Package ‘MOSim’

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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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discretize

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MOSim-package  MOSim

Description

Multiomics simulation package.

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

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")

design_matrix <- experimentalDesign(rnaseq_simulation)
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.

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 omicSim to provide the options to simulated each omic.

**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 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

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. 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.
**MOSimulator-class**

Virtual class containing common methods and slots for child classes.

### Description

Virtual class containing common methods and slots for child classes.

### Slots

- **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.

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**MOSimulatorRegion-class**

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

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**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.
- 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.
omicData

balanceHypoHyper numeric. Balance of hypo/hyper methylation
rateHMMMatrix 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(omic, data = NULL, associationList = NULL)

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  0
## ENSMUSG00000000037  0
## ENSMUSG00000000049  0
```

The helper 'omicData' returns an object with our custom data.

```
rnaseq_customdata <- omicData("RNA-seq", data = custom_rnaseq)
```

---

**omicResults**

Retrieving 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 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 ...
```
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.
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.

Examples
```
optic_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)

rnaseq_options <- c(omicSim("miRNA-seq", totalFeatures = 2500))
# The return value is an associative list compatible with
# 'omicsOptions'
rnaseq_simulation <- mosim(omics = omic_list,
```
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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