Package: MRBEE (via r-universe)

September 24, 2024

Type Package

Title Mendelian Randomization using Bias-Corrected Estimating Equation
and Iterative Pleiotropy Testing

Version 0.1.0

Description This package performs multivariate Mendelian
randomization. It is characterized by the removal of
measurement error bias caused by the estimation error of GWAS
effect size estimates using an unbiased estimating function in
measurement error analysis. It also utilizes a pleiotropy test
to dynamically detect and remove potential pleiotropy, making
the causal effect robust to pleiotropy.

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Encoding UTF-8

LazyData true

Depends R (>= 2.10),

Imports MASS, data.table, FDRestimation, Matrix

RoxygenNote 7.2.3

Suggests testthat (>= 3.0.0)

Repository https://mrcieu.r-universe.dev

RemoteUrl https://github.com/noahlorinczcomi/MRBEE

RemoteRef HEAD

RemoteSha 6295549a1f5a158c6701eb793646d60c8aef11ca

Contents

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errorCov   *Estimate Error Covariance Matrix Using GWAS Insignificant Effects*

Description

This function estimates the error covariance matrix by subsampling a proportion of insignificant GWAS effects and calculating their correlation coefficients.

Usage

```
errorCov(
  ZMatrix,
  Zscore.cutoff = 2,
  subsampling.ratio = 0.1,
  subsampling.time = 1000
)
```

Arguments

ZMatrix	A matrix of Z-scores for exposure and outcome, with the outcome GWAS in the last column.
Zscore.cutoff	The cutoff for significance. Defaults to 2.
subsampling.ratio	
	The proportion of effects to subsample for each iteration. Defaults to 0.1.
subsampling.time	
	The number of subsampling iterations. Defaults to 1000.

Value

A matrix representing the estimated error covariance.

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filter_align   *Filter and Align GWAS Data to a Reference Panel*

Description

The `filter_align` function processes a list of GWAS summary statistics data frames, harmonizes alleles according to a reference panel, removes duplicates, and aligns data to common SNPs. It's used to prepare data for further analysis such as LDSC.

Usage

```
filter_align(gwas_data_list, ref_panel, allele_match = TRUE)
```

Arguments

gwas_data_list	A list of data.frames where each data.frame contains GWAS summary statistics for a trait. Each data.frame should include columns for SNP identifiers, Z-scores of effect size estimates, sample sizes (N), effect allele (A1), and reference allele (A2).
ref_panel	A data.frame containing the reference panel data. It must include columns for SNP, A1, and A2.
allele_match	Logical. Whether to match alleles. Default TRUE.

Details

The function performs several key steps: adjusting alleles according to a reference panel, removing duplicate SNPs, and aligning all GWAS data frames to a set of common SNPs. This is often a necessary preprocessing step before performing genetic correlation and heritability analyses.

Value

A list of data.frames, each corresponding to an input GWAS summary statistics data frame, but filtered, harmonized, and aligned to the common SNPs found across all data frames.

Examples

```
## Not run:
# Assuming GWAS_List and ref_panel are already defined:
GWAS_List <- filter_align(GWAS_List, ref_panel)

## End(Not run)
```

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hapmap3 *HapMap3 and UKBB Genotype SNP Data*

Description

A data frame containing combined SNP data from 1000 Genomes Project Phase 3 and UK Biobank (UKBB) genotypes. It includes a total of 1,664,852 SNPs.

Usage

```
data(hapmap3)
```

Format

A data frame with 1,664,852 rows and 3 variables:

SNP SNP identifier.

A1 Effect allele.

A2 Reference allele.

Source

1000 Genomes Project Phase 3 and UK Biobank genotype data.

Joint.test   *Perform Joint Test on GWAS Summary Data*

Description

This function conducts a joint test on GWAS summary data, calculating Chi-squared values and corresponding P-values based on allele-aligned Z-scores and the correlation matrix of estimation errors for these Z-scores.

Usage

```
Joint.test(bZ, RZ)
```

Arguments

bZ	A matrix of allele-aligned Z-scores from GWAS summary data, where each row represents a different genetic variant and each column represents a different trait or study. The matrix dimensions are n x p, with n being the number of variants and p being the number of traits or studies.
RZ	The correlation matrix of estimation errors for the Z-scores in 'bZ'. This matrix should be p x p, where p is the number of traits or studies.

Value

A data frame with two columns: 'Chi2', containing the Chi-squared values for each genetic variant, and 'P', containing the corresponding P-values.

Examples

```
## Not run:
# Example usage:
# Assuming bZ is your matrix of allele-aligned Z-scores and RZ is the correlation matrix
result <- Joint.test(bZ, RZ)

## End(Not run)
```

MRBEE.IMRP *Estimate Causal Effect with MRBEE*

Description

This function estimates the causal effect using a bias-correction estimating equation, considering potential pleiotropy and measurement errors.

Usage

```
MRBEE.IMRP(
  by,
  bX,
  byse,
  bXse,
  Rxy,
  max.iter = 30,
  max.eps = 1e-04,
  pv.thres = 0.05,
  var.est = "robust",
  FDR = T,
  adjust.method = "Sidak",
  maxdiff = 3
)
```

Arguments

by	A vector (n x 1) of the GWAS effect size of outcome.
bX	A matrix (n x p) of the GWAS effect sizes of p exposures.
byse	A vector (n x 1) of the GWAS effect size SE of outcome.
bXse	A matrix (n x p) of the GWAS effect size SEs of p exposures.
Rxy	A matrix (p+1 x p+1) of the correlation matrix of the p exposures and outcome. The last one should be the outcome.
max.iter	Maximum number of iterations for causal effect estimation. Defaults to 30.
max.eps	Tolerance for stopping criteria. Defaults to 1e-4.
pv.thres	P-value threshold in pleiotropy detection. Defaults to 0.05.
var.est	Method for estimating the variance of residual in pleiotropy test. Can be "robust", "variance", or "ordinal". Defaults is robust that estimates the variance of residual using median absolute deviation (MAD).
FDR	Logical. Whether to apply the FDR to convert the p-value to q-value. Defaults to TRUE.
adjust.method	Method for estimating q-value. Defaults to "Sidak".
maxdiff	The maximum difference between the MRBEE causal estimate and the initial estimator. Defaults to 3.

Value

A list containing the estimated causal effect, its covariance, and pleiotropy

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MRBEE.IMRP.Egger   *Estimate Causal Effect with MRBEE*

Description

This function estimates the causal effect using a bias-correction estimating equation with an intercept, considering potential pleiotropy and measurement errors.

Usage

```
MRBEE.IMRP.Egger(
  by,
  bX,
  byse,
  bXse,
  Rxy,
  max.iter = 30,
  max.eps = 1e-04,
  pv.thres = 0.05,
  var.est = "robust",
  FDR = T,
  adjust.method = "Sidak",
  maxdiff = 3
)
```

Arguments

by	A vector (n x 1) of the GWAS effect size of outcome.
bX	A matrix (n x p) of the GWAS effect sizes of p exposures.
byse	A vector (n x 1) of the GWAS effect size SE of outcome.
bXse	A matrix (n x p) of the GWAS effect size SEs of p exposures.
Rxy	A matrix (p+1 x p+1) of the correlation matrix of the p exposures and outcome. The last one should be the outcome.
max.iter	Maximum number of iterations for causal effect estimation. Defaults to 30.
max.eps	Tolerance for stopping criteria. Defaults to 1e-4.
pv.thres	P-value threshold in pleiotropy detection. Defaults to 0.05.
var.est	Method for estimating the variance of residual in pleiotropy test. Can be "robust", "variance", or "ordinal". Defaults is robust that estimates the variance of residual using median absolute deviation (MAD).
FDR	Logical. Whether to apply the FDR to convert the p-value to q-value. Defaults to TRUE.

adjust.method	Method for estimating q-value. Defaults to "Sidak".
maxdiff	The maximum difference between the MRBEE causal estimate and the initial estimator. Defaults to 3.

Value

A list containing the estimated causal effect, its covariance, and pleiotropy

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MRBEE.IMRP.UV	*Univariable MR Estimation using MRBEE Method*

Description

This function performs univariable Mendelian Randomization (MR) analysis using the MRBEE method.

Usage

```
MRBEE.IMRP.UV(
  by,
  bx,
  byse,
  bxse,
  Rxy,
  max.iter = 30,
  max.eps = 1e-04,
  pv.thres = 0.05,
  var.est = "robust",
  FDR = T,
  adjust.method = "Sidak"
)
```

Arguments

by	Vector of GWAS effect sizes for the outcome (n x 1).
bx	Vector of GWAS effect sizes for the exposure (n x 1).
byse	Vector of standard errors (SE) for the GWAS effect sizes of the outcome (n x 1).
bxse	Vector of SE for the GWAS effect sizes of the exposure (n x 1).
Rxy	Correlation matrix (p+1 x p+1) of the exposures and outcome, with the outcome being the last.
max.iter	Maximum number of iterations for the estimation process. Defaults to 30.
max.eps	Tolerance level for convergence. Defaults to 1e-4.
pv.thres	P-value threshold for pleiotropy detection. Defaults to 0.05.
var.est	Method for estimating the standard error in the pleiotropy test. Can be "robust", "variance", or "ordinal".

FDR   Logical indicating whether to apply False Discovery Rate (FDR) correction.
                      Defaults to TRUE.

adjust.method   Method for estimating q-values, defaults to "Sidak".

Value

A list containing the estimated causal effect, its covariance, and pleiotropy

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