Package ‘SNPassoc’

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Author Juan R González, Lluís Armengol, Elisabet Guinó, Xavier Solé, and Víctor Moreno
Maintainer Juan R González <jrgonzalez@creal.cat>
Description This package carries out most common analysis when performing whole genome association studies. These analyses include descriptive statistics and exploratory analysis of missing values, calculation of Hardy-Weinberg equilibrium, analysis of association based on generalized linear models (either for quantitative or binary traits), and analysis of multiple SNPs (haplotype and epistasis analysis). Permutation test and related tests (sum statistic and truncated product) are also implemented. Max-statistic and genetic risk-allele score exact distributions are also possible to be estimated.
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assocarnation

Association analysis between a single SNP and a given phenotype

Description

This function carries out an association analysis between a single SNP and a dependent variable (phenotype) under five different genetic models (inheritance patterns): codominant, dominant, recessive, overdominant and log-additive. The phenotype may be quantitative or categorical. In the second case (e.g. case-control studies) this variable must be of class 'factor' with two levels.

Usage

association(formula, data, model=c("all"), model.interaction= 
  c("codominant"), subset, name.snp = NULL, quantitative = 
  is.quantitative(formula,data), genotypingRate= 0, 
  level = 0.95, ...)

Arguments

formula a symbolic description of the model to be fitted (a formula object). It might have either a continuous variable (quantitative traits) or a factor variable (case-control studies) as the response on the left of the ~ operator and a term corresponding to the SNP on the right. This term must be of class snp (e.g. ~snp(var), where var is a given SNP), and it is required. Terms with additional covariates on the right of the ~ operator may be added to fit an adjusted model (e.g., ~var1+var2+...+varN+SNP). The formula allows to incorporate more than one
object of class `snp`. In that case, the analysis is done for the first SNP which appears in the formula adjusted by the others covariates and other additional SNPs.

data a required dataframe of class `setupSNP` containing the variables in the model.

model a character string specifying the type of genetic model (mode of inheritance) for the SNP. This indicates how the genotypes should be collapsed. Possible values are "codominant", "dominant", "recessive", "overdominant", "additive" or "all". The default is "all" that fits the 5 possible genetic models. Only the first words are required, e.g "co", "do", etc.

model.interaction a character string specifying the type of genetic model (mode of inheritance) assumed for the SNP when it is included in an interaction term. Possible values are "codominant", "dominant", "recessive", "overdominant". The default is "codominant".

subset an optional vector specifying a subset of observations to be used in the fitting process

name.snp optional label of the SNP variable to be printed.

quantitative logical value indicating whether the phenotype (that which is in the left of the operator `~` in `formula` argument) is quantitative. The function ‘is.quantitative’ returns FALSE when the phenotype is a variable with two categories (i.e. indicating case-control status). Thus, it is not a required argument but it may be modified by the user.

genotypingRate minimum percentage of genotype rate for the SNP to be analyzed. Default is 0% (e.g. all SNPs are analyzed). This parameter should not be changed. It is used in the function `WGassociation`.

level signification level for confidence intervals.

... Other arguments to be passed through glm function

Details

This function should be called by the user when we are interested in analyzing an unique SNP. It is recommended to use `WGassociation` function when more than one SNP is studied.

Value

For each genetic model (codominant, dominant, recessive, overdominant, and log-additive) the function gives a matrix with sample size and percentages for each genotype, the Odds Ratio and its 95% confidence interval (taking the most frequent homozygous genotype as the reference), the p-value corresponding to the likelihood ratio test obtained from a comparison with the null model, and the Akaike Information Criterion (AIC) of each genetic model. In the case of analyzing a quantitative trait, the function returns a matrix with sample size, mean and standard errors for each genotype, mean difference and its 95% confidence interval with respect to the most frequent homozygous genotype, the p-value obtained from an overall gene effect and the Akaike Information Criterion (AIC) of each genetic model.
When an interaction term (a categorical covariate with an SNP) is included in the model, three different tables are given. The first one corresponds to the full interaction matrix where the ORs (or mean differences if a quantitative trait is analyzed) are expressed with respect to the non variant genotype and the first category of the covariate. The other two tables show the ORs and their 95% confidence intervals for both marginal models. P values for interaction and trend are also showed in the output.

References


See Also

WGassoc

Examples

data(SNPs)

# first, we create an object of class 'setupSNP'
datSNP<-setupSNP(SNPs,6:40,sep="\")

# case-control study, crude analysis
association(casco~snp10001, data=datSNP)

# case-control study, adjusted by sex and arterial blood pressure
association(casco~sex+snp10001+blood.pre, data=datSNP)

# quantitative trait, crude analysis
association(log(protein)~snp10001, data=datSNP)
# quantitative trait, adjusted by sex
association(log(protein)~snp10001+sex, data=datSNP)

#
# Interaction analysis
#
#
# Interaction SNP and factor
association(log(protein)~snp10001*sex+blood.pre, data=datSNP,
          model="codominant")

# Interaction SNP and SNP (codominant and codominant)
association(log(protein)~snp10001*factor(snp10002)+blood.pre,
            data=datSNP, model="codominant")
Bonferroni.sig

# Interaction SNP and SNP (dominant and recessive)
association(log(protein)-snp10001+factor(recessive(snp100019))+blood.pre,
  data=datSNP, model="dominant")

Bonferroni.sigBonferroni correction of p values

Description
This function shows the SNPs that are statistically significant after correcting for the number of tests performed (Bonferroni correction) for an object of class "WGassociation"

Usage
Bonferroni.sig(x, model = "codominant", alpha = 0.05,
include.all.SNPs=FALSE)

Arguments

  x an object of class 'WGassociation'.

  model a character string specifying the type of genetic model (mode of inheritance). This indicates how the genotypes should be collapsed when 'plot.summary' is TRUE. Possible values are "codominant", "dominant", "recessive", "overdominant", or "log-additive". The default is "codominant". Only the first words are required, e.g "co", "do"....

  alpha nominal level of significance. Default is 0.05

  include.all.SNPs logical value indicating whether all SNPs are considered in the Bonferroni correction. That is, the number of performed tests is equal to the number of SNPs or equal to the number of SNPs where a p value may be computed. The default value is FALSE indicating that the number of tests is equal to the number of SNPs that are non Monomorphic and the rate of genotyping is greater than the percentage indicated in the GeneticModel.pval function.

Details
After deciding the genetic model, the function shows the SNPs that are statistically significant at alpha level corrected by the number of performed tests.

Value
A data frame with the SNPs and the p values for those SNPs that are statistically significant after Bonferroni correction
See Also

WGassocation

Examples

data(SNPs)
datSNP <- setupSNP(SNPs, 6:40, sep = "")
ans <- WGassocation(protein = 1, data = datSNP, model = "all")
Bonferroni.sig(ans, model = "codominant", alpha = 0.05, include.all.SNPs = FALSE)

GenomicControl          Population substructure

Description

This function estimates an inflation (or deflation) factor, lambda, as indicated in the paper by Devlin et al. (2001) and corrects the p-values using this factor.

Usage

GenomicControl(x, snp.sel)

Arguments

x         an object of class 'WGassocation'.
snp.sel    SNPs used to compute lambda. Not required.

Details

This method is only valid for 2x2 tables. This means that the object of class 'WGassocation' might not have fitted the codominant model.

See reference for further details.

Value

The same object of class 'WGassocation' where the p-values have been corrected for genomic control.

References


See Also

qqpval, WGassocation
getSignificantSNPs

Examples

```r
data(SNPs)
datSNP <- setupSNP(SNPs, 6:40, sep = "")
res <- WGassociation(casco, datSNP, model = c("do", "re", "log-add"))

# Genomic Control
resCorrected <- GenomicControl(res)
plot(resCorrected)
```

getSignificantSNPs  Extract significant SNPs from an object of class 'WGassociation'

Description

Extract significant SNPs from an object of class 'WGassociation' when genomic information is available

Usage

```r
getSignificantSNPs(x, chromosome, model, sig = 1e-15)
```

Arguments

- `x` an object of class 'WGassociation'
- `chromosome` chromosome from which SNPs are extracted
- `model` genetic model from which SNPs are extracted
- `sig` statistical significance level. The default is 1e-15

Value

A list with the following components:

- `names` the name of SNPs
- `column` the columns corresponding to the SNPs in the original data frame

See Also

WGassociation
Examples

```r
data(HapMap)
# resHapMap contains the results for a log-additive genetic model

# to get the significant SNPs for chromosome 12
getSignificantSNPs(resHapMap, chromosome=12)
# to get the significant SNPs for chromosome 5
getSignificantSNPs(resHapMap, 5)
# to get the significant SNPs for chromosome X at level 1e-8
getSignificantSNPs(resHapMap, 5, sig=1e-8)
```

**haplo.interaction**  
*Haplotype interaction with a covariate*

Description

This function computes the ORs (or mean differences if a quantitative trait is analyzed) and their 95% confidence intervals corresponding to an interaction between the haplotypes and a categorical covariate.

Usage

```r
haplo.interaction(formula, data, SNPs.sel, quantitative =
                   is.quantitative(formula, data), haplo.freq.min = 0.05, ...)
```

Arguments

- `formula`: a symbolic description of the model to be fitted (a formula object). It might have either a continuous variable (quantitative traits) or a factor variable (case-control studies) as the response on the left of the `~` operator and a term corresponding to the interaction variable on the right indicated using `interaction` function (e.g. `~int(var)`, where var is a factor variable) and it is required. Terms with additional covariates on the the right of the `~` operator may be added to fit an adjusted model (e.g., `~var1+var2+...+varN+int(var)`).

- `data`: an object of class `setupSNP` containing the variables in the model and the SNPs that will be used to estimate the haplotypes.

- `SNPs.sel`: a vector indicating the names of SNPs that are used to estimate the haplotypes.

- `quantitative`: logical value indicating whether the phenotype (which is on the left of the operator `~` in 'formula' argument) is quantitative. The function `is.quantitative` returns FALSE when the phenotype is a variable with two categories (i.e. indicating case-control status). Thus, it is not a required argument but it may be modified by the user.

- `haplo.freq.min`: control parameter for haplo.glm included in 'haplo.glm.control'. This parameter corresponds to the minimum haplotype frequency for a haplotype to be included in the regression model as its own effect. The haplotype frequency is based on the EM algorithm that estimates haplotype frequencies independently of any trait.
additional parameters for 'haplo.glm.control'.

Details

The function estimates the haplotypes for the SNPs indicated in the 'SNPs.sel' argument. Then, using 'haplo.glm' function (from 'haplo.stats' library) estimates the interaction between these haplotypes and the covariate indicated in the formula by means of 'interaction' function.

Value

Three different tables are given. The first one corresponds to the full interaction matrix where the ORs (or mean differences if a quantitative trait is analyzed) are expressed with respect to the most frequent haplotype and the first category of the covariate. The other two tables show the ORs (or mean differences if a quantitative trait is analyzed) and their 95% confidence intervals for both marginal models. P values for interaction are also showed in the output.

Examples

# not Run
# data(SNPs)
# datSNP<-setupSNP(SNPs,6:40,sep="")
# res<-haplo.interaction(log(protein)-int(sex), data=datSNP,
#     SNPs.sel=c("snp100019","snp10001","snp100029"))
# res

HapMap  

SNPs from HapMap project

Description

Information about 9307 SNPs from the HapMap project belonging to 22 chromosomes. Information about two different population is available: European population (CEU) and Yoruba (YRI). The genomic information (names of SNPs, chromosomes and genetic position) is also available in a data frame called 'HapMap.SNPs.pos'.

Usage

data(HapMap)

Format

A data frame with 120 observations on the 9808 variables (SNPs) and one variable called 'group' indicating the population.

Source

HapMap project (http://www.hapmap.org)
Examples

data(HapMap)

| inheritance | Collapsing (or recoding) genotypes into different categories (generally two) depending on a given genetic mode of inheritance |

Description

codominant function recodifies a variable having genotypes depending on the allelic frequency in descending order.

dominant, recessive, and overdominant functions collapse the three categories of a given SNP into two categories as follows: Let 'AA', 'Aa', and 'aa' be the three genotypes. After determining the most frequent allele (let's suppose that 'A' is the major allele) the functions return a vector with to categories as follows. dominant: 'AA' and 'Aa-aa'; recessive: 'AA-Aa' and 'aa'; overdominant: 'AA-aa' vs 'Aa'.

additive function creates a numerical variable, 1, 2, 3 corresponding to the three genotypes sorted out by descending allelic frequency (this model is referred as log-additive).

Usage

codominant(o)
dominant(o)
recessive(o)
overdominant(o)
additive(o)

Arguments

- o categorical covariate having genotypes

Examples

data(SNPs)
dominant(snp(SNPs$snp10001,sep=""))
overdominant(snp(SNPs$snp10001,sep=""))
**int**

**Identify interaction term**

### Description

This is a special function used for 'haplo.interaction' function. It identifies the variable that will interact with the haplotype estimates. Using int() in a formula implies that the interaction term between this variable and haplotypes is included in 'haplo.glm' function.

### Usage

`int(x)`

### Arguments

- **x**  
  A factor variable.

### Value

- **x**

### See Also

`haplo.interaction`

### Examples

```r
# Not Run  
data(SNPs)  
mod <- haplo.interaction(casco=int(sex)+blood.pre, data=SNPs,  
SNPs.sel=c("snp10001","snp10004","snp10005"))  
```

---

**interactionPval**

**Two-dimensional SNP analysis for association studies**

### Description

Perform a two-dimensional SNP analysis (interaction) for association studies with possible allowance for covariate

### Usage

```r
interactionPval(formula, data, quantitative =  
  is.quantitative(formula, data), model = "codominant")
```
**Arguments**

- **formula**: A formula object. It might have either a continuous variable (quantitative traits) or a factor variable (case-control study) as the response on the left of the `~` operator and the terms corresponding to the covariates to be adjusted. A crude analysis is performed indicating `~1`

- **data**: A required object of class 'setupSNP'.

- **quantitative**: Logical value indicating whether the phenotype (those which is in the left of the operator `~` in 'formula' argument) is quantitative. The function 'is.quantitative' returns FALSE when the phenotype is a variable with two categories (i.e. indicating case-control status). Thus, it is not a required argument but it may be modified by the user.

- **model**: A character string specifying the type of genetic model (mode of inheritance). This indicates how the genotypes should be collapsed. Possible value are "codominant", "dominant", "recessive", "overdominant" or "log-additive". The default is "codominant". Only the first words are required, e.g "co", "do", "re", "ov", "log"

**Details**

The 'interactionPval' function calculates, for each pair of SNPs (i,j), the likelihood underling the null model L0, the likelihood under each of the single-SNP, L(i) and L(j), the likelihood under an additive SNP model La(i,j), and the likelihood under a full SNP model (including SNP-SNP interaction), Lf(i,j).

The upper triangle in matrix from this function contains the p values for the interaction (epistasis) log-likelihood ratio test, LRT, LRTij = -2 (log Lf(i,j) - log La(i,j))

The diagonal contains the p values from LRT for the crude effect of each SNP, LRTii = -2 (log L(i) - log L0)

The lower triangle contains the p values from LRT comparing the two-SNP additive likelihood to the best of the single-SNP models, LRTji = -2 (log La(i,j) - log max(L(i),L(j)))

In all cases the models including the SNPs are adjusted by the covariates indicated in the 'formula' argument. This method is used either for quantitative traits and dicotomous variables (case-control studies).

**Value**

The 'interactionPval' function returns a matrix of class 'SNPinteraction' containing the p values corresponding to the different likelihood ratio tests above describe.

Methods defined for 'SNPinteraction' objects are provided for print and plot. The plot method uses 'image' to plot a grid of p values. The upper triangle contains the interaction (epistasis) p values from LRT. The content in the lower triangle is the p values from the LRT comparing the additive model with the best single model. The diagonal contains the main effects pvalues from LRT. The 'plot.SNPinteraction' function also allows the user to plot the SNPs sorted by genomic position and with the information about chromosomes as in the 'plotMissing' function.

**Note**

two-dimensional SNP analysis on a dense grid can take a great deal of computer time and memory.
intervals

Print ORs and 95% confidence intervals for an object of class 'haplo.glm'

Description

Print ORs and confidence intervals for an object of class 'haplo.glm'

Usage

intervals(o, level=.95, ...)

Arguments

| o         | object of class 'haplo.glm' |
| level     | significance level. Default is 95 percent |
| ...       | other arguments             |

Examples

# Not Run
# data(SNPs)
# tag.SNPs<-c("snp100019","snp10001","snp100029")
# geno<-make.geno(SNPs,tag.SNPs)

# mod<-haplo.glm(casco~geno,data=SNPs,
# family=binomial,
# locus.label=tag.SNPs,
# allele.lev=attributes(geno)$unique.alleles,
# control = haplo.glm.control(haplo.freq.min=0.05))

# intervals(mod)
# summary(mod)

---

**LD**

*max-statistic for a 2x3 table*

### Description

Compute pairwise linkage disequilibrium between genetic markers

### Usage

```r
LD(g1, ...)
```

```r
LD(g1, g2, ...)
```

```r
LD(g1, SNPs, ...)
```

```r
LDplot(x, digits = 3, marker, distance, which = c("D", "D'", "r", "X^2", "P-value", "n", ""), ...)
```

```r
LDtable(x, colorcut = c(0, 0.01, 0.025, 0.05, 0.1, 1),
          colors = heat.colors(length(colorcut)),
          textcol = "black", digits = 3, show.all = FALSE,
          which = c("D", "D'", "r", "X^2", "P-value", "n"),
          colorize = "P-value", cex, ...)
```

### Arguments

- `g1`: genotype object or dataframe containing genotype objects
- `g2`: genotype object (ignored if `g1` is a dataframe)
- `SNPs`: columns containing SNPs
- `x`: LD or LD.data.frame object
- `digits`: Number of significant digits to display
- `which`: Name(s) of LD information items to be displayed
- `colorcut`: P-value cutoffs points for colorizing LDtable
- `colors`: Colors for each P-value cutoff given in 'colorcut' for LDtable
make.geno

- **textcol**: Color for text labels for LDtable
- **marker**: Marker used as 'comparator' on LDplot. If omitted separate lines for each marker will be displayed
- **distance**: Marker location, used for locating of markers on LDplot.
- **show.all**: If TRUE, show all rows/columns of matrix. Otherwise omit completely blank rows/columns.
- **colorize**: LD parameter used for determining table cell colors
- **cex**: Scaling factor for table text. If absent, text will be scaled to fit within the table cells.
- **...**: Optional arguments (‘plot.LD.data.frame’ passes these to ’LDtable’ and ’LDplot’).

**Value**

None

**Author(s)**

functions adapted from LD, LDtable and LDplot in package genetics by Gregory Warnes et al. (warnes@bst.rochester.edu)

**References**

genetics R package by Gregory Warnes et al. (warnes@bst.rochester.edu)

**See Also**

setupSNP snp

---

**Description**

This function prepares the CRITICAL element corresponding to matrix of genotypes necessary to be included in 'haplo.glm' function.

**Usage**

make.geno(data, SNPs.sel)

**Arguments**

- **data**: an object of class 'setupSNP' containing the the SNPs that will be used to estimate the haplotypes.
- **SNPs.sel**: a vector indicating the names of SNPs that are used to estimate the haplotypes.
maxstat

Value

the same as 'setupGeno' function, from 'haplo.stats' library, returns

See Also

snp

Examples

```r
## Not run:
data(SNPs)
# first, we create an object of class 'setupSNP'
datSNP<-setupSNP(SNPs,6:40,sep="")
genoc<-make.geno(datSNP,c("snp10001","snp10002","snp10003"))
## End(Not run)
```

maxstat  

max-statistic for a 2x3 table

Description

Computes the asymptotic p-value for max-statistic for a 2x3 table

Usage

```r
maxstat(x, ...)
```

## Default S3 method:
```r
maxstat(x, y, ...)
```

## S3 method for class 'table'
```r
maxstat(x, ...)
```

## S3 method for class 'setupSNP'
```r
maxstat(x, y, colSNPs=attr(x,"colSNPs"), ...)
```

## S3 method for class 'matrix'
```r
maxstat(x, ...)
```

Arguments

x       a numeric matrix with 2 rows (cases/controls) and 3 columns (genotypes) or a vector with case/control status or an object of class 'setupSNP'.
odds

An optional numeric vector containing the information for a given SNP. In this case 'x' argument must contain a vector indicating case/control status. If 'x' argument is an object of class 'setupSNP' this argument might be the name of the variable containing case/control information.

colSNPs

A vector indicating which columns contain those SNPs to compute max-statistic. By default max-statistic is computed for those SNPs specified when the object of class 'setupSNP' was created.

... further arguments to be passed to or from methods.

Value

A matrix with the chi-square statistic for dominant, recessive, log-additive and max-statistic and its asymptotic p-value.

References


See Also

setupSNP

Examples

# example from Sladek et al. (2007) for the SNP rs1111875
tt<-matrix(c(77,298,310,122,316,231),nrow=2,ncol=3,byrow=TRUE)
maxstat(tt)

data(SNPs)
maxstat(SNPs$casco,SNPs$snp10001)
myDat<-setupSNP(SNPs,6:40,sep="")
maxstat(myDat,casco)

odds

Extract odds ratios, 95% CI and p-values

Description

Extract odds ratios, 95
Usage

```r
odds(x, model=c(\"log-additive\", \"dominant\", \"recessive\", \"overdominant\", \"codominant\"), 
       sorted=c(\"no\", \"p-value\", \"or\"))
```

Arguments

- `x`: an object of class 'WGassociation' output of `WGassociation`
- `model`: model to be extracted. Only first one is used. The first letter is enough, low or upper case.
- `sorted`: Sort the output by P value or OR.

Value

A matrix with OR 95% CI (lower, upper) and P value for the selected model. For codominant model, the OR and 95%CI are given for heterozygous and homozygous.

References


Examples

```r
data(SNPs)
datSNP<-setupSNP(SNPs,6:40,sep=\"\")
ans<-WGassociation(casco=1,data=datSNP,model=\"all\")
odds(ans)
```

---

permTest  
Permutation test analysis

Description

This function extract the p values for permutation approach performed using `scanWGassociation` function

Usage

```r
permTest(x, method=\"minimum\", K)
```

Arguments

- `x`: a required object of class 'WGassociation' with the attribute 'permTest'. See details
- `method`: statistic used in the permutation test. The default is 'minimum' but 'rtp' (rank truncated product) is also available.
- `K`: number of the K most significant p values from the total number of test performed (e.g number of SNPs) used to compute the rank truncated product. This argument is only required when method='rtp'. See references
permTest

Details

This function extracts the p values from an object of class 'WGassociation'. This object might be obtained using the function called 'scanWGassociation' indicating the number of permutations in the argument 'nperm'.

Value

An object of class 'permTest'.

'print' returns a summary indicating the number of SNPs analyzed, the number of valid SNPs (those non-Monomorphic and that pass the calling rate), the p value after Bonferroni correction, and the p values based on permutation approach. One of them is based on considering the empirical percentil for the minimum p values, and the another one on assuming that the minimum p values follow a beta distribution.

'plot' produces a plot of the empirical distribution for the minimum p values (histogram) and the expected distribution assuming a beta distribution. The corrected p value is also showed in the plot.

See examples for further illustration about all previous issues.

References


See Also

scanWGassociation

Examples

data(SNPs)
datSNP<-setupSNP(SNPs,6:40,sep="")
ans<-scanWGassociation(casco~1,data=datSNP,model="co",nperm=1000)

# pPerm<-permTest(ans)
# print(pPerm)
# plot(pPerm)
plot.WGassociation

Function to plot -log p values from an object of class 'WGassociation'

Description

Function to plot -log p values from an object of class 'WGassociation'

Usage

### S3 method for class 'WGassociation'

```r
plot(x, alpha = 0.05, plot.all.SNPs = FALSE,
     print.label.SNPs = TRUE, cutPval = c(0, 1e-10, 1), whole,
     ylim.sup=ifelse(is.null(attr(x,"fast")),1e-40, 1e-30),
     col.legend = c("red", "gray60"), sort.chromosome=TRUE,
     centromere, ...)
```

Arguments

- `x` an object of class 'WGassociation'
- `alpha` statistical significance nominal level. See details
- `plot.all.SNPs` are all SNPs plotted? If not, neither monomorphic nor SNPs with genotyping problems are plotted. The default is FALSE.
- `print.label.SNPs` are labels of SNPs printed? The default is TRUE
- `cutPval` when argument 'whole' is TRUE in the 'x' object (e.g. when whole genome analysis is carried out) 'cutPval' divides the range of p values into intervals and codes these values according to which interval they fall (like 'cut' function). The default is c(0, 1e-10, 1). That is, the p values are divided in those less than 1e-10 and those greater than 1e-10.
- `whole` is a whole genome carried out? If TRUE 'dataSNPs.pos' argument in 'setup-SNP' is required.
- `ylim.sup` superior limit for each panel. This value helps to obtain nicer plots
- `col.legend` the color of the bar corresponding to p values plotted in each panel. The default is "red" for those p values less than 1e-10 and "gray60" for those greater than 1e-10.
- `sort.chromosome` should chromosome be sorted? Set this argument to FALSE when genomic information corresponds to different genes.
- `centromere` numeric vector specifying the centromere positions. If missing, the default centromere value of human genome are used.
- `...` other graphical parameters
A panel with different plots (one for each mode of inheritance) are plotted. Each of them represents the -log(p value) for each SNP. Two horizontal lines are also plotted. One one them indicates the nominal statistical significance level (see 'alpha' argument) whereas the other one indicates the statistical significance level after Bonferroni correction.

A different plot is created when the argument 'whole' the object 'x' is TRUE (see setupSNP function). In that case a plot of p values in the -log scale is plotted for each SNP and for each chromosome.

Value

No return value, just the plot

References


See Also

association setupSNP WGassocation

plotMissing  Plot of missing genotypes

Description

Plot a grid showing which genotypes are missing

Usage

plotMissing(x, print.labels.SNPs = TRUE,
main = "Genotype missing data", ...)

Arguments

x an object of class 'setupSNP'
print.labels.SNPs
should labels of SNPs be printed?
main title to place on plot
... extra arguments of 'image' function

Details

This function uses 'image' function to plot a grid with black pixels where the genotypes are missing.
Description

This function plots ranked observed p values against the corresponding expected p values in -log scale.

Usage

qqpval(p, pch=16, col=4, ...)

Arguments

- **p**: a vector of p values
- **pch**: symbol to use for points
- **col**: color for points
- **...**: other plot arguments

Value

A plot

See Also

GenomicControl, WGassociation
Examples

data(SNPs)
datSNP<-setupSNP(SNPs,6:40,sep="")
res<-WGassocation(casco,datSNP,model=c("do","re","log-add"))

# observed vs expected p values for recessive model
qzpval(recessive(res))

---

ScanWGassociation Whole genome association analysis

Description

This function also performs a whole genome association analysis as the function WGassocation but only computes the p values for each SNP corresponding to likelihood ratio test.

Usage

scanWGassociation(formula, data, model = c("all"), nperm, 
quantitative = is.quantitative(formula, data), genotypingRate = 80)

Arguments

formula either a symbolic description of the model to be fitted (a formula object) without the SNP or the name of response variable in the case of fitting single models (e.g. unadjusted models). It might have either a continuous variable (quantitative traits) or a factor variable (case-control studies) as the response on the left of the ~ operator and terms with additional covariates on the right of the ~. Currently only is possible to write ~1 (that is, non-adjusted analysis). See WGassocation if you are interested in including additional covariates.

data a required dataframe of class 'setupSNP' containing the variables in the model and the SNPs

model a character string specifying the type of genetic model (mode of inheritance) for the SNP. This indicates how the genotypes should be collapsed. Possible values are "codominant", "dominant", "recessive", "overdominant", "log-additive" or "all". The default is "all" that fits the 5 possible genetic models. Only the first words are required, e.g "co", "do", etc.

nperm number of permutations to simulate the null hypotesis (e.g OR=1), conditioning on the empirical correlation structure. Only required to perform a permutation test. Currently this test is only available for binary traits.

quantitative logical value indicating whether the phenotype (that which is in the left of the operator ~ in 'formula' argument) is quantitative. The function 'is.quantitative' returns FALSE when the phenotype is a variable with two categories (i.e. indicating case-control status). Thus, it is not a required argument but it may be modified by the user.
genotypingRate  minimum percentage of genotype rate for a given SNP to be included in the analysis. Default is 80%.

Value

An object of class 'WGassociation'.

The function 'print' is used to print the results. The p values are saved in the attribute 'pvalues' as a matrix. They may be obtained using attr("pvalues") (see examples). The first column indicates whether a problem with genotyping is present.

The function 'plot' is used to obtain a plot of p values in the -log scale. See plot.WGassociation for further details.

References


See Also

WGassociation getSignificantSNPs association setupSNP plot.WGassociation permTest

Examples

# Next steps may be very time consuming. So they are not executed
# data(HapMap)
# myDat<-setupSNP(HapMap, colSNPs=3:9307, sort = TRUE,
# info=HapMap.SNPs.pos, sep="")
# resHapMap<-scanWGassociation(group~1, data=myDat, model="log")

---

**setupSNP**  *Convert columns in a dataframe to class 'snp'*

**Description**

setupSNP Convert columns in a dataframe to class 'snp'

summary.setupSNP gives a summary for an object of class 'setupSNP' including allele names, major allele frequencie, an exact thest of Hardy-Weinberg equilibrium and percentage of missing genotypes

**Usage**

setupSNP(data, colSNPs, sort = FALSE, info, sep = "/", ...)
**setupSNP**

**Arguments**

- `data`: dataframe containing columns with the SNPs to be converted
- `colSNPs`: Vector specifying which columns contain SNPs data
- `sort`: should SNPs be sorted. Default is FALSE
- `info`: if sort is TRUE a dataframe containing information about the SNPs regarding their genomic position and the gene where they are located
- `sep`: character separator used to divide alleles in the genotypes
- `...`: optional arguments

**Value**

A dataframe of class `setupSNP` containing converted SNP variables. All other variables will be unchanged.

**References**


**See Also**

`snp`

**Examples**

```r
data(SNPs)
myDat<-setupSNP(SNPs,6:40,sep="")

# sorted SNPs and having genomic information
data(SNPs.info.pos)
myDat.o<-setupSNP(SNPs,6:40,sep="",sort=TRUE, info=SNPs.info.pos)

# summary
summary(myDat.o)

# plot one SNP
plot(myDat,which=2)
```
snp

SNP object

Description

snp creates an snp object

is returns TRUE if x is of class 'snp'

as attempts to coerce its argument into an object of class 'snp'

reorder change the reference genotype

summary gives a summary for an object of class 'snp' including genotype and allele frequencies and an exact test of Hardy-Weinberg equilibrium

plot gives a summary for an object of class 'snp' including genotype and allele frequencies and an exact test of Hardy-Weinberg equilibrium in a plot. Barplot or pie are allowed

�述 is a copy of [.factor modified to preserve all attributes

Usage

snp(x, sep = "/", name.genotypes, reorder="common",
remove.spaces = TRUE, allow.partial.missing = FALSE)

is.snp(x)

as.snp(x, ...)

## S3 method for class 'snp'
additive(o)

Arguments

x

either an object of class 'snp' or an object to be converted to class 'snp'

sep

character separator used to divide alleles when x is a vector of strings where each string holds both alleles. The default is "/". See below for details.

name.genotypes

the codes for the genotypes. This argument may be useful when genotypes are coded using three different codes (e.g., 0,1,2 or hom1, het, hom2)

reorder

how should genotypes within an individual be reordered. Possible values are 'common' or 'minor'. The default is reorder="common". In that case, alleles are sorted within each individual by common homozygous.

remove.spaces

logical indicating whether spaces and tabs will be removed from the genotypes before processing

allow.partial.missing

logical indicating whether one allele is permitted to be missing. When set to 'FALSE' both alleles are set to 'NA' when either is missing.
o an object of class 'snp' to be coded as a linear covariate: 0,1,2
... optional arguments

Details

SNP objects hold information on which gene or marker alleles were observed for different individuals. For each individual, two alleles are recorded.

The snp class considers the stored alleles to be unordered, i.e., "C/T" is equivalent to "T/C". It assumes that the order of the alleles is not important.

When snp is called, x is a character vector, and it is assumed that each element encodes both alleles. In this case, if sep is a character string, x is assumed to be coded as "Allele1<sep>Allele2". If sep is a numeric value, it is assumed that character locations 1:sep contain allele 1 and that remaining locations contain allele 2.

additive.snp recodes the SNPs for being analyzed as a linear covariate (codes 0,1,2)

Value

The snp class extends "factor" where the levels is a character vector of possible genotype values stored coded by paste( allele1, ",", allele2, sep="/" )

References


See Also

association

Examples

# some examples of snp data in different formats

dat1 <- c("21", "21", "11", "22", "21",
          "22", "22", "11", "11", NA)
ans1 <- snp(dat1, sep="")
ans1

dat2 <- c("A/A","A/G","G/G","A/G","G/G",
          "A/A","A/A","G/G",NA)
ans2 <- snp(dat2, sep="/")
ans2

dat3 <- c("C-C","C-T","C-C","T-T","C-C",
          "C-C","C-C","C-C","T-T",NA)
ans3 <- snp(dat3, sep="-")
ans3

dat4 <- c("het","het","het","hom1","hom2",
          "het","het","het","hom1","hom2"),
### Description

SNPs data frame contains selected SNPs and other clinical covariates for cases and controls in a case-control study.

SNPs.info.pos data frame contains the names of the SNPs included in the data set ‘SNPs’ including their chromosome and their genomic position.

### Usage

data(SNPs)

### Format

‘SNPs’ data frame contains the following columns:

<table>
<thead>
<tr>
<th>Column</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>id</td>
<td>identifier of each subject</td>
</tr>
<tr>
<td>casco</td>
<td>case or control status: 0-control, 1-case</td>
</tr>
<tr>
<td>sex</td>
<td>gender: Male and Female</td>
</tr>
<tr>
<td>blood.pre</td>
<td>arterial blood pressure</td>
</tr>
<tr>
<td>protein</td>
<td>protein levels</td>
</tr>
<tr>
<td>snp10001</td>
<td>SNP 1</td>
</tr>
<tr>
<td>snp10002</td>
<td>SNP 2</td>
</tr>
<tr>
<td>...</td>
<td></td>
</tr>
<tr>
<td>snp100036</td>
<td>SNP 36</td>
</tr>
</tbody>
</table>

‘SNPs.info.pos’ data frame contains the following columns: A data frame with 35 observations on the following 3 variables.

<table>
<thead>
<tr>
<th>snp</th>
<th>name of SNP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
sortSNPs

chr name of chromosome
pos genomic position

Source
Data obtained from our department. The reference and details will be supplied after being published.

sortSNPs HSort a vector of SNPs by genomic position

Description
This function sorts a vector with the position of SNPs in a data frame using another data frame which contains information about SNPs, their chromosome, and their genomic position.

Usage
sortSNPs(data, colSNPs, info)

Arguments
data a required data frame with the SNPs
colSNPs a required vector indicating which columns of ‘data’ contains genotype data
info a required data frame with genomic information for the SNPs (chromosome and position). The first column must have the SNPs, the second one the chromosome and the third one the genomic position.

Details
First of all, the function obtains a vector with the SNPs sorted using the data frame with the genomic positions (see ‘dataSNPs.pos’ argument). Then, the columns which indicate where the information about the genotypes is in our data frame, are sorted using this vector.

This information is useful when WGassociation function is called since it allow the user to summarize the results with the SNPs sorted by genomic position.

Value
a vector indicating the columns where the SNPs are recorded in our data frame (‘data’ argument), sorted using the genomic positions listed in ‘dataSNPs.pos’ argument

Examples
#
# data(SNPs)
# data(SNPs.info.pos)
# colSNPs.order<sortSNPs(SNPs,c(6:40),SNPs.info.pos)
#
#
Table.mean.se

Descriptive sample size, mean, and standard error

Description

This function computes sample size, mean and standard error of a quantitative trait for each genotype (or combination of genotypes)

Usage

Table.mean.se(var, dep, subset = !is.na(var))

Arguments

var          quantitative trait
dep          variable with genotypes or any combination of them
subset       an optional vector specifying a subset of observations to be used in the descriptive analysis

Value

tp           A matrix giving sample size (n), median (me) and standard error (se) for each genotype

See Also

Table.N.Per

Examples

data(SNPs)
  # sample size, mean age and standard error for each genotype
  # Table.mean.se(SNPs$snp10001,SNPs$protein)

  # The same table for a subset (males)
  # Table.mean.se(SNPs$snp10001,SNPs$protein,SNPs$sex=="Male")

  # The same table assuming a dominant model
  # Table.mean.se(dominant(snp(SNPs$snp10001,sep="")),SNPs$protein,SNPs$sex=="Male")
This function computes sample size and percentage for each category of a categorical trait (e.g. case-control status) for each genotype (or combination of genotypes).

```r
Table.N.Per(var, dep, subset = !is.na(var))
```

- **var**: Categorical trait.
- **dep**: Variable with genotypes or any combination of them.
- **subset**: An optional vector specifying a subset of observations to be used in the descriptive analysis.

**Value**

A matrix giving sample size (n), and the percentage (for each genotype).

**See Also**

`Table.mean.se`

**Examples**

```r
data(SNPs)
# Sample size and percentage of cases and controls for each genotype
# Table.N.Per(SNPs$snp10001,SNPs$casco)

# The same table for a subset (males)
# Table.N.Per(SNPs$snp10001,SNPs$casco,SNPs$sex=="Male")

# The same table assuming a dominant model
# Table.N.Per(dominant(snp(SNPs$snp10001,sep=""),SNPs$casco,SNPs$sex=="Male"))
```
Description

Test the null hypothesis that Hardy-Weinberg equilibrium holds in cases, controls and both populations.

print print the information. Number of digits, and significance level can be changed

Usage

tableHWE(x, strata, ...)

Arguments

x an object of class 'setupSNP'
strata a factor variable for a stratified analysis
... optional arguments

Details

This function calculates the HWE test for those variables of class 'snp' in the object x of class 'setupSNP'

Value

A matrix with p values for Hardy-Weinberg Equilibrium

Author(s)

This function is based on an R function which computes an exact SNP test of Hardy-Weinberg Equilibrium written by Wigginton JE, Cutler DJ and Abecasis GR available at http://www.sph.umich.edu/csg/abecasis/Exact/r_instruct.html

References


See Also

setupSNP
WGasssociation

Examples

```r
data(SNPs)
ans<-setupSNP(SNPs,6:40,sep="")
res<-tableHWE(ans)
print(res)
#change the significance level showed in the flag column
print(res,sig=0.001)

#stratified analysis
res<-tableHWE(ans,ans$sex)
print(res)
```

Description

This function carries out a whole genome association analysis between the SNPs and a dependent variable (phenotype) under five different genetic models (inheritance patterns): codominant, dominant, recessive, overdominant and log-additive. The phenotype may be quantitative or categorical. In the second case (e.g. case-control studies) this variable must be of class ‘factor’ with two levels.

Usage

```r
WGasssociation(formula, data, model = c("all"),
    quantitative = is.quantitative(formula, data),
    genotypingRate = 80, level = 0.95, ...)
```

Arguments

- `formula`: either a symbolic description of the model to be fitted (a formula object) without the SNP or the name of response variable in the case of fitting single models (e.g. unadjusted models). It might have either a continuous variable (quantitative traits) or a factor variable (case-control studies) as the response on the left of the `~` operator and terms with additional covariates on the right of the `~` operator may be added to fit an adjusted model (e.g., `~var1+var2+...+varN+SNP`). See details
- `data`: a required dataframe of class ‘setupSNP’ containing the variables in the model and the SNPs
- `model`: a character string specifying the type of genetic model (mode of inheritance) for the SNP. This indicates how the genotypes should be collapsed. Possible values are "codominant", "dominant", "recessive", "overdominant", "log-additive" or "all". The default is "all" that fits the 5 possible genetic models. Only the first words are required, e.g "co", "do", etc.
quantitative logical value indicating whether the phenotype (that which is in the left of the operator ~ in 'formula' argument) is quantitative. The function 'is.quantitative' returns FALSE when the phenotype is a variable with two categories (i.e. indicating case-control status). Thus, it is not a required argument but it may be modified by the user.

genotypingRate minimum percentage of genotype rate for a given SNP to be included in the analysis. Default is 80%.

level signification level for confidence intervals. Default is 95%.

... Other arguments to be passed through glm function

Details

This function assesses the association between the response variable included in the left side in the 'formula' and the SNPs included in the 'data' argument adjusted by those variables included in the right side of the 'formula'. Different genetic models may be analyzed using 'model' argument.

Value

An object of class 'WGassociation'.

'summary' returns a summary table by groups defined in info (genes/chromosomes).

'WGstats' returns a detailed output, similar to the produced by association.

'pvalues' and 'print' return a table of p-values for each genetic model for each SNP. The first column indicates whether a problem with genotyping is present.

'plot' produces a plot of p values in the -log scale. See plot.WGassociation for further details.

'labels' returns the names of the SNPs analyzed.

The functions 'codominat', 'dominant', 'recessive', 'overdominant' and 'additive' are used to obtain the p values under these genetic models.

See examples for further illustration about all previous issues.

References


See Also

scanWGassociation getSignificantSNPs association WGstats setupSNP plot.WGassociation

Examples

data(SNPs)
datSNP<-setupSNP(SNPs,6:40,sep="")
ansAll<-WGassociation(protein=1,data=datSNP,model="all")

# In that case the formula is not required. You can also write:
# ansAll<-WGassociation(protein,data=datSNP,model="all")
#only codominant and log-additive
ansCoAd<-WGassociation(protein~1, data=datSNP, model=c("co","log-add"))

# for printing p values
print(ansAll)
print(ansCoAd)

# for obtaining a matrix with the p values
pvalAll<-pvalues(ansAll)
pvalCoAd<-pvalues(ansCoAd)

# when all models are fitted and we are interested in obtaining
# p values for different genetic models
# codominant model
pvalCod<-codominant(ansAll)

# recessive model
pvalRec<-recessive(ansAll)

# and the same for additive, dominant or overdominant

#summary
summary(ansAll)

# for a detailed report
WGstats(ansAll)

# for plotting the p values
plot(ansAll)

#
# Whole genome analysis
#
data(HapMap)
# Next steps may be very time consuming. So they are not executed

#myDat<-setupSNP(HapMap, colSNPs=3:9809, sort = TRUE,
# info=HapMap.SNP�s.pos, sep="")
#resHapMap<-WGassociation(group~1, data=myDat, model="log")

# However, the results are saved in the object "resHapMap"
# to illustrate print, summary and plot functions
summary(resHapMap)
plot(resHapMap)
print(resHapMap)
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