

Package ‘OmicsLonDA’

July 3, 2022

Type Package

Title Omics Longitudinal Differential Analysis

Version 1.13.0

Date 2021-11-21

Author Ahmed A. Metwally, Tom Zhang, Michael Snyder

Maintainer Ahmed A. Metwally <ametwall@stanford.edu>

URL <https://github.com/aametwally/OmicsLonDA>

BugReports <https://github.com/aametwally/OmicsLonDA/issues>

Description Statistical method that provides robust identification of time intervals where omics features (such as proteomics, lipidomics, metabolomics, transcriptomics, microbiome, as well as physiological parameters captured by wearable sensors such as heart rhythm, body temperature, and activity level) are significantly different between groups.

License MIT + file LICENSE

Depends R(>= 3.6)

Imports SummarizedExperiment, gss, plyr, zoo, pracma, ggplot2, BiocParallel, parallel, grDevices, graphics, stats, utils, methods, BiocGenerics

Suggests knitr, rmarkdown, testthat, devtools, BiocManager

biocViews TimeCourse, Survival, Microbiome, Metabolomics, Proteomics, Lipidomics, Transcriptomics, Regression

NeedsCompilation no

Encoding UTF-8

LazyData true

RoxygenNote 6.1.1

VignetteBuilder knitr

git_url <https://git.bioconductor.org/packages/OmicsLonDA>

git_branch master

git_last_commit 0563fc5

git_last_commit_date 2022-04-26

Date/Publication 2022-07-03

R topics documented:

adjustBaseline	2
curveFitting	3
findSigInterval	4
omicslonda	4
omicslonda_data_example	6
permutationMC	6
testStat	7
testStatPermutation	8
visualizeArea	9
visualizeFeature	10
visualizeFeatureSpline	11
visualizeTestStatHistogram	12

Index	13
--------------	-----------

adjustBaseline	<i>Adjust for baseline differences using Centered-Log Ratio</i>
----------------	---

Description

Adjust for baseline differences using Centered-Log Ratio

Usage

```
adjustBaseline(se_object = NULL)
```

Arguments

se_object SummarizedExperiment object contains omics count/level matrix and metadata

Value

a SummarizedExperiment object with the adjusted baseline assay

References

Ahmed Metwally (ametwall@stanford.edu)

Examples

```
data(omicslonda_data_example)
adjusted_se = adjustBaseline(omicslonda_data_example$omicslonda_se_object)
```

curveFitting	<i>Fit longitudinal data</i>
--------------	------------------------------

Description

Fits longitudinal samples from the same group using negative binomial smoothing splines or LOWESS

Usage

```
curveFitting(formula = Count ~ Time, df = "NULL",
             fit.method = "ssgaussian", points = NULL)
```

Arguments

formula	formula to be passed to the regression model
df	dataframe has the Count, Group, Subject, Time
fit.method	fitting method (ssgaussian)
points	points at which the prediction should happen

Value

a list that contains fitted smoothing spline for each group along with 95

References

Ahmed Metwally (ametwall@stanford.edu)

Examples

```
library(SummarizedExperiment)
data("omicslonda_data_example")
omicslonda_se_object_adjusted = adjustBaseline(
  se_object = omicslonda_data_example$omicslonda_se_object)
se_object = omicslonda_se_object_adjusted[1,]
dt = data.frame(colData(se_object))
dt$Count = as.vector(assay(se_object))
Group = as.character(dt$Group)
group.levels = sort(unique(Group))
gr.1 = as.character(group.levels[1])
gr.2 = as.character(group.levels[2])
df = dt
levels(df$Group) = c(levels(df$Group), "0", "1")
df$Group[which(df$Group == gr.1)] = 0
df$Group[which(df$Group == gr.2)] = 1
group.0 = df[df$Group == 0, ]
group.1 = df[df$Group == 1, ]
points = seq(1, 500)
model = curveFitting(formula = Count ~ Time, df = df, fit.method = "ssgaussian", points = points)
```

findSigInterval	<i>Find Significant Interval based on testStat</i>
-----------------	--

Description

Find Significant Interval based on testStat

Usage

```
findSigInterval(adjusted.pvalue, threshold = 0.05, sign)
```

Arguments

adjusted.pvalue	
threshold	vector of the adjusted p-value
sign	p-value cut off
	vector hold area sign of each time interval

Value

returns a list of the start and end points of all significant time intervals

References

Ahmed Metwally (ametwall@stanford.edu)

Examples

```
library(SummarizedExperiment)
padjusted = abs(rnorm(10, mean = 0.05, sd = 0.04))
sign = sample(x = c(1,-1), 10, replace = TRUE)
intervals = findSigInterval(adjusted.pvalue = padjusted,
                           threshold = 0.05, sign = sign)
```

omicslonda	<i>Omics Longitudinal Differential Analysis for one feature</i>
------------	---

Description

Find significant time intervals of omic feature

Usage

```
omicslonda(se_object = NULL, n.perm = 500, fit.method = "ssgaussian",
           points = NULL, text = "FeatureName", parall = FALSE,
           pvalue.threshold = 0.05, adjust.method = "BH", time.unit = "days",
           ylabel = "Normalized Count", col = c("blue", "firebrick"),
           prefix = "Test")
```

Arguments

<code>se_object</code>	SummarizedExperiment object contains omics count/level matrix and metadata contains (subject, time, group, and any any other covariates)
<code>n.perm</code>	number of permutations.
<code>fit.method</code>	fitting method (ssgaussian).
<code>points</code>	points at which the prediction should happen.
<code>text</code>	Feature's name.
<code>parall</code>	boolean to indicate whether to use multicore.
<code>pvalue.threshold</code>	p-value threshold cutoff for identifying significant time intervals.
<code>adjust.method</code>	multiple testing correction method.
<code>time.unit</code>	time unit used in the Time vector (hours, days, weeks, months, etc.)
<code>ylabel</code>	text to be shown on the y-axis of all generated figures (default: "Normalized Count")
<code>col</code>	two color to be used for the two groups (eg., c("red", "blue")).
<code>prefix</code>	prefix to be used to create directory for the analysis results

Value

a list of the significant time intervals for the tested feature, fitted model for each group, null distribution of the test statistic of the tested feature, and the original input data.

References

Ahmed Metwally (ametwall@stanford.edu)

Examples

```
library(SummarizedExperiment)
data(omicslonda_data_example)
omicslonda_se_object_adjusted = adjustBaseline(
  se_object = omicslonda_data_example$omicslonda_se_object)
omicslonda_test_object = omicslonda_se_object_adjusted[1,]
points = seq(1, 500, length.out = 500)
res = omicslonda(se_object = omicslonda_test_object, n.perm = 10,
  fit.method = "ssgaussian", points = points, text = "Feature_1",
  parall = FALSE, pvalue.threshold = 0.05,
  adjust.method = "BH", time.unit = "days",
  ylabel = "Normalized Count",
  col = c("blue", "firebrick"), prefix = tempfile())
```

omicslonda_data_example
Simulated dataset

Description

Datasets used for examples/testing OmicsLonDA

Usage

omicslonda_data_example

Format

A data frame with 10 simulated features

permutationMC *Permute group labels*

Description

Permutes the group label of the samples in order to construct the testStatistics empirical distribution

Usage

```
permutationMC(formula = Count ~ Time, perm.dat = NULL, n.perm = 500,
  fit.method = "ssgaussian", points, parall = FALSE, prefix = "Test")
```

Arguments

formula	formula to be passed to the regression model
perm.dat	dataframe has the Count, Group, Subject, Time
n.perm	number of permutations
fit.method	The fitting method (ssgaussian)
points	The points at which the prediction should happen
parall	boolean to indicate whether to use multicore.
prefix	prefix to be used to create directory for the analysis results

Value

a list of the fitted model for each group for all the permutations

References

Ahmed Metwally (ametwall@stanford.edu)

Examples

```

library(SummarizedExperiment)
data("omicslonda_data_example")
omicslonda_se_object_adjusted = adjustBaseline(
  se_object = omicslonda_data_example$omicslonda_se_object)
omicslonda_test_object = omicslonda_se_object_adjusted[1,]
se_object = omicslonda_test_object
dt = data.frame(colData(se_object))
dt$Count = as.vector(assay(se_object))
Group = as.character(dt$Group)
group.levels = sort(unique(Group))
gr.1 = as.character(group.levels[1])
gr.2 = as.character(group.levels[2])
df = dt
levels(df$Group) = c(levels(df$Group), "0", "1")
df$Group[which(df$Group == gr.1)] = 0
df$Group[which(df$Group == gr.2)] = 1
group.0 = df[df$Group == 0, ]
group.1 = df[df$Group == 1, ]
points = seq(100, 130)
perm = permutationMC(formula = Count ~ Time, perm.dat = df, n.perm = 10,
  fit.method = "ssgaussian", points = points,
  parall = FALSE, prefix = tempfile())

```

testStat

Calculate Test-Statistic of each feature's time interval

Description

Calculate Test-Statistic of each feature's time interval

Usage

```
testStat(curve.fit.df)
```

Arguments

curve.fit.df gss data object of the fitted spline

Value

a list that has the test statistic for each time interval

References

Ahmed Metwally (ametwall@stanford.edu)

Examples

```
library(SummarizedExperiment)
data("omicslonda_data_example")
model = omicslonda_data_example$omicslonda_results$model
stat = testStat(model)$testStat
```

testStatPermutation *Calculate testStat of each feature's time interval for all permutations*

Description

Calculate testStat of each feature's time interval for all permutations

Usage

```
testStatPermutation(perm)
```

Arguments

perm list has all the permuted models

Value

a list of test statistic for each time interval for all all permutations

References

Ahmed Metwally (ametwall@stanford.edu)

Examples

```
library(SummarizedExperiment)
data("omicslonda_data_example")
omicslonda_se_object_adjusted = adjustBaseline(
  se_object = omicslonda_data_example$omicslonda_se_object)
omicslonda_test_object = omicslonda_se_object_adjusted[1,]
se_object = omicslonda_test_object
dt = data.frame(colData(se_object))
dt$Count = as.vector(assay(se_object))
Group = as.character(dt$Group)
group.levels = sort(unique(Group))
gr.1 = as.character(group.levels[1])
gr.2 = as.character(group.levels[2])
df = dt
levels(df$Group) = c(levels(df$Group), "0", "1")
df$Group[which(df$Group == gr.1)] = 0
df$Group[which(df$Group == gr.2)] = 1
group.0 = df[df$Group == 0, ]
group.1 = df[df$Group == 1, ]
```



```

points = seq(100, 130)
perm = permutationMC(formula = Count ~ Time, perm.dat = df, n.perm = 10,
                     fit.method = "ssgaussian", points = points,
                     parall = FALSE, prefix = tempfile())
test.stat.prem = testStatPermutation(perm)

```

visualizeArea	<i>Visualize significant time interval</i>
---------------	--

Description

Visualize significant time interval

Usage

```

visualizeArea(omicslonda_object = NULL, fit.method = "ssgaussian",
             text = "FeatureName", unit = "days", ylabel = "Normalized Count",
             col = c("blue", "firebrick"), prefix = "Test")

```

Arguments

omicslonda_object	The returned object from omicslonda analysis
fit.method	Fitting method (ssgaussian)
text	Feature name
unit	time unit used in the Time vector (hours, days, weeks, months, etc.)
ylabel	text to be shown on the y-axis of all generated figures (default: "Normalized Count")
col	two color to be used for the two groups (eg., c("red", "blue")).
prefix	prefix to be used to create directory for the analysis results

Value

null

References

Ahmed Metwally (ametwall@stanford.edu)

Examples

```

library(SummarizedExperiment)
data(omicslonda_data_example)
visualizeArea(omicslonda_object = omicslonda_data_example$omicslonda_results,
             fit.method = "ssgaussian",
             text = "Feature_1", unit = "days",
             ylabel = "Normalized Count", col =
             c("blue", "firebrick"), prefix = tempfile())

```

visualizeFeature	<i>Visualize Longitudinal Feature</i>
------------------	---------------------------------------

Description

Visualize Longitudinal Feature

Usage

```
visualizeFeature(se_object = NULL, text = "featureName",  
  unit = "days", ylabel = "Normalized Count", col = c("blue",  
  "firebrick"), prefix = "Test")
```

Arguments

se_object	SummarizedExperiment object contains omics count/level matrix and metadata
text	feature name
unit	time interval unit
ylabel	text to be shown on the y-axis of all generated figures (default: "Normalized Count")
col	two color to be used for the two groups (eg., c("red", "blue")).
prefix	prefix to be used to create directory for the analysis results

Value

null

References

Ahmed Metwally (ametwall@stanford.edu)

Examples

```
library(SummarizedExperiment)  
data("omicslonda_data_example")  
omicslonda_se_object_adjusted = adjustBaseline(  
  se_object = omicslonda_data_example$omicslonda_se_object)  
omicslonda_test_object = omicslonda_se_object_adjusted[1,]  
visualizeFeature(se_object = omicslonda_test_object, text = "Feature_1",  
  unit = "days", ylabel = "Normalized Count",  
  col = c("blue", "firebrick"), prefix = tempfile())
```

 visualizeFeatureSpline

Visualize the feature trajectory with the fitted Splines

Description

Plot the longitudinal features along with the fitted splines

Usage

```
visualizeFeatureSpline(se_object = NULL, omicslonda_object = NULL,
  fit.method = "ssgaussian", text = "FeatureName", unit = "days",
  ylabel = "Normalized Count", col = c("blue", "firebrick"),
  prefix = "Test")
```

Arguments

se_object	SummarizedExperiment object contains omics count/level matrix and metadata
omicslonda_object	The returned object from omicslonda analysis
fit.method	The fitting method (ssgaussian)
text	feature name
unit	time unit used in Time vector (hours, days, weeks, months, etc.)
ylabel	text to be shown on the y-axis of all generated figures (default: "Normalized Count")
col	two color to be used for the two groups (eg., c("red", "blue")).
prefix	prefix to be used to create directory for the analysis results

Value

null

References

Ahmed Metwally (ametwall@stanford.edu)

Examples

```
library(SummarizedExperiment)
data(omicslonda_data_example)
omicslonda_se_object_adjusted = adjustBaseline(
  se_object = omicslonda_data_example$omicslonda_se_object)
omicslonda_test_object = omicslonda_se_object_adjusted[1,]
points = seq(1, 500, length.out = 500)
res = omicslonda(se_object = omicslonda_test_object, n.perm = 10,
  fit.method = "ssgaussian", points = points, text = "Feature_1",
```

```

parall = FALSE, pvalue.threshold = 0.05,
adjust.method = "BH", time.unit = "days",
ylabel = "Normalized Count",
col = c("blue", "firebrick"), prefix = "OmicsLonDA_example")
visualizeFeatureSpline(se_object = omicslonda_test_object, omicslonda_object =
omicslonda_data_example$omicslonda_results, fit.method = "ssgaussian",
text = "Feature_1", unit = "days",
ylabel = "Normalized Count",
col = c("blue", "firebrick"),
prefix = tempfile())

```

visualizeTestStatHistogram

Visualize test statistics empirical distribution

Description

Visualize test statistics empirical distribution

Usage

```

visualizeTestStatHistogram(omicslonda_object = NULL,
text = "FeatureName", fit.method = "ssgaussian", prefix = "Test")

```

Arguments

omicslonda_object	The returned object from omicslonda analysis
text	Feature name
fit.method	fitting method
prefix	prefix to be used to create directory for the analysis results

Value

null

References

Ahmed Metwally (ametwall@stanford.edu)

Examples

```

library(SummarizedExperiment)
data(omicslonda_data_example)
visualizeTestStatHistogram(omicslonda_object = omicslonda_data_example$omicslonda_results,
text = "Feature_1",
fit.method = "ssgaussian", prefix = tempfile())

```

Index

* datasets

- omicslonda_data_example, 6
- adjustBaseline, 2
- curveFitting, 3
- findSigInterval, 4
- omicslonda, 4
- omicslonda_data_example, 6
- permutationMC, 6
- testStat, 7
- testStatPermutation, 8
- visualizeArea, 9
- visualizeFeature, 10
- visualizeFeatureSpline, 11
- visualizeTestStatHistogram, 12