

Package ‘MOSim’

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Title Multi-Omics Simulation (MOSim)

Version 1.16.0

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

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License GPL-3

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MOSim-package	<i>MOSim</i>
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Description

Multomics simulation package.

discretize	<i>Discretize ChIP-Seq counts to simulate a binary dataset</i>
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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

Examples

```
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")
```

experimentalDesign	<i>Retrieves the experimental design</i>
--------------------	--

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)
```

is.declared	<i>Check if a variable is declared.</i>
-------------	---

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.

mosim	<i>mosim</i>
-------	--------------

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 <code>omicSim</code> to provide the options to simulated each omic.
omicsOptions	List containing the options to simulate each omic. We recommend to apply the helper method <code>omicSim</code> to create this list in a friendly way, and the function <code>omicData</code> 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 <code>omicData</code> 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 <code>mosim</code> 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 experimental 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 differentially 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 associations. By default FALSE.

Value

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

Examples

```

moSimulation <- mosim(
  omics = c("RNA-seq"),
  numberReps = 3,
  times = c(0, 2, 6, 12, 24)
)

# Retrieve simulated count matrix for RNA-seq
dataRNAseq <- omicResults(moSimulation, "RNA-seq")

```

MOSimulation-class	<i>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.</i>
--------------------	---

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 % of 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. Overwritten 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.

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.

phaseDiff 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.

omicData	<i>Set customized data for an omic.</i>
----------	---

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.

Examples

```
# 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)
```

```

# In this case, 'custom_rnaseq' is a data frame with
# the structure:
head(custom_rnaseq)
##           Counts
## ENSMUSG00000000001  6572
## ENSMUSG00000000003    0
## ENSMUSG00000000028  4644
## ENSMUSG00000000031    8
## ENSMUSG00000000037    0
## ENSMUSG00000000049    0

# The helper 'omicData' returns an object with our custom data.
rnaseq_customdata <- omicData("RNA-seq", data = custom_rnaseq)

```

omicResults	<i>Retrieves the simulated data.</i>
-------------	--------------------------------------

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 specific, with the simulation data in the format indicated, or a numeric matrix with simulated data if the omic name is directly provided.

Examples

```

omic_list <- c("RNA-seq")
rnaseq_simulation <- mosim(omics = omic_list)
#' # This will be a data frame with RNA-seq counts
rnaseq_simulated <- omicResults(rnaseq_simulation, "RNA-seq")

#           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	421	348	492 ...
# ENSMUSG00000097226	16	14	9 ...
# ENSMUSG00000027857	0	0	0 ...
# ENSMUSG00000032081	1	0	0 ...
# ENSMUSG00000097164	794	822	965 ...
# ENSMUSG00000097871	0	0	0 ...

omicSettings	<i>Retrieves the settings used in a simulation</i>
--------------	--

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.

Examples

```
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")

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

omicSim	<i>Set the simulation settings for an omic.</i>
---------	---

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.

Examples

```
omic_list <- c("RNA-seq", "miRNA-seq")

rnaseq_options <- c(omicSim("miRNA-seq", totalFeatures = 2500))

# The return value is an associative list compatible with
# 'omicsOptions'
rnaseq_simulation <- mosim(omics = omic_list,
```

```
omicsOptions = rnaseq_options)
```

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.

Examples

```
omic_list <- c("RNA-seq", "miRNA-seq")

rnaseq_options <- c(omicSim("miRNA-seq", totalFeatures = 2500))
rnaseq_simulation <- mosim(omics = omic_list,
                           omicsOptions = rnaseq_options)

plotProfile(rnaseq_simulation,
            omics = c("RNA-seq", "miRNA-seq"),
            featureIDS = list("RNA-seq"="ENSMUSG00000007682", "miRNA-seq"="mmu-miR-320-3p")
            )
```

 sampleData

Default data

Description

Dataset with base counts and id-gene tables.

Usage

```
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.

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" column.

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

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