

Package ‘PPMR’

July 21, 2025

Title Probabilistic Two Sample Mendelian Randomization

Type Package

Version 1.0

Description Efficient statistical inference of two-sample MR (Mendelian Randomization) analysis.

It can account for the correlated instruments and the horizontal pleiotropy, and can provide the accurate estimates of both causal effect and horizontal pleiotropy effect as well as the two corresponding p-values. There are two main functions in the 'PPMR' package. One is `PMR_individual()` for individual level data, the other is `PMR_summary()` for summary data.

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Encoding UTF-8

LazyData true

Imports Rcpp (>= 1.0.0)

LinkingTo Rcpp, RcppArmadillo

RoxygenNote 6.1.1.9000

NeedsCompilation yes

BugReports <https://github.com/umich-biostatistics/PPMR/issues>

Author Zhongshang Yuan [aut],
Xiang Zhou [aut],
Michael Kleinsasser [cre]

Maintainer Michael Kleinsasser <mkleinsa@umich.edu>

Depends R (>= 3.5.0)

Repository CRAN

Date/Publication 2019-08-09 10:20:07 UTC

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Exampleindividual	Individual level dataset
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Description

A simulated individual level dataset for PMR.

Usage

Exampleindividual

Format

- A list contains the following objects:
- zx** the standardized genotype matrix for 465 individuals and 50 cis-SNPs in eQTL data.
 - zy** the standardized genotype matrix for 2000 individuals and 50 cis-SNPs in GWAS data.
 - x** the standarized gene expression vector for 465 individuals in eQL data.
 - y** the standarized complex trait vector for 2000 individuals in GWAS data.

Examplesummary	Summary level dataset
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Description

A simulated summary level dataset for PMR

Usage

Examplesummary

Format

- A list contains the following objects:
- betax** the cis-SNP effect size vector for one specific gene in eQTL data.
 - betay** the cis-SNP effect size vector for one specific gene in GWAS data.
 - Sigma1** the LD matrix in eQTL data.
 - Sigma2** the LD matrix in GWAS data.
 - n1** the sample size of eQTL data.
 - n2** the sample size of GWAS data.

PMR_individual	<i>PMR model with individual level data</i>
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Description

Fit the probabilistic MR model with individual level data while accounting for the correlated instruments and horizontal pleiotropy in TWAS framework.

Usage

```
PMR_individual(yin, zin, x1in, x2in, gammain, alphain, max_iterin, epsin)
```

Arguments

yin	standardized exposure vector (e.g. gene expression in TWAS).
zin	standardized complex trait vector.
x1in	standardized cis-genotype matrix in eQTL data.
x2in	standardized cis-genotype matrix in GWAS data.
gammain	indicator variable for constrained PMR model, with 1 for the null model that there is no horizontal pleiotropy.
alphain	indicator variable for constrained PMR model, with 1 for the null model that there is no causal effect.
max_iterin	The maximum iteration.
epsin	The convergence tolerance of the absolute value of the difference between the nth and (n+1)th log likelihood.

Value

a list of estimates of model parameters, including the causal effect alpha, the horizontal pleiotropy effect gamma, and the two corresponding p values

Author(s)

Zhongshang Yuan, Xiang Zhou.

Examples

```
data(Exampleindividual)
attach(Exampleindividual)
fmH1 = PMR_individual(yin=x, zin=y, x1in=zx, x2in=zy,
                      gammain=0, alphain = 0, max_iterin =1000, epsin=1e-5)
alpha<-fmH1$alpha
gamma<-fmH1$gamma
fmH0gamma = PMR_individual(yin=x, zin= y, x1in=zx, x2in=zy, gammain=1,
                           alphain = 0, max_iterin =1000, epsin=1e-5)
fmH0alpha = PMR_individual(yin=x, zin=y, x1in=zx, x2in=zy, gammain=0,
```

```

                                alphain = 1,max_iterin =1000, epsin=1e-5)
loglikH1=max(fmH1$loglik,na.rm=TRUE)
loglikH0gamma=max(fmH0gamma$loglik,na.rm=TRUE)
loglikH0alpha=max(fmH0alpha$loglik,na.rm=TRUE)
stat_alpha = 2 * (loglikH1 - loglikH0alpha)
pvalue_alpha = pchisq(stat_alpha,1,lower.tail=FALSE)
stat_gamma = 2 * (loglikH1 - loglikH0gamma)
pvalue_gamma = pchisq(stat_gamma,1,lower.tail=FALSE)

```

PMR_summary

PMR model with summary data

Description

Fit the probabilistic MR model with summary data while accounting for the correlated instruments and horizontal pleiotropy in TWAS framework.

Usage

```

PMR_summary(betaxin, betayin, Sigma1sin, Sigma2sin, samplen1, samplen2,
            gammain, alphain, max_iterin, epsin)

```

Arguments

betaxin	the cis-SNP effect size vector for one specific gene in eQTL data, which must be calculated based on both the standardized gene expression value and the standardized cis-genotype matrix.
betayin	the cis-SNP effect size vector for one specific gene in GWAS data, which be calculated based on both the standardized complex trait value and the standardized cis-genotype matrix.
Sigma1sin	the LD matrix in eQTL data.
Sigma2sin	the LD matrix in GWAS data. Both Sigma2sin and sigma1sin are often the same from the reference panel.
samplen1	the sample size of eQTL data.
samplen2	the sample size of GWAS data.
gammain	indicator variable for constrained model, with 1 for the null model that there is no horizontal pleiotropy.
alphain	indicator variable for constrained model, with 1 for the null model that there is no causal effect.
max_iterin	The maximum iteration.
epsin	The convergence tolerance of the absolute value of the difference between the nth and (n+1)th log likelihood.

Value

A list of estimates of model parameters, including the causal effect α , the horizontal pleiotropy effect γ , and the two corresponding p values.

Author(s)

Zhongshang Yuan, Xiang Zhou.

Examples

```
data(Examplesummary)
attach(Examplesummary)
fmH1=PMR_summary(betaxin=betax,betayin=betay,Sigma1sin=Sigma1,Sigma2sin=Sigma2,
  samplen1=n1,samplen2=n2,gammain=0,alphain=0,max_iterin =1000, epsin=1e-5)
fmH0alpha=PMR_summary(betaxin=betax,betayin=betay,Sigma1sin=Sigma1,Sigma2sin=Sigma2,
  samplen1=n1,samplen2=n2,gammain=0,alphain=1,max_iterin =1000, epsin=1e-5)
fmH0gamma=PMR_summary(betaxin=betax,betayin=betay,Sigma1sin=Sigma1,Sigma2sin=Sigma2,
  samplen1=n1,samplen2=n2,gammain=1,alphain=0,max_iterin =1000, epsin=1e-5)
loglikH1=max(fmH1$loglik,na.rm=TRUE)
loglikH0alpha=max(fmH0alpha$loglik,na.rm=TRUE)
loglikH0gamma=max(fmH0gamma$loglik,na.rm=TRUE)
stat_alpha = 2 * (loglikH1 - loglikH0alpha)
pvalue_alpha = pchisq(stat_alpha,1,lower.tail=FALSE)
stat_gamma = 2 * (loglikH1 - loglikH0gamma)
pvalue_gamma = pchisq(stat_gamma,1,lower.tail=FALSE)
```

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