

Package ‘MiSTi’

December 13, 2018

Type Package

Title Set-Based Mixed Effects Score Tests for GxE Interactions

Version 0.1.0

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Description Functions to implement set-based tests for GxE interactions on either continuous or dichotomous outcomes under mixed effects models. It includes burden-type test allowing for external weights on each element in the set, kernel-based association test, and two tests, fMiSTi and aMiSTi, based on combinations of the previous two tests. Set-level pvalues are produced and returned.

License GPL (>= 2)

Depends R (>= 3.3.2)

Imports penalized (>= 0.9.50), Matrix (>= 1.2.10), psych (>= 1.7.5),
CompQuadForm (>= 1.4.3), stats

Encoding UTF-8

LazyData true

RoxygenNote 6.0.1

Suggests knitr, rmarkdown, testthat

VignetteBuilder knitr

NeedsCompilation no

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MiSTi *Implementation of set-based mixed effects score tests via MiSTi.*

Description

Implementation of set-based mixed effects score tests via *MiSTi*.

Usage

```
MiSTi(data, outcome_type = "Continuous", p, m, d = 0, R = 1,
      glm_use = FALSE, weight_method = "User", user_weight = rep(1, p),
      ind_burden_return = TRUE, combinations_return = TRUE,
      combination_preference = "All", mac_lower_bound = 6, chisq_app = "3M",
      acc = 5e-10, acc_auto = TRUE, accurate_app_threshold = -log10(0.05),
      max_core = 4)
```

Arguments

<code>data</code>	A $n \times m$ dataframe [Y,E,X,G] with rows represent subjects and columns are Y (outcome), E (environmental risk factors), X (confounders), and G (genotypes).
<code>outcome_type</code>	Either "Continuous" for the values of a quantitative trait, or "Binary" for a dichotomous trait.
<code>p</code>	Number of genetic variants in the set.
<code>m</code>	Number of environmental risk factors.
<code>d</code>	Number of confounders. If d is 0, there is no confounder, and the input data should be arranged as [Y E G].
<code>R</code>	Number of burden scores, including both unweighted and weighted ones. It is always greater than or equal to 0. When R is assigned as 0, only variance component test is performed (more than one GxE terms are required in this situation.)
<code>glm_use</code>	A logical value indicating if generalized linear regression is implemented to fit the null models. A ridge regression is implemented if <code>glm_use</code> is assigned as FALSE (default).
<code>weight_method</code>	One of "User", "No weight", "ScrnStat1", and "ScrnStat2". This specifies weights for calculating burden scores. "User"(default) allows for an equal weight across variants in the set or user-defined weights for each variants (e.g., functional annotations). The weights are specified by the input option "user_weight". "No weight" sets all weights as 0 and tests only the variance component. "ScrnStat1" and "ScrnStat2" use screening test statistics as weights, where "ScrnStat1" use the maximum of G-E correlation and marginal association screening test statistics (Jiao et al. 2015) and "ScrnStat2" uses the sum of squares of marginal association and correlation screening test statistics(Gauderman et al. 2013).
<code>user_weight</code>	A vector or a matrix specifying an equal weight across variants or user-defined weights for calculating weighted burden score. This option only works when <code>weight_method</code> is set as "User". If <code>weight_method</code> is set as "User" and no <code>user_weight</code> is specified, the weight is a vector of 1.
<code>ind_burden_return</code>	A logical value (default: TRUE) indicating if testing results on individual interaction terms between each E and burden score are returned. This option only works when there are more than one ExB terms (i.e. multiple E's or multiple weights for each variant).
<code>combinations_return</code>	A logical value (default: TRUE) indicating if the combination methods, including the optimal linear combination, data-adaptive weighted combination and Fisher's combination method, are implemented. By assigning FALSE, only the burden and variance component tests are conducted.
<code>combination_preference</code>	Either of "All" (default), or a vector containing "OptMin", "AdptWt", or "Fisher" to specify the combination method(s) to be implemented.

<code>mac_lower_bound</code>	The lower bound of minor allele count (MAC) for individual SNPs to be included in the analysis. Default is 6. SNPs with MAC ≤ 5 are excluded from the analysis. A warning message is given when any SNPs are removed from the set.
<code>chisq_app</code>	Either "3M" (default) or "4M" for the moment matching (Liu's) method in quantile approximation in optimal linear combination method. "3M" matches the 3rd moment and "4M" matches the 4th moment of the target and approximate distributions.
<code>acc</code>	A numerical value indicating the precision of Davies method for p-value calculation. Default is 5e-10.
<code>acc_auto</code>	A logical value (default: TRUE) indicating if data adaptive precision is used in optimal linear combination. We recommend to set this as TRUE for computational efficiency.
<code>accurate_app_threshold</code>	A numerical value specifying the threshold to determine when Liu's and Davies methods are used in quantile approximation in the optimal linear combination method. Default is $-\log_{10}(0.05)$.
<code>max_core</code>	An integer specifying the maximum number of cores can be recruited in parallel package. Default is 4 cores.

Value

A list containing `pvalue`, `stat`, `pvalue.ind.f`, `stat.ind.f`, `rho`, and `data.info`. `pvalue` shows p-values from the (joint) burden tests, kernel-based association test, *oMiSTi*, *aMiSTi*, and *fMiSTi*. `stat` shows the corresponding statistics from the aforementioned tests. `pvalue.ind.f` and `stat.ind.f` show p-values and test statistics of individual burden components if multiple E variables are considered jointly. `rho` provides weights of the burden and the kernel-based association tests in *oMiSTi* and *aMiSTi*. `data.info` is a vector including `m`, `p`, `R`, `pm`, and `Rm`, the numbers of E, G, B, GxE, and BxE terms, respectively.

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