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)

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Depends R (>= 3.4), SingleCellExperiment

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

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example_sigmoid  Example sigmoid plot

description
Plot an example sigmoid function. For demonstration and documentation.

usage
example_sigmoid()

value
An object of class ggplot

examples
example_sigmoid()

extract_pars  Extract parameters from fitted model

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 $\mu_0, k$ and $t_0$

### Examples

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

---

#### ex_pseudotime

**Synthetic gene pseudotimes**

**Description**

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

**Usage**

```r
ex_pseudotime
```

**Format**

An object of class `array` of length 100.

**Value**

A vector of length 100

---

#### fit_nzi_model

**Fit a (non-zero-inflated) model for a single gene**

**Description**

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

**Usage**

```r
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 $\mu_0$, $k_0$, $\sigma^2$ and a p-value

Examples

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

---

Description

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

Usage

```r
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 $\mu_0$, $k_0$, $\lambda$, $\sigma^2$ and a p-value

Examples

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

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

Calculate the mean vector given parameters and pseudotimes (mu0 formulation)

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 mu_0, k, t0

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**

```r
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
  - 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 SingleCellExperiment from package SingleCellExperiment
- `pseudotime`: A pseudotime vector with a pseudotime corresponding to every cell. Can be `NULL` if object is of class SCESet and `colData(sce)$pseudotime` 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 SingleCellExperiment 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**

```r
data(synth_gex)
data(ex_pseudotime)
sde <- switchde(synth_gex, ex_pseudotime)
```
### switchplot

**Plot gene behaviour**

**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**

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

### synth_gex

**Synthetic gene expression matrix**

**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.
**Value**

A 12 by 100 matrix
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