

Package ‘HardyWeinberg’

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Title Statistical Tests and Graphics for Hardy-Weinberg Equilibrium

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Description Contains tools for exploring Hardy-Weinberg equilibrium (Hardy, 1908; Weinberg, 1908) <doi:10.1126/science.28.706.49> for bi and multi-allelic genetic marker data. All classical tests (chi-square, exact, likelihood-ratio and permutation tests) with bi-allelic variants are included in the package, as well as functions for power computation and for the simulation of marker data under equilibrium and disequilibrium. Routines for dealing with markers on the X-chromosome are included (Graffelman & Weir, 2016) <doi: 10.1038/hdy.2016.20>, including Bayesian procedures. Some exact and permutation procedures also work with multi-allelic variants. Special test procedures that jointly address Hardy-Weinberg equilibrium and equality of allele frequencies in both sexes are supplied, for the bi and multi-allelic case. Functions for testing equilibrium in the presence of missing data by using multiple imputation are also provided. Implements several graphics for exploring the equilibrium status of a large set of bi-allelic markers: ternary plots with acceptance regions, log-ratio plots and Q-Q plots.

License GPL (>= 2)

URL <https://www.r-project.org>, <http://www-eio.upc.edu/~jan>

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HardyWeinberg-package *Statistical Tests and Graphics for Hardy-Weinberg Equilibrium*

Description

Contains tools for exploring Hardy-Weinberg equilibrium (Hardy, 1908; Weinberg, 1908) for bi and multi-allelic genetic marker data. All classical tests (chi-square, exact, likelihood-ratio and permutation tests) with bi-allelic variants are included in the package, as well as functions for power computation and for the simulation of marker data under equilibrium and disequilibrium. Routines for dealing with markers on the X-chromosome are included (Graffelman & Weir, 2016) including Bayesian procedures. Some exact and permutation procedures also work with multi-allelic variants. Special test procedures that jointly address Hardy-Weinberg equilibrium and equality of allele frequencies in both sexes are supplied, for the bi and multi-allelic case. Functions for testing equilibrium in the presence of missing data by using multiple imputation are also provided. Implements several graphics for exploring the equilibrium status of a large set of bi-allelic markers: ternary plots with acceptance regions, log-ratio plots and Q-Q plots.

Details

Package: HardyWeinberg
 Type: Package
 Version: 1.6.3
 Date: 2019-06-28
 License: GPL Version 2 or later.

With function `HWternaryPlot` one can create ternary plots with acceptance regions for HWE. Several routines implement statistical tests for HWE such as `HWChisq`, `HWExact`, `HWLratio` and `HWPerm`. Bayesian procedures are available using `HWPosterior`. Aikake information criterion for various scenarios can be calculated with `HWaic`. Power computations are possible with `HWPower`.

Author(s)

Jan Graffelman

Maintainer: Jan Graffelman <jan.graffelman@upc.edu>

References

Weir, B.S. (1996) *Genetic Data Analysis II*. Sinauer Associates, Massachusetts.

Graffelman, J. and Morales, J. (2008) Graphical Tests for Hardy-Weinberg Equilibrium Based on the Ternary Plot. *Human Heredity* 65(2):77-84.

Graffelman, J. (2015) Exploring Diallelic Genetic Markers: The HardyWeinberg Package. *Journal of Statistical Software* 64(3): 1-23. <http://www.jstatsoft.org/v64/i03/>.

Graffelman, J. and Weir, B.S. (2016) Testing for Hardy-Weinberg equilibrium at bi-allelic genetic markers on the X chromosome. *Heredity* 116(6): 558-568. <https://doi.org/10.1038/hdy.2016.20> Nature Publishing Group.

Hardy, G.H. (1908) Mendelian Proportions in a Mixed Population. *Science* 28(706): 49-50.

Weinberg, W. (1908) On the Demonstration of Heredity in Man. In: Papers on Human Genetics. S. H. Boyer (Ed.) Englewood Cliffs, NJ:Prentice Hall, translated, 1963.

Examples

```
library(HardyWeinberg)

# draw random SNPs from a population that is in HWE

set.seed(123)

m <- 100 # number of markers
n <- 100 # sample size

X <- HWData(n,m)
out <- HWternaryPlot(X,100,region=1,vertex.cex=2,signifcolour=TRUE)
```

af

Function to compute allele frequencies

Description

Function `af` computes the allele frequencies for a matrix or a vector containing genotypic compositions.

Usage

```
af(x)
```

Arguments

x a vector or matrix with compositions

Value

a vector with allele frequencies

Author(s)

Jan Graffelman (jan.graffelman@upc.edu)

See Also

[maf](#)

Examples

```
X <- as.vector(rmultinom(1,100,c(0.5,0.4,0.1)))
X <- X/sum(X)
print(X)
print(af(X))
```

AFtest

Exact test of equality of allele frequencies for males and females

Description

Function `AFtest` tests equality of allele frequencies for males and females for bi-allelic marker data by means of a Fisher exact test.

Usage

```
AFtest(x, verbose = TRUE, ...)
```

Arguments

x a vector containing the genotypic counts `c(A,B,AA,AB,BB)` for a bi-allelic X-chromosomal markers.

verbose verbose = TRUE prints results, verbose = FALSE is silent.

... additional arguments for function `fisher.test`.

Details

Function `AFtest` constructs the contingency table of sex by allele, and call `fisher.test` to test for equality of allele frequencies. The test assumes Hardy-Weinberg equilibrium.

Value

<code>AC</code>	Two-way table of sex by allele
<code>pval</code>	p-value of the test

Author(s)

Jan Graffelman <jan.graffelman@upc.edu>

See Also

[HWChisq](#), [HWExact](#)

Examples

```
rs5968922 <- c(A=392, B=212, AA=275, AB=296, BB=80)
AFtest(rs5968922)
```

agcounts

Calculate allele and genotype counts for X-chromosomal markers

Description

Function `agcounts` determines sample size, minor and major allele counts, allele counts in females, numbers of males and females and allele frequencies for a vector of genotype counts of an X-chromosomal markers.

Usage

```
agcounts(x, verbose = FALSE)
```

Arguments

<code>x</code>	a vector of X-chromosomal genotype counts (A,B,AA,AB,BB)
<code>verbose</code>	print the counts if (<code>verbose = TRUE</code>)

Value

n	sample size
nA	number of A alleles
nB	number of B alleles
nf	number of females
nm	number of males
nAf	number of A alleles in females
nBf	number of B alleles in females
nt	total number of alleles
fAA	number of AA females
fAB	number of AB females
fBB	number of BB females
pA	overall A allele frequency
pB	overall B allele frequency

Author(s)

Jan Graffelman <jan.graffelman@upc.edu>

See Also

[mac,link{maf}](#)

Examples

```
rs5968922 <- c(A=392, B=212, AA=275, AB=296, BB=80)
counts <- agcounts(rs5968922)
```

alleles

Extract alleles

Description

Function `alleles` extracts the names of the alleles from a named genotype vector.

Usage

```
alleles(x, fromlabels = TRUE)
```

Arguments

x	A named or unnamed genotype vector (e.g. <code>c(AA=10,AB=20,BB=5)</code>)
fromlabels	extract genotypes from the labels of the vector elements, or from the vector elements themselves.

Value

A character vector with the alleles

Author(s)

Jan Graffelman (jan.graffelman@upc.edu)

See Also

[n.alleles](#)

Examples

```
x <- c(AA=10,AG=10,GG=10,AT=5)
als.x <- alleles(x)
```

Alzheimer

Genotype frequencies for 70 SNPs related to Alzheimer's disease

Description

The dataframe contains the genotype frequencies MM, Mm and mm for the 70 SNPs for both cases and controls. The data are taken from table 7.11 in Laird & Lange.

Usage

```
data(Alzheimer)
```

Format

A data frame containing 70 observations.

Source

Laird, N. M. and Lange, C. Table 7.11, p. 124

References

Laird, N. M. and Lange, C. (2011) The fundamentals of modern statistical genetics. Springer.

dgraffelmanweir.bi	<i>Calculate Graffelman-Weir exact density for bi-allelic X-chromosomal variant</i>
--------------------	---

Description

Function `dgraffelmanweir` calculate the probability $P(NAB=nab \text{ and } MA=ma|NA=na)$ for a bi-allelic X-chromosomal variant.

Usage

```
dgraffelmanweir.bi(x, y)
```

Arguments

x	vector with male genotype counts (A,B)
y	vector with female genotype counts (AA,AB,BB)

Value

a single real number

Author(s)

Jan Graffelman <jan.graffelman@upc.edu>

References

Graffelman, J. and Weir, B.S. (2016) Testing for Hardy-Weinberg equilibrium at bi-allelic genetic markers on the X chromosome. *Heredity* 116(6) pp. 558–568.

See Also

[HWExact](#), [HWExactStats](#)

Examples

```
males <- c(A=392, B=212)
females <- c(AA=275, AB=296, BB=80)
prob <- dgraffelmanweir.bi(males, females)
print(prob)
```

`dlevene`*Calculate Levene's exact density for k alleles*

Description

Function `dlevene` calculates Levene's exact density for a diploid system with k alleles.

Usage

```
dlevene(N)
```

Arguments

`N` A lower triangular matrix with genotype counts

Details

The supplied matrix of genotype counts should be triangular, with the homozygote counts on the diagonal, and all heterozygote counts below the diagonal.

Value

a single real number

Author(s)

Jan Graffelman (jan.graffelman@upc.edu)

References

Levene, H. (1949) On a matching problem arising in genetics. *Annals of Mathematical Statistics*, 20, pp. 91-94.

See Also

[HWExact](#)

Examples

```
x <- c(AA=12,AB=19,AC=13,BB=7,BC=5,CC=0)
x <- toTriangular(x)
prob <- dlevene(x)
print(prob)
```

`dlevene.bi`*Calculate Levene's density for a bi-allelic variant*

Description

Program `dlevene.bi` calculates Levene's density ($P(AB|A)$) for a bi-allelic variant.

Usage

```
dlevene.bi(x)
```

Arguments

`x` a vector of genotype counts (AA,AB,BB)

Value

a single real number

Author(s)

Jan Graffelman (jan.graffelman@upc.edu)

References

Levene, H. (1949) On a matching problem arising in genetics. *Annals of Mathematical Statistics*, 20, pp. 91-94.

See Also

[dlevene,HWEExact](#)

Examples

```
x <- c(AA=298,AB=489,BB=213)
prob <- dlvene.bi(x)
print(prob)
```

EAFExact*Exact test for equality of allele frequencies in males and females*

Description

EAFExact uses a Fisher Exact test to compare allele frequencies in males and females for variants with k alleles ($k \geq 2$).

Usage

```
EAFExact(m, f, verbose = TRUE)
```

Arguments

<code>m</code>	vector or triangular matrix with male genotype counts
<code>f</code>	vector or triangular matrix with female genotype counts
<code>verbose</code>	print output (TRUE) or not (FALSE)

Details

For bi-allelic autosomal variants the genotype counts can be supplied as vectors ((AA,AB,BB) for males, and (AA,AB,BB) for females). For X-chromosomal bi-allelic variants the genotype counts can also be supplied as vectors ((A,B) for males, and (AA,AB,BB) for females). For multi-allelic autosomal variants male and female genotype counts can be supplied as vectors (AA,AB,AC,BB,BC,CC,...) or as a triangular matrix, where matrix rows and columns are labelled with the allele name (A,B,C,...). For multi-allelic X-chromosomal variants, male genotype counts must be supplied as a vector (A,B,C,...) and female genotype counts must be supplied as a triangular matrix. See the examples below.

Value

<code>pval</code>	p-value
<code>tab</code>	table with allele counts

Author(s)

Jan Graffelman <jan.graffelman@upc.edu>

See Also

[fisher.test](#)

Examples

```

#
# bi-allelic autosomal
#

m <- c(AA=60, AB=96, BB=44)
f <- c(AA=44, AB=97, BB=59)
EAFtest <- EAFExact(m, f)

#
# bi-allelic X-chromosomal
#

males <- c(A=392, B=212)
females <- c(AA=275, AB=296, BB=80)
EAFtest <- EAFExact(males, females, verbose=TRUE)

#
# tri-allelic autosomal
#

males <- c(AA=20, AB=52, AC=34, BB=17, BC=51, CC=26)
females <- c(AA=28, AB=55, AC=33, BB=18, BC=50, CC=16)
EAFtest <- EAFExact(males, females, verbose=TRUE)

#
# tri-allelic X-chromosomal
#

males <- c(A=15, B=17, C=24)
females <- toTriangular(c(AA=4, AB=2, AC=13, BB=6, BC=19, CC=4))
EAFtest <- EAFExact(males, females, verbose=TRUE)

```

fisherz

*Fisher's z transformation***Description**

Calculates Fisher's z transformation for a correlation coefficient

Usage

```
fisherz(r)
```

Arguments

r a correlation coefficient

Value

a real number

Author(s)

Jan Graffelman (jan.graffelman@upc.edu)

See Also

[cor](#)

Examples

```
r <- 0.5
print(fisherz(r))
```

GenerateSamples	<i>Generate genotypic compositions</i>
-----------------	--

Description

GenerateSamples generates all possible genotypic compositions (AA,AB,BB) for a given sample size n.

Usage

```
GenerateSamples(n = 5)
```

Arguments

n the desired sample size

Value

returns a matrix with in each row a possible genotypic composition for the given sample size.

Author(s)

Jan Graffelman <jan.graffelman@upc.edu>

Examples

```
GenerateSamples(5)
```

genlabels	<i>Label genotype counts of a vector or matrix</i>
-----------	--

Description

Function `genlabels` sets the names of a vector or matrix of genotype counts.

Usage

```
genlabels(X)
```

Arguments

`X` a 3 (or 5) element vector with genotype counts, a matrix of genotype counts (3 or 5 columns)

Value

A vector or a matrix

Author(s)

Jan Graffelman (jan.graffelman@upc.edu)

See Also

[HWChisq](#)

Examples

```
x <- c(25, 50, 25)
x <- genlabels(x)
```

HapMapCHBChr1	<i>Genotype frequencies for 225 SNPs on chromosome 1 of the CHB population.</i>
---------------	---

Description

The dataframe contains the genotype frequencies in generic notation, AA, AB and BB the first 225 polymorphic SNPs without missing data on chromosome 1 of the Han Chinese in Beijing. The data are compiled from the HapMap project, phase 3.2, containing genotype information of 84 individuals.

Usage

```
data(HapMapCHBChr1)
```

Format

A matrix containing 225 rows and 3 columns (AA, AB, BB).

Source

<http://hapmap.ncbi.nlm.nih.gov/>

References

The International HapMap Consortium (2007). A second generation human haplotype map of over 3.1 million SNPs Nature 449, pp. 851–861.

HWABO

Estimate allele frequencies and test for Hardy-Weinberg equilibrium with a tri-allelic ABO system.

Description

Function HWABO takes four genotype counts ("A","B","AB","OO") and estimates the three allele frequencies using the EM algorithm.

Usage

```
HWABO(x, p = c(1/3, 1/3, 1/3), maxiter = 50, tol = 1e-10, verbose = TRUE)
```

Arguments

x	a vector with genotype counts ("A","B","AB","OO").
p	a vector with initial allele frequencies (by default (1/3,1/3,1/3)).
maxiter	maximum number of iterations.
tol	tolerance for convergence, 1e-10 by default
verbose	print iteration history or not.

Value

pn	vector with estimated allele frequencies.
It.hist	iteration history with log-likelihood.
expected	expected genotype counts under HWE.

Author(s)

Jan Graffelman <jan.graffelman@upc.edu>

See Also

[af](#)

Examples

```
x <- c(fA=182, fB=60, nAB=17, n00=176)
al.fre <- HWABO(x)
#a12 <- HWABO(x, p=c(0.99, 0.01, 0.01), maxiter=25)
#a13 <- HWABO(x, p=c(0.01, 0.99, 0.01), maxiter=25)
#a14 <- HWABO(x, p=c(0.01, 0.01, 0.99), maxiter=25)
```

HWAIC	<i>Compute Akaike's Information Criterion (AIC) for HWP and EAF models</i>
-------	--

Description

Function HWAIC calculates Akaike's Information Criterion for ten different models that describe a bi-allelic genetic variant: M11: Hardy-Weinberg proportions and equality of allele frequencies in the sexes (HWP & EAF); M12: EAF and HWP in males only; M13: EAF and HWP in females only; M14: EAF and equality of inbreeding coefficients in the sexes (EIC); M15: EAF only; M21: HWP in both sexes; M22: HWP for males only; M23: HWP for females only; M24: EIC only; M25: None of the previous.

Usage

```
HWAIC(x, y, tracing = 0, tol = 0.000001)
```

Arguments

x	Male genotype counts (AA,AB,BB)
y	Female genotype counts (AA,AB,BB)
tracing	Activate tracing in the maximization of some likelihoods (0=no tracing; 1:tracing)
tol	tolerance for iterative maximization of some likelihoods

Details

The log-likelihood for the six models is calculated. For two models (C and E) this is done numerically using package RSoInp.

Value

A named vector containing 6 values for AIC

Author(s)

Jan Graffelman <jan.graffelman@upc.edu>

References

Graffelman, J. and Weir, B.S. (2017) On the testing of Hardy-Weinberg proportions and equality of allele frequencies in males and females at bi-allelic genetic markers. *Genetic Epidemiology* pp. 1–15.

See Also

[HWRtest](#)

Examples

```
males <- c(AA=11,AB=32,BB=13)
females <- c(AA=14,AB=23,BB=11)
stats <- HWAIC(males,females)
print(stats)
```

HWAlltests

Perform all tests for Hardy-Weinberg equilibrium

Description

HWAlltests performs all classical frequentists tests for Hardy-Weinberg equilibrium and lists their p-values.

Usage

```
HWAlltests(x, verbose = TRUE, include.permutation.test = FALSE, x.linked = FALSE)
```

Arguments

x	a vector with a set of genotype counts (AA, AB, BB)
verbose	print output if set to TRUE
include.permutation.test	turns on the permutation test if set to TRUE
x.linked	x.linked=FALSE indicates the marker is autosomal (default), and x.linked=TRUE indicates it resides on the X-chromosome.

Details

By default the permutation test is not performed in order to reduce computing time.

Value

A dataframe with test statistics and p-values.

Author(s)

Jan Graffelman <jan.graffelman@upc.edu>

See Also

[HWLratio](#), [HWChisq](#), [HWExact](#)

Examples

```
x <- c(298, 489, 213)
names(x) <- c("MM", "MN", "NN")
HWA11tests(x, verbose=TRUE)
```

HWA1r

Compute additive log-ratio transformation

Description

HWA1r computes the additive log-ratio transformation for genotype counts of bi-allelic genetic markers.

Usage

```
HWA1r(X, zeroadj = 0.5, denominator = 2)
```

Arguments

X	A matrix of genotype counts (columns AA, AB and BB)
zeroadj	A zero adjustment parameter (0.5 by default)
denominator	The genotype count put in the denominator of the log-ratio (1=AA, 2=AB, 3=BB)

Value

A matrix or vector of log-ratio coordinates

Author(s)

Jan Graffelman (jan.graffelman@upc.edu)

References

Graffelman, J. and Egozcue, J. J. (2011) Hardy-Weinberg equilibrium: a non-parametric compositional approach. In: Vera Pawlowsky-Glahn and Antonella Buccianti (eds.) *Compositional Data Analysis: Theory and Applications*, John Wiley & Sons, Ltd, pp. 207-215

See Also

[HWC1r](#), [HWI1r](#)

Examples

```
X <- HWDData(100,100)
Y <- HWA1r(X)
```

HWA1rPlot*Plot genetic markers in additive log-ratio coordinates*

Description

HWA1rPlot creates a scatter plot of the log-ratio coordinates of bi-allelic genetic markers. Hardy-Weinberg equilibrium is indicated by a straight line in the plot.

Usage

```
HWA1rPlot(X, zeroadj = 0.5)
```

Arguments

X	A matrix of genotype counts (columns AA, AB, BB)
zeroadj	Zero-adjustment parameter. Zero counts in the count matrix are substituted by zeroadj which is 0.5 by default.

Value

NULL

Author(s)

Jan Graffelman (jan.graffelman@upc.edu)

References

Graffelman, J. and Egozcue, J. J. (2011) Hardy-Weinberg equilibrium: a non-parametric compositional approach. In: Vera Pawlowsky-Glahn and Antonella Buccianti (eds.) *Compositional Data Analysis: Theory and Applications*, John Wiley & Sons, Ltd, pp. 207-215

See Also

[HWC1rPlot](#), [HWI1rPlot](#)

Examples

```
X <- HWC1o(HWDData(100,100))
HWA1rPlot(X)
```

 HWChisq

Chi square tests for Hardy Weinberg equilibrium

Description

HWChisq performs the chi-square test for Hardy-Weinberg equilibrium both for autosomal and X-chromosomal markers.

Usage

```
HWChisq(X, cc = 0.5, verbose = TRUE, x.linked = FALSE, phifixed = NULL)
```

Arguments

X	X a vector containg the genotypic counts (AA,AB,BB for autosomal markers c(A,B,AA,AB,BB) for X-chromosomal markers).
cc	cc the continuity correction parameter (default cc = 0.5).
verbose	verbose = TRUE prints results, verbose = FALSE is silent.
x.linked	x.linked=FALSE indicates the marker is autosomal (default), and x.linked=TRUE indicates it resides on the X-chromosome.
phifixed	(For X-chromosomal markers only) phifixed=NULL indicates that the fraction of males (females) should be estimated from the data (default). If set to any other value (e.g. phifixed=0.5) then the sample is assumed to come from a population with the specified fraction of males.

Details

HWChisq does a chi-square test for Hardy-Weinberg equilibrium, and by default applies a continuity correction. For extreme allele frequencies, the continuity correction can lead to excessive type 1 error rates, and is better turned off in that case. The continuity correction can be turned off by specifying `cc=0`.

HWChisq can do the chi-square test for both autosomal and X-chrosomal markers. By setting `x.linked = TRUE` the marker will be assumed to be on the X-chromosome, and the count vector supplied should have 5 elements instead of 3 elements for an autosomal marker. For X-chromosomal markers argument `phifixed` is in general best left to its default value (NULL). Only in specific situations where the theoretical population sex ratio is known (e.g. in simulation studies where a universe with known gender ratio is sampled) `phifixed` could be set to the theoretical ratio of interest.

When `alternative` is set to `less`, a one-sided test for against a negative inbreeding coefficient (heterozygote excess) is performed. When `alternative` is set to `greater` a one-sided test for against a positive inbreeding coefficient (lack of heterozygotes) is performed.

Value

HWChisq returns a list with the components:

chisq	value of the chi-square statistic. NA is returned if the marker is monomorphic.
pval	p-value of the chi-square test for Hardy-Weinberg equilibrium.
D	Half the deviation from Hardy-Weinberg equilibrium for the AB genotype.
p	the allele frequency of A.
f	the inbreeding coefficient.
expected	the expected counts under Hardy-Weinberg equilibrium

Author(s)

Jan Graffelman <jan.graffelman@upc.edu>

References

Weir, B.S. (1996) Genetic data analysis II. Sinauer Associates, Massachusetts. See Chapter3.

For the chi-square test for X-linked markers:

Graffelman, J. & Weir, B.S. (2016) Testing for Hardy-Weinberg equilibrium at bi-allelic genetic markers on the X chromosome. *Heredity* 116(6) pp. 558–568. <http://dx.doi.org/10.1038/hdy.2016.20>

See Also

[HWLratio](#), [HWChisqStats](#)

Examples

```
#
# Test for an autosomal blood group marker
#
x <- c(MM=298,MN=489,NN=213)
HW.test <- HWChisq(x,verbose=TRUE)
#
# Same test without continuity correction
#
HW.test <- HWChisq(x,cc=0,verbose=TRUE)
#
# Test for an X-chromosomal SNP.
#
rs5968922 <- c(A=392, B=212, AA=275, AB=296, BB=80)
HW.test <- HWChisq(rs5968922,cc=0,x.linked=TRUE,verbose=TRUE)
```

HWChisqMat	<i>Matrix version of HWChisq</i>
------------	----------------------------------

Description

HWChisqMat executes the Chisquare test for HWE for each row in a matrix.

Usage

```
HWChisqMat(X, ...)
```

Arguments

X	A n times 3 matrix of genotypic counts (AA,AB,BB)
...	extra arguments that are passed on to HWChisq

Value

pvalvec	Vector with the p-values of each test
chisqvec	Vector with the chi-square statistics
Dvec	Vector with deviations from independence

Author(s)

Jan Graffelman <jan.graffelman@upc.edu>

See Also

[HWChisq](#)

Examples

```
X <- HWData(100,10)
colnames(X) <- c("MM","MN","NN")
Results <- HWChisqMat(X)
Output <- cbind(X,Results$chisqvec,Results$pvalvec)
print(Output)
```

HWChisqStats	<i>Fast computation of chi-square statistics for Hardy-Weinberg equilibrium</i>
--------------	---

Description

HWChisqStats is a function for the fast computation of chi-square statistics (or the corresponding p-values) for a large set of bi-allelic markers (typically SNPs).

Usage

```
HWChisqStats(X, x.linked = FALSE, pvalues = FALSE)
```

Arguments

X	A matrix with genotype counts, one row per marker. X should have 5 columns for an X-chromosomal data set and 3 columns for an autosomal data set.
x.linked	Logical indicating whether the markers are autosomal (x.linked=FALSE) or X-chromosomal (x.linked=TRUE).
pvalues	Logical indicated whether chi-square statistics should be returned (pvalues=FALSE) or whether p-values should be returned (pvalues=TRUE).

Details

Matrix X should strictly comply with the following format. For an autosomal dataset it should contain the 3 genotype counts in order (AA,AB,BB). For an X-chromosomal dataset it should contain the 5 genotype counts in order (A,B,AA,AB,BB) where A and B are the male counts and AA, AB and BB the female counts.

This function was written for speed improvement, and should be much faster than looping over the rows of X with HWChisq. There is no error checking on the supplied data matrix.

Value

A vector of chi-square statistics

Author(s)

Jan Graffelman <jan.graffelman@upc.edu>

References

Graffelman, J. and Weir, B.S. (2016) Testing for Hardy-Weinberg equilibrium at 2 bi-allelic genetic markers on the X chromosome.

See Also

[HWChisq](#)

Examples

```

#
# Autosomal example
#
set.seed(123)
X <- HWDData(1000,100)
monom <- (X[,2]==0 & X[,1]==0) | (X[,2]==0 & X[,3]==0)
X <- X[!monom,] # exclude monomorphics
Chisq.stats <- HWChisqStats(X,x.linked=FALSE,pvalues=FALSE)
Chisq.pvals <- HWChisqStats(X,x.linked=FALSE,pvalues=TRUE)
#
# X-chromosomal example
#
X <- HWDData(1000,100,n.males=50,nA=75,x.linked=TRUE)
Chisq.stats <- HWChisqStats(X,x.linked=TRUE,pvalues=FALSE)
Chisq.pvals <- HWChisqStats(X,x.linked=TRUE,pvalues=TRUE)

```

HWClo

*Convert genotype counts to compositions***Description**

Function HWClo divides each row of a matrix by its total, and so produces matrix of compositions.

Usage

```
HWClo(X)
```

Arguments

X A matrix of (genotype) counts

Value

A matrix

Author(s)

Jan Graffelman <jan.graffelman@upc.edu>

See Also

[HWA1r](#), [HWC1r](#), [HWI1r](#)

Examples

```

X <- HWDData(2,100)
Y <- HWClo(X)

```

`HWClr`*Compute the centred log-ratio transformation*

Description

HWClr computes the centred log-ratio transformation for genotype counts of bi-allelic genetic markers.

Usage

```
HWClr(X, zeroadj = 0.5)
```

Arguments

<code>X</code>	A matrix of genotype counts (columns AA, AB and BB)
<code>zeroadj</code>	A zero adjustment parameter (0.5 by default)

Value

A matrix or vector of log-ratio coordinates

Author(s)

Jan Graffelman (jan.graffelman@upc.edu)

References

Graffelman, J. and Egozcue, J. J. (2011) Hardy-Weinberg equilibrium: a non-parametric compositional approach. In: Vera Pawlowsky-Glahn and Antonella Buccianti (eds.) *Compositional Data Analysis: Theory and Applications*, John Wiley & Sons, Ltd, pp. 207-215

See Also

[HWA1r](#), [HWI1r](#)

Examples

```
X <- HWDData(100,100)
Y <- HWClr(X)
```

`HWClrPlot`*Plot genetic markers in centred log-ratio coordinates*

Description

HWClrPlot creates a scatter plot of the centred log-ratio coordinates of bi-allelic genetic markers. Hardy-Weinberg equilibrium is indicated by a straight line in the plot.

Usage

```
HWClrPlot(X, zeroadj = 0.5)
```

Arguments

<code>X</code>	A matrix of genotype counts (columns AA, AB, BB)
<code>zeroadj</code>	Zero-adjustment parameter. Zero counts in the count matrix are substituted by <code>zeroadj</code> which is 0.5 by default.

Value

NULL

Author(s)

Jan Graffelman (jan.graffelman@upc.edu)

References

Graffelman, J. and Egozcue, J. J. (2011) Hardy-Weinberg equilibrium: a non-parametric compositional approach. In: Vera Pawlowsky-Glahn and Antonella Buccianti (eds.) *Compositional Data Analysis: Theory and Applications*, John Wiley & Sons, Ltd, pp. 207-215

See Also

[HWAlrPlot](#), [HWIlrPlot](#)

Examples

```
X <- HWC1o(HWDData(100,100))
HWClrPlot(X)
```

`HWCondProbAB`*Compute probability of a genotypic sample*

Description

Computes the probability of a particular genotypic sample given the allele count, sample size and number of heterozygotes.

Usage

```
HWCondProbAB(n, nA, nAB)
```

Arguments

<code>n</code>	<code>n</code> is the total sample size (total number of individuals)
<code>nA</code>	<code>nA</code> is the number of A alleles in the sample
<code>nAB</code>	<code>nAB</code> is the number of heterozygotes in the sample

Value

<code>p</code>	probability of the particular sample
----------------	--------------------------------------

Author(s)

Jan Graffelman (jan.graffelman@upc.edu)

See Also

[HWExact](#)

Examples

```
x <- c(298, 489, 213)
names(x) <- c("MM", "MN", "NN")
n <- sum(x)
nM <- 2*x[1]+x[2]
nMN <- x[2]
p <- HWCondProbAB(n, nM, nMN)
```

HWD*Compute disequilibrium statistic D*

Description

Function HWD computes Weir's disequilibrium coefficient D .

Usage

```
HWD(X)
```

Arguments

X a vector of genotype counts (AA, AB, BB)

Value

Returns the disequilibrium coefficient

Author(s)

Jan Graffelman <jan.graffelman@upc.edu>

References

Weir, B.S. (1996) Genetic data analysis II. Sinauer Associates, Massachusetts. See Chapter3.

See Also

[Hwf HWChisq](#)

Examples

```
x <- c(MM=298,MN=489,NN=213)
D <- HWD(x)
cat("Disequilibrium coefficient: ",D,"\n")
```

HWDData	<i>Generate genetic marker data in or out of Hardy-Weinberg Equilibrium</i>
---------	---

Description

HWDData generates samples of genotypic counts under various schemes. It mainly uses sampling from the multinomial distribution given Hardy-Weinberg allele frequencies.

Usage

```
HWDData(nm = 100, n = rep(100, nm), f = rep(0, nm), p = NULL, conditional
= FALSE, exactequilibrium = FALSE, pdist = "runif", x.linked = FALSE, nA
= NULL,
n.males=rep(round(0.5*n),nm), ...)
```

Arguments

nm	The number of bi-allelic markers.
n	The sample sizes.
f	The inbreeding coefficients (only for autosomal markers)
p	a vector of allele frequencies
conditional	if TRUE Haldane's distribution is used for sampling, if FALSE a multinomial distribution is used. Replaces parameter <code>pfixed</code> from the previous version of the package
exactequilibrium	generates data in exact HWE if set to TRUE
pdist	Take a random allele frequency from a uniform or beta distribution of <code>pfixed = FALSE</code> and <code>p</code> is not given.
x.linked	Simulated autosomal markers (<code>x.linked=FALSE</code> , the default) or X-chromosomal markers (<code>x.linked=TRUE</code>)
nA	A vector of minor allele counts, one for each marker. If not specified, it will be calculated from <code>p</code>
n.males	The number of males (only relevant if <code>x.linked = TRUE</code>)
...	specific parameters for the uniform or beta

Details

The `exactequilibrium` option only takes effects for autosomal markers (`x.linked=FALSE`) and multinomial sampling (`conditional=FALSE`).

Option `pfixed` is deprecated and replaced by `conditional`

HWDData returns a matrix of genotype counts, `nm` by 3 for autosomal markers or `nm` by 5 for X-chromosomal markers. Output is no longer supplied in the compositional form. Function `HWC10` can be used to convert the genotype counts to a composition.

If the inbreeding coefficient is specified (f) it will only take effect for autosomal markers (x.linked=FALSE) and multinomial sampling (conditional=FALSE).

Value

X A matrix containing the genotype counts.

Author(s)

Jan Graffelman (jan.graffelman@upc.edu)

See Also

[HWTernaryPlot](#)

Examples

```
nm <- 100
n <- 100
out <- HWData(nm,n)
```

HWExact

Exact test for Hardy-Weinberg equilibrium

Description

HWExact performs an exact test for Hardy-Weinberg equilibrium

Usage

```
HWExact(X, alternative = "two.sided", pvalue.type = "selome", x.linked =
FALSE, verbose = TRUE)
```

Arguments

X	vector with the genotype counts AA, AB, BB
alternative	two.sided (default) will perform a two-sided test where both an excess and a dearth of heterozygotes count as evidence against HWE. less is a one-sided test where only dearth of heterozygotes counts as evidence against HWE, greater is a one-sided test where only excess of heterozygotes counts as evidence against HWE.
pvalue.type	if pvalue.type is set to dost then the p-value of a two-sided test is computed as twice the tail area of a one-sided test. When set to selome, the p-value is computed as the sum of the probabilities of all samples less or equally likely as the current sample. When set to midp, the p-value is computed as half the probability of the current sample + the probabilities of all samples that are more extreme.

x.linked	x.linked=FALSE indicates the marker is autosomal (default), and x.linked=TRUE indicates it resides on the X-chromosome.
verbose	print results or not.

Details

HWExact uses the recursion equations described by Wigginton et. al.

For testing large sets of bi-allelic variants, use the faster code in [HWExactStats](#).

For large samples, HWExact may give the error message: "evaluation nested too deeply: infinite recursion". This can usually be resolved by increasing R's limit on nested expressions with `options(expressions=10000)` or a higher limit. With higher limits, the error message "protect(): protection stack overflow" can occur. This error can usually be resolved by increasing R's protection stack with the command line option `--max-ppsize 100000` or higher values. However, with such large samples the exact test will give virtually the same result as a chi-square test, and it may be easier to use `HWChisq` in these circumstances.

Value

pval	p-value of the exact test
prob	probabilities of all possible samples with the same sample size and minor allele count
pofthesample	probability of the observed sample

Author(s)

Jan Graffelman (jan.graffelman@upc.edu)

References

Weir, B.S. (1996) Genetic data analysis II. Sinauer Associates, Massachusetts. See Chapter3.

Wigginton, J.E., Cutler, D.J. and Abecasis, G.R. (2005) A note on exact tests of Hardy-Weinberg equilibrium, *American Journal of Human Genetics* (76) pp. 887-893.

Graffelman, J. and Moreno, V. (2013) The mid p-value in exact tests for Hardy-Weinberg equilibrium, *Statistical Applications in Genetics and Molecular Biology* 12(4) pp. 433-448.

See Also

[HWLratio](#), [HWChisq](#), [HWExactStats](#)

Examples

```
#
# Example for an autosomal marker using the standard exact p-value
#
x <- c(298,489,213)
names(x) <- c("MM", "MN", "NN")
HW.test <- HWExact(x, verbose=TRUE)
#
```



```
# Example for an autosomal marker using the mid p-value
#
HW.test <- HWExact(x,verbose=TRUE,pvaluetype="midp")
#
# Example x-linked marker
#
rs5968922 <- c(A=392, B=212, AA=275, AB=296, BB=80 )
HWExact(rs5968922,x.linked=TRUE,verbose=TRUE)
```

HWExactMat

Matrix version of HWExact

Description

HWExactMat executes a fast Exact test for HWE for each row in a matrix.

Usage

```
HWExactMat(X, ...)
```

Arguments

X	A n times 3 matrix of genotypic counts (AA,AB,BB)
...	extra arguments that are passed on to HWExact

Value

pvalvec	Vector with the p-values of each test
---------	---------------------------------------

Author(s)

Jan Graffelman <jan.graffelman@upc.edu>

See Also

[HWExact](#)

Examples

```
X <- HWData(100,10)
colnames(X) <- c("MM","MN","NN")
Results <- HWExactMat(X)
Output <- cbind(X,Results$pvalvec)
print(Output)
```

HWExactPrevious	<i>Exact test for Hardy-Weinberg equilibrium</i>
-----------------	--

Description

HWExactPrevious performs an exact test for Hardy-Weinberg equilibrium

Usage

```
HWExactPrevious(X, alternative = "two.sided", pvalueType = "selome",
x.linked = FALSE, verbose = FALSE)
```

Arguments

X	vector with the genotype counts AA, AB, BB
alternative	two.sided (default) will perform a two-sided test where both an excess and a dearth of heterozygotes count as evidence against HWE. less is a one-sided test where only dearth of heterozygotes counts as evidence against HWE, greater is a one-sided test where only excess of heterozygotes counts as evidence against HWE.
pvalueType	if pvalueType is set to dost then the p-value of a two-sided test is computed as twice the tail area of a one-sided test. When set to selome, the p-value is computed as the sum of the probabilities of all samples less or equally likely as the current sample. When set to midp, the p-value is computed as half the probability of the current sample + the probabilities of all samples that are more extreme.
x.linked	x.linked=FALSE indicates the marker is autosomal (default), and x.linked=TRUE indicates it resides on the X-chromosome.
verbose	print results or not.

Details

HWExactPrevious uses the recursion equations described by Wigginton et. al.

For large samples, HWExactPrevious may give the error message: "evaluation nested too deeply: infinite recursion". This can usually be resolved by increasing R's limit on nested expressions with options(expressions=10000) or a higher limit. With higher limits, the error message "protect(): protection stack overflow" can occur. This error can usually be resolved by increasing R's protection stack with the command line option --max-ppsize 100000 or higher values. However, with such large samples the exact test will give virtually the same result as a chi-square test, and it may be easier to use HWChisq in these circumstances.

Value

pval	p-value of the exact test
prob	probabilities of all possible samples with the same sample size and minor allele count
probOfThisSample	probability of the observed sample

Author(s)

Jan Graffelman (jan.graffelman@upc.edu)

References

Weir, B.S. (1996) Genetic data analysis II. Sinauer Associates, Massachusetts. See Chapter3.
 Wigginton, J.E., Cutler, D.J. and Abecasis, G.R. (2005) A note on exact tests of Hardy-Weinberg equilibrium, American Journal of Human Genetics (76) pp. 887-893.

See Also

[HWLratio](#), [HWChisq](#)

Examples

```
#
# Example autosomal marker
#
x <- c(298,489,213)
names(x) <- c("MM","MN","NN")
## Not run: HW.test <- HWExactPrevious(x,verbose=TRUE)
#
# Example x-linked marker
#
rs5968922 <- c(A=392, B=212, AA=275, AB=296, BB=80 )
## Not run: HWExactPrevious(rs5968922,x.linked=TRUE,verbose=TRUE)
```

HWExactStats

Computation of Exact p-values for Hardy-Weinberg equilibrium for sets of SNPs

Description

HWExactStats is a function for the computation of Exact p-values for a large set of bi-allelic markers (typically SNPs).

Usage

```
HWExactStats(X, x.linked = FALSE, plinkcode = TRUE, midp = FALSE,...)
```

Arguments

X	A matrix with genotype counts, one row per marker. X should have 5 columns for an X-chromosomal data set and 3 columns for an autosomal data set.
x.linked	Logical indicating whether the markers are autosomal (x.linked=FALSE) or X-chromosomal (x.linked=TRUE).
plinkcode	Logical indicating whether to use faster C++ code from the PLINK software.
midp	Logical indicating whether to use the mid p-value for the C++ code or not
...	extra arguments that are passed on to HWExact

Details

Matrix X should strictly comply with the following format. For an autosomal dataset it should contain the 3 genotype counts in order (AA,AB,BB). For an X-chromosomal dataset it should contain the 5 genotype counts in order (A,B,AA,AB,BB) where A and B are the male counts and AA, AB and BB the female counts.

Argument `plinkcode=TRUE` (the default) will use C++ code for faster calculation (functions `SNPHWE2` and `SNPHWEX`) with larger datasets. The C++ code was generously shared by Christopher Chang, and the same code is used in the program [PLINK \(2.0\)](#).

Value

A vector of p-values

Author(s)

Jan Graffelman <jan.graffelman@upc.edu> (R code) and Christopher Chang <chrchang523@gmail.com> (C++ code)

References

Graffelman, J. and Weir, B.S. (2016) Testing for Hardy-Weinberg equilibrium at bi-allelic genetic markers on the X chromosome. [Heredity](#) 116(6) pp. 558–568.

Purcell et al. (2007) PLINK: A Toolset for Whole-Genome Association and Population-Based Linkage Analysis. *American Journal of Human Genetics* 81(3) pp. 559–575.

See Also

[HWExact](#)

Examples

```
#
# Autosomal example
#
set.seed(123)
X <- HWDData(1000,100)
monom <- (X[,2]==0 & X[,1]==0) | (X[,2]==0 & X[,3]==0)
X <- X[!monom,] # exclude monomorphics
Exact.pvalues <- HWExactStats(X,x.linked=FALSE)
#
# X-chromosomal example
#
X <- HWDData(1000,100,n.males=50,nA=75,x.linked=TRUE)
Exact.pvalues <- HWExactStats(X,x.linked=TRUE)
```

HWf*Computation of inbreeding coefficient*

Description

HWf computes the inbreeding coefficient for a sample of genotypes.

Usage

```
HWf(X)
```

Arguments

X a vector of genotype counts (AA, AB, BB)

Details

For monomorphic markers a warning is issued, and the estimate for the inbreeding coefficient is set to zero.

Value

Returns the inbreeding coefficient (intraclass correlation coefficient)

Author(s)

Jan Graffelman <jan.graffelman@upc.edu>

References

Crow, J. F. and Kimura, M. (1970) An introduction to population genetics theory. Harper & Row, publishers, New York

See Also

[HWChisq](#)

Examples

```
x <- c(MM=298,MN=489,NN=213)
f <- HWf(x)
cat("Inbreeding coefficient: ",f,"\n")
```

HWGenotypePlot *Scatter plot of the genotype frequencies*

Description

HWGenotypePlot makes a scatterplots of the AB or BB frequency versus the AA frequency and represents a blue curve indicating the Hardy-Weinberg equilibrium condition.

Usage

```
HWGenotypePlot(X, plottype = 1, xlab = expression(f[AA]), ylab =
  ifelse(plottype == 1, expression(f[AB]), expression(f[BB])), asp = 1,
  pch = 19, xlim = c(0, 1), ylim = c(0, 1), cex = 1, cex.axis = 2, cex.lab = 2, ...)
```

Arguments

X	A matrix of genotype counts or frequencies with three columns (AA, AB, BB)
plottype	plottype=1 produces a plot of AB versus AA, plottype=2 produced a plot of BB versus AA.
xlab	A label for the x axis
ylab	A label for the y axis
asp	Aspec ratio (1 by default)
pch	Plotting charachter (19 by default)
xlim	Limits for the x axis (0-1 by default)
ylim	Limits for the y axis (0-1 by default)
cex	Character expansion factor (1 by default)
cex.axis	Character expansion factor for the axes (2 by default)
cex.lab	Character expansion factor for labels of axis (2 by default)
...	Additional arguments for the plot function

Value

NULL

Author(s)

Jan Graffelman <jan.graffelman@upc.edu>

See Also

[HWTernaryPlot](#)

Examples

```
n <- 100 # sample size
m <- 100 # number of markers
Xc <- HWClo(HWData(n,m))
HWGenotypePlot(Xc,plotype=1,main="Heterozygote-homozygote scatterplot")
```

HWIlr*Compute isometric log ratio coordinates.*

Description

HWIlr computes isometric log ratio coordinates for genotypic compositions (AA, AB, BB)

Usage

```
HWIlr(X, zeroadj = 0.5)
```

Arguments

X	A matrix of genotype counts, markers in rows, counts for AA, AB and BB in three columns
zeroadj	Adjustment for zeros (0.5 by defaults)

Value

A matrix of log ratio coordinates.

Author(s)

Jan Graffelman (jan.graffelman@upc.edu)

References

Egozcue, J.J., Pawlowsky-Glahn, V., Mateu-Figueras, G. and Barcelo-Vidal, C. (2003) Isometric Logratio Transformations for Compositional Data Analysis. *Mathematical Geology* 35(3), pp. 279-300.

Graffelman, J. and Egozcue, J. J. (2011) Hardy-Weinberg equilibrium: a non-parametric compositional approach. In: Vera Pawlowsky-Glahn and Antonella Buccianti (eds.) *Compositional Data Analysis: Theory and Applications*, John Wiley & Sons, Ltd, pp. 207-215

See Also

[HWA1r](#), [HWC1r](#)

Examples

```
X <- HWData(100,100)
Y <- HWIlr(X)
```

`HWIIRPlot`*Plot bi-allelic genetic markers in isometric log ratio coordinates*

Description

HWIIRPlot makes a scatter plot of the isometric log ratio coordinates for bi-allelic markers.

Usage

```
HWIIRPlot(X, zeroadj = 0.5, ...)
```

Arguments

<code>X</code>	Matrix of genotype counts, one marker per row, AA, AB and BB in three columns
<code>zeroadj</code>	Adjustment for zero values (0.5 by default)
<code>...</code>	Additional arguments for function plot

Value

A matrix of log ratio coordinates.

Author(s)

Jan Graffelman (jan.graffelman@upc.edu)

References

Graffelman, J. and Egozcue, J. J. (2011) Hardy-Weinberg equilibrium: a nonparametric compositional approach. In Pawlowsky-Glahn, V. and Buccianti A., editors, *Compositional Data Analysis: Theory and Applications*, pages 208-217, John Wiley & Sons, Ltd.

See Also

[HWAIRPlot](#), [HWCIRPlot](#)

Examples

```
X <- HWC1o(HWDData(100,100))
HWIIRPlot(X)
```

HwLRAllTests	<i>Perform most relevant likelihood ratio test for Hardy-Weinberg equilibrium and equality of allele frequencies</i>
--------------	--

Description

Function `HwLRAllTests` performs a set of likelihood ratio tests in relation with Hardy-Weinberg proportions (HWP) and equality of allele frequencies (EAF) for autosomal bi-allelic genetic variants.

Usage

```
HwLRAllTests(x, y)
```

Arguments

x	Male genotype counts (AA,AB,BB)
y	Female genotype counts (AA,AB,BB)

Details

Function `HwLRAllTests` calls `HwLRtest` and calculates the p-value of six different tests: 1) joint HWP and EAF (A-F); 2) EAF irrespective of HWP (C-F); 3) HWP irrespective of EAF (D-F); 4) HWP versus EIC (given EAF) (A-B); 5) EIC irrespective of EAF (E-F) and 6) HWP versus EIC. Letters refer to scenarios described by Graffelman & Weir (2017).

Value

A named vector with six p-values

Author(s)

Jan Graffelman <jan.graffelman@upc.edu>

References

Graffelman, J. and Weir, B.S. (2017) On the testing of Hardy-Weinberg proportions and equality of allele frequencies in males and females at bi-allelic genetic markers. *Genetic Epidemiology* pp. 1–15.

See Also

[HwLRtest](#)

Examples

```

males <- c(AA=11,AB=32,BB=13)
females <- c(AA=14,AB=23,BB=11)
pvalues <- HWLRA11Tests(males,females)
print(pvalues)

```

HWLratio

Likelihood ratio test for Hardy Weinberg equilibrium

Description

HWLratio performs the Likelihood ratio test for Hardy Weinberg equilibrium, both for autosomal and X-chromosomal markers.

Usage

```
HWLratio(X, verbose = TRUE, x.linked = FALSE)
```

Arguments

X	X a vector containing the genotypic counts (AA,AB,BB).
verbose	verbose = TRUE prints results, verbose = FALSE is silent.
x.linked	x.linked=FALSE indicates the marker is autosomal (default), and x.linked=TRUE indicates it resides on the X-chromosome.

Value

HWLratio returns a list with the components:

Lambda	the likelihood ratio
G2	-2*log(Lambda)
pval	the p-value

Author(s)

Jan Graffelman <jan.graffelman@upc.edu>

References

Weir, B.S. (1996) Genetic data analysis II. Sinauer Associates, Massachusetts. See Chapter 3.

See Also

[HWChisq](#)

Examples

```
x <- c(298,489,213)
names(x) <- c("MM","MN","NN")
HW.test <- HwLRratio(x,verbose=TRUE)
#
# Test for an X-chromosomal SNP.
#
rs5968922 <- c(A=392, B=212, AA=275, AB=296, BB=80)
HW.test <- HwLRratio(rs5968922,x.linked=TRUE,verbose=TRUE)
```

HwLRtest	<i>Perform likelihood ratio test comparing two nested scenarios for a bi-allelic genetic variant, distinguishing the two sexes.</i>
----------	---

Description

Program HwLRtest performs a likelihood ratio test comparing two scenarios for an autosomal bi-allelic genetic variant. The scenarios concern Hardy-Weinberg proportions (HWP) and equality of allele frequencies (EAF) in both sexes. The different scenarios are described by Graffelman & Weir (2017).

Usage

```
HwLRtest(x, y, scene.null = "S1", scene.alt = "S6", verbose = TRUE, tracing = 0)
```

Arguments

x	Male genotype counts
y	Female genotype counts
scene.null	Scenario under the null hypothesis (E.g. "S1")
scene.alt	Scenario under the alternative hypothesis (E.g. "S6")
verbose	print output or not
tracing	Show tracing of the numeric likelihood maximization (1) or not (0).

Details

The different scenarios are indicated with S1, S2, S3, S4, S5 and S6. S1 refers to Hardy-Weinberg proportions and equality of allele frequencies. S2 refers to equality of allele frequencies and equality of inbreeding coefficients for the two sexes. S3 refers to equality of allele frequencies irrespective of HWP. S4 refers to HWP irrespective of allele frequencies. S5 refers to equality of inbreeding coefficients irrespective of allele frequencies. S6 is unrestricted.

Value

G2	Likelihood ratio statistic
df	Degrees of freedom of the likelihood ratio statistic
pval	p-value

Author(s)

Jan Graffelman <jan.graffelman@upc.edu>

References

Graffelman, J. and Weir, B.S. (2017) On the testing of Hardy-Weinberg proportions and equality of allele frequencies in males and females at bi-allelic genetic markers. *Genetic Epidemiology* pp. 1–15.

See Also

[HWAIC](#)

Examples

```

males <- c(AA=11,AB=32,BB=13)
females <- c(AA=14,AB=23,BB=11)

#
# test EAF
#

lr1.out <- HWLRtest(males,females,scene.null="S3",scene.alt="S6")

#
# test EIC given EAF
#

lr2.out <- HWLRtest(males,females,scene.null="S2",scene.alt="S3")

#
# test HWP versus EIC, given EAF.
#

lr3.out <- HWLRtest(males,females,scene.null="S1",scene.alt="S2")

```

HWMissing

Test a bi-allelic marker for Hardy-Weinberg equilibrium in the presence of missing genotype information.

Description

Function HWMissing imputes missing genotype data with a multinomial logit model that uses information from allele intensities and/or neighbouring markers. Multiple imputation algorithms implemented in the Mice package are used to obtain imputed data sets. Inference for HWE is carried out by estimating the inbreeding coefficient or exact p-values for each imputed data set, and by combining all estimates using Rubin's pooling rules.

Usage

```
HWMissing(X, imputecolumn = 1, m = 50, coding = c(0,1,2), verbose = FALSE, alpha = 0.05,
          varest = "oneovern", statistic = "chisquare", alternative =
          "two.sided", ...)
```

Arguments

<code>X</code>	An input data frame. By default, the first column should contain the SNP with missing values.
<code>imputecolumn</code>	Indicates which column of the supplied data frame is to be imputed (by default, the first column, <code>imputecolumn=1</code>)
<code>m</code>	The number of imputations (50 by default)
<code>coding</code>	Indicates how the genotype data is coded (e.g. 0 for AA, 1 for AB, and 2 for BB).
<code>verbose</code>	<code>verbose = TRUE</code> prints results, <code>verbose = FALSE</code> is silent.
<code>alpha</code>	significance level (0.05 by default) used when computing confidence intervals
<code>varest</code>	Estimator for the variance of the inbreeding coefficient. <code>varest="oneovern"</code> is the default and sets the variance under the null ($1/n$). <code>varest="bailey"</code> uses an approximation (see details).
<code>statistic</code>	If <code>statistic = "chisquare"</code> then inbreeding coefficients (equivalent to chisquare statistics) will be computed for each imputed data set and then combined. If <code>statistic = "exact"</code> then one-sided exact tests will be computed for each imputed data set and the resulting p-values will be combined.
<code>alternative</code>	<code>two.sided</code> (default) will perform a two-sided test where both an excess and a dearth of heterozygotes count as evidence against HWE. <code>less</code> is a one-sided test where only dearth of heterozygotes counts as evidence against HWE, <code>greater</code> is a one-sided test where only excess of heterozygotes counts as evidence against HWE.
<code>...</code>	additional options for function <code>mice</code> of the <code>Mice</code> package

Details

The function `HWMissing` tests one genetic marker (e.g. a SNP) with missings for HWE. By default, this marker is supposed to be the first column of dataframe `X`. The other columns of `X` contain covariates to be used in the imputation model. Covariates will typically be other, correlated markers or allele intensities of the SNP to be imputed. Covariate markers should be coded as factor variables whereas allele intensities should be numerical variables. By default, a polytomous regression model will be used to impute the missings. If the covariates also contain missings, an imputation method for each column of `X` can be specified by using the method of `mice` (see example below).

If there are no covariates, missings can be imputed under the MCAR assumption. In that case, missings are imputed by taking a random sample from the observed data. This is what `HWMissing` will do if no covariates are supplied, `X` being a single factor variable.

Several estimators for the variance of the inbreeding coefficient have been described in the literature. The asymptotic variance of the inbreeding coefficient under the null hypothesis is $1/n$, and is used if `varest = "oneovern"` is used. This is the recommended option. Alternatively, the approximation described in Weir (p. 66) can be used with `varest = "bailey"`.

Value

Res A vector with the inbreeding coefficient, a confidence interval for the inbreeding coefficient, a p-value for a HWE test and missing data statistics.

Xmat A matrix with the genotypic composition of each of the *m* imputed data sets.

Author(s)

Jan Graffelman <jan.graffelman@upc.edu>

References

Little, R. J. A. and Rubin, D. B. (2002) Statistical analysis with missing data. Second edition, New York, John Wiley & sons.

Graffelman, J., Sánchez, M., Cook, S. and Moreno, V. (2013) Statistical inference for Hardy-Weinberg proportions in the presence of missing genotype information. PLoS ONE 8(12): e83316. <http://dx.doi.org/10.1371/journal.pone.0083316>

Graffelman, J. (2015) Exploring Diallelic Genetic Markers: The HardyWeinberg Package. *Journal of Statistical Software* 64(3): 1-23. <http://www.jstatsoft.org/v64/i03/>.

See Also

[HWChisq](#)

Examples

```
data(Markers)
## Not run:
set.seed(123)
Results <- HWMissing(Markers[,1],m=50,verbose=TRUE)$Res # no covariates, imputation assuming MCAR.
set.seed(123)
Results <- HWMissing(Markers[,1:3],m=50,verbose=TRUE)$Res # impute with two allele intensities.
set.seed(123)
Results <- HWMissing(Markers[,c(1,4,5)],m=50,verbose=TRUE)$Res # impute with two covariate SNPs

## End(Not run)
```

HWPerm

Permutation test for Hardy-Weinberg equilibrium

Description

Function HWPerm does a permutation test for Hardy-Weinberg equilibrium using a user-supplied test statistic.

Usage

```
HWPerm(x, nperm = 17000, verbose = TRUE, x.linked = FALSE,
FUN = ifelse(x.linked,Chisquare.x,Chisquare), ...)
```

Arguments

x	A vector of genotype counts (AA,AB,BB)
nperm	The number of permutations
verbose	verbose = TRUE will print results, verbose = FALSE is silent.
x.linked	x.linked=FALSE indicates the marker is autosomal (default), and x.linked=TRUE indicates it resides on the X-chromosome.
FUN	An function call for calculating the test statistic for HWE (see examples below)
...	Additional parameters for the function call argument FUN

Details

The set of alleles for the observed sample is permuted. Consequently, the test is conditional on allele frequency.

Value

HWPerm returns a list with the components:

stat	value of the chosen test statistic for the observed sample.
pval	p-value of the permutation test.

Author(s)

Jan Graffelman <jan.graffelman@upc.edu>

References

Ziegler, A. & König, I.R. (2006) A statistical approach to genetic epidemiology. Wiley.

See Also

[HWChisq](#), [HWExact](#), [HwLratio](#)

Examples

```
x <- c(MM=298,MN=489,NN=213)
## Not run:
HW.test <- HWPerm(x,nperm=10000,verbose=TRUE) # uses default chi-square statistic
HW.test <- HWPerm(x,nperm=10000,verbose=TRUE,function(z)
HWChisq(z)$chisq,cc=0.5) # uses chi-square statistic with continuity correction.
HW.test <- HWPerm(x,nperm=10000,verbose=TRUE,function(y) HwLratio(y)$G2)
# uses likelihood ratio statistic.
HWPerm(x,nperm=10000,verbose=TRUE,function(y) 1-HWExact(y)$pval)
# uses exact test p-value
#
# Permutation test for a marker on the X chromosome
#
rs5968922 <- c(A=392, B=212, AA=275, AB=296, BB=80)
HW.test <- HWPerm(rs5968922,nperm=10000,x.linked=TRUE,verbose=TRUE)
```

```
## End(Not run)
```

 HWPerm.mult

Permutation tests fo variants with multiple alleles

Description

Function HWPerm.mult implements permutation tests for Hardy-Weinberg equilibrium for autosomal and X-chromosomal variants.

Usage

```
HWPerm.mult(x, y = NULL, nperm = 17000, eps = 0, verbose = TRUE, ...)
```

Arguments

x	vector or triangular matrix with male genotype counts
y	vector or triangular matrix with female genotype counts
nperm	number of permutations (17.000 by default)
eps	a tolerance that can be set for comparing probabilities in order to include tied outcomes
verbose	print output or not
...	additional arguments

Details

This function approximates exact test probabilities for joint tests for HWE and equality of allele frequencies for variants with multiple alleles. For purely bi-allelic variant HWPerm can be used which allows for more statistics than just probabilities.

If argument y is not specified, gender is considered irrelevant, and x contains total genotype counts. If x and y are specified, x should contain male genotype counts and y female genotype counts. x and y can be vectors if the variant is bi-allelic, but are assumed lower triangular if there are more than two alleles. x is still a vector if there are multiple alleles but the variant is X-chromosomal. See the examples given below.

Value

pofthesample	probability of the observed sample
pseudodist	probabilities of simulated samples
pval	p-value

Author(s)

Jan Graffelman <jan.graffelman@upc.edu>

References

Graffelman, J. and Weir, B.S. (2017) Multi-allelic exact tests for Hardy-Weinberg equilibrium that account for gender. <https://doi.org/10.1111/1755-0998.12748>

See Also

[HWPerm](#)

Examples

```
#
# bi-allelic autosomal
#

x1 <- c(AA=298,AB=489,BB=213)
## Not run:
out <- HWPerm.mult(x1)

## End(Not run)

#
# bi-allelic X-chromosomal
#

x2.m <- c(A=39, B=21)
x2.f <- toTriangular(c(AA=28, AB=30, BB=8))
## Not run:
out <- HWPerm.mult(x2.m,x2.f)

## End(Not run)

#
# autosomal k alleles not accounting for gender
#

x3 <- c(AA=12,AB=19,AC=13,BB=7,BC=5,CC=0)
x3 <- toTriangular(x3)
## Not run:
out <- HWPerm.mult(x3)

## End(Not run)

#
# X-chromosomal k alleles
#

x4.m <- c(A=15,B=17,C=24)
x4.f <- toTriangular(c(AA=4, AB=2, AC=13, BB=6, BC=19, CC=4))
## Not run:
out <- HWPerm.mult(x4.m,x4.f)

## End(Not run)
```

```

#
# Autosomal k alleles accounting for gender
#

x5.m <- toTriangular(c(AA=12,AB=19,AC=13,BB=7,BC=5,CC=0))
x5.f <- toTriangular(c(AA=8,AB=12,AC=13,BB=8,BC=7,CC=0))
## Not run:
out <- HWPerm.mult(x5.m,x5.f)

## End(Not run)

```

HWPosterior

Calculation of posterior probabilities and Bayes factors for Hardy-Weinberg tests at X-chromosomal variants.

Description

Function HWPosterior calculates posterior probabilities and Bayes factors for tests for Hardy-Weinberg equilibrium of autosomal and X-chromosomal variants.

Usage

```

HWPosterior(X, verbose = TRUE, prior.af = c(0.5,0.5), prior.gf =
  c(0.333,0.333,0.333), x.linked = FALSE, precision = 0.05)

```

Arguments

X	A vector of genotype counts. The order c(A,B,AA,AB,BB) is assumed. Differently ordered vectors can be supplied but then elements must be labeled by their genotype
verbose	prints results if verbose = TRUE
prior.af	Beta prior parameters for male and female allele frequencies
prior.gf	Dirichlet prior parameters for female genotype frequencies
x.linked	logical indicating whether the variant is autosomal or X-chromosomal
precision	precision parameter for marginal likelihoods that require numeric integration

Details

For X-chromosomal variants, four possible models are considered, and the posterior probabilities and Bayes factors for each model are calculated.

For autosomal variants, ten possible scenarios are considered, and the posterior probabilities for all models are calculated.

In general, default Dirichlet priors are used for genotype frequencies, and beta prior are used for allele frequencies.

Value

For X-chromosomal variants, a matrix with posterior probabilities and Bayes factors will be produced. For autosomal variants, a vector of posterior probabilities is produced.

Author(s)

Xavi Puig <xavier.puig@upc.edu> and Jan Graffelman <jan.graffelman@upc.edu>

References

Puig, X., Ginebra, J. and Graffelman, J. (2017) A Bayesian test for Hardy-Weinberg equilibrium of bi-allelic X-chromosomal markers. To appear in *Heredity*.

See Also

[HWChisq](#), [HWExact](#), [HWExactStats](#)

Examples

```
#  
# An X-chromosomal example  
#  
x <- c(A=43,B=13,AA=26,AB=19,BB=3)  
out <- HWPow(x,verbose=TRUE,x.linked=TRUE)  
#  
# An autosomal example  
#  
data(JPTsnps)  
post.prob <- HWPow(JPTsnps[1,],x.linked=FALSE)
```

HWPow

Compute the power of a test for Hardy-Weinberg equilibrium.

Description

HWPow is a function that computes the power of a test for Hardy-Weinberg equilibrium.

Usage

```
HWPow(n = 100, nA = 100, pA = 0.5, y = c(AA=25,AB=50,BB=25),  
alpha = 0.05, theta = 4, f = NULL, test = "exact",  
alternative = "two.sided", pvalueType = "selome", cc = 0.5)
```

Arguments

n	The sample size
nA	The minor allele count
pA	The minor allele frequency
y	A sample of genotype counts (AA,AB,BB)
alpha	The significance level (0.05 by default)
theta	The degree of disequilibrium (theta = 4 is equilibrium, theta > 4 is heterozygote excess, theta < 4 is heterozygote dearth)
f	The inbreeding coefficient. Overrides theta if specified.
test	The type of test for which power is to be computed. Can be "exact" (default) or "chisq" (chi-square)
alternative	The nature of the alternative hypothesis ("two.sided" (default), "greater" or "less")
pvaluetype	The type of p-value used in an exact test ("selome", "dost" or "midp")
cc	Continuity correction parameter for the chi-square test (0.5 by default)

Details

HWPowerr uses the Levene-Haldane distribution (distribution of the number of heterozygotes given the minor allele count) for computing power.

HWPowerr can be used in three different way. In principle, the power is calculated on the basis of the sample size (n) and the minor allele count (nA). Alternatively, the user may specify sample size (n) and minor allele frequency (pA). Finally, power can also be calculated directly from a sample of genotype counts. In that case the calculated power is the power for a sample of the given sample size and minor allele count. The three ways to use HWPowerr are illustrated in the example section.

Value

if test = "exact" the power of the exact test is computed for the given significance level and minor allele count.

if test = "chisq" the power of the chi-square test is computed for the given significance level and minor allele count.

Author(s)

Jan Graffelman (jan.graffelman@upc.edu)

References

Graffelman, J. and Moreno, V. (2013) The Mid p-value in exact tests for Hardy-Weinberg proportions. *Statistical Applications in Genetics and Molecular Biology* 12(4): 433-448.

Graffelman, J. (2015) Exploring Diallelic Genetic Markers: The HardyWeinberg Package. *Journal of Statistical Software* 64(3): 1-23. <http://www.jstatsoft.org/v64/i03/>.

See Also

[HWExact](#)

Examples

```

pw.chisq <- HWPow(n=100,nA=100,alpha=0.05,test="chisq",theta=16)
print(pw.chisq)
pw.exact <- HWPow(n=100,nA=100,alpha=0.05,test="exact",theta=16,pvaluetype="selome")
print(pw.exact)
pw.exact <- HWPow(n=100,nA=100)
print(pw.exact)
pw.exact <- HWPow(n=100,pA=0.5)
print(pw.exact)
pw.exact <- HWPow(y=c(AA=25,AB=50,BB=25))
print(pw.exact)

```

HWQqplot

A Q-Q plot for Hardy-Weinberg equilibrium

Description

HWQqplot creates a Q-Q plot for the p-values obtained in an Exact test for Hardy-Weinberg equilibrium. Empirical p-values are plotted against multiple simulated quantiles of the theoretical p-value distribution.

Usage

```

HWQqplot(X, nsim = 100, fit = "curve", logplot = FALSE,
main = "Q-Q plot for HWE", mm = NULL, pvaluetype = "selome", ...)

```

Arguments

X	Data matrix with genotype counts, one row for each sample, 3 columns
nsim	Number of samples drawn from the null distribution (100 by default)
fit	If fit is set to "line" straight lines will be fitted to the simulated samples, if set to "curve", ascending curves will be shown.
logplot	If logplot is set to true, then the log ₁₀ of the p-values will be used in the plot. If not, untransformed p-values will be used.
main	Title for the plot
mm	Maximal value for x and y axis in the plot
pvaluetype	Type of p-value to be used in an exact test. Can be "selome" (default), "midp" or "dost".
...	Any additional arguments for the plot instruction

Details

HWQqplot constructs a Q-Q plot of the p-values of an exact test for Hardy-Weinberg equilibrium. Under the null, this p-value is not uniform. HWQqplot samples from the theoretical null distribution, taking into account that markers may vary in allele frequency and in sample size (due to missing values). For each simulated sample a grey curve or line is shown. A green reference line with intercept 0 and slope 1 is also shown in the plot.

Value

NULL

Author(s)

Jan Graffelman <jan.graffelman@upc.edu>

References

Rohlf, R.V. and Weir, B.S. (2008) Distributions of Hardy-Weinberg equilibrium test statistics. *Genetics* 180, pp. 1609-1616.

See Also

[HWTernaryPlot](#) [HWExact](#) [qqplot](#)

Examples

```
## Not run:
set.seed(1234)
n <- 200 # sample size
m <- 100 # number of markers
X <- HWDData(n,m)$Xt
HWQqplot(X, logplot=TRUE, pvaluetype="selome", main="Q-Q Plot for HWE")

## End(Not run)
```

HWTernaryPlot

Ternary plot with the Hardy-Weinberg acceptance region

Description

HWTernaryPlot is a routine that draws a ternary plot for three-way genotypic compositions (AA,AB,BB), and represents the acceptance region for different tests for Hardy-Weinberg equilibrium (HWE) in the plot. This allows for graphical testing of a large set of markers (e.g. SNPs) for HWE. The (non) significance of the test for HWE can be inferred from the position of the marker in the ternary plot. Different statistical tests for HWE can be done graphically with this routine: the ordinary chisquare test, the chisquare test with continuity correction and the Haldane's exact test.

Usage

```
HWTernaryPlot(X, n = NA, addmarkers = TRUE, newframe = TRUE, hwcurve = TRUE,
vbounds = TRUE, mafbounds = FALSE, mafvalue = 0.05, axis = 0, region = 1,
vertexlab = colnames(X), alpha = 0.05, vertex.cex = 1, pch = 19, cc = 0.5,
markercol = "black", markerbgcol = "black", cex = 0.75, axislab = "",
verbose = FALSE, markerlab = NULL, markerpos = NULL, mcex = 1, connect =
FALSE, curvecols = rep("black",5), signifcolour = TRUE, curtyp =
"solid", ssf = "max", pvaluetype = "selome", ...)
```

Arguments

<code>X</code>	a matrix of n genotypic compositions or counts. If it is a matrix of compositions, X should have (n rows that sum 1, and 3 columns, with the relative frequencies of AA, AB and BB respectively. Argument n should be supplied as well. If X is a matrix of raw genotypic counts, it should have 3 columns with the absolute counts of AA, AB and BB respectively. Argument n may be supplied and will be used for painting acceptance regions. If not supplied n is computed from the data in X .
<code>n</code>	the samples size (for a complete composition with no missing data).
<code>addmarkers</code>	represent markers by dots in the triangle (<code>addmarkers=TRUE</code>) or not (<code>addmarkers=FALSE</code>).
<code>newframe</code>	allows for plotting additional markers in an already existing ternary plot. Overplotting is achieved by setting <code>newframe</code> to <code>FALSE</code> . Setting <code>newframe = TRUE</code> (default) will create a new ternary plot.
<code>hwcurve</code>	draw the HW parabola in the plot (<code>hwcurve=TRUE</code>) or not (<code>hwcurve=FALSE</code>).
<code>vbounds</code>	indicate the area corresponding to expected counts > 5 (<code>vbounds=TRUE</code>) or not (<code>vbounds=FALSE</code>).
<code>mafbounds</code>	indicate the area corresponding to $MAF < mafvalue$.
<code>mafvalue</code>	a critical value for the minor allele frequency (MAF).
<code>axis</code>	draw a vertex axis 0 = no axis is drawn 1 = draw the AA axis 2 = draw the AB axis 3 = draw the BB axis
<code>region</code>	the type of acceptance region to be delimited in the triangle 0 = no acceptance region is drawn 1 = draw the acceptance region corresponding to a Chi-square test 2 = draw the acceptance region corresponding to a Chi-square test with continuity correction 3 = draw the acceptance region corresponding to a Chi-square test with continuity correction for $D > 0$ 4 = draw the acceptance region corresponding to a Chi-square test with continuity correction for $D < 0$ 5 = draw the acceptance regions for all preceding tests simultaneously 6 = draw the acceptance region corresponding to a Chi-square test with continuity correction with the upper limit for $D > 0$ and the lower limit for $D < 0$ 7 = draw the acceptance region corresponding to a two-sided exact test
<code>vertexlab</code>	labels for the three vertices of the triangle
<code>alpha</code>	significance level (0.05 by default)
<code>vertex.cex</code>	character expansion factor for the labels of the vertices of the triangle.
<code>pch</code>	the plotting character used to represent the markers.
<code>cc</code>	value for the continuity correction parameter (0.5 by default).

markercol	vector with colours for the marker points in the triangle.
markerbgcol	vector with background colours for the marker points in the triangle.
cex	expansion factor for the marker points in the triangle.
axislab	a label to be put under the horizontal axis.
verbose	print information on the numerically found cut-points between curves of the acceptance region and the edges of the triangle.
markerlab	labels for the markers in the triangle.
markerpos	positions for the marker labels in the triangle (1,2,3 or 4).
mex	character expansion factor for the labels of the markers in the ternary plot.
connect	connect the represented markers by a line in the ternary plot.
curvecols	a vector with four colour specifications for the different curves that can be used to delimit the HW acceptance region. E.g. curvecols=c("red", "green", "blue", "black", "purple") will paint the Hardy-Weinberg curve red, the limits of the acceptance region for an ordinary chi-square test for HWE green, the limits of the acceptance region for a chi-square test with continuity correction when $D > 0$ blue and the limits of the acceptance region for a chi-square test with continuity correction when $D < 0$ black, and the limits of the exact acceptance region purple.
signifcolour	colour the marker points automatically according to the result of a significance test (green markers non-significant, red markers significant). signifcolour only takes effect if region is set to 1, 2 or 7.
curtyp	style of the drawn curves ("dashed", "solid", "dotted", ...)
ssf	sample size function ("max", "min", "mean", "median", ...). Indicates how the sample size for drawing acceptance regions is determined from the matrix of counts.
pvaluetype	method to compute p-values in an exact test ("dost" or "selome")
...	other arguments passed on to the plot function (e.g. main for a main title).

Details

HWTernaryPlot automatically colours significant markers in red, and non-significant markers in green if region is set to 1, 2 or 7.

Value

minp	minimum allele frequency above which testing for HWE is appropriate (expected counts exceeding 5).
maxp	maximum allele frequency below which testing for HWE is appropriate.
inrange	number of markers in the appropriate range.
percinrange	percentage of markers in the appropriate.
nsignif	number of significant markers (only if region equals 1,2 or 7.)

Author(s)

Jan Graffelman <jan.graffelman@upc.edu>

References

Graffelman, J. and Morales, J. (2008) Graphical Tests for Hardy-Weinberg Equilibrium Based on the Ternary Plot. *Human Heredity* 65(2):77-84.

Graffelman, J. (2015) Exploring Diallelic Genetic Markers: The HardyWeinberg Package. *Journal of Statistical Software* 64(3): 1-23. <http://www.jstatsoft.org/v64/i03/>.

See Also

[HWChisq](#)

Examples

```
n <- 100 # sample size
m <- 100 # number of markers

X <- HWDData(n,m)
HWTernaryPlot(X,100,region=1,hwcurve=TRUE,vbounds=FALSE,vertex.cex=2)
```

HWTriExact	<i>Exact test for Hardy-Weinberg equilibrium and equality of allele frequencies for tri-allelic variants.</i>
------------	---

Description

Function HWTriExact does a standard exact test for Hardy-Weinberg equilibrium of a tri-allelic variant, and also does joint exact tests for equilibrium and equality of allele frequencies if the genotype counts are given separately for both sexes

Usage

```
HWTriExact(x, y = NULL, eps = 0, nperm = 17000, verbose = TRUE)
```

Arguments

x	vector with 6 genotype counts (AA,AB,AC,BB,BC,CC)
y	vector with 6 or 3 genotype counts (AA,AB,AC,BB,BC,CC) or (A,B,C)
eps	a tolerance that can be set for comparing exact probabilities
nperm	number of permutations (only relevant for autosomal stratified by gender)
verbose	print output or not

Details

If only `x` is specified, an exact test for an autosomal variant with three alleles will be performed.

If both `x` and `y` are supplied as vectors with 6 elements, a permutation test for HWE and equality of allele frequencies (EAF) for an autosomal variant is performed, using `nperm` permutations. The distribution of the probabilities is returned in `pseudodist`. The computational cost of a completed enumeration algorithm can be prohibitive in this case.

If `x` is supplied as a length 6 vector, and `y` as a length 3 vector, the variant is assumed to be X-chromosomal, `x` containing female genotype counts and `y` containing male genotype counts. In this case a joint exact test for HWE and EAF for an X-chromosomal tri-allelic variant is executed.

See the examples in the example section below.

Value

<code>pval</code>	The p-value of the sample
<code>pseudodist</code>	Distribution of probabilities obtained by simulation
<code>pofthesample</code>	The probability of the observed sample

Author(s)

Jan Graffelman <jan.graffelman@upc.edu>

References

Graffelman, J. and Weir, B.S. (2017) Multi-allelic exact tests for Hardy-Weinberg equilibrium that account for gender. <https://doi.org/10.1111/1755-0998.12748>

See Also

[HWPerm.mult](#)

Examples

```
#
# Autosomal tri-allelic (not accounting for gender)
#

x <- c(AA=20,AB=31,AC=26,BB=15,BC=12,CC=0)
## Not run: out <- HWTriExact(x)

#
# Autosomal tri-allelic accounting for gender
#

males <- c(A=1,B=21,C=34)
females <- c(AA=0,AB=1,AC=0,BB=8,BC=24,CC=15)
## Not run: out <- HWTriExact(females,males)

#
# X-chromosomal tri-allelic accounting for gender
```

```
#  
males <- c(A=1,B=21,C=34)  
females <- c(AA=0,AB=1,AC=0,BB=8,BC=24,CC=15)  
## Not run: out <- HWTriExact(females,males)
```

ifisherz

Inverse Fisher z transformation

Description

Calculates the inverse of Fisher's z transformation

Usage

```
ifisherz(y)
```

Arguments

y a real number

Value

a correlation coefficient in the range (-1,1)

Author(s)

Jan Graffelman (jan.graffelman@upc.edu)

See Also

[cor](#)

Examples

```
r <- 0.5  
print(ifisherz(fisherz(r)))
```

JPTmultiallelicsChr7 *Multi-allelic autosomal variants of the Japanese population of the 1000 genomes project*

Description

JPTtriallelicsChrX contains three selected multi-allelic variants on chromosome 7 from the Japanese sample of the 1000 genomes project.

Usage

```
data("JPTmultiallelicsChr7")
```

Format

List object with fields m4,f4; m5,f5; m6,f6;

Details

The list object contains male and female genotype counts for 3 multi-allelic variants on chromosome 7 of the JPT sample of the 1000 genomes project.

Source

The [1000 genomes project](#).

References

Graffelman, J. and Weir, B.S. (2017) Multi-allelic exact tests for Hardy-Weinberg equilibrium that account for gender. doi: 10.1101/172874. Table 10.

Examples

```
data(JPTmultiallelicsChr7)
str(JPTmultiallelicsChr7)
```

JPTmultiallelicsChrX *Multi-allelic X-chromosomal variants of the Japanese population of the 1000 genomes project*

Description

JPTtriallelicsChrX contains four selected multi-allelic variants on the X chromosome from the Japanese sample of the 1000 genomes project.

Usage

```
data("JPTmultiallelicsChrX")
```

Format

List object with fields m4,f4; m5,f5; m6,f6; m7,f7

Details

The list object contains male and female genotype counts for four multi-allelic variants of the JPT sample of the 1000 genomes project.

Source

The [1000 genomes project](#).

References

Graffelman, J. and Weir, B.S. (2017) Multi-allelic exact tests for Hardy-Weinberg equilibrium that account for gender. doi: 10.1101/172874. Table 7.

Examples

```
data(JPTmultiallelicsChrX)
m4 <- JPTmultiallelicsChrX$m4
f4 <- JPTmultiallelicsChrX$f4
```

JPTsnps

Bi-allelic SNPs from a Japanese population

Description

JPTsnps contains genotype counts for the two sexes of ten single nucleotide polymorphisms of the Japanese (JPT) sample of the 1000 Genomes project.

Usage

```
data("JPTsnps")
```

Format

data frame

Source

The [1000 genomes project](#).

References

Puig, X., Ginebra, J. and Graffelman, J. (2019) Bayesian model selection for the study of Hardy-Weinberg proportions and homogeneity of gender allele frequencies.

Examples

```
data(JPTsnps)
```

JPTtrialelicsChr7	<i>Tri-allelic variants on chromosome 7 of the Japanese (JPT) sample of the 1000 genomes project</i>
-------------------	--

Description

JPTtrialelics contains six selected tri-allelic variants on chromosome 7 from the Japanese sample of the 1000 genomes project.

Usage

```
data("JPTtrialelicsChr7")
```

Format

A data frame with 6 observations on the following 14 variables.

id RS identifier
 pos position in base pairs
 mAA number of AA males
 mAB number of AB males
 mAC number of AC males
 mBB number of BB males
 mBC number of BC males
 mCC number of CC males
 fAA number of AA females
 fAB number of AB females
 fAC number of AC females
 fBB number of BB females
 fBC number of BC females
 fCC number of CC females

Source

The [1000 genomes project](#).

References

Graffelman, J. and Weir, B.S. (2017) Multi-allelic exact tests for Hardy-Weinberg equilibrium that account for gender. doi: 10.1101/172874. Table 9.

Examples

```
data(JPTtrialelicsChr7)
str(JPTtrialelicsChr7)
```

JPTtrialelicsChrX	<i>Tri-allelic variants on the X-chromosome of the Japanese (JPT) sample of the 1000 genomes project</i>
-------------------	--

Description

JPTtrialelicsChrX contains five selected tri-allelic variants on the X chromosome from the Japanese sample of the 1000 genomes project.

Usage

```
data("JPTtrialelicsChrX")
```

Format

A data frame with 5 observations on the following 12 variables.

id Identifier of the polymorphism
 pos Position of the polymorphism in base pairs
 chr Chromosome
 A Number of males with A genotype
 B Number of males with B genotype
 C Number of males with C genotype
 AA Number of AA females
 AB Number of AB females
 AC Number of AC females
 BB Number of BB females
 BC Number of BC females
 CC Number of CC females

Source

The [1000 genomes project](#).

References

Graffelman, J. and Weir, B.S. (2017) Multi-allelic exact tests for Hardy-Weinberg equilibrium that account for gender. doi: 10.1101/172874. Table 6.

Examples

```
data(JPTtrialelicsChrX)
str(JPTtrialelicsChrX)
```

mac	<i>Compute the minor allele count.</i>
-----	--

Description

mac computes the smallest allele count for a given vector of genotype counts.

Usage

```
mac(X)
```

Arguments

X a vector or matrix with genotype counts (AA, AB, BB)

Value

a vector of the minor allele counts

Author(s)

Jan Graffelman (jan.graffelman@upc.edu)

See Also

[maf](#)

Examples

```
X <- as.vector(rmultinom(1,100,c(0.5,0.4,0.1)))
names(X) <- c("AA", "AB", "BB")
print(X)
print(mac(X))
```

maf *Function to compute minor allele frequencies*

Description

Function maf computes the minor allele frequency for a matrix or vector of compositions.

Usage

```
maf(x)
```

Arguments

x a vector or matrix of genotypic compositions

Value

a vector of minor allele frequencies.

Author(s)

Jan Graffelman (jan.graffelman@upc.edu)

Examples

```
X <- as.vector(rmultinom(1,100,c(0.5,0.4,0.1)))
X <- X/sum(X)
print(X)
print(maf(X))
```

MakeCounts *Create genotype counts from bi-allelic marker data*

Description

MakeCounts creates a matrix of genotype counts, with one row for each bi-allelic marker, containing 4 columns with the counts AA, AB, BB and NA (missings) respectively

Usage

```
MakeCounts(X, alleles, pos1 = 1, pos2 = 3, coding = c(AA=0,AB=1,BB=2))
```

Arguments

X	A matrix or dataframe with bi-allelic genotyping information, markers in columns, individuals in rows
alleles	a vector of alleles for each marker (e.g. c("A/T","A/G",...)). Only relevant if X is a matrix with text entries.
pos1	position of the first allele in the allele string (1 by default)
pos2	position of the second allele in the allele string (3 by default)
coding	indicates how homozygotes and heterozygote are coded as numbers. Only relevant if X is a matrix with numeric entries.

Details

MakeCounts is thought for bi-allelic marker data only. Missings are should be coded by NA. It produces the right input for HWTernaryPlot.

Heterozygotes may be coded in the data as "AB" or "BA". Both entries will be counted as a heterozygote.

Value

A matrix of 4 columns

Author(s)

Jan Graffelman <jan.graffelman@upc.edu>

See Also

[HWTernaryPlot](#)

Examples

```
SNP1 <- c("GG","GG","GG","GG","GG","GG","GG","GG","GG")
SNP2 <- c("CG","GG","CC","GG","GG","CG","CG","CG","CG")
SNP3 <- c("AA","AA","AA","AG","AA","AG","AA","AA","AA")
SNP4 <- c("GG","GG","GG","GG","GG","GG","GG","GG","GG")
SNP5 <- c("CC","CC","CC","CC","CC","CC","CT","CT","CT")
X <- cbind(SNP1,SNP2,SNP3,SNP4,SNP5)
Y <- MakeCounts(X,c("A/G","C/G","A/G","A/G","C/T"))
print(Y)
W <- matrix(sample(c(0,1,2,NA),100,replace=TRUE),ncol=5)
Z <- MakeCounts(W,coding=c(0,1,2))
```

MakeFactor

Make factors from genotyping data

Description

MakeFactor converts bi-allelic genetic marker data, whether coded numerically as (0,1,2) or as (GG,GT,TT), etc. into standard factors coded as AA, AB, BB.

Usage

```
MakeFactor(x, coding = c(0, 1, 2))
```

Arguments

x	A vector containing genotyping results
coding	Describes the numerical coding of the genotype data in order AA, AB and BB. Only relevant if x is numerical

Details

If x is a factor, it will be coerced to a factor with levels AA, AB and BB. Important detail: the produced factors will have only those levels that are observed in the data. E.g., if genotyping results only consist of (0,1), then the resulting factor will not have level BB (which would be an empty category)

Value

A factor variable

Author(s)

Jan Graffelman <jan.graffelman@upc.edu>

See Also

[MakeCounts](#)

Examples

```
y <- c(1,1,0,0,2,2)
data.frame(y, MakeFactor(y))

y <- c(2,2,3,3,1,1)
data.frame(y, MakeFactor(y, coding=c(1,2,3)))

data(Markers)
data.frame(Markers[,1], MakeFactor(Markers[,1], coding=c(1,2,3)))
```

Markers	<i>SNP data and intensities</i>
---------	---------------------------------

Description

The dataframe contains the genotypes of 3 SNPs and two allele intensities of 146 individuals. The first column is a GT polymorphism that has missing values for several individuals. The second and third column (iG and iG) are the allele intensities of this polymorphism. Column 4 and 5 are covariate SNPs (an AC and an AG polymorphism) that have no missing values.

Usage

```
data(Markers)
```

Format

A data frame containing 146 rows and 5 columns

References

Graffelman, J. (2015) Exploring Diallelic Genetic Markers: The HardyWeinberg Package. Journal of Statistical Software, 64(3), 1-23. <http://www.jstatsoft.org/v64/i03/>.

Mourant	<i>Genotype frequencies for blood group locus MN</i>
---------	--

Description

The dataframe contains the genotype frequencies MM, MN and NN for the MN blood group locus for 216 populations. The data are taken from table 2.5 in Mourant et al., using only entries with a sample size of at least 500.

Usage

```
data(Mourant)
```

Format

A data frame containing 216 observations.

Source

Mourant et al, Table 2.5

References

Mourant, A. E. and Kopeł'c, A. C. and Domaniewska-Sobczak, K. (1976) The Distribution of the Human Blood Groups and other Polymorphisms. Second edition. Oxford University Press, London.

n.alleles	<i>Number of alleles</i>
-----------	--------------------------

Description

Function `n.alleles` determines the number of alleles in a named genotype vector.

Usage

```
n.alleles(x, ...)
```

Arguments

x	A named genotype vector (e.g. <code>c(AA=10,AB=20,BB=5)</code>)
...	extra arguments that are passed on to <code>alleles</code>

Value

integer

Author(s)

Jan Graffelman (jan.graffelman@upc.edu)

See Also

[alleles](#)

Examples

```
x <- c(AA=25,AB=50,BB=25)
k <- n.alleles(x)
print(k)
```

recode	<i>Recode genotype information</i>
--------	------------------------------------

Description

function `recode` recodes bi-allelic genetic marker information expressed as strings (e.g. "AA", "AB", "BB") into numerical form.

Usage

```
recode(X, alleles, values = c(0, 1, 2), pos1 = 1, pos2 = 3, minor
= FALSE, verbose = FALSE)
```

Arguments

<code>X</code>	A matrix or dataframe of bi-allelic markers, individuals in rows, markers in columns
<code>alleles</code>	a vector with the alleles for each marker (e.g. <code>c("A/T", "A/G", etc)</code>)
<code>values</code>	a vector of numerical values for AA, AB and BB, ((0,1,2) by default).
<code>pos1</code>	position of the first allele in the allele string (1 by default).
<code>pos2</code>	position of the second allele in the allele string (3 by default).
<code>minor</code>	coding is according to the number of copies of the minor allele. if <code>minor = TRUE</code> , the value of 2 reflects two copies of the minor allele, and the value 0 reflects no copies of the minor allele.
<code>verbose</code>	print progress on the conversion or not.

Details

`recode` is written for bi-allelic marker data only. Heterozygotes may be coded both as AB or BA. By default, the second allele specified (e.g. "T" in "A/T") is counted in the recoding, and homozygotes AA are coded as 0 and homozygotes TT as 2.

Value

A numerical matrix, individuals in rows, markers in columns

Author(s)

Jan Graffelman <jan.graffelman@upc.edu>

See Also

[MakeCounts](#)

Examples

```
SNP1 <- c("GG", "GG", "GG", "GG", "GG", "GG", "GG", "GG", "GG")
SNP2 <- c("CG", "GG", "CC", "GG", "GG", "CG", "CG", "CG", "CG")
SNP3 <- c("AA", "AA", "AA", "AG", "AA", "AG", "AA", "AA", "AA")
SNP4 <- c("GG", "GG", "GG", "GG", "GG", "GG", "GG", "GG", "GG")
SNP5 <- c("CC", "CC", "CC", "CC", "CC", "CC", "CT", "CT", "CT")
X <- cbind(SNP1, SNP2, SNP3, SNP4, SNP5)
Y <- recode(X, c("A/G", "C/G", "A/G", "A/G", "C/T"))
print(Y)
```

strsort	<i>Sort tokens of a set of strings</i>
---------	--

Description

Function `strsort` collapses all tokens of a vector of strings in a single string with sorted tokens

Usage

```
strsort(s)
```

Arguments

`s` a vector of character strings

Value

a string

Author(s)

Jan Graffelman <jan.graffelman@upc.edu>

See Also

[alleles](#)

Examples

```
x <- c("AA", "AB", "BB", "AC", "CC")
print(strsort(x))
```

ThetatoF	<i>Convert theta to an inbreeding coefficient</i>
----------	---

Description

Function `ThetatoF` converts disequilibrium measure `theta` to an inbreeding coefficient.

Usage

```
ThetatoF(p, theta = 4)
```

Arguments

`p` the allele frequency
`theta` the disequilibrium parameter

Value

a real number

Author(s)

Jan Graffelman (jan.graffelman@upc.edu)

References

Rohlf, R.V. and Weir, B.S. (2008) Distributions of Hardy-Weinberg Equilibrium Test Statistics, *Genetics*, 180(3) pp. 1609-1616.

See Also

[HWf](#)

Examples

```
f <- ThetatoF(0.5,4)
```

toTriangular

Convert a vector of genotype counts to triangular format

Description

Function toTriangular converts a named vector of genotype counts into a triangular matrix format, with homozygotes on the diagonal and heterozygotes below the diagonal.

Usage

```
toTriangular(x)
```

Arguments

x A vector of genotype counts

Value

a matrix

Author(s)

Jan Graffelman <jan.graffelman@upc.edu>

Examples

```
x <- c(AA=20, AB=52, AC=34, BB=17, BC=51, CC=26)
print(x)
X <- toTriangular(x)
print(X)
```

UniqueGenotypeCounts *Extract unique genotypic compositions from a matrix*

Description

Function UniqueGenotypeCounts creates a matrix containing only the unique rows in the given matrix, together with their frequency of occurrence

Usage

```
UniqueGenotypeCounts(X, verbose = TRUE)
```

Arguments

X	A n by 3 matrix with genotypic counts (AA,AB,BB)
verbose	If TRUE then print some statistics

Value

A matrix with 4 columns, AA, AB, BB, and frequency of occurrence

Author(s)

Jan Graffelman <jan.graffelman@upc.edu>

See Also

[GenerateSamples](#)

Examples

```
set.seed(123)
X <- HWDData(n=100,nm=100)
print(nrow(X))
Y <- UniqueGenotypeCounts(X)
print(nrow(Y))
print(sum(Y$w))
```

vaf	<i>Computes the sample variance of the allele frequency for a biallelic marker.</i>
-----	---

Description

Function vaf computes the sample variance of the allele frequencies of a single sample or a matrix of samples.

Usage

```
vaf(X, hw = FALSE)
```

Arguments

X	vector or matrix with genotype counts (AA,AB,BB)
hw	assume Hardy-Weinberg proportions (hw=TRUE) or not (hw=FALSE)

Details

For biallelic markers the variance of the minor allele frequency equals the variance of the major allele frequency.

Value

a numeric vector of variances.

Author(s)

Jan Graffelman <jan.graffelman@upc.edu>

References

Weir, B.S. (1996) Genetic data analysis II. Sinauer Associates, Massachusetts. See Chapter 2.

See Also

[af,maf](#)

Examples

```
x <- c(MM=298,MN=489,NN=213)
pA <- af(x)
vA <- vaf(x)
cat("allele frequency:",pA,"\n")
cat("sample variance allele frequency:",vA,"\n")
```

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