

# Package ‘timeSeq’

July 17, 2017

**Type** Package

**Title** Detecting Differentially Expressed Genes in Time Course RNA-Seq Data

**Version** 1.0.3

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**Description** Uses a negative binomial mixed-effects (NBME) model to detect nonparallel differential expression(NPDE) genes and parallel differential expression(PDE) genes in the time course RNA-seq data.

**Depends** R (>= 3.0.1)

**Imports** gss, lattice, pheatmap, reshape, grDevices, graphics

**License** GPL (>= 2)

**Suggests** rmarkdown, knitr

**VignetteBuilder** knitr

**Repository** CRAN

**NeedsCompilation** no

**RoxygenNote** 5.0.1

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timeSeq\_1.0.3-package *Statistical Inference for Time Course RNA-Seq Data using a Negative Binomial Mixed-Effects Model*

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### Description

In this package, we propose a negative binomial mixed-effects (NBME) model to identify differentially expressed (DE) genes, including nonparallel differentially expressed (NPDE) and parallel differentially expressed (PDE) genes, in time course RNA-seq data.

### Details

Package: timeSeq  
Type: Package  
Version: 1.0.3  
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### Author(s)

Fan Gao and Xiaoxiao Sun  
Maintainer: Fan Gao <fangaozh@gmail.com>

### References

Sun, Xiaoxiao, David Dalpiaz, Di Wu, Jun S. Liu, Wenxuan Zhong, and Ping Ma. "Statistical inference for time course RNA-Seq data using a negative binomial mixed-effect model." *BMC Bioinformatics*, 17(1):324, 2016.

Chong Gu. Model diagnostics for smoothing spline ANOVA models. *Canadian Journal of Statistics*, 32(4):347-358, 2004.

Chong Gu. *Smoothing spline ANOVA models*. Springer, second edition, 2013.

Chong Gu and Ping Ma. Optimal smoothing in nonparametric mixed-effect models. *Annals of Statistics*, pages 1357-1379, 2005a.

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pAbp

*Example Data in Vignette*

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### Description

The data 'pAbp'(list) has 5 arguments, including 'data.count', 'exon.length', 'gene.names', 'group.label', 'reads'. Please refer to 'timeSeq.Rd' for more information.

**Usage**

```
data(pAbp)
```

**Format**

A list with 5 arguments:

**Examples**

```
data(pAbp)
str(pAbp)
```

---

simulate.dt

*Example Data in Vignette*

---

**Description**

The data 'simulate.dt'(list) has 4 arguments, including 'data.count', 'gene.names', 'group.label', 'reads'. Please refer to 'timeSeq.Rd' for more information.

**Usage**

```
data(simulate.dt)
```

**Format**

A list with 5 arguments:

**Examples**

```
data(simulate.dt)
str(simulate.dt)
```

---

timeSeq

*Statistical Inference for Time Course RNA-Seq Data using a Negative Binomial Mixed-Effects Model*

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**Description**

Accurately identifying differentially expressed (DE) genes from time course RNA-seq data has been of tremendous significance in creating a global picture of cellular function. DE genes from the time course RNA-seq data can be classified into two types, parallel DE genes (PDE) and non-parallel DE (NPDE) genes. The former are often biologically irrelevant, whereas the latter are often biologically interesting. In this package, we propose a negative binomial mixed-effects (NBME) model to identify both PDE and NPDE genes in time course RNA-seq data.

**Usage**

```
timeSeq(data.count, group.label, gene.names, exon.length = NULL, exon.level = TRUE)
```

**Arguments**

data.count	a n by p matrix of expression values.
group.label	a vector indicating the experimental conditions of each time point.
gene.names	a vector containing all the gene names.
exon.length	a vector containing the length of exons, only used in exon level data.
exon.level	logical:indicating if this is an exon level dataset. Default is TRUE.

**Details**

Nonparallel differential expression(NPDE) genes and parallel differential expression(PDE) genes detection.

**Value**

A list with components

sorted	an object returned by NPDE.sort function. It contains sorted Kullback Leibler Ratios(KLRs) for identifying DE genes
count	the number of exons for each gene.
NPDE.ratio	the NPDE ratios.
PDE.ratio	the PDE ratios.
genenames	gene names.
table	gene expression values.
data	a n by p matrix of expression values.
gene.names	a vector including all the gene names.
exon.length	length of exons.
group.label	a vector indicating the experimental conditions of each time point.
group.length	the total number of time points.
group1.length	the number of time points of condition one.
group2.length	the number of time points of condition two.
exon.level	logical:indicating if this is an exon level dataset. Default is TRUE.

**Author(s)**

Fan Gao and Xiaoxiao Sun

## References

Sun, Xiaoxiao, David Dalpiaz, Di Wu, Jun S. Liu, Wenxuan Zhong, and Ping Ma. "Statistical inference for time course RNA-Seq data using a negative binomial mixed-effect model." *BMC Bioinformatics*, 17(1):324, 2016.

Chong Gu. Model diagnostics for smoothing spline ANOVA models. *Canadian Journal of Statistics*, 32(4):347-358, 2004.

Chong Gu. Smoothing spline ANOVA models. Springer, second edition, 2013.

Chong Gu and Ping Ma. Optimal smoothing in nonparametric mixed-effect models. *Annals of Statistics*, 1357-1379, 2005.

## Examples

```
##Exon level data
data(pAbp)
attach(pAbp)
model.fit <- timeSeq(data.count, group.label, gene.names, exon.length)
detach(pAbp)

##Gene level data (three replicates)
data(simulate.dt)
attach(simulate.dt)
model.fit <- timeSeq(data.count, group.label, gene.names, exon.level=FALSE)
```

---

timeSeq.heatmap

*Heatmap of the Most Significant NDPE Genes*

---

## Description

Plots the heatmap for the significant NDPE genes.

## Usage

```
timeSeq.heatmap(timeSeq.obj, n)
```

## Arguments

timeSeq.obj     an object returned by timeSeq function  
n                the number of the most significant NPDE genes. It must be a positive integer.

## Author(s)

Fan Gao and Xiaoxiao Sun

## References

- Sun, Xiaoxiao, David Dalpiaz, Di Wu, Jun S. Liu, Wenxuan Zhong, and Ping Ma. "Statistical inference for time course RNA-Seq data using a negative binomial mixed-effect model." *BMC Bioinformatics*, 17(1):324, 2016.
- Chong Gu. Model diagnostics for smoothing spline ANOVA models. *Canadian Journal of Statistics*, 32(4):347-358, 2004.
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- Chong Gu and Ping Ma. Optimal smoothing in nonparametric mixed-effect models. *Annals of Statistics*, pages 1357-1379, 2005a.

## Examples

```
data(simulate.dt)
attach(simulate.dt)
model.fit <- timeSeq(data.count, group.label, gene.names, exon.level = FALSE)
timeSeq.heatmap(model.fit, n = 10)
```

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timeSeq.screepLOT	<i>Scree Plot of Kullback Leibler Distance Ratios</i>
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## Description

Plot the scree plot for all genes in the dataset.

## Usage

```
timeSeq.screepLOT(timeSeq.obj, type = c("barplot", "lines"))
```

## Arguments

timeSeq.obj	an object returned by timeSeq function
type	type of plot: "barplot" for bar plot and "lines" for line graph.

## Author(s)

Fan Gao and Xiaoxiao Sun

## References

- Sun, Xiaoxiao, David Dalpiaz, Di Wu, Jun S. Liu, Wenxuan Zhong, and Ping Ma. "Statistical inference for time course RNA-Seq data using a negative binomial mixed-effect model." *BMC Bioinformatics*, 17(1):324, 2016.
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Chong Gu. Smoothing spline ANOVA models. Springer, second edition, 2013.

Chong Gu and Ping Ma. Optimal smoothing in nonparametric mixed-effect models. *Annals of Statistics*, pages 1357-1379, 2005a.

## Examples

```
data(simulate.dt)
attach(simulate.dt)
model.fit <- timeSeq(data.count, group.label, gene.names, exon.level = FALSE)
timeSeq.screepplot(model.fit, "lines")
```

---

timeSeq.sort

*Sort NPDE Genes by Kullback Leibler Distance Ratios*

---

## Description

Sort all genes in the dataset by their Kullback Leibler distance ratios.

## Usage

```
timeSeq.sort(genenames, NPDE.ratio, PDE.ratio, table, count)
```

## Arguments

genenames	a vector of gene names
NPDE.ratio	a vector of Kullback Leibler distance ratios for NPDE genes
PDE.ratio	a vector of Kullback Leibler distance ratios for PDE genes
table	gene expression values.
count	the number of exons for each gene.

## Value

A list with components

NPDE_list	dataframe of NPDE genes sorted by KLRs
PDE_list	dataframe of PDE genes sorted by KLRs
table1	gene expression values for each gene, corresponding to NPDE_list
table2	gene expression values for each gene, corresponding to PDE_list

## Author(s)

Fan Gao and Xiaoxiao Sun

**References**

Sun, Xiaoxiao, David Dalpiaz, Di Wu, Jun S. Liu, Wenxuan Zhong, and Ping Ma. "Statistical inference for time course RNA-Seq data using a negative binomial mixed-effect model." *BMC Bioinformatics*, 17(1):324, 2016.

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