

Package ‘switchde’

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Type Package

Title Switch-like differential expression across single-cell trajectories

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Description Inference and detection of switch-like differential expression across single-cell RNA-seq trajectories.

License GPL (>= 2)

LazyData TRUE

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Depends R (>= 3.4), SingleCellExperiment

Imports SummarizedExperiment, dplyr, ggplot2, methods, stats

Suggests knitr, rmarkdown, BiocStyle, testthat, numDeriv, tidyr

VignetteBuilder knitr

RoxygenNote 6.0.1

URL <https://github.com/kieranrcampbell/switchde>

BugReports <https://github.com/kieranrcampbell/switchde>

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|-----------------|-----------------------------|
| example_sigmoid | <i>Example sigmoid plot</i> |
|-----------------|-----------------------------|

Description

Plot an example sigmoid function. For demonstration and documentation.

Usage

```
example_sigmoid()
```

Value

An object of class `ggplot`

Examples

```
example_sigmoid()
```

| | |
|--------------|---|
| extract_pars | <i>Extract parameters from fitted model</i> |
|--------------|---|

Description

Extract maximum likelihood parameter estimates from a call to `switchde`.

Usage

```
extract_pars(sde, gene)
```

Arguments

sde The data.frame returned by switchde
 gene The gene for which to extract parameters

Value

A vector of length 3 corresponding to the parameters μ_0 , k and t_0

Examples

```
data(synth_gex)
data(ex_pseudotime)
sde <- switchde(synth_gex, ex_pseudotime)
pars <- extract_pars(sde, "Gene1")
```

| | |
|---------------|-----------------------------------|
| ex_pseudotime | <i>Synthetic gene pseudotimes</i> |
|---------------|-----------------------------------|

Description

A vector with example pseudotimes for the synthetic gene expression data in example_gex

Usage

```
ex_pseudotime
```

Format

An object of class array of length 100.

Value

A vector of length 100

| | |
|---------------|--|
| fit_nzi_model | <i>Fit a (non-zero-inflated) model for a single gene</i> |
|---------------|--|

Description

Fits a sigmoidal expression model for a single gene vector, returning MLE model parameters and p-value.

Usage

```
fit_nzi_model(y, pst)
```

Arguments

`y` Vector of gene expression values
`pst` Pseudotime vector, of same length as `y`

Value

A vector with 5 entries: maximum likelihood estimates for μ_0 , k , t_0 , σ^2 and a p-value

Examples

```
data(synth_gex)
data(ex_pseudotime)
y <- synth_gex[1, ]
fit <- fit_nzi_model(y, ex_pseudotime)
```

| | |
|---------------------------|--|
| <code>fit_zi_model</code> | <i>Fit a zero-inflated model for a single gene</i> |
|---------------------------|--|

Description

Fits a zero-inflated sigmoidal model for a single gene vector, returning MLE model parameters and p-value.

Usage

```
fit_zi_model(y, pst, maxiter = 10000, log_lik_tol = 0.001,
  verbose = FALSE)
```

Arguments

`y` Vector of gene expression values
`pst` Pseudotime vector, of same length as `y`
`maxiter` Maximum number of iterations for EM algorithm if zero inflation enabled. Default 100
`log_lik_tol` If the change in the log-likelihood falls below this for zero inflated EM the algorithm is assumed to have converged
`verbose` Print convergence update for EM algorithm

Value

A vector with 6 entries: maximum likelihood estimates for μ_0 , k , t_0 , λ , σ^2 and a p-value

Examples

```
data(synth_gex)
data(ex_pseudotime)
y <- synth_gex[1, ]
fit <- fit_zi_model(y, ex_pseudotime)
```

| | |
|-----------------|------------------------|
| sanitise_inputs | <i>Sanitise inputs</i> |
|-----------------|------------------------|

Description

Sanitise inputs

Usage

```
sanitise_inputs(object, pseudotime, lower_threshold, zero_inflated, sce_assay)
```

Arguments

| | |
|-----------------|--|
| object | The object passed at the entry point (either a SCESet or gene expression matrix) |
| pseudotime | A pseudotime vector |
| lower_threshold | The minimum threshold below which to set expression to zero to avoid numerical issues. Default is 0.01 |
| zero_inflated | Logical. Should zero inflation be implemented? Default FALSE |
| sce_assay | The assay from the SingleCellExperiment to be used as expression, defaulting to "exprs" |

Value

A list with two entries: a gene expression matrix X and a pseudotime vector pst .

| | |
|---------|---|
| sigmoid | <i>Calculate the mean vector given parameters and pseudotimes (mu0 formulation)</i> |
|---------|---|

Description

This function (common to all models) calculates the sigmoidal mean vector given the parameters and factor of pseudotimes

Usage

```
sigmoid(pst, params)
```

Arguments

| | |
|--------|---|
| pst | Vector of pseudotimes |
| params | Vector of length 3 with entries μ_0 , k , t_0 |

Value

Mean sigmoidal vector

 switchde

Switch-like model fitting and differential expression test

Description

Fit sigmoidal differential expression models to gene expression across pseudotime. Parameter estimates are returned along with a p-value for switch-like differential expression over a null model (constant expression).

Usage

```
switchde(object, pseudotime = NULL, zero_inflated = FALSE,
         lower_threshold = 0.01, maxiter = 1000, log_lik_tol = 0.01,
         verbose = FALSE, sce_assay = "exprs")
```

Arguments

| | |
|-----------------|--|
| object | Gene expression data that is either <ul style="list-style-type: none"> • A vector of length number of cells for a single gene • A matrix of dimension number of genes x number of cells • An object of class <code>SingleCellExperiment</code> from package <code>SingleCellExperiment</code> |
| pseudotime | A pseudotime vector with a pseudotime corresponding to every cell. Can be NULL if object is of class <code>SCESet</code> and <code>colData(sce)\$pseudotime</code> is defined. |
| zero_inflated | Logical. Should zero inflation be implemented? Default FALSE |
| lower_threshold | The minimum threshold below which to set expression to zero to avoid numerical issues. Default is 0.01 |
| maxiter | Maximum number of iterations for EM algorithm if zero inflation enabled. Default 100 |
| log_lik_tol | If the change in the log-likelihood falls below this for zero inflated EM the algorithm is assumed to have converged |
| verbose | Print convergence update for EM algorithm |
| sce_assay | The assay from the <code>SingleCellExperiment</code> to be used as expression, defaulting to "exprs" |

Value

A matrix where each column corresponds to a gene, the first row is the p-value for that gene and subsequent rows are model parameters.

Examples

```
data(synth_gex)
data(ex_pseudotime)
sde <- switchde(synth_gex, ex_pseudotime)
```

| | |
|------------|----------------------------|
| switchplot | <i>Plot gene behaviour</i> |
|------------|----------------------------|

Description

Plot gene behaviour and MLE sigmoid as a function of pseudotime.

Usage

```
switchplot(x, pseudotime, pars)
```

Arguments

| | |
|------------|---|
| x | Gene expression vector |
| pseudotime | Pseudotime vector (of same length as x) |
| pars | Fitted model parameters |

Details

This plots expression of a single gene. Fitted model parameters can either be specified manually or can be extracted from the `data.frame` returned by `switchde` using the function `extract_pars`.

Value

A `ggplot2` plot of gene expression and MLE sigmoid

Examples

```
data(synth_gex)
data(ex_pseudotime)
sde <- switchde(synth_gex, ex_pseudotime)
switchplot(synth_gex[1, ], ex_pseudotime, extract_pars(sde, "Gene1"))
```

| | |
|-----------|---|
| synth_gex | <i>Synthetic gene expression matrix</i> |
|-----------|---|

Description

A matrix containing some synthetic gene expression data for 100 cells and 12 genes

Usage

```
synth_gex
```

Format

An object of class `matrix` with 12 rows and 100 columns.

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synth_gex

Value

A 12 by 100 matrix

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