Package 'OPWeight'

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Version 1.29.0 Date 2017-02-26 **Description** This package perform weighted-pvalue based multiple hypothesis test and provides corresponding information such as ranking probability, weight, significant tests, etc. To conduct this testing procedure, the testing method apply a probabilistic relationship between the test rank and the corresponding test effect size. **Depends** R (>= 3.4.0), License Artistic-2.0 LazvData true **Imports** graphics, qvalue, MASS, tibble, stats, Suggests airway, BiocStyle, cowplot, DESeq2, devtools, ggplot2, gridExtra, knitr, Matrix, rmarkdown, scales, testthat VignetteBuilder knitr biocViews ImmunoOncology, BiomedicalInformatics, MultipleComparison,

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opw

Perform Optimal Pvalue Weighting

Description

A function to perform weighted pvalue multiple hypothesis test. This function compute the probabilities of the ranks of the filter statistics given the effect sizes, and consequently the weights if neighter the weights nor the probabilities are given. Then provides the number of rejected null hypothesis and the list of the rejected pvalues as well as the corresponing filter statistics.

Usage

```
opw(pvalue, filter, weight = NULL, ranksProb = NULL,
  mean_filterEffect = NULL, mean_testEffect = NULL,
  effectType = c("continuous", "binary"), alpha = 0.05, nrep = 10000,
  tail = 1L, delInterval = 0.001, method = c("BH", "BON"), ...)
```

	pvalue	Numeric vector of pvalues of the test statistics
	filter	Numeric vector of filter statistics
	weight	An optional numeric weight vector not required
	ranksProb	An optional numeric vector of the ranks probability of the filters given the mean effect
mean_filterEffect		
		Numeric, value of the mean filter effect of the true alternatives
mean_testEffect		
		Numeric, value of the mean test effect of the true alterantives
	effectType	Character ("continuous" or "binary"), type of effect sizes
	alpha	Numeric, significance level of the hypothesis test
	nrep	Integer, number of replications for importance sampling, default value is 10,000, can be increased to obtain smoother probability curves

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tail Integer (1 or 2), right-tailed or two-tailed hypothesis test. default is right-tailed

test.

delInterval Numeric, interval between the delta values of a sequence. Note that, delta is

a LaGrange multiplier, necessary to normalize the weight

method Character ("BH" or "BON"), type of methods is used to obtain the results;

Benjemini-Hochberg or Bonferroni

... Arguments passed to internal functions

Details

If one wants to test

$$H_0: epsilon_i = 0vs.H_a: epsilon_i > 0,$$

then the mean_testEffect and mean_filterEffect should be mean of the test and filter effect sizes, respectively. This is called hypothesis testing for the continuous effect sizes.

If one wants to test

$$H_0: epsilon_i = 0vs. H_a: epsilon_i = epsilon_i$$

then mean_testEffect and mean_filterEffect should be median or any discrete value of the test and filter effect sizes. This is called hypothesis testing for the Binary effect sizes, where epsilon refers to a fixed value.

The main goal of the function is to compute the probabilities of the ranks from the pvalues and the filter statistics, consequently the weights. Although weights ranksProb are optional, opw has the options so that one can compute the probabilities and the weights externally if necessary (see examples).

Internally, opw function compute the ranksProb and consequently the weights, then uses the pvalues to make conclusions about hypotheses. Therefore, if ranksProb is given then mean_filterEffect and are redundant, and should not be provided to the function. Although ranksProb is not required to the function, One can compute ranksProb by using the function prob_rank_givenEffect.

The function internally compute mean_filterEffect and mean_testEffect from a simple linear regression with box-cox transformation between the test and filter statistics, where the filters are regressed on the test statistics. Thus, filters need to be positive to apply boxcox from the R library MASS. Then the estimated mean_filterEffect and mean_testEffect are used to obtian the ranksProb and the weights. Thus, in order to apply the function properly, it is crucial to understand the uses mean_filterEffect and mean_testEffect. If mean_filterEffect and mean_testEffect are not provided then the test statistics computed from the pvalues will be used to compute the relationship between the filter statistics and the test statistics.

If one of the mean effects mean_filterEffect and mean_testEffect are not provided then the missing mean effect will be computed internally.

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Value

totalTests Integer, total number of hypothesis tests evaluated nullProp Numeric, estimated propotion of the true null hypothesis ranksProb Numeric vector of ranks probability given the mean filter effect, p(rank | ey = mean_filterEffect) weight Numeric vector of normalized weight rejections Integer, total number of rejections rejections_list data frame, list of rejected p-values and the corresponding filter statistics and the adjusted p-values if method = "BH" used.

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See Also

prob_rank_givenEffect weight_binary weight_continuous qvalue dnorm

```
# generate pvalues and filter statistics
m = 1000
set.seed(3)
filters = runif(m, min = 0, max = 2.5)
                                                # filter statistics
H = rbinom(m, size = 1, prob = 0.1)
                                              # hypothesis true or false
tests = rnorm(m, mean = H * filters)
                                              # Z-score
pvals = 1 - pnorm(tests)
                                                # pvalue
# general use
results <- opw(pvalue = pvals, filter = filters, effectType = "continuous",
                                              method = "BH")
# supply the mean effects for both the filters and the tests externally
mod <- lm(log(filters) ~ tests)</pre>
et = mean(tests)
ey = mod$coef[[1]] + mod$coef[[2]]*et
results2 <- opw(pvalue = pvals, filter = filters,
               mean_filterEffect = ey, mean_testEffect = et, tail = 2,
               effectType = "continuous", method = "BH")
# supply the rank probabilities externally
library(qvalue)
ranks <- 1:m
nullProp = gvalue(p = pvals, pi0.method = "bootstrap")$pi0
m0 = ceiling(nullProp*m)
m1 = m - m0
probs <- sapply(ranks, prob_rank_givenEffect, et = ey, ey = ey,</pre>
                                        nrep = 10000, m0 = m0, m1 = m1)
results3 <- opw(pvalue = pvals, filter = filters, ranksProb = probs,
                 effectType = "continuous", tail = 2, method = "BH")
```

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prob_rank_givenEffect Probability of rank of test given effect size

Description

Compute the probability of rank of a test being higher than any other tests given the effect size from external information.

Usage

```
prob_rank_givenEffect(k, et, ey, nrep = 10000, m0, m1)
```

Arguments

k	Integer, rank of a test
et	Numeric, effect of the targeted test for importance sampling
ey	Numeric, mean filter efffect from the external information
nrep	Integer, number of replications for importance sampling
m0	Integer, number of true null hypothesis
m1	Integer, number of true alternative hypothesis

Details

If one wants to test

$$H_0: epsilon_i = 0vs.H_a: epsilon_i > 0,$$

then ey should be mean of the filter effect sizes, This is called hypothesis testing for the continuous effect sizes.

If one wants to test

```
H_0: epsilon_i = 0vs.H_a: epsilon_i = epsilon,
```

then ey should be median or any discrete value of the filter effect sizes. This is called hypothesis testing for the Binary effect sizes.

If monitor = TRUE then a window will open to see the progress of the computation. It is useful for a large number of tests

m1 and m0 can be estimated using qvalue from a bioconductor package qvalue.

Value

prob Numeric, probability of the rank of a test

Author(s)

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See Also

dnorm pnorm rnorm qvalue

Examples

```
prob_rank_givenEffect_approx
```

Probability of rank of test given effect size by normal approximation

Description

A normal approximation to commpute the probability of rank of a test being higher than any other test given the effect size from external information.

Usage

```
prob_rank_givenEffect_approx(k, et, ey, nrep = 10000, m0, m1,
  effectType = c("binary", "continuous"))
```

k	Integer, rank of a test
et	Numeric, effect of the targeted test for importance sampling
ey	Numeric, mean/median filter efffect from external information

nrep Integer, number of replications for importance sampling

m0 Integer, number of true null hypothesis

m1 Integer, number of true alternative hypothesis

effectType Character ("continuous" or "binary"), type of effect sizes

Details

If one wants to test

$$H_0: epsilon_i = 0vs.H_a: epsilon_i > 0,$$

then ey should be mean of the filter effect sizes, This is called hypothesis testing for the continuous effect sizes.

If one wants to test

$$H_0: epsilon_i = 0vs.H_a: epsilon_i = epsilon,$$

then ey should be median or any discrete value of the filter effect sizes. This is called hypothesis testing for the Binary effect sizes.

m1 and m0 can be estimated using qvalue from a bioconductor package qvalue.

Value

prob Numeric, probability of the rank of a test

Author(s)

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See Also

dnorm pnorm rnorm qvalue

```
prob_rank_givenEffect_exact
```

Probability of rank of test given effect size by exact method

Description

An exact method to commpute the probability of rank of a test being higher than any other test given the effect size from external information.

Usage

```
prob_rank_givenEffect_exact(k, et, ey, nrep = 10000, m0, m1,
  effectType = c("binary", "continuous"))
```

Arguments

k	Integer, rank of a test
et	Numeric, effect of the targeted test for importance sampling
ey	Numeric, mean/median filter efffect from external information
nrep	Integer, number of replications for importance sampling
mØ	Integer, number of true null hypothesis
m1	Integer, number of true alternative hypothesis
effectTvpe	Character ("continuous" or "binary"), type of effect sizes

Details

If one wants to test

```
H_0: epsilon_i = 0vs.H_a: epsilon_i > 0,
```

then ey should be mean of the filter effect sizes, This is called hypothesis testing for the continuous effect sizes.

If one wants to test

```
H_0: epsilon_i = 0vs.H_a: epsilon_i = epsilon,
```

then ey should be median or any discrete value of the filter effect sizes. This is called hypothesis testing for the Binary effect sizes.

m1 and m0 can be estimated using qvalue from a bioconductor package qvalue.

Value

prob Numeric, probability of the rank of a test

Author(s)

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See Also

dnorm pnorm rnorm qvalue

Examples

```
prob_rank_givenEffect_simu
```

Probability of rank of test given effect size by simulations

Description

A simulation approach to commpute the probability of rank of a test being higher than any other test given the effect size from the external information.

Usage

```
prob_rank_givenEffect_simu(s, ey, e.one, m0, m1, effectType = c("binary",
    "continuous"))
```

S	number of samples of test statistics composed of null and alternative tests
ey	Numeric, filter test efffect from the external information
e.one	Numeric, one test effect that will vary across all tests
mØ	Integer, number of true null hypothesis
m1	Integer, number of true alternative hypothesis
effectType	Character ("continuous" or "binary"), type of effect sizes

Details

If one wants to test

```
H_0: epsilon_i = 0vs.H_a: epsilon_i > 0,
```

then ey should be mean of the filter effect sizes, This is called hypothesis testing for the continuous effect sizes.

If one wants to test

```
H_0: epsilon_i = 0vs.H_a: epsilon_i = epsilon_i
```

then ey should be median or any discrete value of the filter effect sizes. This is called hypothesis testing for the Binary effect sizes.

This is a simulation approach to compute the probability of the rank, $P(\text{rank} \mid \text{effect} = \text{ey})$ to verify the actual $P(\text{rank} \mid \text{effect} = \text{ey})$. Suppose, we have a vector of m = m1+m0 observations, where the first m1 observations are from the true alternative and second m0 are from the true null models. If we pick two tests one from the first position and the other from the (m0+1)-th position, then we would expect that the first observation's rank is greater than m0, and (m1+1)-th observation's rank is less than or equal to m1. However, this is not always true, especially when the effect size of the test statistics is low, but the above scenerio become obvious as the the effect size increases. m1 and m0 can be estimated using qvalue from a bioconductor package qvalue.

Value

```
r0 Integer, rank of the null test statisticr1 Integer, rank of the alternative test statistic
```

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See Also

```
runif rnorm qvalue
```

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```
# probability of the rank of a null test
prob0 <- rep(NA, m)
prob0_x <- tapply(rank[1,], rank[1,], length)/sampleSize
prob0[as.numeric(names(prob0_x))] <- as.vector(prob0_x)

# probability of the rank of an alternative test
prob1 <- rep(NA, m)
prob1_x <- tapply(rank[2,], rank[2,], length)/sampleSize
prob1[as.numeric(names(prob1_x))] <- as.vector(prob1_x)

# plot
matplot(1:m, cbind(prob0, prob1), type = "1")</pre>
```

weight_binary

Weight for the Binary effect sizes

Description

Compute weight from the probability of the rank given the effect size for the binary effect size

Usage

```
weight_binary(alpha, et, m, m1, tail = 1L, delInterval = 0.001, ranksProb)
```

Arguments

alpha	Numeric, significance level of the hypothesis test
et	Numeric, mean effect size of the test statistics
m	Integer, totoal number of hypothesis test
m1	Integer, number of true alternative hypothesis
tail	Integer (1 or 2), right-tailed or two-tailed hypothesis test. default is right-tailed test.
delInterval	Numeric, interval between the delta values of a sequence. Note that, delta is a LaGrange multiplier, necessary to normalize the weight
ranksProb	Numeric vector of the ranks probability of the tests given the effect size

Details

If one wants to test

```
H_0: epsilon_i = 0vs.H_a: epsilon_i = epsilon,
```

then et and ey should be median or any discrete value of the test and filter effect sizes, respectively. This is called hypothesis testing for the Binary effect sizes. m1 can be estimated using qvalue from a bioconductor package qvalue.

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Value

weight Numeric vector of normalized weight of the tests for the binary case

Author(s)

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See Also

```
prob_rank_givenEffect weight_continuous qvalue
```

Examples

weight_by_delta

Find sum of weights for the LaGrange multiplier

Description

Compute sum of weights for a given value of the LaGrange multiplier

Usage

```
weight_by_delta(delta, alpha = 0.05, et, m, m1, tail = 1L, ranksProb,
  effectType = c("continuous", "binary"))
```

delta	Numeric value of the LagRange multiplier
alpha	Numeric, significance level of the hypothesis test
et	Numeric, mean effect size of the test statistics
m	Integer, totoal number of hypothesis test

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m1	Integer, number of true alternative tests
tail	Integer (1 or 2), right-tailed or two-tailed hypothesis test. default is right-tailed test.
ranksProb	Numeric vector of the ranks probability of the filter statistics given the effect size
effectType	Character ("continuous" or "binary"), type of effect sizes

Details

To obtain the normalized weight, and to make sure that the sum of the weights is equal to the number of tests and the weights are positive, an optimal value of the LaGrange multiplier delta needed. This function will compute the weights for a given value of the LaGrange multiplier and provide the sum of the weights in return.

Value

```
sumWeight_per_delta sum of weights per delta value
```

Author(s)

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Examples

weight_continuous

Weight for the continuous effect sizes

Description

Compute weight from the probability of the rank given the effect size for the continuous effect size

Usage

```
weight_continuous(alpha, et, m, tail = 1L, delInterval = 0.001, ranksProb)
```

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Arguments

alpha	Numeric, significance level of the hypothesis test
et	Numeric, mean effect size of the test statistics
m	Integer, totoal number of hypothesis test
tail	Integer (1 or 2), right-tailed or two-tailed hypothesis test. default is right-tailed test.
delInterval	Numeric, interval between the delta values of a sequence. Note that, delta is a LaGrange multiplier, necessary to normalize the weight
ranksProb	Numeric vector of ranks probability of the tests given the effect size

Details

If one wants to test

$$H_0: epsilon_i = 0vs.H_a: \epsilon_i > 0,$$

then et and ey should be mean value of the test and filter effect sizes, respectively. This is called hypothesis testing for the continuous effect sizes.

Value

weight Numeric vector of normalized weight of the tests for the continuous case

Author(s)

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See Also

```
prob_rank_givenEffect weight_binary
```

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