Package 'QMVtest'

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Type Package

Title Robust association tests for quantitative traits on the X chromosome

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Description This code contains sex stratified X chromosome location (mean-based association) tests (QXcat and QZmax), model-based three-degree of freedom test for variance heterogeneity associated with non-additive genotype (wM3VNA3.3) and combining the p-value of QXcat or QZmax with that of wM3VNA3.3, which tests for both the difference of means and that of variances for quantitative trait (QMVXcat or QMVZmax), with or without covariates using unrelated individuals.

LazyData true

License GPL-3

Encoding UTF-8

Imports methods, stats, quantreg, mvtnorm, expm, bigsnpr, xgboost

NeedsCompilation no

RoxygenNote 7.1.2

Depends R (>= 3.6.0)

R topics documented:

Genotype	*a numeric genotype matrix with each row as a different individual and each column as a separate snp.*

Description

For females, each genotype is coded as 0, 1, 2, and NA for AA, Aa, aa, and missing; for males, each genotype is coded as 0, 1, and NA for A, a, and missing.

Usage

```
Genotype
```

Format

a data for 4000 individuals and 31 SNPs.

location_test	*Sex stratified X chromosome location (mean-based association) tests for quantitative traits*

Description

This function takes as input the genotype of SNPs (Genotype), the SEX (Sex), a quantitative trait (Y) in a sample population, and possibly additional covariates, such as principal components. The function returns the location association *p*-values for each SNP (Yang et al., 2021).

Usage

```
location_test(Genotype,Y,Sex,
              Covariate=NULL,
              missing_cutoff=0.15,
              MAF_Cutoff=NULL,
              MGC_Cutoff=30)
```

Arguments

Genotype	a numeric genotype matrix with each row as a different individual and each column as a separate snp, must contain values 0, 1, 2's coded for the number of reference allele. The length/dimension of Genotype should match that of Y, and/or Sex and Covariate.
Y	a numeric vector of quantitative trait, such as human height.
Sex	the genetic sex of individuals in the sample population, must be a vector of 1's and 2's following PLINK default coding, where males are coded as 1 and females 2.
Covariate	optional: a vector or a matrix of covariates, such as age, BMI or principal components.
missing_cutoff	a 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. Only common variants are included in the analysis.

`MGC_Cutoff` Cutoff for the minimum genotype count in either females/males (default=30), SNPs whose minimum genotype count are less than this Cutoff will not be included in the analysis. This is based on the quality control that SNPs with a minimum count below 30 should be removed to avoid inflated type I errors (Deng et al., 2019; Soave et al., 2015).

Details

There are 2 types of Sex stratified X chromosome location (mean-based association) tests: QXcat and QZmax. QXcat: Sex stratified X chromosome association test for quantitative traits considering various XCI patterns; QZmax: Sex stratified X chromosome association test for quantitative traits considering different dosage compensation patterns.

Value

p-values of QXcat and QZmax for each SNP.

Note

QXcat and QZmax are designed for testing mean differences of the trait value. In QXcat, we obtain the *p*-values for females and males, respectively, by testing mean differences of the trait value via weighted linear regression models. Then, we combine these two *p*-values together by Fisher's method. In QZmax, we use different sample sizes as weights, which stand for different dosage compensation patterns according to Wang et al. (2019), to combine the test statistics for females and males.

Author(s)

Zi-Ying Yang, Wei Liu, Yu-Xin Yuan and Ji-Yuan Zhou

References

Zi-Ying Yang, Wei Liu, Yu-Xin Yuan, Yi-Fan Kong, Pei-Zhen Zhao, Wing Kam Fung and Ji-Yuan Zhou. (2022) Robust association tests for quantitative traits on the X chromosome.

Wei Q. Deng, Shihong Mao, Anette Kalnapenkis, Tõnu Esko, Reedik Mägi, Guillaume Paré and Lei Sun. (2019) Analytical strategies to include the X-chromosome in variance heterogeneity analyses: Evidence for trait-specific polygenic variance structure. *Genet Epidemiol*. **43**(7):815-830. doi: 10.1002/gepi.22247. PMID:31332826.

David Soave, Harriet Corvol, Naim Panjwani, Jiafen Gong, Weili Li, Pierre-Yves Boëlle, Peter R. Durie, Andrew D. Paterson, Johanna M. Rommens, Lisa J. Strug and Lei Sun. (2015) A Joint Location-Scale Test Improves Power to Detect Associated SNPs, Gene Sets, and Pathways. *American journal of human genetics*. **97**(1): 125–138. doi: 10.1016/j.ajhg.2015.05.015. PMID: 26140448.

Peng Wang, Si-Qi Xu, Bei-Qi Wang, Wing Kam Fung and Ji-Yuan Zhou. (2019) A robust and powerful test for case-control genetic association study on X chromosome. *Statistical Methods in Medical Research*. **28**(10-11):3260-3272. doi: 10.1177/0962280218799532. PMID: 30232923.

Examples

```
#Phedata: phenotype(Y) and covariates(Sex, age and BMI) data for 4000 individuals
data(Phedata)
#Genotype: a data for 4000 individuals and 31 SNPs
data(Genotype)

#location test
#no covariate
#set "Covariate=NULL"
location_test(Genotype,Phedata$Y,
              Phedata$Sex,
              Covariate=NULL,
              missing_cutoff=0.15,
              MAF_Cutoff=NULL,MGC_Cutoff=10)

#age and BMI as covariates
location_test(Genotype,Phedata$Y,
              Phedata$Sex,
              Covariate=Phedata[,c(-1,-2)],
              missing_cutoff=0.15,
              MAF_Cutoff=NULL,MGC_Cutoff=10)
```

`Phedata` *a phenotype(Y) and covariates(Sex,age,BMI) data for 4000 individuals.*

Description

`Phedata$Sex` must be a vector of 1's and 2's following PLINK default coding, where males are coded as 1 and females 2.

Usage

```
Phedata
```

Format

a data for 4000 individuals and 4 variables.

Y a numeric variable of quantitative trait.

Sex the genetic sex of individuals in the sample population.

age the age of individuals in the sample population

BMI Body mass index

QMV_test *Robust association tests for quantitative traits on the X chromosome*

Description

This function takes as input the genotype of SNPs (Genotype), the SEX (Sex), a quantitative trait (Y) in a sample population, and possibly additional covariates, such as principal components. The function returns the robust X-chromosomal association *p*-values for each SNP (Yang et al., 2021).

Usage

```
QMV_test(Genotype,Y,Sex,
         Covariate=NULL,
         missing_cutoff=0.15,
         MAF_Cutoff=NULL,
         MGC_Cutoff=30,
         method='location')
```

Arguments

Genotype	a numeric genotype matrix with each row as a different individual and each column as a separate snp, must contain values 0, 1, 2's coded for the number of reference allele. The length/dimension of Genotype should match that of Y, and/or Sex and Covariate.
Y	a numeric vector of quantitative trait, such as human height.
Sex	the genetic sex of individuals in the sample population, must be a vector of 1's and 2's following PLINK default coding, where males are coded as 1 and females 2.
Covariate	optional: a vector or a matrix of covariates, such as age, BMI or principal components.
missing_cutoff	a 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. Only common variants are included in the analysis.
MGC_Cutoff	Cutoff for the minimum genotype count in either females/males (default=30), SNPs whose minimum genotype count are less than this Cutoff will not be included in the analysis. This is based on the quality control that SNPs with a minimum count below 30 should be removed to avoid inflated type I errors (Deng et al., 2019; Soave et al., 2015).
method	a character string indicating which kind of association tests is to be computed. One of "location"(default), "scale" , "joint" or "all": can be abbreviated.method="location": QXcat and QZmax; method="scale": wM3VNA3.3; method="joint": QMVXcat and QMVZmax; method="all": All of the above association tests.

Details

QXcat and QZmax: Sex stratified X chromosome location (mean-based association) tests; wM3VNA3.3: Model-based three-degree of freedom test for variance heterogeneity associated with non-additive genotype; QMVXcat (QMVZmax): combining the *p*-value of QXcat (QZmax) with that of wM3VNA3.3, which tests for both the difference of means and that of variances.

Value

robust association *p*-values for each SNP.

Author(s)

Zi-Ying Yang, Wei Liu, Yu-Xin Yuan and Ji-Yuan Zhou

References

Zi-Ying Yang, Wei Liu, Yu-Xin Yuan, Yi-Fan Kong, Pei-Zhen Zhao, Wing Kam Fung and Ji-Yuan Zhou. (2022) Robust association tests for quantitative traits on the X chromosome.

Wei Q. Deng, Shihong Mao, Anette Kalnapenkis, Tõnu Esko, Reedik Mägi, Guillaume Paré and Lei Sun. (2019) Analytical strategies to include the X-chromosome in variance heterogeneity analyses: Evidence for trait-specific polygenic variance structure. *Genet Epidemiol*. **43**(7):815-830. doi: 10.1002/gepi.22247. PMID:31332826.

David Soave, Harriet Corvol, Naim Panjwani, Jiafen Gong, Weili Li, Pierre-Yves Boëlle, Peter R. Durie, Andrew D. Paterson, Johanna M. Rommens, Lisa J. Strug and Lei Sun. (2015) A Joint Location-Scale Test Improves Power to Detect Associated SNPs, Gene Sets, and Pathways. *American journal of human genetics*. **97**(1): 125–138. doi: 10.1016/j.ajhg.2015.05.015. PMID: 26140448.

Peng Wang, Si-Qi Xu, Bei-Qi Wang, Wing Kam Fung and Ji-Yuan Zhou. (2019) A robust and powerful test for case-control genetic association study on X chromosome. *Statistical Methods in Medical Research*. **28**(10-11):3260-3272. doi: 10.1177/0962280218799532. PMID: 30232923.

Examples

```
#Phedata: phenotype(Y) and covariates(Sex,age and BMI) data for 4000 individuals
data(Phedata)
#Genotype: a data for 4000 individuals and 31 SNPs
data(Genotype)

#location tests: QXcat and QZmax
QMV_test(Genotype,Phedata$Y,
         Phedata$Sex,
         Covariate=Phedata[,c(-1,-2)],
         missing_cutoff=0.15,
         MAF_Cutoff=NULL,
         MGC_Cutoff=10,
         method='location')

#scale test: wM3VNA3.3
QMV_test(Genotype,Phedata$Y,
         Phedata$Sex,
         Covariate=Phedata[,c(-1,-2)],
         missing_cutoff=0.15,
         MAF_Cutoff=NULL,
         MGC_Cutoff=10,
         method='scale')

#joint tests: QMVXcat and QMVZmax
QMV_test(Genotype,Phedata$Y,
         Phedata$Sex,
         Covariate=Phedata[,c(-1,-2)],
         missing_cutoff=0.15,
```

```
          MAF_Cutoff=NULL,
          MGC_Cutoff=10,
          method='joint')

#All of the above association tests
QMV_test(Genotype,Phedata$Y,
          Phedata$Sex,
          Covariate=Phedata[,c(-1,-2)],
          missing_cutoff=0.15,
          MAF_Cutoff=NULL,
          MGC_Cutoff=10,
          method='all')
```

`QMV_test_bed` *Read Plink bed files into R, and perform robust association tests for quantitative traits on the X chromosome*

Description

This function takes as input the path to file with extension ".bed" (`bedfile`), and possibly additional path to file with covariates (`Covariate_path`) in a sample population. The function returns the robust X-chromosomal association *p*-values for each SNP (Yang et al., 2021).

Usage

```
QMV_test_bed(bedfile,fastImpute=FALSE,
             Covariate_path=NULL,
             Covariate_missing = NA,
             Covariate.header=FALSE,
             missing_cutoff=0.15,
             MAF_Cutoff=NULL,
             MGC_Cutoff=30,
             method='location')
```

Arguments

`bedfile`	Path to file with extension ".bed" to read. You need the corresponding ".bim" and ".fam" in the same directory.
`fastImpute`	Logical scalar defaulting to False (or F) indicating no imputation for missing genotypes. If fastImpute=TURE, imputation is based on the `bigsnpr::snp_fastImpute`: Fast imputation algorithm based on local XGBoost models.
`Covariate_path`	Path to file with covariates to read. The covariates needed to be adjusted, a text file with a header line, and one line per sample with the following 6+C fields (where C is the number of covariates): Family ID (FID), Individual ID (IID), Paternal within-family ID (PID), Maternal within-family ID (MID), Sex and Main phenotype value(Phenotype). This is followed by one fields per covariate.
`Covariate_missing`	The input variable "covariate_missing" is the missing value for the covariates in the data file, and the default value is NA.

`Covariate.header`
: Logical scalar defaulting to False (or F) indicating whether the covariate file contains variable names or not.

`missing_cutoff`
: a 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 Sample-Size) will be used. Only common variants are included in the analysis.

`MGC_Cutoff`
: Cutoff for the minimum genotype count in either females/males (default=30), SNPs whose minimum genotype count are less than this Cutoff will not be included in the analysis. This is based on the quality control that SNPs with a minimum count below 30 should be removed to avoid inflated type I errors (Deng et al., 2019; Soave et al., 2015).

`method`
: a character string indicating which kind of association tests is to be computed. One of "location"(default), "scale" , "joint" or "all": can be abbreviated.method="location": QXcat and QZmax; method="scale": wM3VNA3.3; method="joint": QMVXcat and QMVZmax; method="all": All of the above association tests.

Value

robust association *p*-values for each SNP.

Author(s)

Zi-Ying Yang, Wei Liu, Yu-Xin Yuan and Ji-Yuan Zhou

References

Zi-Ying Yang, Wei Liu, Yu-Xin Yuan, Yi-Fan Kong, Pei-Zhen Zhao, Wing Kam Fung and Ji-Yuan Zhou. (2022) Robust association tests for quantitative traits on the X chromosome.

Wei Q. Deng, Shihong Mao, Anette Kalnapenkis, Tõnu Esko, Reedik Mägi, Guillaume Paré and Lei Sun. (2019) Analytical strategies to include the X-chromosome in variance heterogeneity analyses: Evidence for trait-specific polygenic variance structure. *Genet Epidemiol*. **43**(7):815-830. doi: 10.1002/gepi.22247. PMID:31332826.

David Soave, Harriet Corvol, Naim Panjwani, Jiafen Gong, Weili Li, Pierre-Yves Boëlle, Peter R. Durie, Andrew D. Paterson, Johanna M. Rommens, Lisa J. Strug and Lei Sun. (2015) A Joint Location-Scale Test Improves Power to Detect Associated SNPs, Gene Sets, and Pathways. *American journal of human genetics*. **97**(1): 125–138. doi: 10.1016/j.ajhg.2015.05.015. PMID: 26140448.

Peng Wang, Si-Qi Xu, Bei-Qi Wang, Wing Kam Fung and Ji-Yuan Zhou. (2019) A robust and powerful test for case-control genetic association study on X chromosome. *Statistical Methods in Medical Research*. **28**(10-11):3260-3272. doi: 10.1177/0962280218799532. PMID: 30232923.

Examples

```
path <- system.file("extdata", package = "QMVtest")

QMV_test_bed(paste(path,"example-missing.bed",sep = '/'),
             fastImpute=FALSE,
             Covariate_path=paste(path,"Covariate.txt",sep = '/'),
             Covariate_missing = NA,
             Covariate.header=TRUE,
```

```
              missing_cutoff=0.15,
              MAF_Cutoff=NULL,
              MGC_Cutoff=30,
              method='location')
```

`QMV_test_ped` *Read Plink Raw files into R, and perform robust association tests for quantitative traits on the X chromosome*

Description

This function takes as input the path to file with extension ".raw" (`ped_raw_path`), the Path to file with extension ".map" (`map_path`), and possibly additional path to file with covariates (`Covariate_path`) in a sample population. The function returns the robust X-chromosomal association *p*-values for each SNP (Yang et al., 2021).

Usage

```
QMV_test_ped(ped_raw_path,trait_missing=NA,
             Genotype_missing=NA,
             ped_raw.header=FALSE,
             Covariate_path=NULL,
             Covariate_missing = NA,
             Covariate.header=FALSE,
             map_path=NULL,map_header=FALSE,
             missing_cutoff=0.15,
             MAF_Cutoff=NULL,MGC_Cutoff=30,
             method='location')
```

Arguments

`ped_raw_path`	Path to file with extension ".raw" to read. Plink raw format, produced by "–recode A" for use with R. A text file with a header line, and then one line per sample with V+6 (for "–recode A") fields, where V is the number of variants. The first six fields are: Family ID (FID), Individual ID (IID), Paternal within-family ID (PID), Maternal within-family ID (MID), Sex and Main phenotype value(Phenotype). This is followed by one fields per variant: Allelic dosage (0/1/2/'NA' for diploid variants). Either Paternal's or Maternal's ID is set to 0 for founders, i.e. individuals with no parents. Numeric coding for Sex is 0 = unknown, 1 = male, 2 = female. For quantitative traits, phenotypes are individuals' trait values. The ped provided to this function should only contain SNPs on X chromosome. The male individuals are hemizygote at all the SNPs on X chromosome.
`trait_missing`	The input variable "trait_missing" is the missing value for the trait in the data file, and the default value is NA. It may be -9 in some data files; or other numeric value.
`Genotype_missing`	The input variable "Genotype_missing" represents that the genotype at the locus is missing, and the default value is NA. It may be -9 in some data files; or other numeric value.

`ped_raw.header` Logical scalar defaulting to False (or F) indicating whether the ped file contains variable names or not.

`Covariate_path` Path to file with covariates to read. The covariates needed to be adjusted, a text file with a header line, and one line per sample with the following 6+C fields (where C is the number of covariates): Family ID (FID), Individual ID (IID), Paternal within-family ID (PID), Maternal within-family ID (MID), Sex and Main phenotype value(Phenotype). This is followed by one fields per covariate.

`Covariate_missing` The input variable "covariate_missing" is the missing value for the covariates in the data file, and the default value is NA.

`Covariate.header` Logical scalar defaulting to False (or F) indicating whether the covariate file contains variable names or not.

`map_path` Path to file with extension ".map" to read. By default, each line of the MAP file describes a single marker and must contain exactly 4 columns:chromosome (1-22, X, Y or 0 if unplaced), rs# or snp identifier, Genetic distance (morgans) and Base-pair position (bp units).

`map_header` Logical scalar defaulting to False (or F) indicating whether the map file contains variable names or not.

`missing_cutoff` a 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. Only common variants are included in the analysis.

`MGC_Cutoff` Cutoff for the minimum genotype count in either females/males (default=30), SNPs whose minimum genotype count are less than this Cutoff will not be included in the analysis. This is based on the quality control that SNPs with a minimum count below 30 should be removed to avoid inflated type I errors (Deng et al., 2019; Soave et al., 2015).

`method` a character string indicating which kind of association tests is to be computed. One of "location"(default), "scale" , "joint" or "all": can be abbreviated.method="location": QXcat and QZmax; method="scale": wM3VNA3.3; method="joint": QMVXcat and QMVZmax; method="all": All of the above association tests.

Value

robust association *p*-values for each SNP.

Author(s)

Zi-Ying Yang, Wei Liu, Yu-Xin Yuan and Ji-Yuan Zhou

References

Zi-Ying Yang, Wei Liu, Yu-Xin Yuan, Yi-Fan Kong, Pei-Zhen Zhao, Wing Kam Fung and Ji-Yuan Zhou. (2022) Robust association tests for quantitative traits on the X chromosome.

Wei Q. Deng, Shihong Mao, Anette Kalnapenkis, Tõnu Esko, Reedik Mägi, Guillaume Paré and Lei Sun. (2019) Analytical strategies to include the X-chromosome in variance heterogeneity analyses: Evidence for trait-specific polygenic variance structure. *Genet Epidemiol*. **43**(7):815-830. doi: 10.1002/gepi.22247. PMID:31332826.

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Examples

```
path <- system.file("extdata", package = "QMVtest")

QMV_test_ped(paste(path,"example.raw",sep = '/'),trait_missing=NA,
             Genotype_missing=NA,
             ped_raw.header=FALSE,
             Covariate_path=paste(path,"Covariate.txt",sep = '/'),
             Covariate_missing = NA,
             Covariate.header=TRUE,
             map_path=paste(path,"example.map",sep = '/'),
             map_header=FALSE,
             missing_cutoff=0.15,
             MAF_Cutoff=NULL,
             MGC_Cutoff=30,
             method='location')
```

`scale_test` *Levene's regression tests for variance homogeneity by SNP genotype*

Description

This function takes as input the genotype of SNPs (`Genotype`), the SEX (`Sex`), a quantitative trait (`Y`) in a sample population, and possibly additional covariates, such as principal components. The function then returns the variance heterogeneity *p*-values using the generalized Levene's test (Deng et al., 2019).

Usage

```
scale_test(Genotype,Y,Sex,
           Covariate=NULL,
           missing_cutoff=0.15,
           MAF_Cutoff=NULL,
           MGC_Cutoff=30)
```

Arguments

`Genotype`	a numeric genotype matrix with each row as a different individual and each column as a separate snp, must contain values 0, 1, 2's coded for the number of reference allele.The length/dimension of `Genotype` should match that of `Y`, and/or `Sex` and `Covariate`.
`Y`	a numeric vector of quantitative trait, such as human height.

`Sex`	the genetic sex of individuals in the sample population, must be a vector of 1's and 2's following PLINK default coding, where males are coded as 1 and females 2.
`Covariate`	optional: a vector or a matrix of covariates, such as age, BMI or principal components.
`missing_cutoff`	a 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.Only common variants are included in the analysis.
`MGC_Cutoff`	Cutoff for the minimum genotype count in either females/males (default=30), SNPs whose minimum genotype count are less than this Cutoff will not be included in the analysis.This is based on the quality control that SNPs with a minimum count below 30 should be removed to avoid inflated type I errors (Deng et al., 2019; Soave et al., 2015).

Details

Deng et al. (2019) assumed that the associations between SNPs and the quantitative trait under study could be biased by sex-specific means or variances because of the different numbers of the copies of X chromosome between females and males. In this regard, wM3VNA3.3 (Model-based three-degree of freedom test for variance heterogeneity associated with non-additive genotype) was proposed.

Value

the Levene's test regression *p*-value according to the model specified.

Author(s)

Zi-Ying Yang, Wei Liu, Yu-Xin Yuan and Ji-Yuan Zhou

References

Zi-Ying Yang, Wei Liu, Yu-Xin Yuan, Yi-Fan Kong, Pei-Zhen Zhao, Wing Kam Fung and Ji-Yuan Zhou. (2022) Robust association tests for quantitative traits on the X chromosome.

Wei Q. Deng, Shihong Mao, Anette Kalnapenkis, Tõnu Esko, Reedik Mägi, Guillaume Paré and Lei Sun. (2019) Analytical strategies to include the X-chromosome in variance heterogeneity analyses: Evidence for trait-specific polygenic variance structure. *Genet Epidemiol*. **43**(7):815-830. doi: 10.1002/gepi.22247. PMID:31332826.

David Soave, Harriet Corvol, Naim Panjwani, Jiafen Gong, Weili Li, Pierre-Yves Boëlle, Peter R. Durie, Andrew D. Paterson, Johanna M. Rommens, Lisa J. Strug and Lei Sun. (2015) A Joint Location-Scale Test Improves Power to Detect Associated SNPs, Gene Sets, and Pathways. *American journal of human genetics*. **97**(1): 125–138. doi: 10.1016/j.ajhg.2015.05.015. PMID: 26140448.

Examples

```
#Phedata: phenotype(Y) and covariates(Sex,age and BMI) data for 4000 individuals
data(Phedata)
#Genotype: a data for 4000 individuals and 31 SNPs
data(Genotype)
```

```
#scale test
#no covariate
#set "Covariate=NULL"
scale_test(Genotype,Phedata$Y,
           Phedata$Sex,
           Covariate=NULL,
           missing_cutoff=0.15,
           MAF_Cutoff=NULL,
           MGC_Cutoff=10)

#age and BMI as covariates
scale_test(Genotype,Phedata$Y,
           Phedata$Sex,
           Covariate=Phedata[,c(-1,-2)],
           missing_cutoff=0.15,
           MAF_Cutoff=NULL,
           MGC_Cutoff=10)
```

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