Package 'LRcontrast'

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Type Package

Title Dose Response Signal Detection under Model Uncertainty

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Imports DoseFinding

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Description Provides functions for calculating test statistics, simulating quantiles
and simulating p-values of likelihood ratio contrast tests in regression models
with a lack of identifiability.

License GPL-3

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LRcontrast-package　　　*Dose Response Signal Detection under Model Uncertainty*

Description

Provides functions for calculating test statistics, simulating quantiles and simulating p-values of likelihood ratio contrast tests in regression models with a lack of identifiability.

Details

Package:	LRcontrast
Type:	Package
Version:	1.0
Date:	2015-06-21
License:	GPL-3

The main functions are:

qLRcontrast: Simulates quantiles of likelihood ratio contrast tests

sLRcontrast: Calculates test statistics of likelihood ratio contrast tests

pLRcontrast: Simulates p-values of likelihood ratio contrast tests

Author(s)

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References

Dette, H., Titoff, S., Volgushev, S. and Bretz, F. (2015), Dose response signal detection under model uncertainty. Biometrics. doi: 10.1111/biom.12357

See Also

[DoseFinding](#)

Examples

```
# Simulate the 90%, 95% and 99% quantiles of the LR contrast tests where the specified
# models are competing against each other.
# The size of each dose group is equal in this case.

qLRcontrast(dose = c(0, 0.05, 0.2, 0.6, 1), probs = c(0.9, 0.95, 0.99), weight
            = c(0.2, 0.2, 0.2, 0.2, 0.2), models = c("linear", "emax",
            "exponential", "linlog"), nsim = 10)

# Calculate the LR test statistics with the same underlying models.
```

```
# In this case the data is generated by the constant model, i.e. the
# null hypothesis of no dose response is true.

resp <- rnorm(n = 50, mean = 0.2)
dose <- c(rep(0, 10), rep(0.05, 10), rep(0.2, 10), rep(0.6, 10), rep(1, 10))

sLRcontrast(dose = dose, resp = resp, models = c("linear", "emax", "exponential", "linlog"))

# Calculate the p-values in this scenario

pLRcontrast(dose = dose, resp = resp, models = c("linear", "emax", "exponential", "linlog"),
            nsim = 10)
```

---

pLRcontrast	*Simulate p-values for LR contrast tests in regression models with a lack of identifiability.*

Description

The function simulates p-values for LR contrast tests. The competing models can be specified by the argument 'models' (see [drmodels](#)) and by 'nsim' you can specify how many simulations should be done. It is recommended to do about 10000 but notice that the simulation can take some time. If the parameter 'info' is set 'TRUE', information of the progress will be shown.

Usage

```
pLRcontrast(dose, resp, models, off = 0.01 * max(dose), scal = 1.2 * max(dose),
            nsim = 1000, info = TRUE)
```

Arguments

dose, resp	Vectors of equal length specifying dose and response values.
models	A subvector of c("linear", "emax", "exponential", "linlog", "sigEmax", "quadratic", "betaMod", "logistic") (see [drmodels](#)) which specifies the competing models.
off	Positive and fixed offset parameter in the 'linlog' model (see [drmodels](#)).
scal	Positive and fixed dose scaling parameter in the 'betaMod' with '$scal \geq \max(dose)$' (see [drmodels](#)).
nsim	A positive integer which specifies the number of simulations that should be done.
info	Logical value which indicates whether progress information should be shown.

Value

A matrix containing the unadjusted and adjusted p-value for one model in each row.

Author(s)

Kevin Kokot

References

Dette, H., Titoff, S., Volgushev, S. and Bretz, F. (2015), Dose response signal detection under model uncertainty. Biometrics. doi: 10.1111/biom.12357

See Also

DoseFinding

Examples

```
# In this case the data is generated by the constant model, i.e. the
# null hypothesis of no dose response is true.

resp <- rnorm(n = 50, mean = 0.2)
dose <- c(rep(0, 10), rep(0.05, 10), rep(0.2, 10), rep(0.6, 10), rep(1, 10))

# Calculate the p-values in this scenario

pLRcontrast(dose = dose, resp = resp, models = c("linear", "emax",
            "exponential", "linlog"), nsim = 10)
```

---

qLRcontrast	*Simulate quantiles of LR contrast tests in regression models with a lack of identifiability.*

Description

The function simulates the desired quantiles of the distribution of LR contrast tests. The competing models can be specified by the argument 'models' (see drmodels). The argument 'dose' is the vector of the different unique dose-levels and 'weight' specifies the weight proportion of each dose group. By 'nsim' you can specify how many simulation should be done. It is recommended to do about 10000 but notice that the simulation can take some time. If the parameter 'info' is set 'TRUE', information of the progress will be shown.

Usage

```
qLRcontrast(dose, probs, models, weight = rep(1/length(dose), length(dose)),
         off = 0.01 * max(dose), scal = 1.2 * max(dose), nsim = 10000, info = TRUE)
```

Arguments

dose	A vector which contains the unique dose-levels.
probs	A vector of probabilities with values in $[0, 1]$ specifying which quantiles should be calculated.
models	A subvector of c("linear", "emax", "exponential", "linlog", "sigEmax", "quadratic", "betaMod", "logistic") (see drmodels) which specifies the competing models.

weight	A vector with values in $[0, 1]$ with 'sum(weight) = 1'. The i-th entry specifies the weight proportion of the i-th dose group.
off	Positive and fixed offset parameter in the 'linlog' model (see [drmodels](#)).
scal	Positive and fixed dose scaling parameter in the 'betaMod' with '$scal \geq \max(\text{dose})$' (see [drmodels](#)).
nsim	A positive integer which specifies the number of simulations that should be done.
info	Logical value which indicates whether progress information should be shown.

Value

A matrix containing the different quantiles for one model in each row. The last row contains the quantiles of the maximum statistic.

Author(s)

Kevin Kokot

References

Dette, H., Titoff, S., Volgushev, S. and Bretz, F. (2015), Dose response signal detection under model uncertainty. Biometrics. doi: 10.1111/biom.12357

See Also

[DoseFinding](#)

Examples

```
# Simulate the 90%, 95% and 99% quantiles of the LR contrast tests where the specified
# models are competing against each other.
# The size of each dose group is equal in this case.

qLRcontrast(dose = c(0, 0.05, 0.2, 0.6, 1), probs = c(0.9, 0.95, 0.99),
            weight = c(0.2, 0.2, 0.2, 0.2, 0.2), models = c("linear", "emax",
            "exponential", "linlog"), nsim = 10)
```

---

sLRcontrast	*Calculate LR test statistics*

Description

The function calculates LR test statistics for the competing models which are defined by the argument 'models' (see [drmodels](#)).

Usage

```
sLRcontrast(dose, resp, models, off = 0.01 * max(dose), scal = 1.2 * max(dose))
```

Arguments

`dose, resp`	Vectors of equal length specifying dose and response values.
`models`	A subvector of c("linear", "emax", "exponential", "linlog", "sigEmax", "quadratic", "betaMod", "logistic") (see [drmodels](#)) which specifies the competing models.
`off`	Positive and fixed offset parameter in the 'linlog' model (see [drmodels](#)).
`scal`	Positive and fixed dose scaling parameter in the 'betaMod' with '$scal \geq \max(dose)$' (see [drmodels](#)).

Value

A matrix containing the LR test statistic for one model in each row. The last row contains the value of the maximum statistic.

Author(s)

Kevin Kokot

References

Dette, H., Titoff, S., Volgushev, S. and Bretz, F. (2015), Dose response signal detection under model uncertainty. Biometrics. doi: 10.1111/biom.12357

See Also

[DoseFinding](#)

Examples

```
## Simulate the power of the LR contrast test

# five dose levels will be used
doselvl <- c(0, 0.05, 0.2, 0.6, 1)
dose <- c(rep(0, 10), rep(0.05, 10), rep(0.2, 10), rep(0.6, 10), rep(1, 10))

# each row of 'resp' will contain one sample of size 50
resp <- matrix(nrow=100, ncol=50)

# the linear model will serve as the data generating model
linear <- function(dose, e0, delta){e0 + delta * dose}

# now 'resp' is generated:
for (i in 1:100)
    {for(j in 1:5)
      {resp[i,(j*10-9):(10*j)]<-rnorm(10, mean=linear(doselvl[j], 0.2, 0.6), sd=1.478)}}

# the simulated 95% quantile in this case:
quantile <- 4.349362

# now the power is simulated
count <- 0
```

```
for (i in 1:100)
    {if(sLRcontrast(dose = dose, resp = resp[i,], models = c("linear", "emax",
                    "exponential", "linlog"))[5] > quantile)
        {count <- count + 1}}

#power:
count/100
```

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