Package ‘splatter’

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**splatter-package**

splatter: Simple Simulation of Single-cell RNA Sequencing Data
**Description**

Splatter is a package for the simulation of single-cell RNA sequencing count data. It provides a simple interface for creating complex simulations that are reproducible and well-documented. Parameters can be estimated from real data and functions are provided for comparing real and simulated datasets.

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**See Also**

Useful links:

- [https://bioconductor.org/packages/splatter/](https://bioconductor.org/packages/splatter/)
- [https://github.com/Oshlack/splatter](https://github.com/Oshlack/splatter)
- Report bugs at [https://github.com/Oshlack/splatter/issues](https://github.com/Oshlack/splatter/issues)

---

**addGeneLengths**

*Add gene lengths*

**Description**

Add gene lengths to an SingleCellExperiment object

**Usage**

```r
addGeneLengths(
  sce,
  method = c("generate", "sample"),
  loc = 7.9,
  scale = 0.7,
  lengths = NULL
)
```
Arguments

sce SingleCellExperiment to add gene lengths to.
method Method to use for creating lengths.
loc Location parameter for the generate method.
scale Scale parameter for the generate method.
lengths Vector of lengths for the sample method.

Details

This function adds simulated gene lengths to the rowData slot of a SingleCellExperiment object that can be used for calculating length normalised expression values such as TPM or FPKM. The generate method simulates lengths using a (rounded) log-normal distribution, with the default loc and scale parameters based on human protein-coding genes. Alternatively the sample method can be used which randomly samples lengths (with replacement) from a supplied vector.

Value

SingleCellExperiment with added gene lengths

Examples

# Default generate method
sce <- simpleSimulate()
sce <- addGeneLengths(sce)
head(rowData(sce))
# Sample method (human coding genes)
# Not run:
library(TxDb.Hsapiens.UCSC.hg19.knownGene)
library(GenomicFeatures)
taxdb <- TxDb.Hsapiens.UCSC.hg19.knownGene
tax.lens <- transcriptLengths(txdb, with.cds_len = TRUE)
tax.lens <- tax.lens[tx.lens$cds_len > 0, ]
gene.lens <- max(splitAsList(tx.lens$tx_len, tx.lens$gene_id))
sce <- addGeneLengths(sce, method = "sample", lengths = gene.lens)

## End(Not run)

BASiCSEstimate Estimate BASiCS simulation parameters

Description

Estimate simulation parameters for the BASiCS simulation from a real dataset.
Usage

```
BASiCSEstimate(
  counts,
  spike.info = NULL,
  batch = NULL,
  n = 20000,
  thin = 10,
  burn = 5000,
  regression = TRUE,
  params = newBASiCSParams(),
  verbose = TRUE,
  progress = TRUE,
  ...
)
```

```r
## S3 method for class 'SingleCellExperiment'
BASiCSEstimate(
  counts,
  spike.info = NULL,
  batch = NULL,
  n = 20000,
  thin = 10,
  burn = 5000,
  regression = TRUE,
  params = newBASiCSParams(),
  verbose = TRUE,
  progress = TRUE,
  ...
)
```

```r
## S3 method for class 'matrix'
BASiCSEstimate(
  counts,
  spike.info = NULL,
  batch = NULL,
  n = 20000,
  thin = 10,
  burn = 5000,
  regression = TRUE,
  params = newBASiCSParams(),
  verbose = TRUE,
  progress = TRUE,
  ...
)
```
Arguments

counts    either a counts matrix or a SingleCellExperiment object containing count data
to estimate parameters from.

spike.info data.frame describing spike-ins with two columns: "Name" giving the names of
the spike-in features (must match rownames(counts)) and "Input" giving the
number of input molecules.

batch vector giving the batch that each cell belongs to.
n    total number of MCMC iterations. Must be >= max(4, thin) and a multiple of
thin.

thin    thining period for the MCMC sampler. Must be >= 2.

burn burn-in period for the MCMC sampler. Must be in the range 1 <= burn < n and
a multiple of thin.

regression logical. Whether to use regression to identify over-dispersion. See BASiCS_MCMC
for details.

params BASiCSParams object to store estimated values in.

verbose logical. Whether to print progress messages.

progress logical. Whether to print additional BASiCS progress messages.

Optional parameters passed to BASiCS_MCMC.

Details

This function is just a wrapper around BASiCS_MCMC that takes the output and converts it to a BA-
SiCSParams object. Either a set of spike-ins or batch information (or both) must be supplied. If
only batch information is provided there must be at least two batches. See BASiCS_MCMC for details.

Value

BASiCSParams object containing the estimated parameters.

Examples

# Load example data
library(scuttle)
set.seed(1)
sce <- mockSCE()

spike.info <- data.frame(
    Name = rownames(sce)[1:10],
    Input = rnorm(10, 500, 200),
    stringsAsFactors = FALSE
)

params <- BASiCSEstimate(sce[1:100, 1:30], spike.info)

params
BASiCSPrams

The BASiCSPrams class

Description

S4 class that holds parameters for the BASiCS simulation.

Parameters

The BASiCS simulation uses the following parameters:

- **nGenes** The number of genes to simulate.
- **nCells** The number of cells to simulate.
- **[seed]** Seed to use for generating random numbers.

**Batch parameters**

- **nBatches** Number of batches to simulate.
- **batchCells** Number of cells in each batch.

**Gene parameters**

- **gene.params** A data.frame containing gene parameters with two columns: Mean (mean expression for each biological gene) and Delta (cell-to-cell heterogeneity for each biological gene).

**Spike-in parameters**

- **nSpikes** The number of spike-ins to simulate.
- **spike.means** Input molecules for each spike-in.

**Cell parameters**

- **cell.params** A data.frame containing gene parameters with two columns: Phi (mRNA content factor for each cell, scaled to sum to the number of cells in each batch) and S (capture efficient for each cell).

**Variability parameters**

- **theta** Technical variability parameter for each batch.

The parameters not shown in brackets can be estimated from real data using BASiCSEstimate. For details of the BASiCS simulation see BASiCSSimulate.

BASiCSSimulate

BASiCS simulation

Description

Simulate counts using the BASiCS method.

Usage

```r
BASiCSSimulate(
    params = newBASiCSPrams(),
    sparsify = TRUE,
    verbose = TRUE,
    ...
)
```
**compareSCEs**

**Arguments**

- `params`: BASiCSPrams object containing simulation parameters.
- `sparsify`: logical. Whether to automatically convert assays to sparse matrices if there will be a size reduction.
- `verbose`: logical. Whether to print progress messages
- `...`: any additional parameter settings to override what is provided in `params`.

**Details**

This function is just a wrapper around `BASiCS_Sim` that takes a `BASiCSPrams`, runs the simulation then converts the output to a `SingleCellExperiment` object. See `BASiCS_Sim` for more details of how the simulation works.

**Value**

`SingleCellExperiment` containing simulated counts

**References**


Paper: [10.1371/journal.pcbi.1004333](https://doi.org/10.1371/journal.pcbi.1004333)

Code: [https://github.com/catavallejos/BASiCS](https://github.com/catavallejos/BASiCS)

**Examples**

```r
if (requireNamespace("BASiCS", quietly = TRUE)) {
  sim <- BASiCSSimulate()
}
```

---

**compareSCEs**

*Compare SingleCellExperiment objects*

**Description**

Combine the data from several `SingleCellExperiment` objects and produce some basic plots comparing them.

**Usage**

```R
compareSCEs(
  sces,
  point.size = 0.1,
  point.alpha = 0.1,
  fits = TRUE,
  colours = NULL
)
```
compareSCEs

Arguments

sces named list of SingleCellExperiment objects to combine and compare.
point.size size of points in scatter plots.
point.alpha opacity of points in scatter plots.
fits whether to include fits in scatter plots.
colours vector of colours to use for each dataset.

Details

The returned list has three items:

RowData Combined row data from the provided SingleCellExperiments.
ColData Combined column data from the provided SingleCellExperiments.
Plots Comparison plots

Means Boxplot of mean distribution.
Variances Boxplot of variance distribution.
MeanVar Scatter plot with fitted lines showing the mean-variance relationship.
LibrarySizes Boxplot of the library size distribution.
ZerosGene Boxplot of the percentage of each gene that is zero.
ZerosCell Boxplot of the percentage of each cell that is zero.
MeanZeros Scatter plot with fitted lines showing the mean-zeros relationship.
VarGeneCor Heatmap of correlation of the 100 most variable genes.

The plots returned by this function are created using ggplot and are only a sample of the kind of plots you might like to consider. The data used to create these plots is also returned and should be in the correct format to allow you to create further plots using ggplot.

Value

List containing the combined datasets and plots.

Examples

```r
sim1 <- splatSimulate(nGenes = 1000, batchCells = 20)
sim2 <- simpleSimulate(nGenes = 1000, nCells = 20)
comparison <- compareSCEs(list(Splat = sim1, Simple = sim2))
names(comparison)
names(comparison$Plots)
```
diffSCEs

**Diff SingleCellExperiment objects**

**Description**

Combine the data from several SingleCellExperiment objects and produce some basic plots comparing them to a reference.

**Usage**

```r
diffSCEs(
  sces,
  ref,
  point.size = 0.1,
  point.alpha = 0.1,
  fits = TRUE,
  colours = NULL
)
```

**Arguments**

- `sces` named list of SingleCellExperiment objects to combine and compare.
- `ref` string giving the name of the SingleCellExperiment to use as the reference.
- `point.size` size of points in scatter plots.
- `point.alpha` opacity of points in scatter plots.
- `fits` whether to include fits in scatter plots.
- `colours` vector of colours to use for each dataset.

**Details**

This function aims to look at the differences between a reference SingleCellExperiment and one or more others. It requires each SingleCellExperiment to have the same dimensions. Properties are compared by ranks, for example when comparing the means the values are ordered and the differences between the reference and another dataset plotted. A series of Q-Q plots are also returned.

The returned list has five items:

- **Reference** The SingleCellExperiment used as the reference.
- **RowData** Combined feature data from the provided SingleCellExperiments.
- **ColData** Combined column data from the provided SingleCellExperiments.
- **Plots** Difference plots
  - **Means** Boxplot of mean differences.
  - **Variances** Boxplot of variance differences.
  - **MeanVar** Scatter plot showing the difference from the reference variance across expression ranks.
LibraeySizes  Boxplot of the library size differences.
ZerosGene  Boxplot of the differences in the percentage of each gene that is zero.
ZerosCell  Boxplot of the differences in the percentage of each cell that is zero.
MeanZeros  Scatter plot showing the difference from the reference percentage of zeros across expression ranks.

QQPlots  Quantile-Quantile plots
  Means  Q-Q plot of the means.
  Variances  Q-Q plot of the variances.
  LibrarySizes  Q-Q plot of the library sizes.
  ZerosGene  Q-Q plot of the percentage of zeros per gene.
  ZerosCell  Q-Q plot of the percentage of zeros per cell.

The plots returned by this function are created using ggplot and are only a sample of the kind of plots you might like to consider. The data used to create these plots is also returned and should be in the correct format to allow you to create further plots using ggplot.

Value
List containing the combined datasets and plots.

Examples

```r
sim1 <- splatSimulate(nGenes = 1000, batchCells = 20)
sim2 <- simpleSimulate(nGenes = 1000, nCells = 20)
difference <- diffSCEs(list(Splat = sim1, Simple = sim2), ref = "Simple")
names(difference)
names(difference$Plots)
```

---

**expandParams**

**Expand parameters**

**Description**
Expand the parameters that can be vectors so that they are the same length as the number of groups. Work is done by paramsExpander called from each method. Expansions are stored using setParamsUnchecked.

**Usage**
```
expandParams(object, ...)
```

## S4 method for signature 'BASiCSParms'
expandParams(object)

## S4 method for signature 'LunParams'
expandParams(object)
```
getLNormFactors

## S4 method for signature 'Params'
expandParams(object, vectors, n)

## S4 method for signature 'SplatParams'
expandParams(object)

## S4 method for signature 'SplatPopParams'
expandParams(object)

paramsExpander(object, vectors, n)

### Arguments

- **object**: object to expand.
- **...**: additional arguments.
- **vectors**: names of vector parameters to expand
- **n**: number of times to repeat each parameter

### Value

Expanded object.

---

**getLNormFactors**  *Get log-normal factors*

**Description**

Randomly generate multiplication factors from a log-normal distribution.

**Usage**

```r
getLNormFactors(n.facs, sel.prob, neg.prob, fac.loc, fac.scale)
```

**Arguments**

- **n.facs**: Number of factors to generate.
- **sel.prob**: Probability that a factor will be selected to be different from 1.
- **neg.prob**: Probability that a selected factor is less than one.
- **fac.loc**: Location parameter for the log-normal distribution.
- **fac.scale**: Scale factor for the log-normal distribution.

**Value**

Vector containing generated factors.
getParam

Get a parameter

Description
Accessor function for getting parameter values.

Usage
getParam(object, name)

## S4 method for signature 'Params'
getParam(object, name)

Arguments
object object to get parameter from.
name name of the parameter to get.

Value
The extracted parameter value

Examples
params <- newSimpleParams()
getParam(params, "nGenes")

getParams

Get parameters

Description
Get multiple parameter values from a Params object.

Usage
getParams(params, names)

Arguments
params Params object to get values from.
names vector of names of the parameters to get.
kersplatEstBCV

Value

List with the values of the selected parameters.

Examples

```r
params <- newSimpleParams()
getParams(params, c("nGenes", "nCells", "mean.rate"))
```

Description

Estimate Biological Coefficient of Variation (BCV) parameters for the Kersplat simulation

Usage

```r
kersplatEstBCV(counts, params, verbose)
```

Arguments

```r
counts  counts matrix.
params  KersplatParams object to store estimated values in.
verbose logical. Whether to print progress messages
```

Details

The `estimateDisp` function is used to estimate the common dispersion across the dataset. An exponential correction is applied based on fitting an exponential relationship between simulated and estimated values. If this results in a negative dispersion a simpler linear correction is applied instead.

Value

KersplatParams object with estimated BCV parameters
kersplatEstimate  

**kersplatEstimate**  
*Estimate Kersplat simulation parameters*

**Description**

Estimate simulation parameters for the Kersplat simulation from a real dataset. See the individual estimation functions for more details on how this is done.

**Usage**

kersplatEstimate(counts, params = newKersplatParams(), verbose = TRUE)

## S3 method for class 'SingleCellExperiment'
kersplatEstimate(counts, params = newKersplatParams(), verbose = TRUE)

## S3 method for class 'matrix'
kersplatEstimate(counts, params = newKersplatParams(), verbose = TRUE)

**Arguments**

- **counts**: either a counts matrix or a SingleCellExperiment object containing count data to estimate parameters from.
- **params**: KersplatParams object to store estimated values in.
- **verbose**: logical. Whether to print progress messages.

**Value**

KersplatParams object containing the estimated parameters.

**See Also**

kersplatEstMean, kersplatEstBCV, kersplatEstLib

**Examples**

```r
if (requireNamespace("igraph", quietly = TRUE)) {
  # Load example data
  library(scuttle)
  set.seed(1)
  sce <- mockSCE()

  params <- kersplatEstimate(sce)
  params
}
```
kersplatEstLib  
*Estimate Kersplat library size parameters*

**Description**

Estimate the library size parameters for the Kersplat simulation

**Usage**

```r
kersplatEstLib(counts, params, verbose)
```

**Arguments**

- `counts`: counts matrix.
- `params`: KersplatParams object to store estimated values in.
- `verbose`: logical. Whether to print progress messages

**Details**

Parameters for the log-normal distribution are estimated by fitting the library sizes using `fitdist`. All the fitting methods are tried and the fit with the best Cramer-von Mises statistic is selected. The density of the library sizes is also estimated using `density`.

**Value**

KersplatParams object with library size parameters

kersplatEstMean  
*Estimate Kersplat means*

**Description**

Estimate mean parameters for the Kersplat simulation

**Usage**

```r
ekthersplatEstMean(norm.counts, params, verbose)
```

**Arguments**

- `norm.counts`: library size normalised counts matrix.
- `params`: KersplatParams object to store estimated values in.
- `verbose`: logical. Whether to print progress messages
Details

Parameters for the gamma distribution are estimated by fitting the mean normalised counts using `fitdist`. All the fitting methods are tried and the fit with the best Cramer-von Mises statistic is selected. The density of the means is also estimated using `density`.

Expression outlier genes are detected using the Median Absolute Deviation (MAD) from median method. If the log2 mean expression of a gene is greater than two MADs above the median log2 mean expression it is designated as an outlier. The proportion of outlier genes is used to estimate the outlier probability. Factors for each outlier gene are calculated by dividing mean expression by the median mean expression. A log-normal distribution is then fitted to these factors in order to estimate the outlier factor location and scale parameters using the `fitdist` MLE method.

Value

KersplatParams object with estimated means

---

**kersplatGenNetwork**  
*Generate Kersplat gene network*

**Description**

Generate a gene network for the Kersplat simulation

**Usage**

`kersplatGenNetwork(params, verbose)`

**Arguments**

- `params`  
  KersplatParams object containing simulation parameters.
- `verbose`  
  logical. Whether to print progress messages

**Details**

Currently a very simple approach is used which needs to be improved. A network is generated using the `sample_forestfire` function and edge weights are sampled from a standard normal distribution.

**Value**

KersplatParams object with gene network
KersplatParams

The KersplatParams class

Description

S4 class that holds parameters for the Kersplat simulation.

Parameters

The Kersplat simulation uses the following parameters:

- nGenes: The number of genes to simulate.
- nCells: The number of cells to simulate.
- [seed]: Seed to use for generating random numbers.
- mean parameters:
  - mean.shape: Shape parameter for the mean gamma distribution.
  - mean.rate: Rate parameter for the mean gamma distribution.
  - mean.outProb: Probability that a gene is an expression outlier.
  - mean.outFacLoc: Location (meanlog) parameter for the expression outlier factor log-normal distribution.
  - mean.outFacScale: Scale (sdlog) parameter for the expression outlier factor log-normal distribution.
  - mean.dens: density object describing the log gene mean density.
  - [mean.method]: Method to use for simulating gene means. Either "fit" to sample from a gamma distribution (with expression outliers) or "density" to sample from the provided density object.
  - [mean.values]: Vector of means for each gene.
- Biological Coefficient of Variation parameters:
  - bcv.common: Underlying common dispersion across all genes.
  - [bcv.df]: Degrees of Freedom for the BCV inverse chi-squared distribution.
- Network parameters:
  - [network.graph]: Graph containing the gene network.
  - [network.nRegs]: Number of regulators in the network.
- Paths parameters:
  - [paths.programs]: Number of expression programs.
  - [paths.design]: data.frame describing path structure. See kersplatSimPaths for details.
- Library size parameters:
  - lib.loc: Location (meanlog) parameter for the library size log-normal distribution, or mean parameter if a normal distribution is used.
  - lib.scale: Scale (sdlog) parameter for the library size log-normal distribution, or sd parameter if a normal distribution is used.
  - lib.dens: density object describing the library size density.
  - [lib.method]: Method to use for simulating library sizes. Either "fit" to sample from a log-normal distribution or "density" to sample from the provided density object.
- Design parameters:
  - [cells.design]: data.frame describing cell structure. See kersplatSimCellMeans for details.
**Doublet parameters**  [doublet.prop] Proportion of cells that are doublets.

**Ambient parameters**  [ambient.scale] Scaling factor for the library size log-normal distribution when generating ambient library sizes.

[ambient.nEmpty] Number of empty cells to simulate.

The parameters not shown in brackets can be estimated from real data using `kersplatEstimate`. For details of the Kersplat simulation see `kersplatSimulate`.

---

**kersplatSample**

*Kersplat sample*

**Description**

Sample cells for the Kersplat simulation

**Usage**

```r
kersplatSample(params, sparsify = TRUE, verbose = TRUE)
```

**Arguments**

- `params`  KersplatParams object containing simulation parameters.
- `sparsify`  logical. Whether to automatically convert assays to sparse matrices if there will be a size reduction.
- `verbose`  logical. Whether to print progress messages

**Details**

The second stage is a two-step Kersplat simulation to generate cells based on a complete `KersplatParams` object. intermediate parameters.

The sampling process involves the following steps:

1. Simulate library sizes for each cell
2. Simulate means for each cell
3. Simulate endogenous counts for each cell
4. Simulate ambient counts for each cell
5. Simulate final counts for each cell

The final output is a `SingleCellExperiment` object that contains the simulated counts but also the values for various intermediate steps. These are stored in the `colData` (for cell specific information), `rowData` (for gene specific information) or `assays` (for gene by cell matrices) slots. This additional information includes:

- `colData`
  - **Cell**  Unique cell identifier.
  - **Type**  Whether the cell is a Cell, Doublet or Empty.
  - **CellLibSize**  The expected number of endogenous counts for that cell.
**AmbientLibSize**  The expected number of ambient counts for that cell.

**Path**  The path the cell belongs to.

**Step**  How far along the path each cell is.

**Path1**  For doublets the path of the first partner in the doublet (otherwise NA).

**Step1**  For doublets the step of the first partner in the doublet (otherwise NA).

**Path2**  For doublets the path of the second partner in the doublet (otherwise NA).

**Step2**  For doublets the step of the second partner in the doublet (otherwise NA).

**rowData**  Gene  Unique gene identifier.

**BaseMean**  The base expression level for that gene.

**AmbientMean**  The ambient expression level for that gene.

**assays**  **CellMeans**  The mean expression of genes in each cell after any differential expression and adjusted for expected library size.

**CellCounts**  Endogenous count matrix.

**AmbientCounts**  Ambient count matrix.

**counts**  Final count matrix.

Values that have been added by Splatter are named using UpperCamelCase in order to differentiate them from the values added by analysis packages which typically use underscore_naming.

**Value**

SingleCellExperiment object containing the simulated counts and intermediate values.

**See Also**

kersplatSimLibSizes, kersplatSimCellMeans, kersplatSimCellCounts, kersplatSimAmbientCounts, kersplatSimCounts

**Examples**

```r
if (requireNamespace("igraph", quietly = TRUE)) {
  params <- kersplatSetup()
  sim <- kersplatSample(params)
}
```

---

**kersplatSelectRegs**  
**Select Kersplat regulators**

**Description**

Select regulator genes in the gene network for a Kersplat simulation

**Usage**

kersplatSelectRegs(params, verbose)
**kersplatSetup**

**Arguments**

params: KersplatParams object containing simulation parameters.

verbose: logical. Whether to print progress messages

**Details**

Regulators are randomly selected, weighted according to the difference between their out degree and in degree. This is an arbitrary weighting and may be improved or replace in the future.

**Value**

KersplatParams object with gene regulators

---

**kersplatSetup**

Kersplat setup

**Description**

Setup the parameters required for the Kersplat simulation

**Usage**

kersplatSetup(params = newKersplatParams(), verbose = TRUE, ...)

**Arguments**

params: KersplatParams object containing simulation parameters.

verbose: logical. Whether to print progress messages

...: any additional parameter settings to override what is provided in params.

**Details**

The first stage is a two-step Kersplat simulation is to generate some of the intermediate parameters. The resulting parameters allow multiple simulated datasets to be generated from the same biological structure (using kersplatSample). As with all the other parameters these values can be manually overwritten if desired.

The setup involves the following steps:

1. Generate a gene network (if not already present)
2. Select regulator genes (if not already present)
3. Simulate gene means (if not already present)
4. Simulate cell paths

The resulting KersplatParams object will have the following parameters set (if they weren’t already).
kersplatSimAmbientCounts

- mean.values
- network.graph
- network.regsSet
- paths.means

See KersplatParams for more details about these parameters and the functions for the individual steps for more details about the process.

Value

A complete KersplatParams object

See Also

kersplatGenNetwork, kersplatSelectRegs, kersplatSimGeneMeans, kersplatSimPaths, KersplatParams

Examples

```r
if (requireNamespace("igraph", quietly = TRUE)) {
  params <- kersplatSetup()
}
```

kersplatSimAmbientCounts

*Simulate Kersplat ambient counts*

Description

Simulate Kersplat ambient counts

Usage

kersplatSimAmbientCounts(sim, params, verbose)

Arguments

- `sim` SingleCellExperiment containing simulation.
- `params` KersplatParams object with simulation parameters.
- `verbose` logical. Whether to print progress messages

Details

The overall expression profile to calculated by averaging the cell counts of the (non-empty) cells. This is then multiplied by the ambient library sizes to get a mean for each cell. Counts are then sampled from a Poisson distribution using these means.

Value

SingleCellExperiment with ambient counts
kersplatSimCellCounts  Simulate Kersplat cell counts

Description
Simulate cell counts for the Kersplat simulation

Usage
kersplatSimCellCounts(sim, params, verbose)

Arguments
- sim: SingleCellExperiment containing simulation.
- params: KersplatParams object with simulation parameters.
- verbose: logical. Whether to print progress messages

Details
Counts are sampled from a Poisson distribution with lambda equal to the cell means matrix.

Value
SingleCellExperiment with cell counts

kersplatSimCellMeans  Simulate Kersplat cell means

Description
Simulate endogenous counts for each cell in a Kersplat simulation

Usage
kersplatSimCellMeans(sim, params, verbose)

Arguments
- sim: SingleCellExperiment containing simulation.
- params: KersplatParams object with simulation parameters.
- verbose: logical. Whether to print progress messages
Details

Cells are first assigned to a path and a step along that path. This is controlled by the `cells.design` parameter which is a `data.frame` with the columns "Path", "Probability", "Alpha" and "Beta". The `Path` field is an ID for each path and the `Probability` field is the probability that a cell will come from that path (must sum to 1). The `Alpha` and `Beta` parameters control the density of cells along the path. After they are assigned to paths the step for each cell is sampled from a Beta distribution with parameters shape1 equals `Alpha` and shape2 equals `Beta`. This approach is very flexible and allows almost any distribution of cells along a path. The distribution can be viewed using `hist(rbeta(10000, Alpha, Beta), breaks = 100)`. Some useful combinations of parameters are:

- `Alpha = 1, Beta = 1` Uniform distribution along the path
- `Alpha = 0, Beta = 1` All cells at the start of the path.
- `Alpha = 1, Beta = 0` All cells at the end of the path.
- `Alpha = 0, Beta = 0` Cells only at each end of the path.
- `Alpha = 1, Beta = 2` Linear skew towards the start of the path
- `Alpha = 0.5, Beta = 1` Curved skew towards the start of the path
- `Alpha = 2, Beta = 1` Linear skew towards the end of the path
- `Alpha = 1, Beta = 0.5` Curved skew towards the end of the path
- `Alpha = 0.5, Beta = 0.5` Curved skew towards both ends of the path
- `Alpha = 0.5, Beta = 0.5` Curved skew away from both ends of the path

Once cells are assigned to paths and steps the correct means are extracted from the `paths.means` parameter and adjusted based on each cell’s library size. An adjustment for BCV is then applied. Doublets are also simulated at this stage by selecting two path/step combinations and averaging the means.

Value

SingleCellExperiment with cell means

Usage

```r
cersplatSimCounts(sim, params, verbose)
```

Arguments

- `sim` SingleCellExperiment containing simulation.
- `params` KersplatParams object with simulation parameters.
- `verbose` logical. Whether to print progress messages
kersplatSimGeneMeans

Details

The cell counts matrix and ambient counts matrix are added together. The result is then downsampled to the cell library size (for cells and doublets) or the ambient library size (for empty cells) using the `downsampleMatrix` function.

Value

SingleCellExperiment with counts matrix

See Also

downsampleMatrix

kersplatSimGeneMeans  Simulate Kersplat gene means

Description

Simulate Kersplat gene means

Usage

kersplatSimGeneMeans(params, verbose)

Arguments

params  KersplatParams object containing simulation parameters.
verbose  logical. Whether to print progress messages

Details

Gene means are simulated in one of two ways depending on the value of the mean.method parameter.

If mean.method is "fit" (default) then means are sampled from a Gamma distribution with shape equals mean.shape and rate equals mean.rate. Expression outliers are then added by replacing some values with the median multiplied by a factor from a log-normal distribution. This is the same process used for the Splat simulation.

If mean.method is "density" then means are sampled from the density object in the mean.density parameter using a rejection sampling method. This approach is more flexible but may violate some statistical assumptions.

Value

KersplatParams object with gene means
kersplatSimLibSizes  
**Simulate Kersplat library sizes**

**Description**
Generate library sizes for cells in the Kersplat simulation

**Usage**
kersplatSimLibSizes(sim, params, verbose)

**Arguments**
- `sim` SingleCellExperiment containing simulation.
- `params` KersplatParams object with simulation parameters.
- `verbose` logical. Whether to print progress messages

**Details**
Library sizes are simulated in one of two ways depending on the value of the `lib.method` parameter. If `lib.method` is "fit" (default) then means are sampled from a log-normal distribution with mean-log equals `lib.loc` and sd-log equals `lib.scale`.

If `mean.method` is "density" then library sizes are sampled from the density object in the `lib.density` parameter using a rejection sampling method. This approach is more flexible but may violate some statistical assumptions.

Ambient library sizes are also generated from a log-normal distribution based on the parameters for the cell library size and adjusted using the `ambient.scale` parameter.

**Value**
SingleCellExperiment with library sizes

kersplatSimPaths  
**Simulate Kersplat paths**

**Description**
Simulate gene means for each step along each path of a Kersplat simulation

**Usage**
kersplatSimPaths(params, verbose)
The method of simulating paths is inspired by the method used in the PROSSTT simulation. Changes in expression are controlled by paths.nPrograms regulatory programs. Each of the regulatory genes in the gene network has some association with each program. This is analogous to there being changes in the environment (the programs) which are sensed by receptors (regulatory genes) and cause changes in expression downstream. For each path a random walk is generated for each program and the changes passed on to the regulatory genes. At each step the changes propagate through the network according to the weights on edges between genes. This algorithm is fairly simple but should result in correlation relationships between genes. However it is likely to be improved and adjusted in the future.

The path structure itself is specified by the paths.design parameter. This is a data.frame with three columns: "Path", "From", and "Steps". The Path field is an ID for each path while the Steps field controls the length of each path. Increasing the number of steps will increase the difference in expression between the ends of the paths. The From field sets the originating point of each path. For example a From of 0, 0, 0 would indicate three paths from the origin while a From of 0, 1, 1 would give a branching structure with Path 1 beginning at the origin and Path 2 and Path 3 beginning at the end of Path 1.

Value

KersplatParams object with path means

References


kersplatSimulate Kersplat simulation

Description

Simulate scRNA-seq count data using the Kersplat model

Usage

kersplatSimulate(
  params = newKersplatParams(),
  sparsify = TRUE,
  verbose = TRUE,
  ...
)
Arguments

- `params` - KersplatParams object containing simulation parameters.
- `sparsify` - logical. Whether to automatically convert assays to sparse matrices if there will be a size reduction.
- `verbose` - logical. Whether to print progress messages
- `...` - any additional parameter settings to override what is provided in `params`.

Details

This function is for simulating data in a single step. It consists of a call to `kersplatSetup` followed by a call to `kersplatSample`. Please see the documentation for those functions for more details of the individual steps.

Value

SingleCellExperiment containing simulated counts and intermediate values

See Also

- `kersplatSetup`, `kersplatSample`

Examples

```r
if (requireNamespace("igraph", quietly = TRUE)) {
  sim <- kersplatSimulate
}
```

Description

List all the simulations that are currently available in Splatter with a brief description.

Usage

```r
listSims(print = TRUE)
```

Arguments

- `print` - logical. Whether to print to the console.

Value

Invisibly returns a data.frame containing the information that is displayed.
Estimate Lun2 simulation parameters

Description

Estimate simulation parameters for the Lun2 simulation from a real dataset.

Usage

```r
lun2Estimate(
  counts,  
  plates,  
  params = newLun2Params(),  
  min.size = 200,  
  verbose = TRUE,  
  BPPARAM = SerialParam()
)

## S3 method for class 'SingleCellExperiment'

lun2Estimate(
  counts,  
  plates,  
  params = newLun2Params(),  
  min.size = 200,  
  verbose = TRUE,  
  BPPARAM = SerialParam()
)

## S3 method for class 'matrix'

lun2Estimate(
  counts,  
  plates,  
  params = newLun2Params(),  
  min.size = 200,  
  verbose = TRUE,  
  BPPARAM = SerialParam()
)
```

Arguments

- **counts**: either a counts matrix or a SingleCellExperiment object containing count data to estimate parameters from.
- **plates**: integer vector giving the plate that each cell originated from.
Lun2Params object to store estimated values in.

min.size minimum size of clusters when identifying group of cells in the data.

verbose logical. Whether to show progress messages.

BPPPARAM A BiocParallelParam instance giving the parallel back-end to be used. Default is SerialParam which uses a single core.

Details

See Lun2Params for more details on the parameters.

Value

LunParams object containing the estimated parameters.

Examples

# Load example data
library(scuttle)
set.seed(1)
sce <- mockSCE()
plates <- as.numeric(factor(colData(sce)$Mutation_Status))
params <- lun2Estimate(sce, plates, min.size = 20)
params

---

Lun2Params The Lun2Params class

Description

S4 class that holds parameters for the Lun2 simulation.

Parameters

The Lun2 simulation uses the following parameters:

nGenes The number of genes to simulate.
nCells The number of cells to simulate.
[seed] Seed to use for generating random numbers.

Gene parameters gene.params A data.frame containing gene parameters with two columns: Mean (mean expression for each gene) and Disp (dispersion for each gene).
zi.params A data.frame containing zero-inflated gene parameters with three columns: Mean (mean expression for each gene), Disp (dispersion for each gene), and Prop (zero proportion for each gene).

[nPlates] The number of plates to simulate.
Plate parameters  plate.ingroup  Character vector giving the plates considered to be part of the "ingroup".
  plate.mod  Plate effect modifier factor. The plate effect variance is divided by this value.
  plate.var  Plate effect variance.

Cell parameters  cell.plates  Factor giving the plate that each cell comes from.
  cell.libSizes  Library size for each cell.
  cell.libMod  Modifier factor for library sizes. The library sizes are multiplied by this value.

Differential expression parameters  de.nGenes  Number of differentially expressed genes.
  de.fc  Fold change for differentially expressed genes.

The parameters not shown in brackets can be estimated from real data using lun2Estimate. For details of the Lun2 simulation see lun2Simulate.

---

lun2Simulate  Lun2 simulation

Description

Simulate single-cell RNA-seq count data using the method described in Lun and Marioni "Overcoming confounding plate effects in differential expression analyses of single-cell RNA-seq data".

Usage

lun2Simulate(
  params = newLun2Params(),
  zinb = FALSE,
  sparsify = TRUE,
  verbose = TRUE,
  ...
)

Arguments

  params  Lun2Params object containing simulation parameters.
  zinb  logical. Whether to use a zero-inflated model.
  sparsify  logical. Whether to automatically convert assays to sparse matrices if there will be a size reduction.
  verbose  logical. Whether to print progress messages.
  ...  any additional parameter settings to override what is provided in params.
Details

The Lun2 simulation uses a negative-binomial distribution where the means and dispersions have been sampled from a real dataset (using `lun2Estimate`). The other core feature of the Lun2 simulation is the addition of plate effects. Differential expression can be added between two groups of plates (an "ingroup" and all other plates). Library size factors are also applied and optionally a zero-inflated negative-binomial can be used.

If the number of genes to simulate differs from the number of provided gene parameters or the number of cells to simulate differs from the number of library sizes the relevant parameters will be sampled with a warning. This allows any number of genes or cells to be simulated regardless of the number in the dataset used in the estimation step but has the downside that some genes or cells may be simulated multiple times.

Value

`SingleCellExperiment` containing simulated counts.

References


Paper: dx.doi.org/10.1093/biostatistics/kxw055

Code: https://github.com/MarioniLab/PlateEffects2016

Examples

```r
sim <- lun2Simulate()
```

---

```
| lunEstimate      | Estimate Lun simulation parameters |
```

Description

Estimate simulation parameters for the Lun2 simulation from a real dataset.

Usage

```r
lunEstimate(counts, params = newLunParams())
```

```r
# S3 method for class 'SingleCellExperiment'
lunEstimate(counts, params = newLunParams())
```

```r
# S3 method for class 'matrix'
lunEstimate(counts, params = newLunParams())
```
Arguments

- **counts**: either a counts matrix or a SingleCellExperiment object containing count data to estimate parameters from.
- **params**: LunParams object to store estimated values in.

Details

The `nGenes` and `nCells` parameters are taken from the size of the input data. No other parameters are estimated. See `LunParams` for more details on the parameters.

Value

LunParams object containing the estimated parameters.

Examples

```r
# Load example data
library(scuttle)
set.seed(1)
sce <- mockSCE()
params <- lunEstimate(sce)
params
```

Description

S4 class that holds parameters for the Lun simulation.

Parameters

The Lun simulation uses the following parameters:

- **nGenes**: The number of genes to simulate.
- **nCells**: The number of cells to simulate.
- **[nGroups]**: The number of groups to simulate.
- **[groupCells]**: Vector giving the number of cells in each simulation group/path.
- **[seed]**: Seed to use for generating random numbers.

**Mean parameters**

- **[mean.shape]**: Shape parameter for the mean gamma distribution.
- **[mean.rate]**: Rate parameter for the mean gamma distribution.

**Counts parameters**

- **[count.disp]**: The dispersion parameter for the counts negative binomial distribution.

**Differential expression parameters**

- **[de.nGenes]**: The number of genes that are differentially expressed in each group.
[de.upProp] The proportion of differentially expressed genes that are up-regulated in each group
[de.upFC] The fold change for up-regulated genes
[de.downFC] The fold change for down-regulated genes

The parameters not shown in brackets can be estimated from real data using `lunEstimate`. For details of the Lun simulation see `lunSimulate`.

---

**lunSimulate**

**Lun simulation**

**Description**

Simulate single-cell RNA-seq count data using the method described in Lun, Bach and Marioni "Pooling across cells to normalize single-cell RNA sequencing data with many zero counts".

**Usage**

```r
lunSimulate(params = newLunParams(), sparsify = TRUE, verbose = TRUE, ...)```

**Arguments**

- `params` LunParams object containing Lun simulation parameters.
- `sparsify` logical. Whether to automatically convert assays to sparse matrices if there will be a size reduction.
- `verbose` logical. Whether to print progress messages.
- `...` any additional parameter settings to override what is provided in `params`.

**Details**

The Lun simulation generates gene mean expression levels from a gamma distribution with shape = mean.shape and rate = mean.rate. Counts are then simulated from a negative binomial distribution with mu = means and size = 1 / bcv.common. In addition each cell is given a size factor (2 ^ rnorm(nCells, mean = 0, sd = 0.5)) and differential expression can be simulated with fixed fold changes.

See `LunParams` for details of the parameters.

**Value**

SingleCellExperiment object containing the simulated counts and intermediate values.

**References**

Lun ATL, Bach K, Marioni JC. Pooling across cells to normalize single-cell RNA sequencing data with many zero counts. Genome Biology (2016).


Code: https://github.com/MarioniLab/Deconvolution2016
Examples

```r
sim <- lunSimulate()
```

makeCompPanel

**Make comparison panel**

**Description**

Combine the plots from `compareSCEs` into a single panel.

**Usage**

```r
makeCompPanel(
  comp,
  title = "Comparison",
  labels = c("Means", "Variance", "Mean-variance relationship", "Library size",
             "Zeros per gene", "Zeros per cell", "Mean-zeros relationship")
)
```

**Arguments**

- `comp`: list returned by `compareSCEs`.
- `title`: title for the panel.
- `labels`: vector of labels for each of the seven plots.

**Value**

Combined panel plot

**Examples**

```r
sim1 <- splatSimulate(nGenes = 1000, batchCells = 20)
sim2 <- simpleSimulate(nGenes = 1000, nCells = 20)
comparison <- compareSCEs(list(Splat = sim1, Simple = sim2))
panel <- makeCompPanel(comparison)
```
makeDiffPanel

Make difference panel

Description

Combine the plots from diffSCEs into a single panel.

Usage

makeDiffPanel(
  diff,
  title = "Difference comparison",
  labels = c("Means", "Variance", "Library size", "Zeros per cell", "Zeros per gene",
             "Mean-variance relationship", "Mean-zeros relationship")
)

Arguments

diff  list returned by diffSCEs.
title  title for the panel.
labels  vector of labels for each of the seven sections.

Value

Combined panel plot

Examples

sim1 <- splatSimulate(nGenes = 1000, batchCells = 20)
sim2 <- simpleSimulate(nGenes = 1000, nCells = 20)
difference <- diffSCEs(list(Splat = sim1, Simple = sim2), ref = "Simple")
panel <- makeDiffPanel(difference)

makeOverallPanel

Make overall panel

Description

Combine the plots from compSCEs and diffSCEs into a single panel.
Usage

makeOverallPanel(
  comp,
  diff,
  title = "Overall comparison",
  row.labels = c("Means", "Variance", "Mean-variance relationship", "Library size",
                 "Zeros per cell", "Zeros per gene", "Mean-zeros relationship")
)

Arguments

comp list returned by compareSCEs.
diff list returned by diffSCEs.
title title for the panel.
row.labels vector of labels for each of the seven rows.

Value

Combined panel plot

Examples

sim1 <- splatSimulate(nGenes = 1000, batchCells = 20)
sim2 <- simpleSimulate(nGenes = 1000, nCells = 20)
comparison <- compareSCEs(list(Splat = sim1, Simple = sim2))
difference <- diffSCEs(list(Splat = sim1, Simple = sim2), ref = "Simple")
panel <- makeOverallPanel(comparison, difference)

<table>
<thead>
<tr>
<th>mfaEstimate</th>
<th>Estimate mfa simulation parameters</th>
</tr>
</thead>
</table>

Description

Estimate simulation parameters for the mfa simulation from a real dataset.

Usage

mfaEstimate(counts, params = newMFAParams())

## S3 method for class 'SingleCellExperiment'
mfaEstimate(counts, params = newMFAParams())

## S3 method for class 'matrix'
mfaEstimate(counts, params = newMFAParams())
Arguments

counts: either a counts matrix or a SingleCellExperiment object containing count data to estimate parameters from.

params: MFAParams object to store estimated values in.

Details

The nGenes and nCells parameters are taken from the size of the input data. The dropout lambda parameter is estimate using empirical_lambda. See MFAParams for more details on the parameters.

Value

MFAParams object containing the estimated parameters.

Examples

```r
# Load example data
if (requireNamespace("mfa", quietly = TRUE)) {
  library(mfa)
  synth <- create_synthetic(
    C = 20, G = 5, zero_negative = TRUE,
    model_dropout = TRUE
  )
  
  params <- mfaEstimate(synth$X)
  params
}
```

---

**MFAParams**

The MFAParams class

Description

S4 class that holds parameters for the mfa simulation.

Parameters

The mfa simulation uses the following parameters:

nGenes: The number of genes to simulate.

nCells: The number of cells to simulate.

[seed]: Seed to use for generating random numbers.

[trans.prop]: Proportion of genes that show transient expression. These genes are briefly up or down-regulated before returning to their initial state.

[zero.neg]: Logical. Whether to set negative expression values to zero. This will zero-inflate the data.

[dropout.present]: Logical. Whether to simulate dropout.
dropout.lambda  Lambda parameter for the exponential dropout function.

The parameters not shown in brackets can be estimated from real data using mfaEstimate. See create_synthetic for more details about the parameters. For details of the Splatter implementation of the mfa simulation see mfaSimulate.

---

**mfaSimulate**  
*MFA simulation*

**Description**

Simulate a bifurcating pseudotime path using the mfa method.

**Usage**

mfaSimulate(params = newMFAParams(), sparsify = TRUE, verbose = TRUE, ...)

**Arguments**

- **params** 
  MFAParams object containing simulation parameters.
- **sparsify** 
  logical. Whether to automatically convert assays to sparse matrices if there will be a size reduction.
- **verbose** 
  Logical. Whether to print progress messages.
- **...** 
  any additional parameter settings to override what is provided in params.

**Details**

This function is just a wrapper around create_synthetic that takes a MFAParams, runs the simulation then converts the output from log-expression to counts and returns a SingleCellExperiment object. See create_synthetic and the mfa paper for more details about how the simulation works.

**Value**

SingleCellExperiment containing simulated counts

**References**


Paper: 10.12688/wellcomeopenres.11087.1

Code: https://github.com/kieranrcampbell/mfa

**Examples**

if (!requireNamespace("mfa", quietly = TRUE)) {
  sim <- mfaSimulate()
}


minimiseSCE

Description

Reduce the size of a SingleCellExperiment object by unneeded information.

Usage

minimiseSCE(
  sce,
  rowData.keep = FALSE,
  colData.keep = FALSE,
  metadata.keep = FALSE,
  assays.keep = "counts",
  sparsify = c("auto", "all", "none"),
  verbose = TRUE
)

Arguments

sce
  SingleCellExperiment object
rowData.keep
  Either TRUE (keep all rowData columns), FALSE (remove all rowData columns) or a character vector with the names of the rowData columns to keep
colData.keep
  Either TRUE (keep all colData columns), FALSE (remove all colData columns) or a character vector with the names of the colData columns to keep
metadata.keep
  Either TRUE (keep all metadata), FALSE (remove all metadata) or a character vector with the names of the metadata items to keep
assays.keep
  Either TRUE (keep all assays), FALSE (remove all assays) or a character vector with the names of the assays to keep
sparsify
  Whether to convert assay matrices to sparse format. Either "all", "none" or "auto" (default) to only convert those matrices that will result in a size reduction
verbose
  Whether to print status messages

Value

SingleCellExperiment object

Examples

sce <- splatSimulate(verbosr = FALSE)
sce.min <- minimiseSCE(sce, verbose = FALSE)
object.size(sce)
object.size(sce.min)
mockBulkeQTL Generate mock eQTL mapping results

Description
Quick function to generate mock eQTL mapping results, with parameters estimated using real eQTL mapping results from GTEx using thyroid tissue.

Usage
mockBulkeQTL(n.genes = 500, seed = NULL)

Arguments
- n.genes: Number of genes in mock eQTL data.
- seed: Optional: seed for random seed

Value
data.frame containing mock bulk eQTL mapping results.

Examples
eqtl <- mockBulkeQTL()

mockBulkMatrix Generate mock bulk population scale expression data

Description
Quick function to generate mock bulk expression data for a population, with parameters estimated using real thyroid tissue data from GTEx.

Usage
mockBulkMatrix(n.genes = 100, n.samples = 50, seed = NULL)

Arguments
- n.genes: Number of genes in mock bulk data.
- n.samples: Number of samples in mock bulk data.
- seed: Optional: seed for random seed
Value

matrix containing mock bulk expression data.

Examples

bulk <- mockBulkMatrix

mockEmpiricalSet

Generate set of "empirical" mock data

Description

Quick function to generate matching mock VCF, bulk expression, and eQTL data, useful for running splatPopEmpiricalMeans

Usage

mockEmpiricalSet(
  n.genes = 20,
  n.snps = 1000,
  n.samples = 10,
  chromosome = 1,
  chr.length = 2e+06,
  seed = NULL
)

Arguments

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>n.genes</td>
<td>Number of genes in mock eQTL data.</td>
</tr>
<tr>
<td>n.snps</td>
<td>Number of SNPs in mock vcf file.</td>
</tr>
<tr>
<td>n.samples</td>
<td>Number of samples in mock bulk data.</td>
</tr>
<tr>
<td>chromosome</td>
<td>Chromosome name</td>
</tr>
<tr>
<td>chr.length</td>
<td>Length of mock chromosome</td>
</tr>
<tr>
<td>seed</td>
<td>Optional: seed for random seed</td>
</tr>
</tbody>
</table>

Value

list(gff=mockGFF, vcf=mockVCF, means=mockMEANS, eqtl=mockEQTL)

Examples

empirical <- mockEmpiricalSet()
mockGFF

Generate mock gff

Description

Quick function to generate a mock gff.

Usage

mockGFF(n.genes = 50, chromosome = 1, chr.length = 2e+06, seed = NULL)

Arguments

- n.genes: Number of genes in mock gff file
- chromosome: Chromosome name
- chr.length: Length of mock chromosome
- seed: Optional: seed for random seed

Value

data.frame containing mock gff data.

Examples

gff <- mockGFF()

mockVCF

Generate mock vcf

Description

Quick function to generate mock vcf file. Note this data has unrealistic population structure.

Usage

mockVCF(
    n.snps = 200,
    n.samples = 5,
    chromosome = 1,
    chr.length = 2e+06,
    seed = NULL
)

)
Arguments

- **n.snps**: Number of SNPs in mock vcf file.
- **n.samples**: Number of samples in mock bulk data.
- **chromosome**: Chromosome name
- **chr.length**: Length of mock chromosome
- **seed**: Optional: seed for random seed

Value

data.frame containing mock vcf data.

Examples

```r
vcf <- mockVCF()
```

---

**Description**

Create a new Params object. Functions exist for each of the different Params subtypes.

**Usage**

```r
newBASiCSParams(...)
newKersplatParams(...)
newLun2Params(...)
newLunParams(...)
newMFAParams(...)
newPhenoParams(...)
newSCDDParams(...)
newSimpleParams(...)
newSparseDCParams(...)
newSplatParams(...)
newSplatPopParams(...)
newZINBParams(...)
```
**Params**

**Description**

Virtual S4 class that all other Params classes inherit from.

**Parameters**

The Params class defines the following parameters:

- `nGenes` The number of genes to simulate.
- `nCells` The number of cells to simulate.
- `[seed]` Seed to use for generating random numbers.

The parameters not shown in brackets can be estimated from real data.

---

**phenoEstimate**

*Estimate PhenoPath simulation parameters*

**Description**

Estimate simulation parameters for the PhenoPath simulation from a real dataset.

**Usage**

```r
phenoEstimate(counts, params = newPhenoParams())
```

```r
## S3 method for class 'SingleCellExperiment'
phenoEstimate(counts, params = newPhenoParams())
```

```r
## S3 method for class 'matrix'
phenoEstimate(counts, params = newPhenoParams())
```
Arguments

counts either a counts matrix or an SingleCellExperiment object containing count data to estimate parameters from.
params PhenoParams object to store estimated values in.

Details

The nGenes and nCells parameters are taken from the size of the input data. The total number of genes is evenly divided into the four types. See PhenoParams for more details on the parameters.

Value

PhenoParams object containing the estimated parameters.

Examples

```r
if (requireNamespace("phenopath", quietly = TRUE)) {
  # Load example data
  library(scuttle)
  set.seed(1)
  sce <- mockSCE()

  params <- phenoEstimate(sce)
  params
}
```

PhenoParams The PhenoParams class

Description

S4 class that holds parameters for the PhenoPath simulation.

Parameters

The PhenoPath simulation uses the following parameters:

nGenes The number of genes to simulate.
nCells The number of cells to simulate.
[seed] Seed to use for generating random numbers.
[n.de] Number of genes to simulate from the differential expression regime
[n.pst] Number of genes to simulate from the pseudotime regime
[n.pst.beta] Number of genes to simulate from the pseudotime + beta interactions regime
[n.de.pst.beta] Number of genes to simulate from the differential expression + pseudotime + interactions regime

The parameters not shown in brackets can be estimated from real data using phenoEstimate. For details of the PhenoPath simulation see phenoSimulate.
**PhenoSimulate**

**PhenoPath simulation**

**Description**

Simulate counts from a pseudotime trajectory using the PhenoPath method.

**Usage**

```r
phenoSimulate(params = newPhenoParams(), sparsify = TRUE, verbose = TRUE, ...)
```

**Arguments**

- `params`: PhenoParams object containing simulation parameters.
- `sparsify`: logical. Whether to automatically convert assays to sparse matrices if there will be a size reduction.
- `verbose`: logical. Whether to print progress messages
- `...`: any additional parameter settings to override what is provided in `params`.

**Details**

This function is just a wrapper around `simulate_phenopath` that takes a `PhenoParams`, runs the simulation then converts the output from log-expression to counts and returns a `SingleCellExperiment` object. The original simulated log-expression values are returned in the `LogExprs` assay. See `simulate_phenopath` and the PhenoPath paper for more details about how the simulation works.

**Value**

`SingleCellExperiment` containing simulated counts

**References**


Paper: [10.1101/159913](https://10.1101/159913)

Code: [https://github.com/kieranrcampbell/phenopath](https://github.com/kieranrcampbell/phenopath)

**Examples**

```r
if (requireNamespace("phenopath", quietly = TRUE)) {
  sim <- phenoSimulate()
}
```
Estimate simulation parameters for the scDD simulation from a real dataset.

Usage

scDDEstimate(  
  counts,  
  params = newSCDDParams(),  
  verbose = TRUE,  
  BPPARAM = SerialParam(),  
  ...  
)

## S3 method for class 'matrix'
scDDEstimate(  
  counts,  
  params = newSCDDParams(),  
  verbose = TRUE,  
  BPPARAM = SerialParam(),  
  conditions,  
  ...  
)

## S3 method for class 'SingleCellExperiment'
scDDEstimate(  
  counts,  
  params = newSCDDParams(),  
  verbose = TRUE,  
  BPPARAM = SerialParam(),  
  condition = "condition",  
  ...  
)

## Default S3 method:
scDDEstimate(  
  counts,  
  params = newSCDDParams(),  
  verbose = TRUE,  
  BPPARAM = SerialParam(),  
  condition,  
  ...  
)
SCDDParams

Arguments

counts either a counts matrix or a SingleCellExperiment object containing count data to estimate parameters from.
params SCDDParams object to store estimated values in.
verbose logical. Whether to show progress messages.
BPPARAM A BiocParallelParam instance giving the parallel back-end to be used. Default is SerialParam which uses a single core.
... further arguments passed to or from other methods.
conditions Vector giving the condition that each cell belongs to. Conditions can be 1 or 2.
condition String giving the column that represents biological group of interest.

Details

This function applies preprocess to the counts then uses scDD to estimate the numbers of each gene type to simulate. The output is then converted to a SCDDParams object. See preprocess and scDD for details.

Value

SCDDParams object containing the estimated parameters.

Examples

if (requireNamespace("scDD", quietly = TRUE)) {
  library(scuttle)
  set.seed(1)
  sce <- mockSCE(ncells = 20, ngenes = 100)
  colData(sce)$condition <- sample(1:2, ncol(sce), replace = TRUE)
  params <- scDDEstimate(sce, condition = "condition")
  params
}

The SCDDParams class

Description

S4 class that holds parameters for the scDD simulation.
Parameters

The SCDD simulation uses the following parameters:

- **nGenes**: The number of genes to simulate (not used).
- **nCells**: The number of cells to simulate in each condition.
- **[seed]**: Seed to use for generating random numbers.
- **SCdat**: `SingleCellExperiment` containing real data.
- **nDE**: Number of DE genes to simulate.
- **nDP**: Number of DP genes to simulate.
- **nDM**: Number of DM genes to simulate.
- **nDB**: Number of DB genes to simulate.
- **nEE**: Number of EE genes to simulate.
- **nEP**: Number of EP genes to simulate.
- **[sd.range]**: Interval for fold change standard deviations.
- **[modeFC]**: Values for DP, DM and DB mode fold changes.
- **[varInflation]**: Variance inflation factors for each condition. If all equal to 1 will be set to NULL (default).
- **[condition]**: String giving the column that represents biological group of interest.

The parameters not shown in brackets can be estimated from real data using `scDDEstimate`. See `simulateSet` for more details about the parameters. For details of the Splatter implementation of the scDD simulation see `scDDSimulate`.

---

**scDDSimulate**

*scDD simulation*

---

Description

Simulate counts using the scDD method.

Usage

```r
scDDSimulate(
    params = newSCDDParams(),
    plots = FALSE,
    plot.file = NULL,
    sparsify = TRUE,
    verbose = TRUE,
    BPPPARAM = SerialParam(),
    ...
)
```
Arguments

- params: SCDDParams object containing simulation parameters.
- plots: logical. whether to generate scDD fold change and validation plots.
- plot.file: File path to save plots as PDF.
- sparsify: logical. Whether to automatically convert assays to sparse matrices if there will be a size reduction.
- verbose: logical. Whether to print progress messages
- BPPARAM: A BiocParallelParam instance giving the parallel back-end to be used. Default is SerialParam which uses a single core.
- ... any additional parameter settings to override what is provided in params.

Details

This function is just a wrapper around simulateSet that takes a SCDDParams, runs the simulation then converts the output to a SingleCellExperiment object. See simulateSet for more details about how the simulation works.

Value

SingleCellExperiment containing simulated counts

References


Code: https://github.com/kdkorthauer/scDD

Examples

```r
sim <- scDDsimulate()
```
setParam(object, name, value)

## S4 method for signature 'BASiCSParams'
setParam(object, name, value)

## S4 method for signature 'KersplatParams'
setParam(object, name, value)

## S4 method for signature 'Lun2Params'
setParam(object, name, value)

## S4 method for signature 'LunParams'
setParam(object, name, value)

## S4 method for signature 'Params'
setParam(object, name, value)

## S4 method for signature 'PhenoParams'
setParam(object, name, value)

## S4 method for signature 'SCDDParams'
setParam(object, name, value)

## S4 method for signature 'SplatParams'
setParam(object, name, value)

## S4 method for signature 'SplatPopParams'
setParam(object, name, value)

## S4 method for signature 'ZINBParams'
setParam(object, name, value)

Arguments

object object to set parameter in.
name name of the parameter to set.
value value to set the parameter to.

Value

Object with new parameter value.

Examples

params <- newSimpleParams()
setParam(params, "nGenes", 100)
setParams

Set parameters

Description
Set multiple parameters in a Params object.

Usage
setParams(object, update = NULL, ...)

## S4 method for signature 'KersplatParams'
setParams(object, update = NULL, ...)

## S4 method for signature 'Params'
setParams(object, update = NULL, ...)

## S4 method for signature 'SplatParams'
setParams(object, update = NULL, ...)

Arguments
- object: Params object to set parameters in.
- update: list of parameters to set where names(update) are the names of the parameters to set and the items in the list are values.
- ...: additional parameters to set. These are combined with any parameters specified in update.

Details
Each parameter is set by a call to setParam. If the same parameter is specified multiple times it will be set multiple times. Parameters can be specified using a list via update (useful when collecting parameter values in some way) or individually (useful when setting them manually), see examples.

Value
Params object with updated values.

Examples
params <- newSimpleParams()
params
# Set individually
params <- setParams(params, nGenes = 1000, nCells = 50)
params
# Set via update list
params <- setParams(params, list(mean.rate = 0.2, mean.shape = 0.8))
params
setParamsUnchecked  
Set parameters UNCHECKED

Description
Set multiple parameters in a Params object.

Usage
setParamsUnchecked(params, update = NULL, ...)

Arguments
- params: Params object to set parameters in.
- update: list of parameters to set where names(update) are the names of the parameters to set and the items in the list are values.
- ... additional parameters to set. These are combined with any parameters specified in update.

Details
Each parameter is set by a call to setParam. If the same parameter is specified multiple times it will be set multiple times. Parameters can be specified using a list via update (useful when collecting parameter values in some way) or individually (useful when setting them manually), see examples. THE FINAL OBJECT IS NOT CHECKED FOR VALIDITY!

Value
Params object with updated values.

setParamUnchecked  
Set a parameter UNCHECKED

Description
Function for setting parameter values. THE OUTPUT IS NOT CHECKED FOR VALIDITY!

Usage
setParamUnchecked(object, name, value)

## S4 method for signature 'Params'
setParamUnchecked(object, name, value)
simpleEstimate

Arguments

- **object**: object to set parameter in.
- **name**: name of the parameter to set.
- **value**: value to set the parameter to.

Value

Object with new parameter value.

---

**simpleEstimate**

*Estimate simple simulation parameters*

**Description**

Estimate simulation parameters for the simple simulation from a real dataset.

**Usage**

```r
simpleEstimate(counts, params = newSimpleParams())
```

```r
## S3 method for class 'SingleCellExperiment'
simpleEstimate(counts, params = newSimpleParams())
```

```r
## S3 method for class 'matrix'
simpleEstimate(counts, params = newSimpleParams())
```

**Arguments**

- **counts**: either a counts matrix or a SingleCellExperiment object containing count data to estimate parameters from.
- **params**: SimpleParams object to store estimated values in.

**Details**

The nGenes and nCells parameters are taken from the size of the input data. The mean parameters are estimated by fitting a gamma distribution to the library size normalised mean expression level using `fitdist`. See `SimpleParams` for more details on the parameters.

**Value**

SimpleParams object containing the estimated parameters.
# Load example data
library(scuttle)
set.seed(1)
sce <- mockSCE()

params <- simpleEstimate(sce)
params

---

### SimpleParams

#### The SimpleParams class

#### Description

S4 class that holds parameters for the simple simulation.

#### Parameters

The simple simulation uses the following parameters:

- nGenes: The number of genes to simulate.
- nCells: The number of cells to simulate.
- [seed]: Seed to use for generating random numbers.
- mean.shape: The shape parameter for the mean gamma distribution.
- mean.rate: The rate parameter for the mean gamma distribution.
- [count.disp]: The dispersion parameter for the counts negative binomial distribution.

The parameters not shown in brackets can be estimated from real data using `simpleEstimate`. For details of the simple simulation see `simpleSimulate`.

---

### simpleSimulate

#### Simple simulation

#### Description

Simulate counts from a simple negative binomial distribution without simulated library sizes, differential expression etc.

#### Usage

```r
simpleSimulate(
  params = newSimpleParams(),
  sparsify = TRUE,
  verbose = TRUE,
  ...
)
```
sparseDCEstimate

**Arguments**

- **params**: SimpleParams object containing simulation parameters.
- **sparsify**: logical. Whether to automatically convert assays to sparse matrices if there will be a size reduction.
- **verbose**: logical. Whether to print progress messages
- ... any additional parameter settings to override what is provided in `params`.

**Details**

Gene means are simulated from a gamma distribution with `shape = mean.shape` and `rate = mean.rate`. Counts are then simulated from a negative binomial distribution with `mu = means` and `size = 1 / counts.disp`. See `SimpleParams` for more details of the parameters.

**Value**

SingleCellExperiment containing simulated counts

**Examples**

```r
sim <- simpleSimulate()
# Override default parameters
sim <- simpleSimulate(nGenes = 1000, nCells = 50)
```

---

**sparseDCEstimate**

*Estimate SparseDC simulation parameters*

**Description**

Estimate simulation parameters for the SparseDC simulation from a real dataset.

**Usage**

```r
sparseDCEstimate(
  counts, conditions, nclusters, norm = TRUE, 
  params = newSparseDCParams()
)
```

### S3 method for class 'SingleCellExperiment'

```r
sparseDCEstimate(
  counts, conditions, nclusters, norm = TRUE,
)
params = newSparseDCParams()

## S3 method for class 'matrix'
sparseDCEstimate(
  counts,
  conditions,
  nclusters,
  norm = TRUE,
  params = newSparseDCParams()
)

Arguments

- **counts**
  - either a counts matrix or an SingleCellExperiment object containing count data to estimate parameters from.

- **conditions**
  - numeric vector giving the condition each cell belongs to.

- **nclusters**
  - number of cluster present in the dataset.

- **norm**
  - logical, whether to library size normalise counts before estimation. Set this to FALSE if counts is already normalised.

- **params**
  - PhenoParams object to store estimated values in.

Details

The nGenes and nCells parameters are taken from the size of the input data. The counts are preprocessed using `pre_proc_data` and then parameters are estimated using `sparsedc_cluster` using lambda values calculated using `lambda1_calculator` and `lambda2_calculator`.

See `SparseDCParams` for more details on the parameters.

Value

SparseParams object containing the estimated parameters.

Examples

```r
if (requireNamespace("SparseDC", quietly = TRUE)) {
  # Load example data
  library(scuttle)
  set.seed(1)
  sce <- mockSCE(ncells = 20, ngenes = 100)

  conditions <- sample(1:2, ncol(sce), replace = TRUE)

  params <- sparseDCEstimate(sce, conditions, nclusters = 3)
  params
}
```
**Description**

S4 class that holds parameters for the SparseDC simulation.

**Parameters**

The SparseDC simulation uses the following parameters:

- `nGenes`  The number of genes to simulate in each condition.
- `nCells`  The number of cells to simulate.
- `[seed]`  Seed to use for generating random numbers.
- `markers.n`  Number of marker genes to simulate for each cluster.
- `markers.shared`  Number of marker genes for each cluster shared between conditions. Must be less than or equal to `markers.n`.
- `[markers.same]`  Logical. Whether each cluster should have the same set of marker genes.
- `clusts.c1`  Numeric vector of clusters present in condition 1. The number of times a cluster is repeated controls the proportion of cells from that cluster.
- `clusts.c2`  Numeric vector of clusters present in condition 2. The number of times a cluster is repeated controls the proportion of cells from that cluster.
- `[mean.lower]`  Lower bound for cluster gene means.

The parameters not shown in brackets can be estimated from real data using `sparseDCEstimate`. For details of the SparseDC simulation see `sparseDCSimulate`.

---

**sparseDCSimulate**

*SparseDC simulation*

**Description**

Simulate counts from cluster in two conditions using the SparseDC method.

**Usage**

```r
sparseDCSimulate(
    params = newSparseDCParams(),
    sparsify = TRUE,
    verbose = TRUE,
    ...
)
```
Estimate Splat Biological Coefficient of Variation parameters

splatEstBCV

Arguments

- **params**: SparseDCParams object containing simulation parameters.
- **sparsify**: logical. Whether to automatically convert assays to sparse matrices if there will be a size reduction.
- **verbose**: logical. Whether to print progress messages
- **...**: any additional parameter settings to override what is provided in params.

Details

This function is just a wrapper around `sim_data` that takes a SparseDCParams, runs the simulation then converts the output from log-expression to counts and returns a SingleCellExperiment object. The original simulated log-expression values are returned in the LogExprs assay. See `sim_data` and the SparseDC paper for more details about how the simulation works.

Value

SingleCellExperiment containing simulated counts

References


Paper: 10.1093/nar/gkx1113

Examples

```r
if (requireNamespace("SparseDC", quietly = TRUE)) {
  sim <- sparseDCSimulate()
}
```

Description

Parameters are estimated using the estimateDisp function in the edgeR package.

Usage

`splatEstBCV(counts, params)`

Arguments

- **counts**: counts matrix to estimate parameters from.
- **params**: SplatParams object to store estimated values in.
splatEstDropout

Details

The `estimateDisp` function is used to estimate the common dispersion and prior degrees of freedom. See `estimateDisp` for details. When estimating parameters on simulated data we found a broadly linear relationship between the true underlying common dispersion and the edgR estimate, therefore we apply a small correction, \( \text{disp} = 0.1 + 0.25 \times \text{edgeR\_disp} \).

Value

SplatParams object with estimated values.

---

**splatEstDropout**  
*Estimate Splat dropout parameters*

Description

Estimate the midpoint and shape parameters for the logistic function used when simulating dropout.

Usage

`splatEstDropout(norm.counts, params)`

Arguments

- `norm.counts`: library size normalised counts matrix.
- `params`: SplatParams object to store estimated values in.

Details

Logistic function parameters are estimated by fitting a logistic function to the relationship between log2 mean gene expression and the proportion of zeros in each gene. See `nls` for details of fitting. Note this is done on the experiment level, more granular (eg. group or cell) level dropout is not estimated.

Value

SplatParams object with estimated values.
splatEstimate

Estimate Splat simulation parameters

Description

Estimate simulation parameters for the Splat simulation from a real dataset. See the individual estimation functions for more details on how this is done.

Usage

splatEstimate(counts, params = newSplatParams())

## S3 method for class 'SingleCellExperiment'
splatEstimate(counts, params = newSplatParams())

## S3 method for class 'matrix'
splatEstimate(counts, params = newSplatParams())

Arguments

- **counts**: either a counts matrix or a SingleCellExperiment object containing count data to estimate parameters from.
- **params**: SplatParams object to store estimated values in.

Value

SplatParams object with estimated values.

See Also

splatEstMean, splatEstLib, splatEstOutlier, splatEstBCV, splatEstDropout

Examples

# Load example data
library(scuttle)
set.seed(1)
sce <- mockSCE()
params <- splatEstimate(sce)
params
splatEstLib  Estimate Splat library size parameters

Description
The Shapiro-Wilks test is used to determine if the library sizes are normally distributed. If so a normal distribution is fitted to the library sizes, if not (most cases) a log-normal distribution is fitted and the estimated parameters are added to the params object. See fitdist for details on the fitting.

Usage
splatEstLib(counts, params)

Arguments
- counts: counts matrix to estimate parameters from.
- params: splatParams object to store estimated values in.

Value
SplatParams object with estimated values.

splatEstMean  Estimate Splat mean parameters

Description
Estimate rate and shape parameters for the gamma distribution used to simulate gene expression means.

Usage
splatEstMean(norm.counts, params)

Arguments
- norm.counts: library size normalised counts matrix.
- params: SplatParams object to store estimated values in.

Details
Parameters for the gamma distribution are estimated by fitting the mean normalised counts using fitdist. The 'maximum goodness-of-fit estimation' method is used to minimise the Cramer-von Mises distance. This can fail in some situations, in which case the 'method of moments estimation' method is used instead. Prior to fitting the means are winsorized by setting the top and bottom 10 percent of values to the 10th and 90th percentiles.
splatEstOutlier  Estimate Splat expression outlier parameters

Description

Parameters are estimated by comparing means of individual genes to the median mean expression level.

Usage

splatEstOutlier(norm.counts, params)

Arguments

- **norm.counts**: library size normalised counts matrix.
- **params**: SplatParams object to store estimated values in.

Details

Expression outlier genes are detected using the Median Absolute Deviation (MAD) from median method. If the log2 mean expression of a gene is greater than two MADs above the median log2 mean expression it is designated as an outlier. The proportion of outlier genes is used to estimate the outlier probability. Factors for each outlier gene are calculated by dividing mean expression by the median mean expression. A log-normal distribution is then fitted to these factors in order to estimate the outlier factor location and scale parameters using `fitdist`.

Value

SplatParams object with estimated values.

SplatParams  The SplatParams class

Description

S4 class that holds parameters for the Splat simulation.
Parameters

The Splat simulation requires the following parameters:

nGenes  The number of genes to simulate.
nCells  The number of cells to simulate.
[seed]  Seed to use for generating random numbers.

**Batch parameters**  nBatches  The number of batches to simulate.

[batchCells]  Vector giving the number of cells in each batch.
[batch.facLoc]  Location (meanlog) parameter for the batch effect factor log-normal distribution. Can be a vector.
[batch.facScale]  Scale (sdlog) parameter for the batch effect factor log-normal distribution. Can be a vector.
[batch.rmEffect]  Logical, removes the batch effect and continues with the simulation when TRUE. This allows the user to test batch removal algorithms without having to calculate the new expected cell means with batch removed.

**Mean parameters**  mean.shape  Shape parameter for the mean gamma distribution.
mean.rate  Rate parameter for the mean gamma distribution.

**Library size parameters**  lib.loc  Location (meanlog) parameter for the library size log-normal distribution, or mean parameter if a normal distribution is used.
lib.scale  Scale (sdlog) parameter for the library size log-normal distribution, or sd parameter if a normal distribution is used.
lib.norm  Logical. Whether to use a normal distribution for library sizes instead of a log-normal.

**Expression outlier parameters**  out.prob  Probability that a gene is an expression outlier.
out.facLoc  Location (meanlog) parameter for the expression outlier factor log-normal distribution.
out.facScale  Scale (sdlog) parameter for the expression outlier factor log-normal distribution.

**Group parameters**  nGroups  The number of groups or paths to simulate.
[group.prob]  Probability that a cell comes from a group.

**Differential expression parameters**  de.prob  Probability that a gene is differentially expressed in a group. Can be a vector.
de.downProb  Probability that a differentially expressed gene is down-regulated. Can be a vector.
de.facLoc  Location (meanlog) parameter for the differential expression factor log-normal distribution. Can be a vector.
de.facScale  Scale (sdlog) parameter for the differential expression factor log-normal distribution. Can be a vector.

**Biological Coefficient of Variation parameters**  bcv.common  Underlying common dispersion across all genes.
bcv.df  Degrees of Freedom for the BCV inverse chi-squared distribution.
**splatPopAssignMeans**  

Sample expression mean and variance for each gene

### Description

A mean and coefficient of variation is assigned to each gene by sampling from gamma distributions parameterized from real data in `splatPopEstimate`. The cv gamma distributions are binned by gene mean because the distribution of variance in real data is not independent from the mean. The degree of similarity between individuals can be further tuned using the similarity.scale parameter in `SplatPopParams`.

### Usage

```r
splatPopAssignMeans(params, key)
```

### Arguments

- **params**: SplatPopParams object containing parameters for population scale simulations. See `SplatPopParams` for details.
- **key**: Partial splatPop key data.frame.
splatPopCleanSCE

Value
The key updated with assigned means and variances.

splatPopCleanSCE Clean up the population-scale SCE to remove redundant information

Description
Clean up the population-scale SCE to remove redundant information

Usage
splatPopCleanSCE(sim.all)

Arguments

sim.all SingleCellExperiment object with counts for all samples

Value
SingleCellExperiment with simulated sc counts.

splatPopConditionalEffects

Description
Add conditional DE effects to means matrix

Usage
splatPopConditionalEffects(id, key, vcf, means.pop)

Arguments

id The group ID (e.g. "global" or "g1")
key Partial splatPop key data.frame.
vcf VariantAnnotation object containing genotypes of samples.
means.pop Population mean gene expression matrix

Value
data.frame of gene mean expression levels WITH eQTL effects.
splatPopConditionEffects

Assign Condition-specific eQTL and DEGs.

Description
If nConditions > 1, n eSNP-eGene pairs (n = 'eqtl.condition.specific') are randomly assigned as condition specific.

Usage
splatPopConditionEffects(params, key, conditions)

Arguments
- params: SplatPopParams object containing parameters for population scale simulations. See SplatPopParams for details.
- key: Partial splatPop key data.frame.
- conditions: array of condition names

Value
The key updated with conditional eQTL and DE effects.

splatPopDesignBatches

Set up pooled experimental design

Description
Set up pooled experimental design

Usage
splatPopDesignBatches(params, samples, verbose)

Arguments
- params: SplatParams object with simulation parameters.
- samples: List of samples from vcf.
- verbose: logical. Whether to print progress messages.

Value
Vector with batch assignments for each sample.
splatPopDesignConditions

*Set up designed experiments conditions*

**Description**

Set up designed experiments conditions

**Usage**

`splatPopDesignConditions(params, samples)`

**Arguments**

- `params` SplatParams object with simulation parameters.
- `samples` List of samples from vcf.

**Value**

Vector with condition assignments for each sample.

---

splatPopeQTLEffects

*Assign eGenes-eSNPs pairs and effect sizes.*

**Description**

Randomly pairs N genes (eGene) a SNP (eSNP) within the window size (eqtl.dist) and assigns each pair an effect size sampled from a gamma distribution parameterized using the effect sizes from a real eQTL study.

**Usage**

`splatPopeQTLEffects(params, key, vcf)`

**Arguments**

- `params` SplatPopParams object containing parameters for population scale simulations. See SplatPopParams for details.
- `key` Partial splatPop key data.frame.
- `vcf` VariantAnnotation object containing genotypes of samples.

**Value**

The key updated with assigned eQTL effects.
splatPopEstimate  

**Estimate population/eQTL simulation parameters**

**Description**

Estimate simulation parameters for the eQTL population simulation from real data. See the individual estimation functions for more details on how this is done.

**Usage**

```r
splatPopEstimate(
  counts = NULL,
  means = NULL,
  eqtl = NULL,
  params = newSplatPopParams()
)
```

**Arguments**

- **counts**: either a counts matrix or a SingleCellExperiment object containing count data to estimate parameters from.
- **means**: Matrix of real gene means across a population, where each row is a gene and each column is an individual in the population.
- **eqtl**: data.frame with all or top eQTL pairs from a real eQTL analysis. Must include columns: 'gene_id', 'pval_nominal', and 'slope'.
- **params**: SplatPopParams object containing parameters for the simulation of the mean expression levels for the population. See `SplatPopParams` for details.

**Value**

SplatPopParams object containing the estimated parameters.

**See Also**

`splatPopEstimateEffectSize, splatPopEstimateMeanCV`

**Examples**

```r
if (requireNamespace("VariantAnnotation", quietly = TRUE) &&
    requireNamespace("preprocessCore", quietly = TRUE)) {
  # Load example data
  library(scuttle)

  sce <- mockSCE()
  params <- splatPopEstimate(sce)
}
```
splatPopEstimateEffectSize

Estimate eQTL Effect Size parameters

Description

Estimate rate and shape parameters for the gamma distribution used to simulate eQTL (eSNP-eGene) effect sizes.

Usage

splatPopEstimateEffectSize(params, eqtl)

Arguments

params SplatPopParams object containing parameters for the simulation of the mean expression levels for the population. See SplatPopParams for details.
eqtl data.frame with all or top eQTL pairs from a real eQTL analysis. Must include columns: gene_id, pval_nominal, and slope.

Details

Parameters for the gamma distribution are estimated by fitting the top eSNP-eGene pair effect sizes using fitdist. The maximum goodness-of-fit estimation method is used to minimise the Cramer-von Mises distance. This can fail in some situations, in which case the method of moments estimation method is used instead.

Value

params object with estimated values.

splatPopEstimateMeanCV

Estimate gene mean and gene mean variance parameters

Description

Estimate gene mean and gene mean variance parameters

Usage

splatPopEstimateMeanCV(params, emp.gene.means)
Arguments

params SplatPopParams object containing parameters for the simulation of the mean expression levels for the population. See SplatPopParams for details.

emp.gene.means data.frame of empirical gene means across a population, where rows are genes and columns are individuals.

Details

Parameters for the mean gamma distribution are estimated by fitting the mean (across the population) expression of genes that meet the criteria (<50 samples have exp < 0.1) and parameters for the cv gamma distribution are estimated for each bin of mean expression using the cv of expression across the population for genes in that bin. Both are fit using fitdist. The "Nelder-Mead" method is used to fit the mean gamma distribution and the maximum goodness-of-fit estimation method is used to minimise the Cramer-von Mises distance for the CV distribution.

Value

params object with estimated values.

splatPopGroupEffects Assign group-specific eQTL and DEGs.

Description

If groups > 1, n eSNP-eGene pairs (n = 'eqtl.group.specific') are randomly assigned as group specific.

Usage

splatPopGroupEffects(params, key, groups)

Arguments

params SplatPopParams object containing parameters for population scale simulations. See SplatPopParams for details.

key Partial splatPop key data.frame.

groups array of group names

Value

The key updated with group eQTL and DE effects.
The SplatPopParams class

Description

S4 class that holds parameters for the splatPop simulation.

Parameters

In addition to the SplatParams parameters, splatPop simulation requires the following parameters:

- **[similarity.scale]** Scaling factor for pop.cv.param.rate, where values larger than 1 increase the similarity between individuals in the population and values less than one make the individuals less similar.

- **[eqtl.n]** The number (>1) or percent (<=1) of genes to assign eQTL effects.

- **[eqtl.dist]** Maximum distance between eSNP and eGene

- **[eqtl.maf.min]** Minimum Minor Allele Frequency of eSNPs.

- **[eqtl.maf.max]** Maximum Minor Allele Frequency of eSNPs.

- **[eqtl.coreg]** Proportion of eGenes to have a shared eSNP (i.e., co-regulated genes)

- **[eqtl.group.specific]** Percent of eQTL effects to simulate as group specific.

- **[eqtl.condition.specific]** Percent of eQTL effects to simulate as condition specific.

**eQTL Effect size distribution parameters.** Defaults estimated from GTEx eQTL mapping results, see vignette for more information.

- **eqtl.ES.shape** Shape parameter for the effect size gamma distribution.

- **eqtl.ES.rate** Rate parameter for the effect size gamma distribution.

**Bulk Mean Expression distribution parameters.** Defaults estimated from GTEx data, see vignette for more information.

- **pop.mean.shape** Shape parameter for the mean (i.e. bulk) expression gamma distribution

- **pop.mean.rate** Rate parameter for the mean (i.e. bulk) expression gamma distribution

**Bulk Expression Coefficient of Variation distribution parameters binned.** Defaults estimated from GTEx data, see vignette for more information.

- **pop.cv.param** Dataframe containing gene mean bin range, and the CV shape, and CV rate parameters for each of those bins.

Specify number of samples per batch. Note that splatPop will randomly assign donors to be present in multiple batches to...

The number of donors in each pool/batch.

Specify shape and rate of gamma distribution to sample number of cells per batch per donor. Will only be used if nCells parameter is set to 0.

- **nCells.shape** Shape parameter for the nCells per batch per donor distribution.

- **nCells.rate** Rate parameter for the nCells per batch per donor distribution.

**Condition/treatment differential expression parameters** [nConditions] The number of conditions/treatments to divide samples into.

- **[condition.prob]** Probability that a sample belongs to each condition/treatment group. Can be a vector.
[cde.prob] Probability that a gene is differentially expressed in a condition group. Can be a vector.
[cde.downProb] Probability that a conditionally differentially expressed gene is down-regulated. Can be a vector.
[cde.facLoc] Location (meanlog) parameter for the conditional differential expression factor log-normal distribution. Can be a vector.
[cde.facScale] Scale (sdlog) parameter for the conditional differential expression factor log-normal distribution. Can be a vector.

The parameters not shown in brackets can be estimated from real data using `splatPopEstimate`. For details of the eQTL simulation see `splatPopSimulate`.

---

`splatPopParseEmpirical`

`splatPopParseEmpirical`

**Description**

Parse splatPop key information from empirical data provided.

**Usage**

```r
splatPopParseEmpirical(
  vcf = vcf,
  gff = gff,
  eqtl = eqtl,
  means = means,
  params = params
)
```

**Arguments**

- `vcf`: VariantAnnotation object containing genotypes of samples.
- `gff`: Either NULL or a data.frame object containing a GFF/GTF file.
- `eqtl`: Either NULL or if simulating population parameters directly from empirical data, a data.frame with empirical/desired eQTL results. To see required format, run `mockEmpiricalSet()` and see eqtl output.
- `means`: Either NULL or if simulating population parameters directly from empirical data, a Matrix of real gene means across a population, where each row is a gene and each column is an individual in the population. To see required format, run `mockEmpiricalSet()` and see means output.
- `params`: SplatPopParams object containing parameters for population scale simulations. See `SplatPopParams` for details.
Details

NOTE: This function will cause some of the parameters in the splatPopParams object to be ignored, such as population level gene mean and variance and eQTL parameters.

This function will ignore a number of parameters defined in splatPopParams, instead pulling key information directly from provided VCF, GFF, gene means, and eQTL mapping result data provided.

Value

A partial splatPop ‘key’

---

**splatPopParseGenes**

*Generate population key matrix from random or gff provided gene information*

---

**Description**

Generate population key matrix from random or gff provided gene information

**Usage**

`splatPopParseGenes(params, gff)`

**Arguments**

- **params**: SplatPopParams object containing parameters for population scale simulations. See `SplatPopParams` for details.
- **gff**: Either NULL or a data.frame object containing a GFF/GTF file.

**Value**

The Partial splatPop key data.frame.

---

**splatPopParseVCF**

*Format and subset genotype data from a VCF file.*

---

**Description**

Extract numeric alleles from vcf object and filter out SNPs missing genotype data or outside the Minor Allele Frequency range in `SplatPopParams`.

**Usage**

`splatPopParseVCF(vcf, params)`
splatPopQuantNorm

Arguments

- **vcf** VariantAnnotation object containing genotypes of samples.
- **params** SplatPopParams object containing parameters for population scale simulations. See SplatPopParams for details.

Value

Genotype data.frame

---

**splatPopQuantNorm**  
Quantile normalize by sample to fit sc expression distribution.

Description

For each sample, expression values are quantile normalized (qgamma) using the gamma distribution parameterized from splatEstimate(). This ensures the simulated gene means reflect the distribution expected from a sc dataset and not a bulk dataset.

Usage

splatPopQuantNorm(params, means)

Arguments

- **params** SplatPopParams object containing parameters for population scale simulations. See SplatPopParams for details.
- **means** Mean gene expression matrix with eQTL effects.

Value

matrix of quantile normalized gene mean expression levels.

Examples

```r
if (requireNamespace("VariantAnnotation", quietly = TRUE) && requireNamespace("preprocessCore", quietly = TRUE)) {
  bulk.means <- mockBulkMatrix(n.genes = 100, n.samples = 100)
  bulk.qnorm <- splatPopQuantNorm(newSplatPopParams(), bulk.means)
}
```
splatPopQuantNormKey

Add quantile normalized gene mean and cv info the eQTL key.

Description
Add quantile normalized gene mean and cv info the eQTL key.

Usage
splatPopQuantNormKey(key, means)

Arguments
key
Partial splatPop key data.frame.
means
matrix or list of matrices containing means from ‘splatPopQuantNorm’

Value
Final eQTL key.

splatPopSimBatchEffects
Simulate batch effects

Description
Simulate batch effects. Batch effect factors for each batch are produced using getLNormFactors and these are added along with updated means for each batch.

Usage
splatPopSimBatchEffects(sim, params)

Arguments
sim
SingleCellExperiment to add batch effects to.
params
SplatParams object with simulation parameters.

Value
SingleCellExperiment with simulated batch effects.
**splatPopSimConditionalEffects**

*Add conditional DE effects to means matrix*

**Description**

Add conditional DE effects to means matrix

**Usage**

`splatPopSimConditionalEffects(key, means.pop, conditions)`

**Arguments**

- **key**: Partial splatPop key data.frame.
- **means.pop**: matrix or list of matrices with gene means.
- **conditions**: array of condition assignments for each sample

**Value**

data.frame of gene mean expression levels WITH conditional DE effects.

**splatPopSimEffects**

*Add eQTL effects to means matrix*

**Description**

Add eQTL effects and non-eQTL group effects to simulated means matrix. The eQTL effects are incorporated using the following equation:

\[ Y_{gs} = (E_{g}xM_{gs}xG_{s}) + M_{gs} \]

Where \( Y_{gs} \) is the mean for gene \( g \) and sample \( s \), \( E_{g} \) is the effect size assigned to \( g \), \( M_{gs} \) is the mean expression assigned to \( g \) for \( s \), and \( G_{s} \) is the genotype (number of minor alleles) for \( s \). Non-eQTL group effects are incorporated as:

\[ Y_{gs} = M_{gs}xG_{E_{g}} \]

Where \( G_{E_{g}} \) is the group effect (i.e. differential expression) assigned to \( g \). To simulate multiple gene mean matrices with different group effects, this function can be run with 'id' designating the group id.

**Usage**

`splatPopSimEffects(id, key, conditions, vcf, means.pop)`
splatPopSimGeneMeans

Arguments

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>id</td>
<td>The group ID (e.g. &quot;global&quot; or &quot;g1&quot;)</td>
</tr>
<tr>
<td>key</td>
<td>Partial splatPop key data.frame.</td>
</tr>
<tr>
<td>conditions</td>
<td>array of condition assignments for each sample</td>
</tr>
<tr>
<td>vcf</td>
<td>VariantAnnotation object containing genotypes of samples.</td>
</tr>
<tr>
<td>means.pop</td>
<td>Population mean gene expression matrix</td>
</tr>
</tbody>
</table>

Value

data.frame of gene mean expression levels WITH eQTL effects.

Usage

splatPopSimGeneMeans(sim, params, base.means.gene)

Arguments

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>sim</td>
<td>SingleCellExperiment to add gene means to.</td>
</tr>
<tr>
<td>params</td>
<td>SplatParams object with simulation parameters.</td>
</tr>
<tr>
<td>base.means.gene</td>
<td>List of gene means for sample from matrix generated by `splatPopSimulateMeans` and with the sample specified in `splatPopSimulateSC`.</td>
</tr>
</tbody>
</table>

Value

SingleCellExperiment with simulated gene means.
splatPopSimMeans

Simulate mean gene expression matrix without eQTL effects

Description

Gene mean expression levels are assigned to each gene for each pair randomly from a normal distribution parameterized using the mean and cv assigned to each gene in the key. If gene means matrix is provided, those will be used instead.

Usage

splatPopSimMeans(vcf, key, means)

Arguments

vcf      VariantAnnotation object containing genotypes of samples.
key      Partial splatPop key data.frame.
means    Null or matrix of gene means to use

Value

matrix of gene mean expression levels WITHOUT eQTL effects.

splatPopSimulate  splatPop simulation

Description

Simulate scRNA-seq count data using the splat model for a population of individuals with correlation structure.

Usage

splatPopSimulate(
  params = newSplatPopParams(nGenes = 50),
  vcf = mockVCF(),
  method = c("single", "groups", "paths"),
  gff = NULL,
  eqtl = NULL,
  means = NULL,
  key = NULL,
  counts.only = FALSE,
  sparsify = TRUE,
  verbose = TRUE,
  ...
)

)
splatPopSimulate

Arguments

params SplatPopParams object containing parameters for population scale simulations. See SplatPopParams for details.

vcf VariantAnnotation object containing genotypes of samples.

method which simulation method to use. Options are "single" which produces a single population, "groups" which produces distinct groups (eg. cell types), "paths" which selects cells from continuous trajectories (eg. differentiation processes).

gff Either NULL or a data.frame object containing a GFF/GTF file.
eqtl Either NULL or if simulating population parameters directly from empirical data, a data.frame with empirical/desired eQTL results. To see required format, run 'mockEmpiricalSet()' and see eqtl output.

means Either NULL or if simulating population parameters directly from empirical data, a Matrix of real gene means across a population, where each row is a gene and each column is an individual in the population. To see required format, run 'mockEmpiricalSet()' and see means output.

key Either NULL or a data.frame object containing a full or partial splatPop key.

counts.only logical. Whether to save only counts in sce object.

sparsify logical. Whether to automatically convert assays to sparse matrices if there will be a size reduction.

verbose logical. Whether to print progress messages.

... any additional parameter settings to override what is provided in params.

Details

This functions is for simulating data in a single step. It consists of a call to splatPopSimulateMeans, which simulates a mean expression level per gene per sample, followed by a call to splatPopSimulateSC, which uses the splat model to simulate single-cell counts per individual. Please see the documentation for those functions for more details.

Value

SingleCellExperiment object containing simulated counts, intermediate values like the gene means simulated in 'splatPopSimulateMeans', and information about the differential expression and eQTL effects assigned to each gene.

See Also

splatPopSimulateMeans, splatPopSimulateSC

Examples

if (requireNamespace("VariantAnnotation", quietly = TRUE) &
   requireNamespace("preprocessCore", quietly = TRUE)) {
  vcf <- mockVCF()
  gff <- mockGFF()
  sim <- splatPopSimulate(vcf = vcf, gff = gff, sparsify = FALSE)
splatPopSimulateMeans

Description

Simulate mean expression levels for all genes for all samples, with between sample correlation structure simulated with eQTL effects and with the option to simulate multiple groups (i.e. cell-types).

Usage

splatPopSimulateMeans(
  vcf = mockVCF(),
  params = newSplatPopParams(nGenes = 1000),
  verbose = TRUE,
  key = NULL,
  gff = NULL,
  eqtl = NULL,
  means = NULL,
  ...
)

Arguments

- **vcf**: VariantAnnotation object containing genotypes of samples.
- **params**: SplatPopParams object containing parameters for population scale simulations. See SplatPopParams for details.
- **verbose**: logical. Whether to print progress messages.
- **key**: Either FALSE or a data.frame object containing a full or partial splatPop key.
- **gff**: Either NULL or a data.frame object containing a GFF/GTF file.
- **eqtl**: Either NULL or if simulating population parameters directly from empirical data, a data.frame with empirical/desired eQTL results. To see required format, run ‘mockEmpiricalSet()’ and see eqtl output.
- **means**: Either NULL or if simulating population parameters directly from empirical data, a Matrix of real gene means across a population, where each row is a gene and each column is an individual in the population. To see required format, run ‘mockEmpiricalSet()’ and see means output.
- **...**: any additional parameter settings to override what is provided in params.
Details

SplatPopParams can be set in a variety of ways. 1. If not provided, default parameters are used. 2. Default parameters can be overridden by supplying desired parameters using `setParams`. 3. Parameters can be estimated from real data of your choice using `splatPopEstimate`.

‘splatPopSimulateMeans’ involves the following steps:

1. Load population key or generate random or GFF/GTF based key.
2. Format and subset genotype data from the VCF file.
3. If not in key, assign expression mean and variance to each gene.
4. If not in key, assign eGenes-eSNPs pairs and effect sizes.
5. If not in key and groups >1, assign subset of eQTL associations as group-specific and assign DEG group effects.
6. Simulate mean gene expression matrix without eQTL effects
7. Quantile normalize by sample to fit single-cell expression distribution as defined in ‘splatEstimate’.
8. Add quantile normalized gene mean and cv info the eQTL key.
9. Add eQTL effects to means matrix.

Value

A list containing: ‘means’ a matrix (or list of matrices if n.groups > 1) with the simulated mean gene expression value for each gene (row) and each sample (column), ‘key’ a data.frame with population information including eQTL and group effects, and ‘condition’ a named array containing conditional group assignments for each sample.

See Also

`splatPopParseVCF`, `splatPopParseGenes`, `splatPopAssignMeans`, `splatPopQuantNorm`, `splatPopQuantNormKey`, `splatPopQTLEffects`, `splatPopGroupEffects`, `splatPopSimMeans`, `splatPopSimEffects`,

Examples

```r
if (requireNamespace("VariantAnnotation", quietly = TRUE) && requireNamespace("preprocessCore", quietly = TRUE)) {
  means <- splatPopSimulateMeans()
}
```
splatPopSimulateSample

splatPopSimulateSample simulation

Description

Simulate count data for one sample from a fictional single-cell RNA-seq experiment using the Splat method.

Usage

splatPopSimulateSample(
  params = newSplatPopParams(),
  method = c("single", "groups", "paths"),
  batch = "batch1",
  counts.only = FALSE,
  verbose = TRUE,
  sample.means,
  ...
)

Arguments

- **params**: SplatPopParams object containing parameters for population scale simulations. See SplatPopParams for details.
- **method**: which simulation method to use. Options are "single" which produces a single population, "groups" which produces distinct groups (eg. cell types), "paths" which selects cells from continuous trajectories (eg. differentiation processes).
- **batch**: Batch number.
- **counts.only**: logical. Whether to return only the counts.
- **verbose**: logical. Whether to print progress messages.
- **sample.means**: Gene means to use if running splatSimulatePop().
- **...**: any additional parameter settings to override what is provided in params.

Details

This function closely mirrors splatSimulate. The main difference is that it takes the means simulated by splatPopSimulateMeans instead of randomly sampling a mean for each gene. For details about this function see the documentation for splatSimulate.

Value

SingleCellExperiment object containing the simulated counts and intermediate values for one sample.
splatPopSimulateSC

See Also
splatSimLibSizes, splatPopSimGeneMeans, splatSimBatchEffects, splatSimBatchCellMeans, splatSimDE, splatSimCellMeans, splatSimBCVMeans, splatSimTrueCounts, splatSimDropout, splatPopSimulateSC

Description
Simulate count data for a population from a fictional single-cell RNA-seq experiment using the Splat method.

Usage
splatPopSimulateSC(
  sim.means, 
  params, 
  key, 
  method = c("single", "groups", "paths"), 
  counts.only = FALSE, 
  conditions = NULL, 
  sparsify = TRUE, 
  verbose = TRUE, 
  ... 
)

Arguments
- sim.means: Matrix or list of matrices of gene means for the population. Output from `splat-PopSimulateMeans()`.
- params: SplatPopParams object containing parameters for population scale simulations. See SplatPopParams for details.
- key: data.frame object containing a full or partial splatPop key. Output from `splat-PopSimulateMeans()`.
- method: which simulation method to use. Options are "single" which produces a single cell population for each sample, "groups" which produces distinct groups (eg. cell types) for each sample (note, this creates separate groups from those created in 'popSimulate' with only DE effects), and "paths" which selects cells from continuous trajectories (eg. differentiation processes).
- counts.only: logical. Whether to return only the counts.
- conditions: named array with conditional group assignment for each sample. Output from `splat-PopSimulateMeans()`.
- sparsify: logical. Whether to automatically convert assays to sparse matrices if there will be a size reduction.
- verbose: logical. Whether to print progress messages.
- ...: any additional parameter settings to override what is provided in params.
splatSimBatchCellMeans

Description

Simulate a mean for each gene in each cell incorporating batch effect factors.

Usage

splatSimBatchCellMeans(sim, params)

Arguments

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>sim</td>
<td>SingleCellExperiment to add batch means to.</td>
</tr>
<tr>
<td>params</td>
<td>SplatParams object with simulation parameters.</td>
</tr>
</tbody>
</table>

Value

SingleCellExperiment with simulated batch means.
splatSimBatchEffects

Description

Simulate batch effects. Batch effect factors for each batch are produced using `getLNormFactors` and these are added along with updated means for each batch.

Usage

`splatSimBatchEffects(sim, params)`

Arguments

- `sim` : SingleCellExperiment to add batch effects to.
- `params` : SplatParams object with simulation parameters.

Value

SingleCellExperiment with simulated batch effects.

splatSimBCVMeans

Description

Simulate means for each gene in each cell that are adjusted to follow a mean-variance trend using Biological Coefficient of Variation taken from and inverse gamma distribution.

Usage

`splatSimBCVMeans(sim, params)`

Arguments

- `sim` : SingleCellExperiment to add BCV means to.
- `params` : SplatParams object with simulation parameters.

Value

SingleCellExperiment with simulated BCV means.
splatSimCellMeans  

*Simulate cell means*

**Description**

Simulate a gene by cell matrix giving the mean expression for each gene in each cell. Cells start with the mean expression for the group they belong to (when simulating groups) or cells are assigned the mean expression from a random position on the appropriate path (when simulating paths). The selected means are adjusted for each cell’s expected library size.

**Usage**

- `splatSimSingleCellMeans(sim, params)`
- `splatSimGroupCellMeans(sim, params)`
- `splatSimPathCellMeans(sim, params)`

**Arguments**

- `sim` 
  *SingleCellExperiment to add cell means to.*
- `params` 
  *SplatParams object with simulation parameters.*

**Value**

*SingleCellExperiment with added cell means.*

splatSimDE  

*Simulate group differential expression*

**Description**

Simulate differential expression. Differential expression factors for each group are produced using `getLNormFactors` and these are added along with updated means for each group. For paths care is taken to make sure they are simulated in the correct order.

**Usage**

- `splatSimGroupDE(sim, params)`
- `splatSimPathDE(sim, params)`

**Arguments**

- `sim` 
  *SingleCellExperiment to add differential expression to.*
- `params` 
  *splatParams object with simulation parameters.*
**splatSimDropout**

**Value**

SingleCellExperiment with simulated differential expression.

**Description**

A logistic function is used to form a relationship between the expression level of a gene and the probability of dropout, giving a probability for each gene in each cell. These probabilities are used in a Bernoulli distribution to decide which counts should be dropped.

**Usage**

`splatSimDropout(sim, params)`

**Arguments**

- `sim` SingleCellExperiment to add dropout to.
- `params` SplatParams object with simulation parameters.

**Value**

SingleCellExperiment with simulated dropout and observed counts.

**splatSimGeneMeans**

**Simulate gene means**

**Description**

Simulate gene means from a gamma distribution. Also simulates outlier expression factors. Genes with an outlier factor not equal to 1 are replaced with the median mean expression multiplied by the outlier factor.

**Usage**

`splatSimGeneMeans(sim, params)`

**Arguments**

- `sim` SingleCellExperiment to add gene means to.
- `params` SplatParams object with simulation parameters.

**Value**

SingleCellExperiment with simulated gene means.
splatSimLibSizes | Simulate library sizes

**Description**

Simulate expected library sizes. Typically a log-normal distribution is used but there is also the option to use a normal distribution. In this case any negative values are set to half the minimum non-zero value.

**Usage**

`splatSimLibSizes(sim, params)`

**Arguments**

- `sim` SingleCellExperiment to add library size to.
- `params` SplatParams object with simulation parameters.

**Value**

SingleCellExperiment with simulated library sizes.

splatSimTrueCounts | Simulate true counts

**Description**

Simulate a true counts matrix. Counts are simulated from a poisson distribution where each gene in each cell has its own mean based on the group (or path position), expected library size and BCV.

**Usage**

`splatSimTrueCounts(sim, params)`

**Arguments**

- `sim` SingleCellExperiment to add true counts to.
- `params` SplatParams object with simulation parameters.

**Value**

SingleCellExperiment with simulated true counts.
splatSimulate

Splat simulation

Description

Simulate count data from a fictional single-cell RNA-seq experiment using the Splat method.

Usage

splatSimulate(
  params = newSplatParams(),
  method = c("single", "groups", "paths"),
  sparsify = TRUE,
  verbose = TRUE,
  ...
)

splatSimulateSingle(params = newSplatParams(), verbose = TRUE, ...)

splatSimulateGroups(params = newSplatParams(), verbose = TRUE, ...)

splatSimulatePaths(params = newSplatParams(), verbose = TRUE, ...)

Arguments

params  SplatParams object containing parameters for the simulation. See SplatParams for details.
method  which simulation method to use. Options are "single" which produces a single population, "groups" which produces distinct groups (eg. cell types), or "paths" which selects cells from continuous trajectories (eg. differentiation processes).
sparsify logical. Whether to automatically convert assays to sparse matrices if there will be a size reduction.
verbose logical. Whether to print progress messages.
...  any additional parameter settings to override what is provided in params.

Details

Parameters can be set in a variety of ways. If no parameters are provided the default parameters are used. Any parameters in params can be overridden by supplying additional arguments through a call to setParams. This design allows the user flexibility in how they supply parameters and allows small adjustments without creating a new SplatParams object. See examples for a demonstration of how this can be used.

The simulation involves the following steps:

1. Set up simulation object
2. Simulate library sizes
3. Simulate gene means
4. Simulate groups/paths
5. Simulate BCV adjusted cell means
6. Simulate true counts
7. Simulate dropout
8. Create final dataset

The final output is a SingleCellExperiment object that contains the simulated counts but also the values for various intermediate steps. These are stored in the colData (for cell specific information), rowData (for gene specific information) or assays (for gene by cell matrices) slots. This additional information includes:

**colData**
- **Cell** Unique cell identifier.
- **Group** The group or path the cell belongs to.
- **ExpLibSize** The expected library size for that cell.
- **Step** (paths only) how far along the path each cell is.

**rowData**
- **Gene** Unique gene identifier.
- **BaseGeneMean** The base expression level for that gene.
- **OutlierFactor** Expression outlier factor for that gene. Values of 1 indicate the gene is not an expression outlier.
- **GeneMean** Expression level after applying outlier factors.
- **BatchFac[Batch]** The batch effects factor for each gene for a particular batch.
- **DEFac[Group]** The differential expression factor for each gene in a particular group. Values of 1 indicate the gene is not differentially expressed.
- **SigmaFac[Path]** Factor applied to genes that have non-linear changes in expression along a path.

**assays**
- **BatchCellMeans** The mean expression of genes in each cell after adding batch effects.
- **BaseCellMeans** The mean expression of genes in each cell after any differential expression and adjusted for expected library size.
- **BCV** The Biological Coefficient of Variation for each gene in each cell.
- **CellMeans** The mean expression level of genes in each cell adjusted for BCV.
- **TrueCounts** The simulated counts before dropout.
- **Dropout** Logical matrix showing which values have been dropped in which cells.

Values that have been added by Splatter are named using UpperCamelCase in order to differentiate them from the values added by analysis packages which typically use underscore_naming.

**Value**

SingleCellExperiment object containing the simulated counts and intermediate values.

**References**


Paper: 10.1186/s13059-017-1305-0

Code: https://github.com/Oshlack/splatter
See Also

splatSimLibSizes, splatSimGeneMeans, splatSimBatchEffects, splatSimBatchCellMeans,
splatSimDE, splatSimCellMeans, splatSimBCVMeans, splatSimTrueCounts, splatSimDropout

Examples

# Simulation with default parameters
sim <- splatSimulate()

# Simulation with different number of genes
sim <- splatSimulate(nGenes = 1000)
# Simulation with custom parameters
params <- newSplatParams(nGenes = 100, mean.rate = 0.5)
sim <- splatSimulate(params)
# Simulation with adjusted custom parameters
sim <- splatSimulate(params, mean.rate = 0.6, out.prob = 0.2)
# Simulate groups
sim <- splatSimulate(method = "groups")
# Simulate paths
sim <- splatSimulate(method = "paths")

summariseDiff

Summarise diffSCEs

Description

Summarise the results of diffSCEs. Calculates the Median Absolute Deviation (MAD), Mean Absolute Error (MAE), Root Mean Squared Error (RMSE) and Kolmogorov-Smirnov (KS) statistics for the various properties and ranks them.

Usage

summariseDiff(diff)

Arguments

diff Output from diffSCEs

Value

data.frame with MADs, MAEs, RMSEs, scaled statistics and ranks
Examples

```r
sim1 <- splatSimulate(nGenes = 1000, batchCells = 20)
sim2 <- simpleSimulate(nGenes = 1000, nCells = 20)
difference <- diffSCEs(list(Splat = sim1, Simple = sim2), ref = "Simple")
summary <- summariseDiff(difference)
head(summary)
```

**znbEstimate**

*Estimate ZINB-WaVE simulation parameters*

**Description**

Estimate simulation parameters for the ZINB-WaVE simulation from a real dataset.

**Usage**

```r
znbEstimate(
  counts,
  design.samples = NULL,
  design.genes = NULL,
  common.disp = TRUE,
  iter.init = 2,
  iter.opt = 25,
  stop.opt = 1e-04,
  params = newZINBParams(),
  verbose = TRUE,
  BPPARAM = SerialParam(),
  ...
)
```

## S3 method for class 'SingleCellExperiment'

```r
znbEstimate(
  counts,
  design.samples = NULL,
  design.genes = NULL,
  common.disp = TRUE,
  iter.init = 2,
  iter.opt = 25,
  stop.opt = 1e-04,
  params = newZINBParams(),
  verbose = TRUE,
  BPPARAM = SerialParam(),
  ...
)
```

## S3 method for class 'matrix'

```r
znbEstimate(
```

counts,
design.samples = NULL,
design.genes = NULL,
common.disp = TRUE,
iter.init = 2,
iter.opt = 25,
stop.opt = 1e-04,
params = newZINBParams(),
verbose = TRUE,
BPPARAM = SerialParam(),
...)

Arguments

counts either a counts matrix or a SingleCellExperiment object containing count data
to estimate parameters from.
design.samples design matrix of sample-level covariates.
design.genes design matrix of gene-level covariates.
common.disp logical. Whether or not a single dispersion for all features is estimated.
iter.init number of iterations to use for initialization.
iter.opt number of iterations to use for optimization.
stop.opt stopping criterion for optimization.
params ZINBParams object to store estimated values in.
verbose logical. Whether to print progress messages.
BPPARAM A BiocParallelParam instance giving the parallel back-end to be used. Default
is SerialParam which uses a single core.
... additional arguments passes to zinbFit.

Details

The function is a wrapper around zinbFit that takes the fitted model and inserts it into a ZINBParams
object. See ZINBParams for more details on the parameters and zinbFit for details of the estima-
tion procedure.

Value

ZINBParams object containing the estimated parameters.

Examples

if (requireNamespace("zinbwave", quietly = TRUE)) {
  library(scuttle)
sce <- mockSCE(ncells = 20, ngenes = 100)
  params <- zinbEstimate(sce)
ZINBParams

The ZINBParams class

Description

S4 class that holds parameters for the ZINB-WaVE simulation.

Parameters

The ZINB-WaVE simulation uses the following parameters:

- nGenes  The number of genes to simulate.
- nCells  The number of cells to simulate.
- [seed]  Seed to use for generating random numbers.
- model   Object describing a ZINB model.

The majority of the parameters for this simulation are stored in a ZinbModel object. Please refer to the documentation for this class and its constructor(zinbModel) for details about all the parameters.

The parameters not shown in brackets can be estimated from real data using zinbEstimate. For details of the ZINB-WaVE simulation see zinbSimulate.

zinbSimulate

ZINB-WaVE simulation

Description

Simulate counts using the ZINB-WaVE method.

Usage

zinbSimulate(params = newZINBParams(), sparsify = TRUE, verbose = TRUE, ...)

Arguments

- params  ZINBParams object containing simulation parameters.
- sparsify logical. Whether to automatically convert assays to sparse matrices if there will be a size reduction.
- verbose logical. Whether to print progress messages
- ... any additional parameter settings to override what is provided in params.
**Details**

This function is just a wrapper around `zinbSim` that takes a `ZINBParams`, runs the simulation then converts the output to a `SingleCellExperiment` object. See `zinbSim` and the ZINB-WaVE paper for more details about how the simulation works.

**Value**

`SingleCellExperiment` containing simulated counts

**References**


Paper: 10.1101/125112

Code: https://github.com/drisso/zinbwave

**Examples**

```r
if (requireNamespace("zinbwave", quietly = TRUE)) {
  sim <- zinbSimulate()
}
```
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