

Package ‘MultiMed’

October 18, 2017

Title Testing multiple biological mediators simultaneously

Version 1.10.0

Date 2013-07-07

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Depends R (>= 3.1.0)

Suggests RUnit, BiocGenerics

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Description Implements permutation method with joint correction for testing multiple mediators

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biocViews MultipleComparison, StatisticalMethod, Software

NeedsCompilation no

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medTest	<i>Permutation test for multiple mediators which uses a joint correction</i>
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Description

Implements Boca et al. 2014 method of testing multiple biological mediators simultaneously, which uses a permutation test with a joint correction based on the maximal test statistics.

Usage

```
medTest(E, M, Y, Z = NULL, useWeightsZ = TRUE, nperm = 100, w = 1)
```

Arguments

E	Exposure: numerical vector of length n or numerical n x 1 matrix, where n is the number of samples or subjects.
M	Mediators: numerical matrix of dimension n x p, where p is the number of mediators.
Y	Outcome: numerical vector of length n or numerical n x 1 matrix
Z	Additional covariates: NULL or numerical matrix having n rows. If it is not NULL, then the exposure, mediators, and outcome will all be initially regressed on Z, with the residuals being used in the mediation analysis.
nperm	Number of permutations performed. One of the permutations always consists of the observed data.
w	Weight assigned to each subject or sample for the E-M associations. Useful for case-control sampling.
useWeightsZ	If TRUE, use the weights in w for the initial regression of E and M on Z, in the case where Z is not null. If FALSE, use equal weights.

Details

See Boca et al. 2014 paper for a more in-depth description of this method.

Value

Matrix with p rows and 2 columns, where the first column (labeled "S") gives the S-statistics and the second column (labeled "p") gives the p-values for each mediator, where the mediators correspond to the rows. For each mediator, the S-statistic is the absolute value of the product of the correlation between the exposure and the mediator and the conditional (or partial) correlation between the mediator and the outcome conditional on the exposure. Thus, the larger the S-statistic is, the smaller the p-value is, and the more likely it is that the mediator is statistically significant.

Author(s)

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References

Boca SM, Sinha R, Cross AJ, Moore SC, Sampson JN. (2014) Testing multiple biological mediators simultaneously. *Bioinformatics*, 30(2), 214-220.

See Also

NavyAdenoma

Examples

```
##More details on this example are given in the accompanying vignette.

data(NavyAdenoma)

##the exposure of interest is the daily intake of fish
##the possible mediators are 149 normalized serum metabolite values
##the outcome of interest is colorectal adenoma case-control status
```

```

##get weights needed due to retrospective sampling, to use for all regressions
##that do not have adenoma status as the outcome
prev <- 0.228
p <- sum(NavyAdenoma$Adenoma==1)/nrow(NavyAdenoma)
w <- rep(NA, nrow(NavyAdenoma))
w[NavyAdenoma$Adenoma == 1] <- prev/p
w[NavyAdenoma$Adenoma == 0] <- (1-prev)/(1-p)

##perform the test of mediation, adjusting for the covariates
##BMI, gender, age, and current smoking status
##(only running 10 permutations in this example - would need to
##perform more to get an accurate p-value)
set.seed(840218)
medsFish <- medTest(E=NavyAdenoma$Fish,
                   M=NavyAdenoma[, 6:154],
                   Y=NavyAdenoma$Adenoma,
                   Z=NavyAdenoma[, 2:5],
                   nperm=10, w=w)

##get metabolite with lowest p-value
medsFish[which.min(medsFish[, "p"]),]
colnames(NavyAdenoma[, -(1:5)])[which.min(medsFish[, "p"])]

```

NavyAdenoma

Data from the Sinha et al. 1999 and Boca et al. 2014 studies concerning the Navy Colorectal Adenoma case-control study.

Description

The data consists of a dietary exposures of interest (daily intake of fish in grams/day), the outcome of interest (colorectal adenoma status), and 149 serum metabolites which are possible mediators between either of the exposures and the outcome. Four other additional covariates of interest are included (body mass index, gender, age, current smoking status.)

Usage

```
data(NavyAdenoma)
```

Format

Data frame with 258 rows, representing 129 cases and 129 controls in the Navy Colorectal Adenoma study. There are 155 columns, ordered as follows: fish intake (*Fish*), body mass index (*BMI*), gender (*Female* - coded as 0 for male, 1 for female), age in years (*Age*), current smoking status (*Smoking* - coded as 0 for non-smoker, 1 for current smoker), 149 serum metabolites (values were previously batch normalized and log transformed), and case-control status for adenoma (*Adenoma* - coded as 0 for control, 1 for case.)

References

- Sinha, R, Chow WH, Kulldorff M, Denobile J, Butler J, Garcia-Closas M, Weil R, Hoover RN, Rothman N. (1999) Well-done, grilled red meat increases the risk of colorectal adenomas. *Cancer Res.*, 59(17), 4320-4324.
- Boca SM, Sinha R, Cross AJ, Moore SC, Sampson JN. (2014) Testing multiple biological mediators simultaneously. *Bioinformatics*, 30(2), 214-220.

See Also

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