Package 'MQMVtest'

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Title X chromosome-wide association studies for quantitative trait loci based on the mixture of general pedigrees and additional unrelated individuals

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Description An R package of X chromosome-wide association studies for quantitative trait loci based on the mixture of general pedigrees and additional unrelated individuals. In this package, the nine methods (MQXcat, MQZmax, MTplink, MTchen, MwM3VNA, MQMVXcat, MQMVZmax, MpMV and McMV) can not only handle the mixed data but also be applied to only general pedigrees, where the latter case simply requires reducing the block matrix to a kinship matrix.

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Imports GMMAT, lmtest, quantreg, gJLS2, mvtnorm, expm, bigsnpr, xgboost

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R topics documented:

McMV_test *mean-variance-based method:McMV,simultaneously test for differences in both the means and variances of a quantitative trait.*

Description

A function to obtain the p value and the test statistics of the MTchenw_test (i.e., MTchenw), the variance test (i.e.,MwM3VNA), the McMV_test(i.e., McMV) or all.

Usage

```
McMV_test(
  Genotype,
  Y,
  Sex,
  Covariate = NULL,
  missing_cutoff = 0.15,
  MAF_Cutoff = NULL,
  MGC_Cutoff = 20,
  kins = NULL,
  method = "joint"
)
```

Arguments

Genotype	A numeric genotype matrix with each row as a different individual and each column as a separate SNP. Each genotype is coded as 0, 1 or 2 for females and coded as 0 or 1 for males, indicating the number of reference allele.
Y	A numeric vector of a quantitative trait, such as height.
Sex	A vector of the genetic sex following PLINK default coding, where males are coded as 1 and females are coded as 2.
Covariate	ptional: a vector or a matrix of covariates, such as age.
missing_cutoff	Cutoff of the missing rates of SNPs (default=0.15). Any SNPs with missing rates higher than the cutoff will be excluded from the analysis.
MAF_Cutoff	MAF cutoff for common vs. rare variants (default=NULL). It should be a numeric value between 0 and 0.5, or NULL.
MGC_Cutoff	Cutoff for the minimum genotype count in either females or males.
kins	For the mixed data, kins=GRM is a block matrix, interpreted as the genetic relatedness among these individuals, including general pedigrees and unrelated individuals. For general pedigrees, GRM is a kinship matrix, indicating the genetic relatedness among individuals within general pedigrees, calculated using the dedicated method for kinship coefficients of X chromosome provided by the "kinship2" package in R software.
method	Optional: A character string indicating which kind of association tests is to be conducted. There are four options: "MTchenw", "variance", "joint" (default) and "all". method="MTchenw": MTchenw; method="variance": MwM3VNA; method="joint": McMV; method="all": all of the above association tests.

Value

The p values and the test statistics of association tests selected by the method option for each SNP.

Examples

```
McMV_test(Genotype,Y,Sex,
                    Covariate=mixed[,"Age"],
                    missing_cutoff=0.15,
                    MAF_Cutoff=NULL,
                    MGC_Cutoff=20,
                    kins=GRM,
                    method='joint')
```

`mean_test` *The mean-based methods:MQXcat and MQZmax*

Description

A function to obtain the p values and the test statistics of MQXcat and MQZmax for testing the mean difference of the trait value across genotypes.

Usage

```
mean_test(
  Genotype,
  Y,
  Sex,
  Covariate = NULL,
  missing_cutoff = 0.15,
  MAF_Cutoff = NULL,
  MGC_Cutoff = 20,
  kins = NULL
)
```

Arguments

`Genotype`	A numeric genotype matrix with each row as a different individual and each column as a separate SNP. Each genotype is coded as 0, 1 or 2 for females and coded as 0 or 1 for males, indicating the number of reference allele.
`Y`	A numeric vector of a quantitative trait, such as height.
`Sex`	A vector of the genetic sex following PLINK default coding, where males are coded as 1 and females are coded as 2.
`Covariate`	Optional: a vector or a matrix of covariates, such as age.
`missing_cutoff`	Cutoff of the missing rates of SNPs (default=0.15). Any SNPs with missing rates higher than the cutoff will be excluded from the analysis.
`MAF_Cutoff`	MAF cutoff for common vs. rare variants (default=NULL). It should be a numeric value between 0 and 0.5, or NULL. When it is NULL, 1/ sqrt(2 SampleSize) will be used (Ionita-Laza et al. 2013). Only common variants are included in the analysis.
`MGC_Cutoff`	Cutoff for the minimum genotype count in either females or males.

kins	For the mixed data, kins is a block matrix, interpreted as the genetic relatedness among these individuals, including general pedigrees and unrelated individuals. For general pedigrees, it is a kinship matrix, indicating the genetic relatedness among individuals within general pedigrees, calculated using the dedicated method for kinship coefficients of X chromosome provided by the "kinship2" package in R software.

Value

The p values and test statistics of MQXcat and MQZmax

Examples

```
mean_test(Genotype,Y,Sex,
                    Covariate=mixed[,"Age"],
                    missing_cutoff=0.15,
                    MAF_Cutoff=NULL,
                    MGC_Cutoff=20)
```

MpMV_test *mean-variance-based method:MpMV, simultaneously test for differences in both the means and variances of a quantitative trait,*

Description

A function to obtain the p value and the test statistics of the MTplinkw_test (i.e., MTplinkw), the variance test (i.e.,MwM3VNA), the MpMV_test(i.e., MpMV) or all.

Usage

```
MpMV_test(
  Genotype,
  Y,
  Sex,
  Covariate = NULL,
  missing_cutoff = 0.15,
  MAF_Cutoff = NULL,
  MGC_Cutoff = 20,
  kins = NULL,
  method = "joint"
)
```

Arguments

Genotype	A numeric genotype matrix with each row as a different individual and each column as a separate SNP. Each genotype is coded as 0, 1 or 2 for females and coded as 0 or 1 for males, indicating the number of reference allele.
Y	A numeric vector of a quantitative trait, such as height.
Sex	A vector of the genetic sex following PLINK default coding, where males are coded as 1 and females are coded as 2.
Covariate	Optional: a vector or a matrix of covariates, such as age.

`missing_cutoff` Cutoff of the missing rates of SNPs (default=0.15). Any SNPs with missing rates higher than the cutoff will be excluded from the analysis.

`MAF_Cutoff` MAF cutoff for common vs. rare variants (default=NULL). It should be a numeric value between 0 and 0.5, or NULL.

`MGC_Cutoff` Cutoff for the minimum genotype count in either females or males.

`kins` For the mixed data, kins is a block matrix, interpreted as the genetic relatedness among these individuals, including general pedigrees and unrelated individuals. For general pedigrees, it is a kinship matrix, indicating the genetic relatedness among individuals within general pedigrees, calculated using the dedicated method for kinship coefficients of X chromosome provided by the "kinship2" package in R software.

`method` Optional: A character string indicating which kind of association tests is to be conducted. There are four options: "MTplinkw", "variance", "joint" (default) and "all". method="MTplinkw": MTplinkw; method="variance": MwM3VNA; method="joint": MpMV; method="all": all of the above association tests.

Value

The p values and the test statistics of association tests selected by the method option for each SNP.

Examples

```
MpMV_test(Genotype,Y,Sex,
                    Covariate=mixed[,"Age"],
                    missing_cutoff=0.15,
                    MAF_Cutoff=NULL,
                    MGC_Cutoff=20,
                    kins=GRM,
                    method='joint')
```

MQMV_test

The mean-variance-based methods: MQMVXcat and MQMVZmax, where MQMVXcat is a method that accounts for different XCI patterns and simultaneously test for differences in both the means and variances of a quantitative trait, while MQMVZmax is a mean-variance-based method that considers different DC patterns.

Description

A function to obtain the p values and the test statistics of the mean_test (i.e., MQXcat and MQZmax), the variance_test (i.e.,MwM3VNA), the MQMV_test (i.e., MQMVXcat and MQMVZmax) or all. MQMVXcat and MQMVZmax are designed to test for both the mean differences and the variance heterogeneity of the trait value across genotypes. MQXcat and MQZmax are used for testing the mean differences of the trait value only. MwM3VNA is for testing the variance heterogeneity only.

Usage

```
MQMV_test(
  Genotype,
  Y,
  Sex,
  Covariate = NULL,
  missing_cutoff = 0.15,
  MAF_Cutoff = NULL,
  MGC_Cutoff = 20,
  kins = NULL,
  method = "joint"
)
```

Arguments

Genotype	A numeric genotype matrix with each row as a different individual and each column as a separate SNP. Each genotype is coded as 0, 1 or 2 for females and coded as 0 or 1 for males, indicating the number of reference allele.
Y	A numeric vector of a quantitative trait, such as height.
Sex	A vector of the genetic sex following PLINK default coding, where males are coded as 1 and females are coded as 2.
Covariate	Optional: a vector or a matrix of covariates, such as age.
missing_cutoff	Cutoff of the missing rates of SNPs (default=0.15). Any SNPs with missing rates higher than the cutoff will be excluded from the analysis.
MAF_Cutoff	MAF cutoff for common vs. rare variants (default=NULL). It should be a numeric value between 0 and 0.5, or NULL. When it is NULL, 1/ sqrt(2 SampleSize) will be used (Ionita-Laza et al. 2013). Only common variants are included in the analysis.
MGC_Cutoff	Cutoff for the minimum genotype count in either females or males.
kins	For the mixed data, kins is a block matrix, interpreted as the genetic relatedness among these individuals, including general pedigrees and unrelated individuals. For general pedigrees, it is a kinship matrix, indicating the genetic relatedness among individuals within general pedigrees, calculated using the dedicated method for kinship coefficients of X chromosome provided by the "kinship2" package in R software.
method	Optional: A character string indicating which kind of association tests is to be conducted. There are four options: "mean", "variance", "joint" (default) and "all". method="mean": MQXcat and MQZmax; method="variance": MwM3VNA; method="joint": MQMVXcat and MQMVZmax; method="all": all of the above association tests.

Value

The p values and the test statistics of association tests selected by the method option for each SNP.

Examples

```
MQMV_test(Genotype,Y,Sex,
                    Covariate=mixed[,"Age"],
                    missing_cutoff=0.15,
```

```
MAF_Cutoff=NULL,
MGC_Cutoff=20,
kins=GRM,
method='joint')
```

`MTchenw_test` *mean-based method: MTchenw, including a dominant effect of heterozygous (Aa) females*

Description

A function to obtain the p value and the test statistic of MTchenw for testing the mean difference of the trait value across genotypes.

Usage

```
MTchenw_test(
  Genotype,
  Y,
  Sex,
  Covariate = NULL,
  missing_cutoff = 0.15,
  MAF_Cutoff = NULL,
  MGC_Cutoff = 20,
  kins = kins
)
```

Arguments

`Genotype`	A numeric genotype matrix with each row as a different individual and each column as a separate SNP. Each genotype is coded as 0, 1 or 2 for females and coded as 0 or 1 for males, indicating the number of reference allele.
`Y`	A numeric vector of a quantitative trait, such as height.
`Sex`	A vector of the genetic sex following PLINK default coding, where males are coded as 1 and females are coded as 2.
`Covariate`	Optional: a vector or a matrix of covariates, such as age.
`missing_cutoff`	Cutoff of the missing rates of SNPs (default=0.15). Any SNPs with missing rates higher than the cutoff will be excluded from the analysis.
`MAF_Cutoff`	MAF cutoff for common vs. rare variants (default=NULL). It should be a numeric value between 0 and 0.5, or NULL. When it is NULL, 1/ sqrt(2 SampleSize) will be used (Ionita-Laza et al. 2013). Only common variants are included in the analysis.
`MGC_Cutoff`	Cutoff for the minimum genotype count in either females or males.
`kins`	For the mixed data, kins is a block matrix, interpreted as the genetic relatedness among these individuals, including general pedigrees and unrelated individuals. For general pedigrees, it is a kinship matrix, indicating the genetic relatedness among individuals within general pedigrees, calculated using the dedicated method for kinship coefficients of X chromosome provided by the "kinship2" package in R software.

Value

The p value and test statistic of MTchenw.

Examples

```
MTchenw_test(Genotype,Y,Sex,
                        Covariate=mixed[,"Age"],
                        missing_cutoff=0.15,
                        MAF_Cutoff=NULL,
                        MGC_Cutoff=20,
                        kins=GRM)
```

MTplinkw_test *mean-based method:MTplinkw*

Description

A function to obtain the p value and the test statistic of MTplinkw for testing the mean difference of the trait value across genotypes.

Usage

```
MTplinkw_test(
  Genotype,
  Y,
  Sex,
  Covariate = NULL,
  missing_cutoff = 0.15,
  MAF_Cutoff = NULL,
  MGC_Cutoff = 20,
  kins = kins
)
```

Arguments

Genotype	A numeric genotype matrix with each row as a different individual and each column as a separate SNP. Each genotype is coded as 0, 1 or 2 for females and coded as 0 or 1 for males, indicating the number of reference allele.
Y	A numeric vector of a quantitative trait, such as height.
Sex	A vector of the genetic sex following PLINK default coding, where males are coded as 1 and females are coded as 2.
Covariate	Optional: a vector or a matrix of covariates, such as age.
missing_cutoff	Cutoff of the missing rates of SNPs (default=0.15). Any SNPs with missing rates higher than the cutoff will be excluded from the analysis.
MAF_Cutoff	MAF cutoff for common vs. rare variants (default=NULL). It should be a numeric value between 0 and 0.5, or NULL. When it is NULL, 1/ sqrt(2 SampleSize) will be used (Ionita-Laza et al. 2013). Only common variants are included in the analysis.
MGC_Cutoff	Cutoff for the minimum genotype count in either females or males.

kins — For the mixed data, kins is a block matrix, interpreted as the genetic relatedness among these individuals, including general pedigrees and unrelated individuals. For general pedigrees, it is a kinship matrix, indicating the genetic relatedness among individuals within general pedigrees, calculated using the dedicated method for kinship coefficients of X chromosome provided by the "kinship2" package in R software.

Value

The p value and test statistic of MTplinkw.

Examples

```
MTplinkw_test(Genotype,Y,Sex,
                        Covariate=mixed[,"Age"],
                        missing_cutoff=0.15,
                        MAF_Cutoff=NULL,
                        MGC_Cutoff=20,
                        kins=GRM)
```

Tchenw_test

mean-based method: Tchenw for unrelated individuals, including a dominant effect of heterozygous (Aa) females Similar to the MTchen method, Tchenw is an approach designed for unrelated individuals and therefore does not incorporate a kinship matrix to account for correlations between individuals.

Description

mean-based method: Tchenw for unrelated individuals, including a dominant effect of heterozygous (Aa) females Similar to the MTchen method, Tchenw is an approach designed for unrelated individuals and therefore does not incorporate a kinship matrix to account for correlations between individuals.

Usage

```
Tchenw_test(
  Genotype,
  Y,
  Sex,
  Covariate = NULL,
  missing_cutoff = 0.15,
  MAF_Cutoff = NULL,
  MGC_Cutoff = 20
)
```

Arguments

Genotype — A numeric genotype matrix with each row as a different individual and each column as a separate SNP. Each genotype is coded as 0, 1 or 2 for females and coded as 0 or 1 for males, indicating the number of reference allele.

Y — A numeric vector of a quantitative trait, such as height.

Sex	A vector of the genetic sex following PLINK default coding, where males are coded as 1 and females are coded as 2.
Covariate	Optional: a vector or a matrix of covariates, such as age.
missing_cutoff	Cutoff of the missing rates of SNPs (default=0.15). Any SNPs with missing rates higher than the cutoff will be excluded from the analysis.
MAF_Cutoff	MAF cutoff for common vs. rare variants (default=NULL). It should be a numeric value between 0 and 0.5, or NULL. When it is NULL, 1/ sqrt(2 SampleSize) will be used (Ionita-Laza et al. 2013). Only common variants are included in the analysis.
MGC_Cutoff	Cutoff for the minimum genotype count in either females or males.

Value

The p value and test statistic of Tchenw.

Examples

```
Tchenw_test(Genotype,Y,Sex,
                      Covariate=unrelated[,"Age"],
                      missing_cutoff=0.15,
                      MAF_Cutoff=NULL,
                      MGC_Cutoff=20)
```

TcMV_test *mean-variance-based method for unrelated individuals:TcMV, simultaneously test for differences in both the means and variances of a quantitative trait.*

Description

A function to obtain the p value and the test statistics of the Tchenw_test (i.e., Tchenw), the scale test (i.e.,wM3VNA) from the "QMVtest" package, the TcMV_test(i.e., TcMV) or all.

Usage

```
TcMV_test(
  Genotype,
  Y,
  Sex,
  Covariate = NULL,
  missing_cutoff = 0.15,
  MAF_Cutoff = NULL,
  MGC_Cutoff = 20,
  method = "joint"
)
```

Arguments

Genotype	A numeric genotype matrix with each row as a different individual and each column as a separate SNP. Each genotype is coded as 0, 1 or 2 for females and coded as 0 or 1 for males, indicating the number of reference allele.
Y	A numeric vector of a quantitative trait, such as height.
Sex	A vector of the genetic sex following PLINK default coding, where males are coded as 1 and females are coded as 2.
Covariate	ptional: a vector or a matrix of covariates, such as age.
missing_cutoff	Cutoff of the missing rates of SNPs (default=0.15). Any SNPs with missing rates higher than the cutoff will be excluded from the analysis.
MAF_Cutoff	MAF cutoff for common vs. rare variants (default=NULL). It should be a numeric value between 0 and 0.5, or NULL.
MGC_Cutoff	Cutoff for the minimum genotype count in either females or males.
method	Optional: A character string indicating which kind of association tests is to be conducted. There are four options: "Tchenw", "scale", "joint" (default) and "all". method="Tchenw": Tchenw; method="scale": wM3VNA; method="joint": TcMV; method="all": all of the above association tests.

Value

The p values and the test statistics of association tests selected by the method option for each SNP.

Examples

```
TcMV_test(Genotype,Y,Sex,
                  Covariate=unrelated[,"Age"],
                  missing_cutoff=0.15,
                  MAF_Cutoff=NULL,
                  MGC_Cutoff=20,
                  method='joint')
```

Tplinkw_test *mean-based method: Tplinkw for unrelated data*

Description

#' Similar to the MTplink method, Tplinkw is an approach designed for unrelated individuals and therefore does not incorporate a kinship matrix to account for correlations between individuals.

Usage

```
Tplinkw_test(
  Genotype,
  Y,
  Sex,
  Covariate = NULL,
  missing_cutoff = 0.15,
  MAF_Cutoff = NULL,
  MGC_Cutoff = 20
)
```

Arguments

Genotype	A numeric genotype matrix with each row as a different individual and each column as a separate SNP. Each genotype is coded as 0, 1 or 2 for females and coded as 0 or 1 for males, indicating the number of reference allele.
Y	A numeric vector of a quantitative trait, such as height.
Sex	A vector of the genetic sex following PLINK default coding, where males are coded as 1 and females are coded as 2.
Covariate	ptional: a vector or a matrix of covariates, such as age.
missing_cutoff	Cutoff of the missing rates of SNPs (default=0.15). Any SNPs with missing rates higher than the cutoff will be excluded from the analysis.
MAF_Cutoff	MAF cutoff for common vs. rare variants (default=NULL). It should be a numeric value between 0 and 0.5, or NULL.
MGC_Cutoff	Cutoff for the minimum genotype count in either females or males.

Value

The p value and test statistic of Tplinknw.

Examples

```
Tplinkw_test(Genotype,Y,Sex,
                      Covariate=unrelated[,"Age"],
                      missing_cutoff=0.15,
                      MAF_Cutoff=NULL,
                      MGC_Cutoff=20)
```

TpMV_test *mean-variance-based method for unrelated individuals:TpMV, simultaneously test for differences in both the means and variances of a quantitative trait.*

Description

A function to obtain the p value and the test statistics of the Tplinkw_test (i.e., Tplinkw), the scale test (i.e.,wM3VNA) from the "QMVtest" package, the TpMV_test(i.e., TpMV) or all.

Usage

```
TpMV_test(
  Genotype,
  Y,
  Sex,
  Covariate = NULL,
  missing_cutoff = 0.15,
  MAF_Cutoff = NULL,
  MGC_Cutoff = 20,
  method = "joint"
)
```

Arguments

Genotype	A numeric genotype matrix with each row as a different individual and each column as a separate SNP. Each genotype is coded as 0, 1 or 2 for females and coded as 0 or 1 for males, indicating the number of reference allele.
Y	A numeric vector of a quantitative trait, such as height.
Sex	A vector of the genetic sex following PLINK default coding, where males are coded as 1 and females are coded as 2.
Covariate	ptional: a vector or a matrix of covariates, such as age.
missing_cutoff	Cutoff of the missing rates of SNPs (default=0.15). Any SNPs with missing rates higher than the cutoff will be excluded from the analysis.
MAF_Cutoff	MAF cutoff for common vs. rare variants (default=NULL). It should be a numeric value between 0 and 0.5, or NULL.
MGC_Cutoff	Cutoff for the minimum genotype count in either females or males.
method	Optional: A character string indicating which kind of association tests is to be conducted. There are four options: "Tplinkw", "scale", "joint" (default) and "all". method="Tplinkw": Tplinkw; method="scale": wM3VNA; method="joint": TpMV; method="all": all of the above association tests.

Value

The p values and the test statistics of association tests selected by the method option for each SNP.

Examples

```
TpMV_test(Genotype,Y,Sex,
                  Covariate = unrelated[,"Age"],
                  missing_cutoff = 0.15,
                  MGC_Cutoff = 2,
                  method = 'all')
```

---

variance_test *variance-based method–MwM3VNA:variance_test*

Description

A function to obtain the p-value and the test statistic of MwM3VNA testing for the variance heterogeneity of the trait values across genotypes. This function takes the genotype of SNPs (Genotype), the sex (Sex), the quantitative trait (Y) in the sample population, and possibly additional covariates, such as age, as input.

Usage

```
variance_test(
  Genotype,
  Y,
  Sex,
  Covariate = NULL,
  missing_cutoff = 0.15,
```

```
  MAF_Cutoff = NULL,
  MGC_Cutoff = 20,
  kins = NULL
)
```

Arguments

Genotype	A numeric genotype matrix with each row as a different individual and each column as a separate SNP. Each genotype is coded as 0, 1 or 2 for females and coded as 0 or 1 for males, indicating the number of reference allele.
Y	A numeric vector of a quantitative trait, such as height.
Sex	A vector of the genetic sex following PLINK default coding, where males are coded as 1 and females are coded as 2.
Covariate	Optional: a vector or a matrix of covariates, such as age.
missing_cutoff	Cutoff of the missing rates of SNPs (default=0.15). Any SNPs with missing rates higher than the cutoff will be excluded from the analysis.
MAF_Cutoff	MAF cutoff for common vs. rare variants (default=NULL). It should be a numeric value between 0 and 0.5, or NULL. When it is NULL, 1/ sqrt(2 SampleSize) will be used (Ionita-Laza et al. 2013). Only common variants are included in the analysis.
MGC_Cutoff	Cutoff for the minimum genotype count in either females or males.
kins	For the mixed data, kins is a block matrix, interpreted as the genetic relatedness among these individuals, including general pedigrees and unrelated individuals. For general pedigrees, it is a kinship matrix, indicating the genetic relatedness among individuals within general pedigrees, calculated using the dedicated method for kinship coefficients of X chromosome provided by the "kinship2" package in R software.

Value

The p value and test statistic of MwM3VNA

Examples

```
variance_test(Genotype,Y,Sex,
                        Covariate=mixed[,"Age"],
                        missing_cutoff=0.15,
                        MAF_Cutoff=NULL,
                        MGC_Cutoff=20)
```