Package ‘neutralitytestr’

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Title Test for a Neutral Evolutionary Model in Cancer Sequencing Data

Version 0.0.3

Description Package takes frequencies of mutations as reported by high throughput sequencing data from cancer and fits a theoretical neutral model of tumour evolution. Package outputs summary statistics and contains code for plotting the data and model fits. See Williams et al 2016 <doi:10.1038/ng.3489> and Williams et al 2017 <doi:10.1101/096305> ther details of the method.

Depends R (>= 3.4)

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Encoding UTF-8

LazyData true

Imports dplyr, ggplot2, scales, pracma, ggpmisc, cowplot

Suggests knitr, rmarkdown, testthat

VignetteBuilder knitr

URL `https://github.com/marcjwilliams1/neutralitytestr`

BugReports `https://github.com/marcjwilliams1/neutralitytestr/issues`

RoxygenNote 7.1.1

NeedsCompilation no

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Repository CRAN

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`lsq_plot` *Plot cumulative distribution* `lsq_plot` *Plots the cumulative distribution of the data as well as the best fit linear model line.*

Description

Plot cumulative distribution `lsq_plot` Plots the cumulative distribution of the data as well as the best fit linear model line.

Usage

```
lsq_plot(object)
```

Arguments

`object`	neutrality test object

Value

ggplot object.

Examples

```
lsq_plot(neutralitytest(VAFselection, fmin = 0.1, fmax = 0.25))
```

`neutralitytest` *Testing for neutrality on cancer sequencing data*

Description

`neutralitytest` returns a neutralitytest object which contains the result of various test statistics to test for neutrality as described in Williams et al. Nature Genetics 2018. WARNING: This package has been superseded by MOBSTER, see Caravagna et al. Nature Genetics 2020.

Usage

```
neutralitytest(
  VAF,
  fmin = 0.1,
  fmax = 0.25,
  read_depth = NULL,
  rho = 0,
  cellularity = 1,
  ploidy = 2
)
```

Arguments

`VAF`	Vector of variant allele frequencies (VAFs) from a deep sequencing experiment, numbers should be between 0 and 1
`fmin`	Minimum VAF of integration range, default is 0.1
`fmax`	Maximum VAF of integration range, default is 0.25
`read_depth`	Read depth of sample, if this is specified it will be used to calculate an approptiate integration range. default is NULL in which case the default or inputted fmin and fmax will be used.
`rho`	Overdispersion of sample if known, default is 0.0. Will be used to calculate integration range if read_depth != NULL
`cellularity`	Cellularity of sample, default is 1.0. Will be used to calculate integration range if read_depth != NULL
`ploidy`	Ploidy of the genome, default is 2. Ideally mutations should be filtered for this ploidy before running the test. Will be used to calculate integration range if read_depth != NULL

Value

neutralitytest object which contains test statistics which tests if the sequencing data is consistent a neutral evolutionary model. Test statistics are area between theoretical and empirical curves, kolmogorov distance, mean distance and R^2 statistics from linear model fit. Also returns an estimate of the mutation rate per tumour tumour doubling, the raw VAFs and cumulative distribution

Examples

```
neutralitytest(runif(100))
neutralitytest(VAFselection, fmin = 0.1, fmax = 0.25)
neutralitytest(VAFneutral, read_depth = 100.0, cellularity = 0.8)
```

`neutralitytestr` `neutralitytestr` *package*

Description

Package to test a neutral evolutionary model on deep sequencing data.

Details

See the README on GitHub

`normalized_plot` *Plot normalized cumulative distribution* `normalized_plot` *Plots the (normalized) cumulative distribution of the data as well as the theoretical expectation from a neutral evolutionary model.*

Description

Plot normalized cumulative distribution `normalized_plot` Plots the (normalized) cumulative distribution of the data as well as the theoretical expectation from a neutral evolutionary model.

Usage

```
normalized_plot(object)
```

Arguments

`object`	neutrality test object

Value

ggplot object.

Examples

```
normalized_plot(neutralitytest(VAFselection, fmin = 0.1, fmax = 0.25))
```

`plot_all` *Plot all plots in the package and make composite figure.* `plot_all` *Plots histogram, linear model best fit plot and normalized plot and plot and makes composite figure.*

Description

Plot all plots in the package and make composite figure. `plot_all` Plots histogram, linear model best fit plot and normalized plot and plot and makes composite figure.

Usage

```
plot_all(object)
```

Arguments

`object`	neutrality test object

Value

ggplot object.

Examples

```
plot_all(neutralitytest(VAFselection, fmin = 0.1, fmax = 0.25))
```

`VAFneutral` *Synthetic sequencing data generated from a evolutionary based cancer simulation.*

Description

This data is generated from a neutral evolutionary model where all subclonal mutations are neutral.

Usage

```
VAFneutral
```

Format

A vector with variant allele frequencies (VAFs) ranging from 0 to 1

Source

Generated using cancer sequencing simulation `https://github.com/marcjwilliams1/CancerSeqSim.jl`

`VAFselection` *Synthetic sequencing data generated from a evolutionary based cancer simulation.*

Description

This data is generated from an evolutionary model where there is on subclonal population and all other mutations are neutral passengers.

Usage

```
VAFselection
```

Format

A vector with variant allele frequencies (VAFs) ranging from 0 to 1

Source

Generated using cancer sequencing simulation https://github.com/marcjwilliams1/CancerSeqSim.jl

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`vaf_histogram` *Plot VAF histogram* `vaf_histogram` *Plots a histogram of the variant allele frequencies.*

Description

Plot VAF histogram `vaf_histogram` Plots a histogram of the variant allele frequencies.

Usage

```
vaf_histogram(object)
```

Arguments

`object`	neutrality test object

Value

ggplot object.

Examples

```
vaf_histogram(neutralitytest(VAFselection, fmin = 0.1, fmax = 0.25))
```

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