Package 'milorGWAS'

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Type Package

Title Mixed Logistic Regression for Genome-Wide Analysis Studies (GWAS)

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Description Fast approximate methods for mixed logistic regression in genome-wide analysis studies (GWAS).
Two computationnally efficient methods are proposed for obtaining effect size estimates (beta) in Mixed Logistic Regression in GWAS: the Approximate Maximum Likelihood Estimate (AMLE), and the Offset
method. The wald test obtained with AMLE is identical to the score test. Data can be genotype matrices
in plink format, or dosage (VCF files). The methods are described in details in
Milet et al (2020) <doi:10.1101/2020.01.17.910109>.

License GPL-3

Imports Rcpp (>= 1.0.2)

Depends gaston (>= 1.6)

LinkingTo Rcpp, RcppEigen, gaston

Suggests knitr, rmarkdown, png

VignetteBuilder knitr

NeedsCompilation yes

RoxygenNote 7.3.2

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Contents

`association.test.logistic`

Mixed logistic regression for GWAS

Description

Mixed logistic regression for GWAS

Usage

```
association.test.logistic(
  x,
  Y = x@ped$pheno,
  X = matrix(1, nrow(x)),
  K,
  beg = 1,
  end = ncol(x),
  algorithm = c("amle", "offset"),
  eigenK,
  p = 0,
  model = c("additive", "dominant", "recessive"),
  ...
)
```

Arguments

`x`	a bedmatrix
`Y`	phenotype vector. Default is column `pheno` of `x@ped`
`X`	A matrix of covariates (defaults to a column of ones for the intercept)
`K`	A genetic relationship matrix (or a list of such matrices)
`beg`	Index of the first SNP tested for association
`end`	Index of the last SNP tested for association
`algorithm`	Algorithm to use
`eigenK`	eigen decomposition of K (only if p > 0)
`p`	Number of principal components to include in the model
`model`	Model for the effect allele (allele A2)
`...`	Additional parameter for `gaston::logistic.mm.aireml`

Details

Tests the association between the phenotype and requested SNPs in `x`. The phenotype `Y` is a binary trait. A Wald test is performed using an approximate method defined by the parameter `algorithm`.

Parameter `model` allows to specify an additive model (genotypes A1 A1, A1 A2, and A2 A2 are recoded for analysis as 0, 1 and 2 respectively), a dominant model (genotypes recoded as 0, 1, and 1) or a recessive model (recoded as 0, 0 and 1).

All other arguments are as in `gaston::association.test`.

Value

A data frame giving for each SNP the association statistics.

See Also

`association.test`

Examples

```
data(TTN)
x <- as.bed.matrix(TTN.gen, TTN.fam, TTN.bim)
## Simulation data ##
set.seed(1)
# some covariables
X <- cbind(1, runif(nrow(x)))
# A random GRM
ran <- random.pm( nrow(x))
# random effects (tau = 1)
omega <- lmm.simu(1, 0, eigenK=ran$eigen)$omega
# linear term of the model
lin <- X %*% c(0.1,-0.2) + omega
# vector of probabilitues
pi <- 1/(1+exp( -lin ))
# vector of binary phenotypes
y <- rbinom(nrow(x), 1, pi)
# testing association with 1) the score test, 2) the offset algorithm, 3) the 'amle' algorithm
a1 <- association.test(x, y, X, K = ran$K, method = "lmm", response = "bin")
a2 <- association.test.logistic(x, y, X, K = ran$K, algorithm = "offset")
a3 <- association.test.logistic(x, y, X, K = ran$K, algorithm = "amle")
```

---

association.test.logistic.dosage

Mixed logistic regression for GWAS, using dosages

Description

Mixed logistic regression for GWAS, using dosages

Usage

```
association.test.logistic.dosage(
  filename,
  Y,
  X,
  K,
  beg,
  end,
  algorithm = c("amle", "offset"),
  eigenK,
  p = 0,
  n.cores = 1L,
  ...
)
```

Arguments

filename	Name of a dosage file
Y	phenotype vector. Default is column pheno of x@ped
X	A matrix of covariates (defaults to a column of ones for the intercept)
K	A genetic relationship matrix (or a list of such matrices)
beg	Index of the first SNP tested for association
end	Index of the last SNP tested for association
algorithm	Algorithm to use
eigenK	eigen decomposition of K (only if p > 0)
p	Number of principal components to include in the model
n.cores	number of cores to use
...	Additional parameter for gaston::logistic.mm.aireml

Details

Dosage files can be VCF files with 'DS' or 'GP' fields. It is also possible to use a file with columns 'id"', 'chr', 'pos', 'A1', 'A2', 'sample1', 'sample2', etc. These files should have a header with column names.

For more details refer to association.test.logistic and association.test.

Value

A data frame giving for each SNP the association statistics.

See Also

association.test.logistic, association.test

`qqplot.pvalues` *Stratified QQ-plot of p-values*

Description

Draws a QQ plot of p-values

Usage

```
qqplot.pvalues(
  p,
  snp.cat,
  col.cat,
  col.abline = "red",
  CB = TRUE,
  col.CB = "gray80",
  CB.level = 0.95,
  thinning = TRUE,
  ...
)
```

Arguments

`p`	vector of p-values, or a data.frame with a column named `p`
`snp.cat`	(optional) A factor giving the SNP categories.
`col.cat`	(optional) A vector of colors used to plot the SNP categories.
`col.abline`	Color of the line of slope 1. Set to `NA` to suppress.
`CB`	`Logical`. If `TRUE`, a confidence band is included in the plot.
`col.CB`	The color of the confidence band.
`CB.level`	The level of the confidence band.
`thinning`	`Logical`. If `TRUE`, not all points are displayed.
`...`	Graphical parameters to be passed to `plot` and `points`

Details

This function draws a QQ plot of p-values, stratified by categories. If the parameter `snp.cat` is missing, the function falls back on `gaston::qqplot.pvalues`.

Value

Returns a 'NULL'

See Also

`SNP.category`, `qqplot.pvalues` (in gaston)

Examples

```
# a random vector of categories
ca <- sample(c("A","B","C"), 1e6, TRUE, c(0.05, 0.9, 0.05))
# a vector of p-values, with different distribution depending on the strata
p <- runif(1e6)**ifelse(ca == "A", .8, ifelse(ca == "B", 1, 1.2))
qqplot.pvalues(p, ca)
```

SNP.category *SNP.category*

Description

SNP.category

Usage

```
SNP.category(bed, Z, threshold = 0.8)
```

Arguments

bed	A bed matrix
Z	A vector of length nrow(bed)
threshold	Variance thresholds

Details

This function determines a SNP Category from a covariable Z, which can be for example an indicator variable for a population strata, or the first genomic principal component.

Value

A factor giving the category of each SNP

See Also

qqplot.pvalues

Examples

```
# a random vector of categories
ca <- sample(c("A","B","C"), 1e6, TRUE, c(0.05, 0.9, 0.05))
# a vector of p-values, with different distribution depending on the strata
p <- runif(1e6)**ifelse(ca == "A", .8, ifelse(ca == "B", 1, 1.2))
qqplot.pvalues(p, ca)
```

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