4_TEM' = c(21:30),
'Memory_B' = c(31:40))
#estimated_params <- sc_param_estimation(omicsList, cell_types)</pre>
```

shuffle_group_matrix

shuffle_group_matrix, Reorder cell type-specific expression matrix during co-expression simulation. Copied from ACORDE (https://github.com/ConesaLab/acorde) to facilitate stability and running within our scripts This function is a slightly modified copy of the 'shuffle_group_matrix' function from the 'Acorde' package (v1.0.0), originally developed by Arzalluz-Luque A, Salguero P, Tarazona S, Conesa A. (2022). acorde unravels functionally interpretable networks of isoform co-usage from single cell data. Nature communications 1828. DOI: 10.1038/s41467-022-29497-w. The original package is licensed under the GPL-3 license.

Description

This function is used internally by accorde to perform the shuffling of simulated features for an individual cell type, as part of the co-expression simulation process. The function is called recursively by simulate_coexpression() to perform the simulation on a full scRNA-seq matrix.

Usage

```
shuffle_group_matrix(sim_data, feature_ids, group_pattern, ngroups)
```

Arguments

sim_data A count matrix with features as rows and cells as columns. Feature IDs must be

included in an additional column named feature.

feature_ids A two-column tibble containing top and bottom columns, each including the

feature IDs of features to be used as highly or lowly expressed when shuffling

by the indicated expression pattern.

group_pattern A logical vector, containing TRUE to indicate that high expression in that cell

type is desired and FALSE if the opposite. The vector must be ordered as the cell

types in sim_data.

ngroups An integer indicating the number of groups that top and bottom features should

be divided into. It is computed by dividing the number of features selected as

highly/lowly expressed by the size of the clusters that are to be generated.

Value

An expression matrix, with the same characteristics as sim_data, and a number of features defined as the total amount of top/bottom features selected divided by the number of clusters for which co-expression patterns where supplied.

simulate_coexpression simulate coexpression

Description

Adapted from ACORDE (https://github.com/ConesaLab/acorde) to adapt to our data input type. Simulates coexpression of genes along celltypes

Usage

```
simulate_coexpression(
   sim_matrix,
   feature_no,
   cellTypes,
   patterns,
   cluster_size = NULL
)
```

Arguments

sim_matrix Matrix with rows as features and columns as cells

feature_no Total number of features to be distributed between the coexpression clusters cellTypes list where the i-th element of the list contains the column indices for i-th exper-

imental conditions. List must be a named list.

patterns Tibble with TRUE FALSE depicting the cluster patterns to simulate. Generated

by the user or by make_cluster_patterns.

cluster_size OPTIONAL. It may be inputted by the user. By default, its the number of fea-

tures divided by the number of patterns to generate.

simulate_hyper 29

Details

This function is a slightly modified copy of the 'simulate_coexpression' function from the 'Acorde' package (v1.0.0), originally developed by Arzalluz-Luque A, Salguero P, Tarazona S, Conesa A. (2022). acorde unravels functionally interpretable networks of isoform co-usage from single cell data. Nature communications 1828. DOI: 10.1038/s41467-022-29497-w. The original package is licensed under the GPL-3 license.

Value

the simulated coexpression

late_hyper Simulate technical variabilit
--

Description

Function to simulate the technical variability (i.e. a multivariate hypergeometric on a gamma expression value array)

Usage

```
simulate_hyper(avgAbund, seqdepth = NULL, digits, max_val)
```

Arguments

avgAbund	array containing the intensity values for each feature. It describes the intensity of a single sample
seqdepth	sequencing depth (i.e. sample size of the MH)
digits	number of digits for random number generation
max_val	max value for random number generation

Details

This function is a copy of the 'simulate_hyper' function from the 'SPARSim' package (v0.9.5), originally developed by Giacomo Baruzzo, Ilaria Patuzzi, Barbara Di Camillo (2020). The original package is licensed under the GPL-3 license.

Value

An array of length(avgAbund) elements representing the count values for the current sample

Description

Function to create a SPARSim simulation parameter. This function is a copy of the 'SPARSIM_create_simulation_parameter' function from the 'SPARSim' package (v0.9.5), originally developed by Giacomo Baruzzo, Ilaria Patuzzi, Barbara Di Camillo (2020). The original package is licensed under the GPL-3 license. To simulate N feature (e.g. genes), user must specify N values of gene expression level and gene expression variability in the function input parameters intensity and variability, respectively. To simulate M samples (i.e. cells), user must specify M values of sample library size in the function input parameter library_size.

Usage

```
sparsim_create_simulation_parameter(
  intensity,
  variability,
  library_size,
  feature_names = NA,
  sample_names = NA,
  condition_name = NA,
  intensity_2 = NULL,
  variability_2 = NULL,
  p_bimod = NULL
)
```

Arguments

intensity	Array of gene expression intensity values
variability	Array of gene expression variability values
library_size	Array of library size values
feature_names	Array of feature names. It must be of the same length of intensity array. If NA (default), feature will be automatically named "gene_1", "gene_2", "gene_ $<$ N>", where N = length(intensity)
sample_names	Array of sample names. It must be of the same length of library_size array. If NA (defatul), sample will be automatically named " <condition_name>_cell1", "<condition_name>_cell2",, "<condition_name>_cell<m>", where $M = length(library_size)$</m></condition_name></condition_name></condition_name>
condition_name	Name associated to the current experimental condition. If NA (default), it will be set to "cond<11><12>", where 11 and 12 are two random letters.
intensity_2	Array of gene expression intensity values for the second expression mode, if simulating genes with bimodal gene expression. Entries containing NAs will be ignored. If NULL (default), no bimodal gene expression is simulated.

variability_2 Array of gene expression variability values for the second expression mode, if

simulating genes with bimodal gene expression. If NULL (default), no bimodal

gene expression is simulated.

p_bimod Array of bimodal gene expression probabilities; the i-th value indicates the prob-

ability p of the i-th gene to be expressed in the first mode (i.e. the one specified in the i-th entries of parameters intensity and variability); with probability 1-p the i-th gene will be expressed in the second mode (i.e. the one specified in

the i-th entries of parameters intensity_2 and variability_2)

Details

User can optionally specify the names to assign at the single feature and sample to simulate (function input parameters feature_names and sample_names, respectively, as well as the name of the experimental condition (function input parameter condition_name). If the user does not specify such information, the function will set some default values.

To simulate T different experimental conditions in a single count table, then T different simulation parameters must be created.

Value

SPARSim simulation parameter describing one experimental condition

sparsim_estimate_intensity

Estimate SPARSIm "intensity" parameter

Description

Function to estimate the intensity values from the genes in data. The intensity is computed as mean of normalized counts for each gene.

Usage

sparsim_estimate_intensity(data)

Arguments

data

normalized count data matrix (gene on rows, samples on columns). rownames(data) must contain gene names.

Details

This function is a copy of the 'SPARSIM_estimate_intensity' function from the 'SPARSim' package (v0.9.5), originally developed by Giacomo Baruzzo, Ilaria Patuzzi, Barbara Di Camillo (2020).

The original package is licensed under the GPL-3 license. This function is used in sparsim_estimate_parameter_from_date to compute SPARSim "intensity" parameter, given a real count table as input. If the count table contains more than one experimental condition, then the function is applied to each experimental conditions.

Value

An array of intensity values having N_genes elements (N_genes = nrow(data)). Array entries are named with gene names.

```
sparsim_estimate_library_size
```

Estimate SPARSim "library size" parameter

Description

Function to estimate the library sizes from the samples in data.

Usage

```
sparsim_estimate_library_size(data)
```

Arguments

data

raw count data matrix (gene on rows, samples on columns)

Details

This function is a copy of the 'SPARSIM_estimate_library_size' function from the 'SPARSim' package (v0.9.5), originally developed by Giacomo Baruzzo, Ilaria Patuzzi, Barbara Di Camillo (2020). The original package is licensed under the GPL-3 license. This function is used in sparsim_estimate_parameter_f to compute SPARSim "library size" parameter, given a real count table as input. If the count table contains more than one experimental condition, then the function is applied to each experimental conditions.

Value

An array of library size values having N_samples elements (N_samples = ncol(data))

```
sparsim_estimate_parameter_from_data
```

Estimate SPARSim simulation parameter from a given count table

Description

Function to estimate SPARSim simulation parameters (intensity, variability and library sizes) from a real count table. If the real count table contains more than one experimental condition, it is possible to estimate the parameters for each experimental condition.

Usage

```
sparsim_estimate_parameter_from_data(raw_data, norm_data, conditions)
```

Arguments

norm_data

raw_data count matrix (gene on rows, samples on columns) containing raw count data

count matrix (gene on rows, samples on columns) containing normalized count

data

conditions list where the i-th element of the list contains the column indices for i-th exper-

imental conditions. List must be a named list.

Details

This function is a copy of the 'SPARSIM_estimate_parameter_from_data' function from the 'SPAR-Sim' package (v0.9.5), originally developed by Giacomo Baruzzo, Ilaria Patuzzi, Barbara Di Camillo (2020). The original package is licensed under the GPL-3 license.

Value

A SPARSim simulation parameters

sparsim_estimate_variability

Estimate SPARSim "variability" parameter

Description

Function to estimate the variability values from the genes in data.

Usage

```
sparsim_estimate_variability(data)
```

Arguments

data raw count data matrix (gene on rows, samples on columns)

Details

This function is a copy of the 'SPARSIM_estimate_variability' function from the 'SPARSim' package (v0.9.5), originally developed by Giacomo Baruzzo, Ilaria Patuzzi, Barbara Di Camillo (2020). The original package is licensed under the GPL-3 license. This function is used in sparsim_estimate_parameter_from_date to compute SPARSim "variability" parameter, given a real count table as input. If the count table contains more than one experimental condition, then the function is applied to each experimental conditions.

Value

An array of variability values having N_genes elements (N_genes = nrow(data))

34 sparsim_simulation

sparsim_simulation

Function to simulate a raw count table

Description

This function is a copy of the 'SPARSIM_simulation' function from the 'SPARSim' package (v0.9.5), originally developed by Giacomo Baruzzo, Ilaria Patuzzi, Barbara Di Camillo (2020). The original package is licensed under the GPL-3 license.

Usage

```
sparsim_simulation(
  dataset_parameter,
  output_sim_param_matrices = FALSE,
  output_batch_matrix = FALSE,
  count_data_simulation_seed = NULL
)
```

Arguments

dataset_parameter

list containing, the intensity, variability and lib sizes of each experimental condition. It is the return value of "estimate_parameter_from_data" or could be created by the users

output_sim_param_matrices

boolean flag. If TRUE, the function will output two additional matrices, called abundance_matrix and variability_matrix, containing the gene intensities and gene variabilities used as simulation input. (Default: FALSE)

output_batch_matrix

boolean flag. If TRUE, the function will output an additional matrix, called batch_factors_matrix, containing the multiplicative factors used in batch effect simulation. (Default: FALSE)

count_data_simulation_seed

inherited from sparsim

Value

A list of 5 elements:

- count_matrix: the simulated count matrix (genes on rows, samples on columns)
- gene_matrix: the simulated gene expression levels (genes on rows, samples on columns)
- abundance_matrix: the input gene intensity values provided as input (genes on rows, samples on columns), if output_sim_param_matrices = TRUE. NULL otherwise.
- variability_matrix: the input gene variability values provided as input (genes on rows, samples on columns), if output_sim_param_matrices = TRUE. NULL otherwise.
- batch_factors_matrix: the multiplicative factor used in batch generation (genes on rows, samples on columns), if output_batch_matrix = TRUE. NULL otherwise.

TF_human 35

TF_human

Data to extract human TF

Description

Data to extract human TF

Usage

```
data("TF_human")
```

Format

vector of gene names

data.frame gene names corresponding to TF and to Target genes

@source https://tflink.net/

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