

Package ‘scMultiSim’

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Title Simulation of Multi-Modality Single Cell Data Guided By Gene
Regulatory Networks and Cell-Cell Interactions

Version 1.7.0

Description

scMultiSim simulates paired single cell RNA-seq, single cell ATAC-seq and RNA velocity data, while incorporating mechanisms of gene regulatory networks, chromatin accessibility and cell-cell interactions. It allows users to tune various parameters controlling the amount of each biological factor, variation of gene-expression levels, the influence of chromatin accessibility on RNA sequence data, and so on. It can be used to benchmark various computational methods for single cell multi-omics data, and to assist in experimental design of wet-lab experiments.

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<code>.amplifyOneCell</code>	<i>This function simulates the amplification, library prep, and the sequencing processes.</i>
------------------------------	---

Description

This function simulates the amplification, library prep, and the sequencing processes.

Usage

```
.amplifyOneCell(  
  true_counts_1cell,  
  protocol,  
  rate_2cap,  
  gene_len,  
  amp_bias,  
  rate_2PCR,  
  nPCR1,  
  nPCR2,  
  LinearAmp,  
  LinearAmp_coef,  
  N_molecules_SEQ  
)
```

Arguments

<code>true_counts_1cell</code>	the true transcript counts for one cell (one vector)
<code>protocol</code>	a string, can be "nonUMI" or "UMI"
<code>rate_2cap</code>	the capture efficiency for this cell
<code>gene_len</code>	gene lengths for the genes/transcripts, sampled from real human transcript length
<code>amp_bias</code>	amplification bias for each gene, a vector of length ngenes
<code>rate_2PCR</code>	PCR efficiency, usually very high

nPCR1	the number of PCR cycles
nPCR2	the number of PCR cycles
LinearAmp	if linear amplification is used for pre-amplification step, default is FALSE
LinearAmp_coef	the coefficient of linear amplification, that is, how many times each molecule is amplified by
N_molecules_SEQ	number of molecules sent for sequencing; sequencing depth

Value

read counts (if protocol="nonUMI") or UMI counts (if protocol="UMI")

<i>.calAmpBias</i>	<i>Simulate technical biases</i>
--------------------	----------------------------------

Description

Simulate technical biases

Usage

```
.calAmpBias(lenslope, nbins, gene_len, amp_bias_limit)
```

Arguments

lenslope	amount of length bias. This value should be less than $2 * \text{amp_bias_limit}[2] / (\text{nbins} - 1)$
nbins	number of bins for gene length
gene_len	transcript length of each gene
amp_bias_limit	range of amplification bias for each gene, a vector of length ngenes

Value

a vector

<code>.continuousCIF</code>	<i>Generates cifs for cells sampled along the trajectory of cell development</i>
-----------------------------	--

Description

Generates cifs for cells sampled along the trajectory of cell development

Usage

```
.continuousCIF(  
  seed,  
  N,  
  options,  
  ncell_key = "cell",  
  is_spatial = FALSE,  
  spatial_params = NULL,  
  .plot = FALSE,  
  .plot.name = "cont_cif.pdf"  
)
```

Arguments

<code>seed</code>	random seed
<code>N</code>	the number list
<code>options</code>	the option list
<code>ncell_key</code>	the key for the number of cells in N
<code>is_spatial</code>	return a list of cifs for spatial
<code>spatial_params</code>	the spatial parameters
<code>.plot</code>	save the CIF plot
<code>.plot.name</code>	plot name

Value

a list containing the cif and meta data

<code>.divideBatchesImpl</code>	<i>Divide the observed counts into multiple batches by adding batch effect to each batch</i>
---------------------------------	--

Description

Divide the observed counts into multiple batches by adding batch effect to each batch

Usage

```
.divideBatchesImpl(
  counts,
  meta_cell,
  nbatch,
  batch_effect_size = 1,
  randseed = 0
)
```

Arguments

<code>counts</code>	gene cell matrix
<code>meta_cell</code>	the meta information related to cells, will be combined with technical cell level information and returned
<code>nbatch</code>	number of batches
<code>batch_effect_size</code>	amount of batch effects. Larger values result in bigger differences between batches. Default is 1.
<code>randseed</code>	random seed

Value

a list with two elements: counts and meta_cell

<code>.expandToBinary</code>	<i>expand transcript counts to a vector of binaries of the same length of as the number of transcripts</i>
------------------------------	--

Description

expand transcript counts to a vector of binaries of the same length of as the number of transcripts

Usage

```
.expandToBinary(true_counts_1cell)
```

Arguments

true_counts_1cell
number of transcript in one cell

Value

a list of two vectors, the first vector is a vector of 1s, the second vector is the index of transcripts

.getCountCorrMatrix *This function finds the correlation between every pair of genes*

Description

This function finds the correlation between every pair of genes

Usage

```
.getCountCorrMatrix(counts)
```

Arguments

counts rna seq counts

Value

the correlation matrix

.getParams *Get Kineic Parameters for all cells and genes*

Description

Get Kineic Parameters for all cells and genes

Usage

```
.getParams(seed, sim, sp_cell_i = NULL, sp_path_i = NULL)
```

Arguments

seed random seed
sim the simulation environment
sp_cell_i spatial cell index
sp_path_i the pre-sampled path along the tree for this cell

Value

the kinetic parameters

.normalizeGRNParams	<i>Rename the original gene IDs in the GRN table to integers.</i>
---------------------	---

Description

Rename the original gene IDs in the GRN table to integers.

Usage

```
.normalizeGRNParams(params)
```

Arguments

params GRN parameters.

Value

list

.rnormTrunc	<i>sample from truncated normal distribution</i>
-------------	--

Description

sample from truncated normal distribution

Usage

```
.rnormTrunc(n, mean, sd, a, b)
```

Arguments

n number of values to create
mean mean of the normal distribution
sd standard deviation of the normal distribution
a the minimum value allowed
b the maximum value allowed

Value

a vector of length n

add_expr_noise	<i>Add experimental noise to true counts</i>
----------------	--

Description

Add experimental noise to true counts

Usage

```
add_expr_noise(results, ...)
```

Arguments

results	The scMultisim result object
...	randseed: The random seed protocol: UMI or non-UMI gene_len: A vector with lengths of all genes alpha_mean, alpha_sd: rate of subsampling of transcripts during capture step depth_mean, depth_sd: The sequencing depth

Value

none

See Also

The underlying methods [True2ObservedCounts](#) and [True2ObservedATAC](#)

Examples

```
results <- sim_example(ncells = 10)
add_expr_noise(results)
```

add_outliers	<i>Add outliers to the observed counts</i>
--------------	--

Description

Add outliers to the observed counts

Usage

```
add_outliers(
  res,
  prob = 0.01,
  factor = 2,
  sd = 0.5,
  cell.num = 1,
  max.var = Inf
)
```

Arguments

res	The scMultisim result object
prob	The probability of adding outliers for each gene
factor	The factor of the outliers
sd	The standard deviation of the outliers
cell.num	For a gene, the number of cells chosen to add outliers
max.var	The maximum variance allowed

Value

none

cci_cell_type_params *Generate cell-type level CCI parameters*

Description

See the return value if you want to specify the cell-type level ground truth.

Usage

```
cci_cell_type_params(
  tree,
  total.lr,
  ctype.lr = 4:6,
  step.size = 1,
  rand = TRUE,
  discrete = FALSE
)
```

Arguments

tree	Use the same value for sim_true_counts().
total.lr	Total number of LR pairs in the database. Use the same value for sim_true_counts().
ctype.lr	If rand is TRUE, how many LR pairs should be enabled between each cell type pair. Should be a range, e.g. 4:6.
step.size	Use the same value for sim_true_counts().
rand	Whether fill the matrix randomly
discrete	Whether the cell population is discrete. Use the same value for sim_true_counts().

Value

A 3D matrix of (n_cell_type, n_cell_type, n_lr). The value at (i, j, k) is 1 if there exist CCI of LR-pair k between cell type i and cell type j.

Examples

```
cci_cell_type_params(Phyla3(), 100, 4:6, 0.5, TRUE, FALSE)
```

dens_nonzero	<i>this is the density function of $\log(x+1)$, where x is the non-zero values for ATAC-SEQ data</i>
--------------	--

Description

this is the density function of $\log(x+1)$, where x is the non-zero values for ATAC-SEQ data

Usage

```
data(dens_nonzero)
```

Format

a vector.

Value

a vector.

Examples

```
data(dens_nonzero)
```

divide_batches	<i>Divide batches for observed counts</i>
----------------	---

Description

Divide batches for observed counts

Usage

```
divide_batches(results, nbatch = 2, effect = 3, randseed = 0)
```

Arguments

results	The scMultisim result object, after running addExprNoise()
nbatch	Number of batches
effect	Batch effect size, default is 3
randseed	Random seed

Value

none

Examples

```
results <- sim_example(ncells = 10)
add_expr_noise(results)
divide_batches(results)
```

gene_corr_cci

Plot the ligand-receptor correlation summary

Description

Plot the ligand-receptor correlation summary

Usage

```
gene_corr_cci(
  results = .getResultsFromGlobal(),
  all.genes = FALSE,
  .pair = NULL,
  .exclude.same.types = TRUE
)
```

Arguments

results	The scMultisim result object
all.genes	Whether to use all genes or only the ligand/receptor genes
.pair	Return the raw data for the given LR pair
.exclude.same.types	Whether to exclude neighbor cells with same cell type

Value

none

Examples

```
results <- sim_example_spatial(ncells = 10)
gene_corr_cci(results)
```

gene_corr_regulator	<i>Print the correlations between targets of each regulator</i>
---------------------	---

Description

Print the correlations between targets of each regulator

Usage

```
gene_corr_regulator(results = .getResultsFromGlobal(), regulator)
```

Arguments

results	The scMultisim result object
regulator	The regulator ID in the GRN params

Value

none

Examples

```
results <- sim_example(ncells = 10)
gene_corr_regulator(results, 2)
```

gene_len_pool	<i>a pool of gene lengths to sample from</i>
---------------	--

Description

a pool of gene lengths to sample from

Usage

```
data(gene_len_pool)
```

Format

a vector.

Value

a vector of gene lengths.

Examples

```
data(gene_len_pool)
```

gen_1branch

Generate true transcript counts for linear structure

Description

Generate true transcript counts for linear structure

Usage

```
gen_1branch(
  kinet_params,
  start_state,
  start_s,
  start_u,
  randpoints1,
  ncells1,
  ngenes,
  beta_vec,
  d_vec,
  cycle_length_factor,
  cell
)
```

Arguments

kinet_params	kinetic parameters, include k_on, k_off, s and beta
start_state	the starting state: on or off of each gene
start_s	spliced count of the root cell in the branch
start_u	unspliced count of the root cell in the branch
randpoints1	the value which evf mean is generated from
ncells1	number of cells in the branch
ngenes	number of genes
beta_vec	splicing rate of each gene
d_vec	degradation rate of each gene
cycle_length_factor	for generating velocity data, a factor which is multiplied by the expected time to transition from kon to koff and back to to form the the length of a cycle
cell	the cell number currently having counts generated

Value

a list of 4 elements, the first element is true counts, second is the gene level meta information, the third is cell level meta information, including a matrix of evf and a vector of cell identity, and the fourth is the parameters kon, koff and s used to simulation the true counts

gen_clutter	<i>generate a clutter of cells by growing from the center</i>
-------------	---

Description

generate a clutter of cells by growing from the center

Usage

```
gen_clutter(
  n_cell,
  grid_size = NA,
  center = c(0, 0),
  existing_loc = NULL,
  existing_grid = NULL
)
```

Arguments

n_cell	the number of cells
grid_size	the width and height of the grid
center	the center of the grid
existing_loc	only place cells on the specified existing locations
existing_grid	manually specify what locations are in the grid

Value

a matrix of locations

Examples

```
gen_clutter(10, 10, c(5, 5))
```

Get_1region_ATAC_correlation

This function gets the average correlation rna seq counts and region effect on genes for genes which are only associated with 1 chromatin region

Description

This function gets the average correlation rna seq counts and region effect on genes for genes which are only associated with 1 chromatin region

Usage

```
Get_1region_ATAC_correlation(counts, atacseq_data, region2gene)
```

Arguments

counts	rna seq counts
atacseq_data	atac seq data
region2gene	a 0 1 coupling matrix between regions and genes of shape (nregions) x (num_genes), where a value of 1 indicates the gene is affected by a particular region

Value

the correlation value

Examples

```
results <- sim_example(ncells = 10)
Get_1region_ATAC_correlation(results$counts, results$atacseq_data, results$region_to_gene)
```

Get_ATAC_correlation *This function gets the average correlation rna seq counts and chromatin region effect on genes*

Description

This function gets the average correlation rna seq counts and chromatin region effect on genes

Usage

```
Get_ATAC_correlation(counts, atacseq_data, num_genes)
```

Arguments

counts	rna seq counts
atacseq_data	atac seq data
num_genes	number of genes

Value

the correlation value

Examples

```
results <- sim_example(ncells = 10)
Get_ATAC_correlation(results$counts, results$atacseq_data, results$num_genes)
```

GRN_params_100	<i>100_gene_GRN is a matrix of GRN params consisting of 100 genes where: # - column 1 is the target gene ID, # - column 2 is the gene ID which acts as a transcription factor for the target (regulated) gene # - column 3 is the effect of the column 2 gene ID on the column 1 gene ID</i>
----------------	--

Description

100_gene_GRN is a matrix of GRN params consisting of 100 genes where: # - column 1 is the target gene ID, # - column 2 is the gene ID which acts as a transcription factor for the target (regulated) gene # - column 3 is the effect of the column 2 gene ID on the column 1 gene ID

Usage

```
data(GRN_params_100)
```

Format

a data frame.

Value

a data frame with three columns: target gene ID, TF gene ID, and the effect of TF on target gene.

Examples

```
data(GRN_params_100)
```

GRN_params_1139	<i>GRN_params_1139 is a matrix of GRN params consisting of 1139 genes where: # - column 1 is the target gene ID, # - column 2 is the gene ID which acts as a transcription factor for the target (regulated) gene # - column 3 is the effect of the column 2 gene ID on the column 1 gene ID</i>
-----------------	--

Description

GRN_params_1139 is a matrix of GRN params consisting of 1139 genes where: # - column 1 is the target gene ID, # - column 2 is the gene ID which acts as a transcription factor for the target (regulated) gene # - column 3 is the effect of the column 2 gene ID on the column 1 gene ID

Usage

```
data(GRN_params_1139)
```

Format

a data frame.

Value

a data frame with three columns: target gene ID, TF gene ID, and the effect of TF on target gene.

Examples

```
data(GRN_params_1139)
```

len2nfrag	<i>from transcript length to number of fragments (for the nonUMI protocol)</i>
-----------	--

Description

from transcript length to number of fragments (for the nonUMI protocol)

Usage

```
data(len2nfrag)
```

Format

a vector.

Value

a vector.

Examples

```
data(len2nfrag)
```

match_params	<i>distribution of kinetic parameters learned from the Zeisel UMI cortex datasets</i>
--------------	---

Description

distribution of kinetic parameters learned from the Zeisel UMI cortex datasets

Usage

data(param_realdata.zeisel.imputed)

Format

a data frame.

Value

a data frame.

Examples

data(param_realdata.zeisel.imputed)

OP	<i>Get option from an object in the current environment</i>
----	---

Description

Get option from an object in the current environment

Usage

OP(..., .name = "options")

Arguments

- ... the parameter name
- .name get option from this object

Value

the parameter value

Phyla1

Creating a linear example tree

Description

Creating a linear example tree

Usage

```
Phyla1(len = 1)
```

Arguments

len length of the tree

Value

a R phylo object

Examples

```
Phyla1(len = 1)
```

Phyla3

Creating an example tree with 3 tips

Description

Creating an example tree with 3 tips

Usage

```
Phyla3(plotting = FALSE)
```

Arguments

plotting True for plotting the tree on console, False for no plot

Value

a R phylo object

Examples

```
Phyla3()
```

Phyla5*Creating an example tree with 5 tips*

Description

Creating an example tree with 5 tips

Usage

```
Phyla5(plotting = FALSE)
```

Arguments

plotting True for plotting the tree on console, False for no plot

Value

a R phylo object

Examples

```
Phyla5()
```

plot_cell_loc*Plot cell locations*

Description

Plot cell locations

Usage

```
plot_cell_loc(  
  results = .getResultsFromGlobal(),  
  size = 4,  
  show.label = FALSE,  
  show.arrows = TRUE,  
  lr.pair = 1,  
  .cell.pop = NULL,  
  .locs = NULL  
)
```

Arguments

results	The scMultisim result object
size	Fig size
show.label	Show cell numbers
show.arrows	Show arrows representing cell-cell interactions
lr.pair	The ligand-receptor pair used to plot CCI arrows results\$cci_cell_type_param[lr.pair]
.cell.pop	Specify the cell population metadata
.locs	Manually specify the cell locations as a 2xncells matrix

Value

none

Examples

```
results <- sim_example_spatial(ncells = 10)
plot_cell_loc(results)
```

plot_gene_module_cor_heatmap

Plot the gene module correlation heatmap

Description

Plot the gene module correlation heatmap

Usage

```
plot_gene_module_cor_heatmap(
  results = .getResultsFromGlobal(),
  seed = 0,
  grn.genes.only = TRUE,
  save = FALSE
)
```

Arguments

results	The scMultisim result object
seed	The random seed
grn.genes.only	Plot the GRN gens only
save	save the plot as pdf

Value

none

Examples

```
results <- sim_example(ncells = 10)
plot_gene_module_cor_heatmap(results)
```

`plot_grid`*Plot the CCI grid*

Description

In normal cases, please use `plotCellLoc` instead.

Usage

```
plot_grid(results = .getResultsFromGlobal())
```

Arguments

`results` The `scMultisim` result object

Value

none

Examples

```
results <- sim_example_spatial(ncells = 10)
plot_grid(results)
```

`plot_grn`*Plot the GRN network*

Description

Plot the GRN network

Usage

```
plot_grn(params)
```

Arguments

`params` The GRN params data frame

Value

none

Examples

```
data(GRN_params_100, envir = environment())
plot_grn(GRN_params_100)
```

plot_phyla	<i>Plot a R phylogenic tree</i>
------------	---------------------------------

Description

Plot a R phylogenic tree

Usage

```
plot_phyla(tree)
```

Arguments

tree	The tree
------	----------

Value

none

Examples

```
plot_phyla(Phyla5())
```

plot_rna_velocity	<i>Plot RNA velocity as arrows on tSNE plot</i>
-------------------	---

Description

Plot RNA velocity as arrows on tSNE plot

Usage

```
plot_rna_velocity(
  results = .getResultsFromGlobal(),
  velocity = results$velocity,
  perplexity = 70,
  arrow.length = 1,
  save = FALSE,
  randseed = 0,
  ...
)
```

Arguments

results	The scMultiSim result object
velocity	The velocity matrix, by default using the velocity matrix in the result object
perplexity	The perplexity for tSNE
arrow.length	The length scaler of the arrow
save	Whether to save the plot
randseed	The random seed
...	Other parameters passed to ggplot

Value

The plot

Examples

```
results <- sim_example(ncells = 10, velocity = TRUE)
plot_rna_velocity(results, perplexity = 3)
```

plot_tsne

Plot t-SNE visualization of a data matrix

Description

Plot t-SNE visualization of a data matrix

Usage

```
plot_tsne(
  data,
  labels,
  perplexity = 60,
  legend = "",
  plot.name = "",
  save = FALSE,
  rand.seed = 0,
  continuous = FALSE,
  labels2 = NULL,
  lim = NULL,
  runPCA = FALSE,
  alpha = 1
)
```

Arguments

data	The dxn matrix
labels	A vector of length n, usually cell clusters
perplexity	Perplexity value used for t-SNE
legend	A list of colors for the labels
plot.name	The plot title
save	If TRUE, save as plot.name.pdf
rand.seed	The random seed
continuous	Whether labels should be treated as continuous, e.g. pseudotime
labels2	Additional label
lim	Specify the xlim and y lim c(x_min, x_max, y_min, y_max)
runPCA	Whether to run PCA before t-SNE
alpha	The alpha value for the points

Value

the figure if not save, otherwise save the figure as plot.name.pdf

Examples

```
results <- sim_example(ncells = 10)
plot_tsne(log2(results$counts + 1), results$cell_meta$pop, perplexity = 3)
```

run_shiny

Launch the Shiny App to configure the simulation

Description

Launch the Shiny App to configure the simulation

Usage

```
run_shiny()
```

SampleDen	<i>sample from smoothed density function</i>
-----------	--

Description

sample from smoothed density function

Usage

```
SampleDen(nsample, den_fun, reduce.mem = FALSE)
```

Arguments

nsample	number of samples needed
den_fun	density function estimated from density() from R default
reduce.mem	use alternative implementation to reduce memory usage

Value

a vector of samples

scmultisim_help	<i>Show detailed documentations of scMultiSim's parameters</i>
-----------------	--

Description

Show detailed documentations of scMultiSim's parameters

Usage

```
scmultisim_help(topic = NULL)
```

Arguments

topic	Can be options, dynamic.GRN, or cci
-------	-------------------------------------

Value

none

Examples

```
scmultisim_help()
```

sim_example	<i>Simulate a small example dataset with 200 cells and the 100-gene GRN</i>
-------------	---

Description

Simulate a small example dataset with 200 cells and the 100-gene GRN

Usage

```
sim_example(ncells = 10, velocity = FALSE)
```

Arguments

ncells	number of cells, please increase this number on your machine
velocity	whether to simulate RNA velocity

Value

the simulation result

Examples

```
sim_example(ncells = 10)
```

sim_example_spatial	<i>Simulate a small example dataset with 200 cells and the 100-gene GRN, with CCI enabled</i>
---------------------	---

Description

Simulate a small example dataset with 200 cells and the 100-gene GRN, with CCI enabled

Usage

```
sim_example_spatial(ncells = 10)
```

Arguments

ncells	number of cells, please increase this number on your machine
--------	--

Value

the simulation result

Examples

```
sim_example_spatial(ncells = 10)
```

sim_true_counts	<i>Simulate true scRNA and scATAC counts from the parameters</i>
-----------------	--

Description

Simulate true scRNA and scATAC counts from the parameters

Usage

```
sim_true_counts(options, return_summarized_exp = FALSE)
```

Arguments

options See `scMultiSim_help()`.
return_summarized_exp Whether to return a `SummarizedExperiment` object.

Value

`scMultiSim` returns an environment with the following fields:

- `counts`: Gene-by-cell scRNA-seq counts.
- `atac_counts`: Region-by-cell scATAC-seq counts.
- `region_to_gene`: Region-by-gene 0-1 matrix indicating the corresponding relationship between chromatin regions and genes.
- `atacseq_data`: The "clean" scATAC-seq counts without added intrinsic noise.
- `cell_meta`: A dataframe containing cell type labels and pseudotime information.
- `cif`: The CIF used during the simulation.
- `giv`: The GIV used during the simulation.
- `kinetic_params`: The kinetic parameters used during the simulation.
- `.grn`: The GRN used during the simulation.
- `.grn$regulators`: The list of TFs used by all gene-by-TF matrices.
- `.grn$geff`: Gene-by-TF matrix representing the GRN used during the simulation.
- `.n`: Other metadata, e.g. `.n$cells` is the number of cells.

If `do.velocity` is enabled, it has these additional fields:

- `unspliced_counts`: Gene-by-cell unspliced RNA counts.
- `velocity`: Gene-by-cell RNA velocity ground truth.
- `cell_time`: The pseudotime at which the cell counts were generated.

If dynamic GRN is enabled, it has these additional fields:

- `cell_specific_grn`: A list of length `n_cells`. Each element is a gene-by-TF matrix, indicating the cell's GRN.

If cell-cell interaction is enabled, it has these additional fields:

- `grid`: The grid object used during the simulation.
 - `grid$get_neighbours(i)`: Get the neighbour cells of cell `i`.
- `cci_locs`: A dataframe containing the X and Y coordinates of each cell.
- `cci_cell_type_param`: A dataframe containing the CCI network ground truth: all ligand-receptor pairs between each pair of cell types.
- `cci_cell_types`: For continuous cell population, the sub-divided cell types along the trajectory used when simulating CCI.

If it is a debug session (`debug = TRUE`), a `sim` field is available, which is an environment contains all internal states and data structures.

Examples

```
data(GRN_params_100, envir = environment())
sim_true_counts(list(
  rand.seed = 0,
  GRN = GRN_params_100,
  num.cells = 100,
  num.cifs = 50,
  tree = Phyla5()
))
```

spatialGrid-class	<i>The class for spatial grids</i>
-------------------	------------------------------------

Description

The class for spatial grids

Value

a `spatialGrid` object

Fields

`method` the method to generate the cell layout
`grid_size` the width and height of the grid
`ncells` the number of cells
`grid` the grid matrix
`locs` a list containing the locations of all cells
`loc_order` deprecated, don't use; the order of the locations
`cell_types` a map to save the cell type of each allocated cell
`same_type_prob` the probability of a new cell placed next to a cell with the same type

max_nbs the maximum number of neighbors for each cell
 nb_map a list containing the neighbors for each cell
 nb_adj adjacency matrix for neighbors
 nb_radius the radius of neighbors
 final_types the final cell types after the final time step
 pre_allocated_pos the pre-allocated positions for each cell, if any
 method_param additional parameters for the layout method

True2observedATAC	<i>Simulate observed ATAC-seq matrix given technical noise and the true counts</i>
-------------------	--

Description

Simulate observed ATAC-seq matrix given technical noise and the true counts

Usage

```
True2observedATAC(
  atacseq_data,
  randseed,
  observation_prob = 0.3,
  sd_frac = 0.1
)
```

Arguments

atacseq_data	true ATAC-seq data
randseed	(should produce same result if nregions, nevf and randseed are all the same)
observation_prob	for each integer count of a particular region for a particular cell, the probability the count will be observed
sd_frac	the fraction of ATAC-seq data value used as the standard deviation of added normally distributed noise

Value

a matrix of observed ATAC-seq data

Examples

```
results <- sim_example(ncells = 10)
True2observedATAC(results$atac_counts, randseed = 1)
```

True2ObservedCounts	<i>Simulate observed count matrix given technical biases and the true counts</i>
---------------------	--

Description

Simulate observed count matrix given technical biases and the true counts

Usage

```
True2ObservedCounts(
  true_counts,
  meta_cell,
  protocol,
  randseed,
  alpha_mean = 0.1,
  alpha_sd = 0.002,
  alpha_gene_mean = 1,
  alpha_gene_sd = 0,
  gene_len,
  depth_mean,
  depth_sd,
  lenslope = 0.02,
  nbins = 20,
  amp_bias_limit = c(-0.2, 0.2),
  rate_2PCR = 0.8,
  nPCR1 = 16,
  nPCR2 = 10,
  LinearAmp = FALSE,
  LinearAmp_coef = 2000
)
```

Arguments

true_counts	gene cell matrix
meta_cell	the meta information related to cells, will be combined with technical cell level information and returned
protocol	a string, can be "nonUMI" or "UMI"
randseed	(should produce same result if nregions, nev and randseed are all the same)
alpha_mean	the mean of rate of subsampling of transcripts during capture step, default at 10 percent efficiency
alpha_sd	the std of rate of subsampling of transcripts
alpha_gene_mean	the per-gene scale factor of the alpha parameter, default at 1

<code>alpha_gene_sd</code>	the standard deviation of the per-gene scale factor of the alpha parameter, default at 0
<code>gene_len</code>	a vector with lengths of all genes
<code>depth_mean</code>	mean of sequencing depth
<code>depth_sd</code>	std of sequencing depth
<code>lenslope</code>	amount of length bias
<code>nbins</code>	number of bins for gene length
<code>amp_bias_limit</code>	range of amplification bias for each gene, a vector of length ngenes
<code>rate_2PCR</code>	PCR efficiency, usually very high, default is 0.8
<code>nPCR1</code>	the number of PCR cycles in "pre-amplification" step, default is 16
<code>nPCR2</code>	the number of PCR cycles used after fragmentation.
<code>LinearAmp</code>	if linear amplification is used for pre-amplification step, default is FALSE
<code>LinearAmp_coef</code>	the coefficient of linear amplification, that is, how many times each molecule is amplified by

Value

if UMI, a list with two elements, the first is the observed count matrix, the second is the metadata;
if nonUMI, a matrix

Examples

```
results <- sim_example(ncells = 10)
data(gene_len_pool)
gene_len <- sample(gene_len_pool, results$num_genes, replace = FALSE)
True2ObservedCounts(
  results$counts, results$cell_meta, protocol = "nonUMI", randseed = 1,
  alpha_mean = 0.1, alpha_sd = 0.05, gene_len = gene_len, depth_mean = 1e5, depth_sd = 3e3
)
```

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