

# Package ‘gap’

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**Title** Genetic analysis package

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**Depends** R (>= 2.10)

**Suggests** BradleyTerry2, rms, MASS, NCBI2R, grid, haplo.stats, kinship2, magic, pedigree, survival

**LazyData** Yes

**LazyLoad** Yes

**Description** It is designed as an integrated package for genetic data analysis of both population and family data. Currently, it contains functions for sample size calculations of both population-based and family-based designs, probability of familial disease aggregation, kinship calculation, some statistics in linkage analysis, and association analysis involving one or more genetic markers including haplotype analysis with or without environmental covariates.

**License** GPL (>= 2)

**URL** <http://www.mrc-epid.cam.ac.uk/~jinghua.zhao>

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**R topics documented:**

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gap-package	<i>Genetic analysis package</i>
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**Description**

It is designed as an integrated package for genetic data analysis of both population and family data. Currently, it contains functions for sample size calculations of both population-based and family-based designs, classic twin models, probability of familial disease aggregation, kinship calculation, some statistics in linkage analysis, and association analysis involving one or more genetic markers including haplotype analysis with or without environmental covariates.

**Details**

Package: gap  
Version: 1.1-6  
Depends: R(>= 2.1.0)  
Suggests: BradleyTerry2, rms, Hmisc, MASS, grid, haplo.stats, magic, pedigree, survival  
License: GPL (>=2)  
URL: <http://www.mrc-epid.cam.ac.uk/~jinghua.zhao>

Index:

BFDP	Bayesian false-discovery probability
FPRP	False-positive report probability
PD	A study of Parkinson's disease and APOE, LRRK2, SNCA makers
SNP	Functions for single nucleotide polymorphisms (SNPs)
ab	Test/Power calculation for mediating effect
aldh2	ALDH2 markers and Alcoholism
apoeapoc	APOE/APOC1 markers and Alzheimer's
asplot	Regional association plot
bt	Bradley-Terry model for contingency table
b2r	Obtain correlation coefficients and their variance-covariances
ccsize	Power and sample size for case-cohort design
chow.test	Chow's test for heterogeneity in two regressions
cf	Cystic Fibrosis data
comp.score	score statistics for testing genetic linkage of quantitative trait
crohn	Crohn disease data
ESplot	Effect-size plot
fa	Friedreich Ataxia data
fbsize	Sample size for family-based linkage and association design
fsnps	A case-control data involving four SNPs with missing genotype
gc.em	Gene counting for haplotype analysis
gcontrol	genomic control
gcontrol2	genomic control based on p values
gcp	Permutation tests using GENECOUNTING
genecounting	Gene counting for haplotype analysis
gif	Kinship coefficient and genetic index of familiarity
h2	Heritability estimation according to twin correlations
hap	Haplotype reconstruction
hap.em	Gene counting for haplotype analysis
hap.score	Score Statistics for Association of Traits with Haplotypes
hla	HLA markers and Schizophrenia
htr	Haplotype trend regression
hwe	Hardy-Weinberg equilibrium test for multiallelic marker
hwe.cc	A likelihood ratio test of population Hardy-Weinberg equilibrium for case-control studies
hwe.hardy	Hardy-Weinberg equilibrium test using MCMC
kin.morgan	kinship matrix for simple pedigree
klem	Haplotype frequency estimation based on a genotype table of two multiallelic markers
LD22	LD statistics for two diallelic markers
LDkl	LD statistics for two multiallelic markers
lukas	An example pedigree
makeped	A function to prepare pedigrees in post-MAKEPED format
masize	Sample size calculation for mediation analysis
mao	A study of Parkinson's disease and MAO gene
metap	Meta-analysis of p values
metareg	Fixed and random effects model for meta-analysis
mhtdata	An example data for Manhattan plot
mhtplot	Manhattan plot of p values

mia	multiple imputation analysis for hap
mtdt	Transmission/disequilibrium test of a multiallelic marker
mtdt2	Transmission/disequilibrium test of a multiallelic marker by Bradley-Terry model
muvar	Means and variances under 1- and 2- locus (diallelic) QTL model
mvmeta	Multivariate meta-analysis based on generalized least squares
nep499	A study of Alzheimer's disease with eight SNPs and APOE
pysize	Power for population-based association design
pysize2	Power for case-control association design
pedtodot	Converting pedigree(s) to dot file(s)
pf	Probability of familial clustering of disease
pf.sim	Probability of familial clustering of disease
pgc	Preparing weight for GENECOUNTING
plot.hap.score	Plot Haplotype Frequencies versus Haplotype Score Statistics
print.hap.score	Print a hap.score object
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qqunif	Q-Q plot for uniformly distributed random variable
read.ms.output	A utility function to read ms output
s2k	Statistics for 2 by K table
tsc	Power calculation for two-stage case-control design
whscore	Whittemore-Halpern scores for allele-sharing

We have incorporated functions for a wide range of problems. Nevertheless, this largely remains as a preliminary work to be consolidated in the near future.

#### Author(s)

Author: Jing Hua Zhao in collaboration with other colleagues, and with help from Kurt Hornik and Brian Ripley of the R core development team

Maintainer: Jing Hua Zhao <jinghua.zhao@mrc-epid.cam.ac.uk>

#### References

Zhao JH, gap: genetic analysis package. Journal of Statistical Software 2007, 23(8):1-18

---

ab

*Test/Power calculation for mediating effect*

---

#### Description

This function tests for or obtains power of mediating effect based on estimates of two regression coefficients and their standard errors. Note that for binary outcome or mediator, one should use log-odds ratio and its standard error.

**Usage**

```
ab(type,n=25000,a=0.15,sa=0.01,b=log(1.19),sb=0.01,alpha=0.05,fold=1)
```

**Arguments**

type	string option: "test", "power"
n	default sample size to be used for power calculation
a	regression coefficient from independent variable to mediator
sa	SE(a)
b	regression coefficient from mediator variable to outcome
sb	SE(b)
alpha	size of significance test for power calculation
fold	fold change for power calculation, as appropriate for a range of sample sizes

**Value**

The returned value are z-test and significance level for significant testing or sample size/power for a given fold change of the default sample size.

**References**

Freathy RM, Timpson NJ, Lawlor DA, Pouta A, Ben-Shlomo Y, Ruukonen A, Ebrahim S, Shields B, Zeggini E, Weedon MN, Lindgren CM, Lango H, Melzer D, Ferrucci L, Paolisso G, Neville MJ, Karpe F, Palmer CN, Morris AD, Elliott P, Jarvelin MR, Smith GD, McCarthy MI, Hattersley AT, Frayling TM. Common variation in the FTO Gene alters diabetes-related metabolic traits to the extent expected given its effect on BMI. *Diabetes* 57:1419-1426, 2008.

Kline RB. Principles and practice of structural equation modeling, Second Edition. The Guilford Press 2005.

MacKinnon DP. Introduction to Statistical Mediation Analysis. Taylor & Francis Group 2008.

Preacher KJ, Leonardelli GJ. Calculation for the Sobel Test-An interactive calculation tool for mediation tests <http://www.people.ku.edu/~preacher/sobel/sobel.htm>

**Author(s)**

Jing Hua Zhao

**See Also**

[ccsize](#)

**Examples**

```
## Not run:

ab()
n <- power <- vector()
for (j in 1:10)
{
  z <- ab(fold=j*0.01)
  n[j] <- z[1]
  power[j] <- z[2]
}
plot(n,power,xlab="Sample size",ylab="Power")
title("SNP-BMI-T2D association in EPIC-Norfolk study")

## End(Not run)
```

---

aldh2

*ALDH2 markers and Alcoholism*

---

**Description**

This data set contains eight ALDH2 markers and Japanese alcoholic patients ( $y=1$ ) and controls ( $y=0$ ). There are genotypes for 8 loci, with a prefix name (e.g., "EXON12") and a suffix for each of two alleles (".a1" and ".a2").

The eight markers loci follows the following map (base pairs)

D12S2070	(> 450 000),
D12S839	(> 450 000),
D12S821	(~ 400 000),
D12S1344	( 83 853),
EXON12	( 0),
EXON1	( 37 335),
D12S2263	( 38 927),
D12S1341	(> 450 000)

**Usage**

```
data(aldh2)
```

**Format**

A data frame

**Source**

Prof Ian Craig of Oxford and SGDP Centre, KCL

## References

Koch HG, McClay J, Loh E-W, Higuchi S, Zhao J-H, Sham P, Ball D, et al (2000) Allele association studies with SSR and SNP markers at known physical distances within a 1 Mb region embracing the ALDH2 locus in the Japanese, demonstrates linkage disequilibrium extending up to 400 kb. Hum. Mol. Genet. 9:2993-2999

---

apoeapoc

*APOE/APOC1 markers and Alzheimer's*

---

## Description

This data set contains APOE/APOC1 markers and Chinese Alzheimer's patients and controls. Variable id is subject id and y takes value 0 for controls and 2 for Alzheimer's.

The last six variables are age, sex and genotypes for APOE and APOC with suffixes for each of two alleles (".a1" and ".a2").

## Usage

```
data(apoeapoc)
```

## Format

A data frame

## Source

Shi J, Zhang S, Ma C, Liu X, Li T, Tang M, Han H, Guo Y, Zhao JH, Zheng K, Kong X, Zhang K, Su Z, Zhao Z. Association between apolipoprotein CI HpaI polymorphism and sporadic Alzheimer's disease in Chinese. Acta Neurol Scan 2004, 109:140-145.

---

asplot

*Regional association plot*

---

## Description

This function obtains regional association plot for a particular locus, based on the information about recombination rates, linkage disequilibria between the SNP of interest and neighbouring ones, and single-point association tests p values.

Note that the best p value is not necessarily within locus in the original design.

## Usage

```
asplot(locus, map, genes, flanking=1e3, best.pval=NULL, sf=c(4,4), logpmax=10, pch=21)
```

**Arguments**

locus	Data frame with columns c("CHR", "POS", "NAME", "PVAL", "RSQR") containing association results
map	Genetic map, i.e. c("POS", "THETA", "DIST")
genes	Gene annotation with columns c("START", "STOP", "STRAND", "GENE")
flanking	Flanking length
best.pval	Best p value for the locus of interest
sf	scale factors for p values and recombination rates, smaller values are necessary for gene dense regions
logpmax	Maximum value for $-\log_{10}(p)$
pch	Plotting character for the SNPs to be highlighted, e.g., 21 and 23 refer to circle and diamond

**References**

DGI. Whole-genome association analysis identifies novel loci for type 2 diabetes and triglyceride levels. *Science* 2007;316(5829):1331-6

**Author(s)**

Paul de Bakker, Jing Hua Zhao, Shengxu Li

**Examples**

```
## Not run:
asplot(CDKNlocus, CDKNmap, CDKNgenes)
title("CDKN2A/CDKN2B Region")
asplot(CDKNlocus, CDKNmap, CDKNgenes, best.pval=5.4e-8, sf=c(3,6))

## NCBI2R

options(stringsAsFactors=FALSE)
p <- with(CDKNlocus, data.frame(SNP=NAME, PVAL))
hit <- subset(p, PVAL==min(PVAL, na.rm=TRUE))$SNP

library(NCBI2R)
# LD under build 36
pos <- apply(as.data.frame(p$SNP), 1, GetSNPPosHapmap)
chr_pos <- do.call("rbind", pos)
l <- with(chr_pos, min(as.numeric(chrpos), na.rm=TRUE))
u <- with(chr_pos, max(as.numeric(chrpos), na.rm=TRUE))
LD <- with(chr_pos, GetLDInfo(unique(chr), l, u))
hit_LD <- subset(LD, SNPA==hit)
hit_LD <- within(hit_LD, {RSQR=r2})
info <- GetSNPInfo(p$SNP)
haldane <- function(x) 0.5*(1-exp(-2*x))
locus <- with(info, data.frame(CHR=chr, POS=chrpos, NAME=marker,
                             DIST=(chrpos-min(chrpos))/1000000,
                             THETA=haldane((chrpos-min(chrpos))/10000000)))
```

```

locus <- merge.data.frame(locus,hit_LD,by.x="NAME",by.y="SNPB",all=TRUE)
locus <- merge.data.frame(locus,p,by.x="NAME",by.y="SNP",all=TRUE)
locus <- subset(locus,!is.na(POS))
ann <- AnnotateSNPList(p$SNP)
genes <- with(ann,data.frame(ID=locusID,CLASS=fxn_class,PATH=pathways,
                             START=GeneLowPoint,STOP=GeneHighPoint,
                             STRAND=ori,GENE=genesymbol,BUILD=build,CYTO=cyto))

attach(genes)
ugenes <- unique(GENE)
ustart <- as.vector(as.table(by(START,GENE,min))[ugenes])
ustop <- as.vector(as.table(by(STOP,GENE,max))[ugenes])
ustrand <- as.vector(as.table(by(as.character(STRAND),GENE,max))[ugenes])
detach(genes)
genes <- data.frame(START=ustart,STOP=ustop,STRAND=ustrand,GENE=ugenes)
genes <- subset(genes,START!=0)
rm(l,u,ugenes,ustart,ustop,ustrand)
# Assume we have the latest map as in CDKNmap
asplot(locus,CDKNmap,genes)

## End(Not run)

```

b2r

*Obtain correlation coefficients and their variance-covariances***Description**

This function converts linear regression coefficients of phenotype on single nucleotide polymorphisms (SNPs) into Pearson correlation coefficients with their variance-covariance matrix. It is useful as a preliminary step for meta-analyze SNP-trait associations at a given region. Between-SNP correlations (e.g., from HapMap) are required as auxiliary information.

**Usage**

```
b2r(b,s,rho,n)
```

**Arguments**

b	the vector of linear regression coefficients
s	the corresponding vector of standard errors
rho	triangular array of between-SNP correlation
n	the sample size

**Value**

The returned value is a list containing:

r	the vector of correlation coefficients
V	the variance-covariance matrix of correlations

**References**

- Becker BJ (2004). Multivariate meta-analysis. in Tinsley HEA, Brown SD (Ed.) Handbook of Applied Multivariate Statistics and Mathematical Modeling (Chapter 17, pp499-525). Academic Press.
- Casella G, Berger RL (2002). Statistical Inference, 2nd Edition, Duxbury.
- Elston RC (1975). On the correlation between correlations. Biometrika 62:133-40

**Author(s)**

Jing Hua Zhao

**See Also**

[mvmeta, LD22](#)

**Examples**

```
## Not run:
n <- 10
r <- c(1,0.2,1,0.4,0.5,1)
b <- c(0.1,0.2,0.3)
s <- c(0.4,0.3,0.2)
bs <- b2r(b,s,r,n)

## End(Not run)
```

---

BFDP

*Bayesian false-discovery probability*

---

**Description**

This function calculates BFDP, the approximate  $P(H_0|\hat{\theta})$ , given an estimate of the log relative risk,  $\hat{\theta}$ , the variance of this estimate,  $V$ , the prior variance,  $W$ , and the prior probability of a non-null association. When `logscale=TRUE`, the function accepts an estimate of the relative risk,  $\hat{RR}$ , and the upper point of a 95% confidence interval  $RR_{hi}$ .

**Usage**

```
BFDP(a,b,pi1,W,logscale=FALSE)
```

**Arguments**

<code>a</code>	parameter value at which the power is to be evaluated
<code>b</code>	the variance for a, or the upper point ( $RR_{hi}$ ) of a 95%CI if <code>logscale=FALSE</code>
<code>pi1</code>	the prior probability of a non-null association
<code>W</code>	the prior variance
<code>logscale</code>	FALSE=the original scale, TRUE=the log scale

**Value**

The returned value is a list with the following components:

PH0	probability given a,b)
PH1	probability given a,b,W)
BF	Bayes factor, $P_{H_0}/P_{H_1}$
BFDP	Bayesian false-discovery probability
ABF	approximate Bayes factor
ABFDP	approximate Bayesian false-discovery probability

**References**

Wakefield J (2007) Bayesian measure of the probability of false discovery in genetic epidemiology studies. *Am J Hum Genet* 81:208-227

**Note**

adapted from BFDP functions by Jon Wakefield on 17th April, 2007

**Author(s)**

Jon Wakefield, Jing Hua Zhao

**See Also**

[FPRP](#)

**Examples**

```
## Not run:

# Example from BDFP.xls by Jon Wakefield and Stephanie Monnier
# Step 1 - Pre-set an BFDP-level threshold for noteworthiness: BFDP values below this threshold are noteworthy
# The threshold is given by  $R/(1+R)$  where R is the ratio of the cost of a false non-discovery to the cost of a false d

T <- 0.8

# Step 2 - Enter up values for the prior that there is an association

pi0 <- c(0.7,0.5,0.01,0.001,0.00001,0.6)

# Step 3 - Enter the value of the OR that is the 97.5% point of the prior, for example if we pick the value 1.5 we
# believe that the prior probability that the odds ratio is bigger than 1.5 is 0.025.

ORhi <- 3

W <- (log(ORhi)/1.96)^2
W
```

```

# Step 4 - Enter OR estimate and 95% confidence interval (CI) to obtain BFDP

OR <- 1.316
OR_L <- 1.10
OR_U <- 2.50
logOR <- log(OR)
selogOR <- (log(OR_U)-log(OR))/1.96
r <- W/(W+selogOR^2)
r
z <- logOR/selogOR
z
ABF <- exp(-z^2*r/2)/sqrt(1-r)
ABF
FF <- (1-pi0)/pi0
FF
BFDPex <- FF*ABF/(FF*ABF+1)
BFDPex
pi0[BFDPex>T]

## now turn to BFDP

pi0 <- c(0.7,0.5,0.01,0.001,0.00001,0.6)
ORhi <- 3
OR <- 1.316
OR_U <- 2.50
W <- (log(ORhi)/1.96)^2
z <- BFDP(OR,OR_U,pi0,W)
z

```

---

bt

*Bradley-Terry model for contingency table*


---

### Description

This function calculates statistics under Bradley-Terry model.

### Usage

```
bt(x)
```

### Arguments

x                    the data table

### Value

The returned value is a list containing:

y                    A column of 1  
count                the frequency count/weight

allele	the design matrix
bt.glm	a glm.fit object
etdt.dat	a data table that can be used by ETDT

## References

Bradley RA, Terry ME (1952) Rank analysis of incomplete block designs I. the method of paired comparisons. *Biometrika* 39:324–345

Sham PC, Curtis D (1995) An extended transmission/disequilibrium test (TDT) for multi-allelic marker loci. *Ann. Hum. Genet.* 59:323-336

## Note

```

/*Adapted from the SAS macro below for data in the example section*/
%macro mtdt(data,n);
data _bt_;
  set &data;
  array x {&n} x1-x&n;
  array allele {&n} y1-y&n;
  do i=1 to &n; allele{i}=0; end;
  y=1;
  do i=1 to &n;
    allele{_n_}=1;
    allele{i}=-1;
    count=x{i};
    if _n_ ne i then output;
    allele{i}=0;
  end;
  keep y count y1-y&n;
run;
/*Bradly-Terry model*/
proc logistic data=_bt_;
  freq count;
  model y=y1-y&n / noint;
  output out=out p=p;
run;
/*Bowker's test of symmetry*/
data b;
  array x x1-x&n;
  do i=1 to &n;
    set &data;
    do j=1 to &n; w=x[j]; output; end;
  end;
  drop x1-x&n;
run;
proc freq;
  weight w;
  table i*j / agree noprint;

```

```

run;
%mend;
data a;
input x1-x12;
cards;
0 0 0 2 0 0 0 0 0 0 0 0
0 0 1 3 0 0 0 2 3 0 0 0
2 3 26 35 7 0 2 10 11 3 4 1
2 3 22 26 6 2 4 4 10 2 2 0
0 1 7 10 2 0 0 2 2 1 1 0
0 0 1 4 0 1 0 1 0 0 0 0
0 2 5 4 1 1 0 0 0 2 0 0
0 0 2 6 1 0 2 0 2 0 0 0
0 3 6 19 6 0 0 2 5 3 0 0
0 0 3 1 1 0 0 0 1 0 0 0
0 0 0 2 0 0 0 0 0 0 0 0
0 0 1 0 0 0 0 0 0 0 0 0
;
%mtdt(a,12);

```

**Author(s)**

Jing Hua Zhao

**See Also**

[mtdt](#)

**Examples**

```

## Not run:
# Copeman JB, Cucca F, Hearne CM, Cornall RJ, Reed PW,
# Ronningen KS, Undlien DE, Nistico L, Buzzetti R, Tosi R, et al.
# (1995) Linkage disequilibrium mapping of a type 1
# diabetes susceptibility gene (IDDM7) to chromosome 2q31-q33.
# Nat Genet 9: 80-5

x <- matrix(c(0,0, 0, 2, 0,0, 0, 0, 0, 0, 0, 0,
             0,0, 1, 3, 0,0, 0, 2, 3, 0, 0, 0,
             2,3,26,35, 7,0, 2,10,11, 3, 4, 1,
             2,3,22,26, 6,2, 4, 4,10, 2, 2, 0,
             0,1, 7,10, 2,0, 0, 2, 2, 1, 1, 0,
             0,0, 1, 4, 0,1, 0, 1, 0, 0, 0, 0,
             0,2, 5, 4, 1,1, 0, 0, 0, 2, 0, 0,
             0,0, 2, 6, 1,0, 2, 0, 2, 0, 0, 0,
             0,3, 6,19, 6,0, 0, 2, 5, 3, 0, 0,
             0,0, 3, 1, 1,0, 0, 0, 1, 0, 0, 0,
             0,0, 0, 2, 0,0, 0, 0, 0, 0, 0, 0,
             0,0, 1, 0, 0,0, 0, 0, 0, 0, 0, 0),nrow=12)

# Bradley-Terry model, only deviance is available in glm

```

```
# (SAS gives score and Wald statistics as well)
bt.ex<-bt(x)
anova(bt.ex$bt.glm)
summary(bt.ex$bt.glm)

## End(Not run)
```

---

ccsize

*Power and sample size for case-cohort design*


---

### Description

The power of the test is according to

$$\Phi \left( Z_{\alpha} + m^{1/2} \theta \sqrt{\frac{p_1 p_2 p_D}{q + (1-q)p_D}} \right)$$

where  $\alpha$  is the significance level,  $\theta$  is the log-hazard ratio for two groups,  $p_j$ ,  $j=1, 2$ , are the proportion of the two groups in the population.  $m$  is the total number of subjects in the subcohort,  $p_D$  is the proportion of the failures in the full cohort, and  $q$  is the sampling fraction of the subcohort.

Alternatively, the sample size required for the subcohort is

$$m = n B p_D / (n - B(1 - p_D))$$

where  $B = (Z_{1-\alpha} + Z_{\beta})^2 / (\theta^2 p_1 p_2 p_D)$ , and  $n$  is the size of cohort.

When infeasible configurations are specified, a sample size of -999 is returned.

### Usage

```
ccsize(n,q,pD,p1,alpha,theta,power=NULL,verbose=FALSE)
```

### Arguments

n	the total number of subjects in the cohort
q	the sampling fraction of the subcohort
pD	the proportion of the failures in the full cohort
p1	proportions of the two groups (p2=1-p1)
alpha	significant level
theta	log-hazard ratio for two groups
power	if specified, the power for which sample size is calculated
verbose	error messages are explicitly printed out

### Value

The returned value is a value indicating the power or required sample size.

## References

Cai J, Zeng D. Sample size/power calculation for case-cohort studies. *Biometrics* 2004, 60:1015-1024

## Note

Programmed for EPIC study

## Author(s)

Jing Hua Zhao

## See Also

[pbsize](#)

## Examples

```
# Table 1 of Cai & Zeng (2004).
outfile <- "table1.txt"
cat("n", "pD", "p1", "theta", "q", "power\n", file=outfile, sep="\t")
alpha <- 0.05
n <- 1000
for(pD in c(0.10,0.05))
{
  for(p1 in c(0.3,0.5))
  {
    for(theta in c(0.5,1.0))
    {
      for(q in c(0.1,0.2))
      {
        power <- ccsize(n,q,pD,p1,alpha,theta)
        cat(n,"\t",pD,"\t",p1,"\t",theta,"\t",q,"\t",signif(power,3),"\n",
            file=outfile,append=TRUE)
      }
    }
  }
}
n <- 5000
for(pD in c(0.05,0.01))
{
  for(p1 in c(0.3,0.5))
  {
    for(theta in c(0.5,1.0))
    {
      for(q in c(0.01,0.02))
      {
        power <- ccsize(n,q,pD,p1,alpha,theta)
        cat(n,"\t",pD,"\t",p1,"\t",theta,"\t",q,"\t",signif(power,3),"\n",
            file=outfile,append=TRUE)
      }
    }
  }
}
```

```

    }
  }
  table1<-read.table(outfile,header=TRUE,sep="\t")
  unlink(outfile)
  # ARIC study
  outfile <- "aric.txt"
  n <- 15792
  pD <- 0.03
  p1 <- 0.25
  alpha <- 0.05
  theta <- c(1.35,1.40,1.45)
  beta1 <- 0.8
  s_nb <- c(1463,722,468)
  cat("n", "pD", "p1", "hr", "q", "power", "ssize\n", file=outfile, sep="\t")
  for(i in 1:3)
  {
    q <- s_nb[i]/n
    power <- ccsize(n,q,pD,p1,alpha,log(theta[i]))
    ssize <- ccsize(n,q,pD,p1,alpha,log(theta[i]),beta1)
    cat(n, "\t", pD, "\t", p1, "\t", theta[i], "\t", q, "\t", signif(power,3), "\t", ssize, "\n",
        file=outfile, append=TRUE)
  }
  aric<-read.table(outfile,header=TRUE,sep="\t")
  unlink(outfile)
  # EPIC study
  outfile <- "epic.txt"
  n <- 25000
  alpha <- 0.00000005
  power <- 0.8
  s_pD <- c(0.3,0.2,0.1,0.05)
  s_p1 <- seq(0.1,0.5,by=0.1)
  s_hr <- seq(1.1,1.4,by=0.1)
  cat("n", "pD", "p1", "hr", "alpha", "ssize\n", file=outfile, sep="\t")
  # direct calculation
  for(pD in s_pD)
  {
    for(p1 in s_p1)
    {
      for(hr in s_hr)
      {
        ssize <- ccsize(n,q,pD,p1,alpha,log(hr),power)
        if (ssize>0) cat(n, "\t", pD, "\t", p1, "\t", hr, "\t", alpha, "\t", ssize, "\n",
            file=outfile, append=TRUE)
      }
    }
  }
  }
  epic<-read.table(outfile,header=TRUE,sep="\t")
  unlink(outfile)
  # exhaustive search
  outfile <- "search.txt"
  s_q <- seq(0.01,0.5,by=0.01)
  cat("n", "pD", "p1", "hr", "nq", "alpha", "power\n", file=outfile, sep="\t")
  for(pD in s_pD)

```

```
{
  for(p1 in s_p1)
  {
    for(hr in s_hr)
    {
      for(q in s_q)
      {
        power <- ccsize(n,q,pD,p1,alpha,log(hr))
        cat(n,"\t",pD,"\t",p1,"\t",hr,"\t",q*n,"\t",alpha,"\t",power,"\n",
            file=outfile,append=TRUE)
      }
    }
  }
}
search<-read.table(outfile,header=TRUE,sep="\t")
unlink(outfile)
```

---

CDKN

*Example data for association plot*

---

## Description

These data are adapted from the DGI study on CDKN2A/CDKN2B region.

## Usage

```
data(CDKN)
```

## Format

There are three data objects in the dataset: CDKNgenes, the gene list from the Chromosome 9 according to UCSC browser (<http://genome.ucsc.edu/>); CDKNmap, the genetic map as from the HapMap website ([http://www.hapmap.org/downloads/recombination/2006-10\\_re121\\_phaseI+II/rates/](http://www.hapmap.org/downloads/recombination/2006-10_re121_phaseI+II/rates/)); CDKNlocus, the results from the association analysis of the locus based on DGI data.

## Source

The data were obtained from the Harvard-MIT Broad Institute (see <http://www.broad.mit.edu/diabetes/>)

## References

Diabetes Genetics Initiative of Broad Institute of Harvard and MIT, Lund University and Novartis Institute for BioMedical Research. *Whole-genome association analysis identifies novel loci for type 2 diabetes and triglyceride levels* Science 2007;316(5829):1331-6

**Examples**

```
## Not run:
data(CDKN)
CDKlocus

## End(Not run)
```

---

cf	<i>Cystic fibrosis data</i>
----	-----------------------------

---

**Description**

This data set contains a case-control indicator and 23 SNPs.

The inter-marker distances (Morgan) are as follows

```
0.000090, 0.000158, 0.005000, 0.000100, 0.000200, 0.000150, 0.000250, 0.000200, 0.000050,
0.000350, 0.000300, 0.000250, 0.000350, 0.000350, 0.000800, 0.000100, 0.000200, 0.000150,
0.000550, 0.006000, 0.000700, 0.001000
```

**Usage**

```
data(cf)
```

**Format**

A data frame containing 186 rows and 24 columns

**Note**

This can be used as an example of converting PL-EM to matrix format,

```
cfdata <- vector("numeric")
cfname <- vector("character")
for (i in 2:dim(cf)[2])
{
  tmp <- plem2m(cf[,i])
  a1 <- tmp[[1]]
  a2 <- tmp[[2]]
  cfdata <- cbind(cfdata,a1,a2)
  a1name <- paste("loc",i-1,".a1",sep="")
  a2name <- paste("loc",i-1,".a2",sep="")
  cfname <- cbind(cfname,a1name,a2name)
}
cfdata <- as.data.frame(cfdata)
names(cfdata) <- cfname
```

**Source**

Liu JS, Sabatti C, Teng J, Keats BJB, Risch N (2001). Bayesian Analysis of Haplotypes for Linkage Disequilibrium Mapping. *Genome Research* 11:1716-1724

---

chow.test

*Chow's test for heterogeneity in two regressions*


---

**Description**

Chow's test is for differences between two or more regressions. Assuming that errors in regressions 1 and 2 are normally distributed with zero mean and homoscedastic variance, and they are independent of each other, the test of regressions from sample sizes  $n_1$  and  $n_2$  is then carried out using the following steps. 1. Run a regression on the combined sample with size  $n = n_1 + n_2$  and obtain within group sum of squares called  $S_1$ . The number of degrees of freedom is  $n_1 + n_2 - k$ , with  $k$  being the number of parameters estimated, including the intercept. 2. Run two regressions on the two individual samples with sizes  $n_1$  and  $n_2$ , and obtain their within group sums of square  $S_2 + S_3$ , with  $n_1 + n_2 - 2k$  degrees of freedom. 3. Conduct an  $F_{(k, n_1 + n_2 - 2k)}$  test defined by

$$F = \frac{[S_1 - (S_2 + S_3)]/k}{[(S_2 + S_3)/(n_1 + n_2 - 2k)]}$$

If the  $F$  statistic exceeds the critical  $F$ , we reject the null hypothesis that the two regressions are equal.

In the case of haplotype trend regression, haplotype frequencies from combined data are known, so can be directly used.

**Usage**

```
chow.test(y1, x1, y2, x2, x=NULL)
```

**Arguments**

y1	a vector of dependent variable
x1	a matrix of independent variables
y2	a vector of dependent variable
x2	a matrix of independent variables
x	a known matrix of independent variables

**Value**

The returned value is a vector containing (please use subscript to access them):

F	the F statistic
df1	the numerator degree(s) of freedom
df2	the denominator degree(s) of freedom
p	the p value for the F test

**References**

Chow GC (1960). Tests of equality between sets of coefficients in two linear regression. *Econometrica* 28:591-605

**Note**

adapted from chow.R

**Author(s)**

Shigenobu Aoki, Jing Hua Zhao

**Source**

<http://aoki2.si.gunma-u.ac.jp/R/>

**See Also**

[htr](#)

**Examples**

```
## Not run:
dat1 <- matrix(c(
  1.2, 1.9, 0.9,
  1.6, 2.7, 1.3,
  3.5, 3.7, 2.0,
  4.0, 3.1, 1.8,
  5.6, 3.5, 2.2,
  5.7, 7.5, 3.5,
  6.7, 1.2, 1.9,
  7.5, 3.7, 2.7,
  8.5, 0.6, 2.1,
  9.7, 5.1, 3.6), byrow=TRUE, ncol=3)

dat2 <- matrix(c(
  1.4, 1.3, 0.5,
  1.5, 2.3, 1.3,
  3.1, 3.2, 2.5,
  4.4, 3.6, 1.1,
  5.1, 3.1, 2.8,
  5.2, 7.3, 3.3,
  6.5, 1.5, 1.3,
  7.8, 3.2, 2.2,
  8.1, 0.1, 2.8,
  9.5, 5.6, 3.9), byrow=TRUE, ncol=3)

y1<-dat1[,3]
y2<-dat2[,3]
x1<-dat1[,1:2]
x2<-dat2[,1:2]
```

```
chow.test.r<-chow.test(y1,x1,y2,x2)

## End(Not run)
```

---

 comp.score

*score statistics for testing genetic linkage of quantitative trait*


---

## Description

The function empirically estimate the variance of the score functions. The variance-covariance matrix consists of two parts: the additive part and the part for the individual-specific environmental effect. Other reasonable decompositions are possible.

This program has the following improvement over "score.r":

1. It works with selected nuclear families
2. Trait data on parents (one parent or two parents), if available, are utilized.
3. Besides a statistic assuming no locus-specific dominance effect, it also computes a statistic that allows for such effect. It computes two statistics instead of one.

Function "merge" is used to merge the IBD data for a pair with the transformed trait data (i.e.,  $w_k w_l$ ).

## Usage

```
comp.score(ibddata="ibd_dist.out", phenotype="pheno.dat", mean=0, var=1, h2=0.3)
```

## Arguments

ibddata	The output file from GENEHUNTER using command "dump ibd". The default file name is <i>ibd_dist.out</i> .
phenotype	The file of pedigree structure and trait value. The default file name is "pheno.dat". Columns (no headings) are: family ID, person ID, father ID, mother ID, gender, trait value, where Family ID and person ID must be numbers, not characters. Use character "NA" for missing phenotypes.
mean	(population) mean of the trait, with a default value of 0
var	(population) variance of the trait, with a default value of 1
h2	heritability of the trait, with a default value of 0.3

## Value

a matrix with each row containing the location and the statistics and their p-values.

## References

- Kruglyak L, Daly MJ, Reeve-Daly MP, Lander ES (1996) Parametric and Nonparametric linkage analysis: a unified multipoint approach. *Am J Hum Genet* 58:1347-1363
- Kruglyak L, Lander ES (1998) Faster multipoint linkage analysis using Fourier transforms *J Comp Bio* 1998 5:1-7
- Wang K (2005) A likelihood approach for quantitative-trait-locus mapping with selected pedigrees. *Biometrics* 61:465-473

## Note

Adapt from score2.r

## Author(s)

Yingwei Peng, Kai Wang

## Examples

```
# An example based on GENEHUNTER version 2.1, with quantitative trait data in file "pheno.dat"
# generated from the standard normal distribution. The following exmaple shows that it is
# possible to automatically call GENEHUNTER using R function "system".
```

```
cwd <- getwd()
cs.dir <- file.path(.path.package("gap"), "doc", "comp.score")
setwd(cs.dir)
dir()
# system("gh < gh.inp")
cs.default <- comp.score()
setwd(cwd)
```

---

crohn

*Crohn's disease data*

---

## Description

The data set consist of 103 common (>5% minor allele frequency) SNPs genotyped in 129 trios from an European-derived population. These SNPs are in a 500-kb region on human chromosome 5q31 implicated as containing a genetic risk factor for Crohn disease.

The positions, names and haplotype blocks reported are as follows,

```
274044   IGR1118a_1 BLOCK 1
274541   IGR1119a_1 *
286593   IGR1143a_1 *
287261   IGR1144a_1 *
299755   IGR1169a_2 *
324341   IGR1218a_2 *
```

324379 IGR1219a\_2 \*  
358048 IGR1286a\_1 BLOCK 1  
366811 TSC0101718  
395079 IGR1373a\_1 BLOCK 2  
396353 IGR1371a\_1 \*  
397334 IGR1369a\_2 \*  
397381 IGR1369a\_1 \*  
398352 IGR1367a\_1 BLOCK 2  
411823 IGR2008a\_2  
411873 IGR2008a\_1 BLOCK 3  
412456 IGR2010a\_3 \*  
413233 IGR2011b\_1 \*  
415579 IGR2016a\_1 \*  
417617 IGR2020a\_15 \*  
419845 IGR2025a\_2 \*  
424283 IGR2033a\_1 \*  
425376 IGR2036a\_2 \*  
425549 IGR2036a\_1 BLOCK 3  
433467 IGR2052a\_1 BLOCK 4  
435282 IGR2055a\_1 \*  
437682 IGR2060a\_1 \*  
438883 IGR2063b\_1 \*  
443565 IGR2072a\_2 \*  
443750 IGR2073a\_1 \*  
445337 IGR2076a\_1 \*  
447791 IGR2081a\_1 \*  
449895 IGR2085a\_2 \*  
455246 IGR2096a\_1 \*  
463136 IGR2111a\_3 BLOCK 4  
482171 IGR2150a\_1 BLOCK 5  
485828 IGR2157a\_1 \*  
495082 IGR2175a\_2 \*  
506266 IGR2198a\_1 \*  
506890 IGR2199a\_1 BLOCK 5  
507208 IGR2200a\_1 BLOCK 6  
508338 IGR2202a\_1 \*  
508858 IGR2203a\_1 \*  
510951 IGR2207a\_1 \*  
518478 IGR2222a\_2 BLOCK 6  
519387 IGR2224a\_2 BLOCK 7  
519962 IGR2225a\_1 \*  
520521 IGR2226a\_3 \*  
522600 IGR2230a\_1 \*  
525243 IGR2236a\_1 \*  
529556 IGR2244a\_4 \*  
532363 IGR2250a\_4 \*  
545062 IGR2276a\_1 \*  
553189 IGR2292a\_1 \*

570978 IGR3005a\_1 \*  
571022 IGR3005a\_2 \*  
576586 IGR3016a\_1 \*  
577141 IGR3018a\_2 \*  
577838 IGR3019a\_2 \*  
578122 IGR3020a\_1 \*  
579217 IGR3022a\_1 \*  
579529 IGR3023a\_1 \*  
579818 IGR3023a\_3 \*  
582651 IGR3029a\_1 \*  
582948 IGR3029a\_2 \*  
583131 IGR3030a\_1 \*  
587836 IGR3039a\_1 \*  
590425 IGR3044a\_1 \*  
590585 IGR3045a\_1 \*  
594115 IGR3051a\_1 \*  
594812 IGR3053a\_1 \*  
598805 IGR3061a\_1 \*  
601294 IGR3066a\_1 \*  
608759 IGR3081a\_1 \*  
610447 IGR3084a\_1 \*  
611177 IGR3086a\_1 BLOCK 7  
613488 IGR3090a\_1  
616241 IGR3096a\_1 BLOCK 8  
616763 IGR3097a\_1 \*  
617299 IGR3098a\_1 \*  
626881 IGR3117a\_1 \*  
633786 IGR3131a\_1 \*  
635072 IGR3134a\_1 \*  
637441 IGR3138a\_1 BLOCK 8  
648564 IGR3161a\_1  
649061 IGR3162a\_1 BLOCK 9  
649903 IGR3163a\_1 \*  
657234 IGR3178a\_1 \*  
662077 IGR3188a\_1 \*  
662819 IGR3189a\_2 \*  
676688 IGRX100a\_1 BLOCK 9  
683387 IGR3230a\_1 BLOCK 10  
686249 IGR3236a\_1 \*  
692320 IGR3248a\_1 \*  
718291 IGR3300a\_2 \*  
730313 IGR3324a\_1 \*  
731025 IGR3326a\_1 \*  
738461 IGR3340a\_1 BLOCK 10  
871978 GENS021ex1\_2 BLOCK 11  
877571 GENS020ex3\_3 \*  
877671 GENS020ex3\_2 \*  
877809 GENS020ex3\_1 \*

890710 GENS020ex1\_1 BLOCK 11

However it has been updated after the paper was published (posted on <http://www.broad.mit.edu/humgen/IBD5/haplodata.html>)

### Usage

```
data(crohn)
```

### Format

A data frame containing 387 rows and 212 columns

### Source

MJ Daly, JD Rioux, SF Schaffner, TJ Hudson, ES Lander (2001) High-resolution haplotype structure in the human genome *Nature Genetics* 29:229-232

---

ESplot	<i>Effect-size plot</i>
--------	-------------------------

---

### Description

The function accepts parameter estimates and their standard errors for a range of models.

### Usage

```
ESplot(ESdat, SE=TRUE, logscale=TRUE, alpha=0.05, xlim=c(-2, 8), v=1, ...)
```

### Arguments

ESdat	A data frame consisting of model id, parameter estimates and standard errors or confidence limits
SE	If TRUE, the third column of ESdata contains the standard error estimates
logscale	If TRUE, indicates log-scale as appropriate for odds ratio
alpha	Type-I error rate used to construct 100(1-alpha) confidence interval
xlim	Lower and upper limits of the horizontal axis, roughly corresponding to confidence limits
...	Other options for plot
v	Location of the vertical line

### Author(s)

Jing Hua Zhao

## Examples

```
## Not run:
# 7-4-2008 MRC-Epid JHZ
options(stringsAsFactors=FALSE)
testdata <- data.frame(models=c("Basic model", "Adjusted", "Moderately adjusted", "Heavily adjusted", "Other"),
OR = c(4.5, 3.5, 2.5, 1.5, 1),
SElogOR = c(0.2, 0.1, 0.5, 0.5, 0.2))
ESplot(testdata, v=1)
title("This is a fictitious plot")
#
# Quantitative trait, as appropriate for linear regression
# testdata <- data.frame(modelid, beta, se(beta))
# ESplot(testdata, logscale=FALSE)
#
# Other scenarios
# OR with CI
# ESplot(testdata, SE=FALSE)

## End(Not run)
```

---

fa

*Friedreich Ataxia data*


---

## Description

This data set contains a case-control indicator and twelve microsatellite markers. An extra unphased individual with the following genotype

```
2 7 7 7 1 3 2 2 2 2 6 3
3 8 10 8 3 9 3 4 2 2 7 5
```

has not been included.

The inter-marker distances (Morgan) are as follows,

0.03, 0.065, 0.00125, 0.00125, 0.00125, 0.00125, 0.00125, 0.00125, 0.00125, 0.00125, 0.00125, 0.045

## Usage

```
data(fa)
```

## Format

A data frame containing 127 rows and 13 columns

## Source

Liu JS, Sabatti C, Teng J, Keats BJB, Risch N (2001). Bayesian analysis of haplotypes for linkage disequilibrium mapping *Genome Research* 11:1716-1724

---

fbsize *Sample size for family-based linkage and association design*

---

### Description

This function implements Risch and Merikangas (1996) statistics evaluating power for family-based linkage (affected sib pairs, ASP) and association design. They are potentially useful in the prospect of genome-wide association studies.

The function calls auxiliary functions `sn()` and `strlen`; `sn()` contains the necessary thresholds for power calculation while `strlen()` evaluates length of a string (generic).

### Usage

```
fbsize(gamma,p,alpha=c(1e-4,1e-8,1e-8),beta=0.2,debug=0,error=0)
```

### Arguments

gamma	genotype relative risk assuming multiplicative model
p	frequency of disease allele
alpha	Type I error rates for ASP linkage, TDT and ASP-TDT
beta	Type II error rate
debug	verbose output
error	0=use the correct formula,1=the original paper

### Value

The returned value is a list containing:

gamma	input gamma
p	input p
n1	sample size for ASP
n2	sample size for TDT
n3	sample size for ASP-TDT
lambdao	lambda o
lambdas	lambda s

### References

Risch, N. and K. Merikangas (1996). The future of genetic studies of complex human diseases. *Science* 273(September): 1516-1517.

Risch, N. and K. Merikangas (1997). Reply to Scott et al. *Science* 275(February): 1329-1330.

Scott, W. K., M. A. Pericak-Vance, et al. (1997). Genetic analysis of complex diseases. *Science* 275: 1327.

**Note**

extracted from rm.c

**Author(s)**

Jing Hua Zhao

**See Also**

[pbsize](#)

**Examples**

```
models <- matrix(c(
  4.0, 0.01,
  4.0, 0.10,
  4.0, 0.50,
  4.0, 0.80,
  2.0, 0.01,
  2.0, 0.10,
  2.0, 0.50,
  2.0, 0.80,
  1.5, 0.01,
  1.5, 0.10,
  1.5, 0.50,
  1.5, 0.80), ncol=2, byrow=TRUE)
outfile <- "fbsize.txt"
cat("gamma", "p", "Y", "N_asp", "P_A", "H1", "N_tdt", "H2", "N_asp/tdt", "L_o", "L_s\n", file=outfile, sep="\t")
for(i in 1:12) {
  g <- models[i,1]
  p <- models[i,2]
  z <- fbsize(g,p)
  cat(z$gamma, z$p, z$y, z$n1, z$pA, z$h1, z$n2, z$h2, z$n3, z$lambdao, z$lambdao, file=outfile, append=TRUE, sep="\t")
  cat("\n", file=outfile, append=TRUE)
}
table1 <- read.table(outfile, header=TRUE, sep="\t")
nc <- c(4,7,9)
table1[,nc] <- ceiling(table1[,nc])
dc <- c(3,5,6,8,10,11)
table1[,dc] <- round(table1[,dc],2)
unlink(outfile)
# APOE-4, Scott WK, Pericak-Vance, MA & Haines JL
# Genetic analysis of complex diseases 1327
g <- 4.5
p <- 0.15
cat("\nAlzheimer's:\n\n")
fbsize(g,p)
# note to replicate the Table we need set alpha=9.961139e-05, 4.910638e-08 and beta=0.2004542.
# or reset the quantiles in fbsize.R
```

FPRP

False-positive report probability

**Description**

The function calculates the false positive report probability (FPRP), the probability of no true association between a genetic variant and disease given a statistically significant finding, which depends not only on the observed P value but also on both the prior probability that the association is real and the statistical power of the test. An associate result is the false negative reported probability (FNRP). See example for the recommended steps.

The FPRP and FNRP are derived as follows. Let  $H_0$ =null hypothesis (no association),  $H_A$ =alternative hypothesis (association). Since classic frequentist theory considers they are fixed, one has to resort to Bayesian framework by introducing prior,  $\pi = P(H_0 = TRUE) = P(\text{association})$ . Let  $T$ =test statistic, and  $P(T > z_\alpha | H_0 = TRUE) = P(\text{rejecting } H_0 | H_0 = TRUE) = \alpha$ ,  $P(T > z_\alpha | H_0 = FALSE) = P(\text{rejecting } H_0 | H_A = TRUE) = 1 - \beta$ . The joint probability of test and truth of hypothesis can be expressed by  $\alpha$ ,  $\beta$  and  $\pi$ .

Truth of $H_A$	significant	nonsignificant	Total
TRUE	$(1 - \beta)\pi$	$\beta\pi$	$\pi$
FALSE	$\alpha(1 - \pi)$	$(1 - \alpha)(1 - \pi)$	$1 - \pi$
Total	$(1 - \beta)\pi + \alpha(1 - \pi)$	$\beta\pi + (1 - \alpha)(1 - \pi)$	1

We have  $FPRP = P(H_0 = TRUE | T > z_\alpha) = \alpha(1 - \pi) / [\alpha(1 - \pi) + (1 - \beta)\pi] = \{1 + \pi / (1 - \pi) [(1 - \beta) / \alpha]\}^{-1}$  and similarly  $FNRP = \{1 + [(1 - \alpha) / \beta] [(1 - \pi) / \pi]\}^{-1}$ .

**Usage**

```
FPRP(a,b,pi0,ORlist,logscale=FALSE)
```

**Arguments**

a	parameter value at which the power is to be evaluated
b	the variance for a, or the upper point of a 95%CI if logscale=FALSE
pi0	the prior probability that $H_0$ is true
ORlist	a vector of ORs that is most likely
logscale	FALSE=a,b in original scale, TRUE=a, b in log scale

**Value**

The returned value is a list with components,

p	p value corresponding to a,b
power	the power corresponding to the vector of ORs
FPRP	False-positive report probability
FNRP	False-negative report probability

## References

Wacholder S, Chanock S, Garcia-Closas M, El ghomli L, Rothman N. (2004) Assessing the probability that a positive report is false: an approach for molecular epidemiology studies. *J Natl Cancer Inst* 96:434-442

## Author(s)

Jing Hua Zhao

## See Also

[BFDP](#)

## Examples

```
## Not run:
# Example by Laure El ghormli & Sholom Wacholder on 25-Feb-2004
# Step 1 - Pre-set an FPRP-level criterion for noteworthiness

T <- 0.2

# Step 2 - Enter values for the prior that there is an association

pi0 <- c(0.25,0.1,0.01,0.001,0.0001,0.00001)

# Step 3 - Enter values of odds ratios (OR) that are most likely, assuming that there is a non-null association

ORlist <- c(1.2,1.5,2.0)

# Step 4 - Enter OR estimate and 95

OR <- 1.316
ORlo <- 1.08
ORhi <- 1.60

logOR <- log(OR)
selogOR <- abs(logOR-log(ORhi))/1.96
p <- ifelse(logOR>0,2*(1-pnorm(logOR/selogOR)),2*pnorm(logOR/selogOR))
p
q <- qnorm(1-p/2)
POWER <- ifelse(log(ORlist)>0,1-pnorm(q-log(ORlist)/selogOR),pnorm(-q-log(ORlist)/selogOR))
POWER
FPRPex <- t(p*(1-pi0)/(p*(1-pi0)+POWER%o%pi0))
row.names(FPRPex) <- pi0
colnames(FPRPex) <- ORlist
FPRPex
FPRPex>T

## now turn to FPRP
OR <- 1.316
ORhi <- 1.60
ORlist <- c(1.2,1.5,2.0)
```

```
pi0 <- c(0.25,0.1,0.01,0.001,0.0001,0.00001)
z <- FPRP(OR,ORhi,pi0,ORlist,logscale=FALSE)
z

## End(Not run)
```

---

fsnps

*A case-control data involving four SNPs with missing genotype*

---

### Description

This is a simulated data of four SNPs with their alleles coded in characters. The variable y contains phenotypes (1=case, 0=control).

### Usage

```
data(fsnps)
```

### Format

A data frame

### Source

Dr Sebastien Lissarrague of Genset

---

gc.em

*Gene counting for haplotype analysis*

---

### Description

Gene counting for haplotype analysis with missing data, adapted for hap.score

### Usage

```
gc.em(data, locus.label=NA, converge.eps=1e-06, maxiter=500,
       handle.miss=0, miss.val=0, control=gc.control())
```

**Arguments**

<code>data</code>	Matrix of alleles, such that each locus has a pair of adjacent columns of alleles, and the order of columns corresponds to the order of loci on a chromosome. If there are $K$ loci, then $\text{ncol}(\text{data}) = 2 * K$ . Rows represent alleles for each subject.
<code>locus.label</code>	Vector of labels for loci, of length $K$ (see definition of data matrix).
<code>converge.eps</code>	Convergence criterion, based on absolute change in log likelihood ( $\ln\text{like}$ ).
<code>maxiter</code>	Maximum number of iterations of EM.
<code>handle.miss</code>	a flag for handling missing genotype data, 0=no, 1=yes
<code>miss.val</code>	missing value
<code>control</code>	a function, see <a href="#">genecounting</a>

**Value**

List with components:

<code>converge</code>	Indicator of convergence of the EM algorithm (1=converged, 0 = failed).
<code>niter</code>	Number of iterations completed in the EM algorithm.
<code>locus.info</code>	A list with a component for each locus. Each component is also a list, and the items of a locus- specific list are the locus name and a vector for the unique alleles for the locus.
<code>locus.label</code>	Vector of labels for loci, of length $K$ (see definition of input values).
<code>haplotype</code>	Matrix of unique haplotypes. Each row represents a unique haplotype, and the number of columns is the number of loci.
<code>hap.prob</code>	Vector of mle's of haplotype probabilities. The $i$ th element of <code>hap.prob</code> corresponds to the $i$ th row of <code>haplotype</code> .
<code>hap.prob.noLD</code>	Similar to <code>hap.prob</code> , but assuming no linkage disequilibrium.
<code>lnlike</code>	Value of $\ln\text{like}$ at last EM iteration (maximum $\ln\text{like}$ if converged).
<code>lr</code>	Likelihood ratio statistic to test no linkage disequilibrium among all loci.
<code>indx.subj</code>	Vector for index of subjects, after expanding to all possible pairs of haplotypes for each person. If $\text{indx}=i$ , then $i$ is the $i$ th row of input matrix <code>data</code> . If the $i$ th subject has $n$ possible pairs of haplotypes that correspond to their marker phenotype, then $i$ is repeated $n$ times.
<code>nreps</code>	Vector for the count of haplotype pairs that map to each subject's marker genotypes.
<code>hap1code</code>	Vector of codes for each subject's first haplotype. The values in <code>hap1code</code> are the row numbers of the unique haplotypes in the returned matrix <code>haplotype</code> .
<code>hap2code</code>	Similar to <code>hap1code</code> , but for each subject's second haplotype.
<code>post</code>	Vector of posterior probabilities of pairs of haplotypes for a person, given their marker phenotypes.
<code>htrtable</code>	A table which can be used in haplotype trend regression

## References

- Zhao, J. H., Lissarrague, S., Essioux, L. and P. C. Sham (2002). GENECOUNTING: haplotype analysis with missing genotypes. *Bioinformatics* 18(12):1694-1695
- Zhao, J. H. and P. C. Sham (2003). Generic number systems and haplotype analysis. *Comp Meth Prog Biomed* 70: 1-9

## Note

Adapted from GENECOUNTING

## Author(s)

Jing Hua Zhao

## See Also

[genecounting](#), [LDkl](#)

## Examples

```
## Not run:
data(hla)
gc.em(hla[,3:8], locus.label=c("DQR", "DQA", "DQB"), control=gc.control(assignment="t"))

## End(Not run)
```

---

gcontrol

*genomic control*

---

## Description

The Bayesian genomic control statistics with the following parameters,

n	number of loci under consideration
lambdahat	median(of the n trend statistics)/0.46 Prior for noncentrality parameter $A_i$ is Normal( $\sqrt{\text{lambdahat}}\kappa, \text{lambdahat}*\tau^2$ )
kappa	multiplier in prior above, set at $1.6 * \sqrt{\log(n)}$
tau2	multiplier in prior above
epsilon	prior probability a marker is associated, set at $10/n$
ngib	number of cycles for the Gibbs sampler after burn in
burn	number of cycles for the Gibbs sampler to burn in

Armitage's trend test along with the posterior probability that each marker is associated with the disorder is given. The latter is not a p-value but any value greater than 0.5 (pout) suggests association.

**Usage**

```
gcontrol(data,zeta,kappa,tau2,epsilon,ngib,burn,idum)
```

**Arguments**

data	the data matrix
zeta	program constant with default value 1000
kappa	multiplier in prior for mean with default value 4
tau2	multiplier in prior for variance with default value 1
epsilon	prior probability of marker association with default value 0.01
ngib	number of Gibbs steps, with default value 500
burn	number of burn-ins with default value 50
idum	seed for pseudorandom number sequence

**Value**

The returned value is a list containing:

deltot	the probability of being an outlier
x2	the $\chi^2$ statistic
A	the A vector

**References**

Devlin B, Roeder K (1999) Genomic control for association studies. *Biometrics* 55:997-1004

**Note**

Adapted from gcontrol by Bobby Jones and Kathryn Roeder, use -Dexecutable for standalone program, function getnum in the original code needs %\*s to skip id string

**Author(s)**

Bobby Jones, Jing Hua Zhao

**Source**

<http://www.stat.cmu.edu>

**Examples**

```
## Not run:
test<-c(1,2,3,4,5,6, 1,2,1,23,1,2, 100,1,2,12,1,1,
        1,2,3,4,5,61, 1,2,11,23,1,2, 10,11,2,12,1,11)
test<-matrix(test,nrow=6,byrow=T)
gcontrol(test)

## End(Not run)
```

---

`gcontrol2`*genomic control based on p values*

---

**Description**

The function obtains 1-df  $\chi^2$  statistics (observed) according to a vector of p values, and the inflation factor (lambda) according to medians of the observed and expected statistics. The latter is based on the empirical distribution function (EDF) of 1-df  $\chi^2$  statistics.

It would be appropriate for genetic association analysis as of 1-df Armitage trend test for case-control data; for 1-df additive model with continuous outcome one has to consider the compatibility with p values based on z-/t- statistics.

**Usage**

```
gcontrol2(p,col=palette()[4],lcol=palette()[2],...)
```

**Arguments**

<code>p</code>	a vector of observed p values
<code>col</code>	colour for points in the Q-Q plot
<code>lcol</code>	colour for the diagonal line in the Q-Q plot
<code>...</code>	other options for plot

**Value**

A list containing:

<code>x</code>	the expected $\chi^2$ statistics
<code>y</code>	the observed $\chi^2$ statistics
<code>lambda</code>	the inflation factor

**References**

Devlin B, Roeder K (1999) Genomic control for association studies. *Biometrics* 55:997-1004

**Author(s)**

Jing Hua Zhao

**Examples**

```
## Not run:
x2 <- rchisq(100,1,.1)
p <- pchisq(x2,1,lower.tail=FALSE)
r <- gcontrol2(p)
print(r$lambda)

## End(Not run)
```

gcp

*Permutation tests using GENECOUNTING***Description**

This function is a R port of the GENECOUNTING/PERMUTE program which generates EHPLUS-type statistics including z-tests for individual haplotypes

**Usage**

```
gcp(y, cc, g, handle.miss=1, miss.val=0, n.sim=0,
    locus.label=NULL, quietly=FALSE)
```

**Arguments**

y	A column of 0/1 indicating cases and controls
cc	analysis indicator, 0 = marker-marker, 1 = case-control
g	the multilocus genotype data
handle.miss	a flag with value 1 indicating missing data are allowed
miss.val	missing value
n.sim	the number of permutations
locus.label	label of each locus
quietly	a flag if TRUE will suppress the screen output

**Value**

The returned value is a list containing (p.sim and ph when n.sim > 0):

x2obs	the observed chi-squared statistic
pobs	the associated p value
zobs	the observed z value for individual haplotypes
p.sim	simulated p value for the global chi-squared statistic
ph	simulated p values for individual haplotypes

**References**

Zhao JH, Curtis D, Sham PC (2000). Model-free analysis and permutation tests for allelic associations. *Human Heredity* 50(2): 133-139

Zhao JH (2004). 2LD, GENECOUNTING and HAP: Computer programs for linkage disequilibrium analysis. *Bioinformatics* 20: 1325-1326

Zhao JH, Qian WD Association analysis of unrelated individuals using polymorphic genetic markers – methods, implementation and application, Royal Statistical Society 2003, Hassallt-Diepenbeek, Belgium.

**Note**

Built on gcp.c

**Author(s)**

Jing Hua Zhao

**See Also**

[genecounting](#)

**Examples**

```
## Not run:

data(fsnps)
y<-fsnps$y
cc<-1
g<-fsnps[,3:10]

gcp(y,cc,g,miss.val="Z",n.sim=5)
hap.score(y,g,method="hap",miss.val="Z")

## End(Not run)
```

---

genecounting

*Gene counting for haplotype analysis*

---

**Description**

Gene counting for haplotype analysis with missing data

**Usage**

```
genecounting(data,weight=NULL,loci=NULL,control=gc.control())
```

**Arguments**

data	genotype table
weight	a column of frequency weights
loci	an array containing number of alleles at each locus
control	is a function with the following arguments:

1. xdata. a flag indicating if the data involves X chromosome, if so, the first column of data indicates sex of each subject: 1=male, 2=female. The marker data are no different from the autosomal version for females, but for males, two copies of the single allele present at a given locus.

2. convll. set convergence criteria according to log-likelihood, if its value set to 1
3. handle.miss. to handle missing data, if its value set to 1
4. eps. the actual convergence criteria, with default value 1e-5
5. tol. tolerance for genotype probabilities with default value 1e-8
6. maxit. maximum number of iterations, with default value 50
7. pl. criteria for trimming haplotypes according to posterior probabilities
8. assignment. filename containing haplotype assignment
9. verbose. If TRUE, yields print out from the C routine

### Value

The returned value is a list containing:

h	haplotype frequency estimates under linkage disequilibrium (LD)
h0	haplotype frequency estimates under linkage equilibrium (no LD)
prob	genotype probability estimates
l0	log-likelihood under linkage equilibrium
l1	log-likelihood under linkage disequilibrium
hapid	unique haplotype identifier (defunct, see gc.em)
npusr	number of parameters according user-given alleles
npdat	number of parameters according to observed
htrtable	design matrix for haplotype trend regression (defunct, see gc.em)
iter	number of iterations used in gene counting
converge	a flag indicating convergence status of gene counting
di0	haplotype diversity under no LD, defined as $1 - \sum(h_0^2)$
di1	haplotype diversity under LD, defined as $1 - \sum(h^2)$
resid	residuals in terms of frequency weights = o - e

### References

- Zhao, J. H., Lissarrague, S., Essioux, L. and P. C. Sham (2002). GENECOUNTING: haplotype analysis with missing genotypes. *Bioinformatics* 18(12):1694-1695
- Zhao, J. H. and P. C. Sham (2003). Generic number systems and haplotype analysis. *Comp Meth Prog Biomed* 70: 1-9
- Zhao, J. H. (2004). 2LD, GENECOUNTING and HAP: Computer programs for linkage disequilibrium analysis. *Bioinformatics*, 20, 1325-1326

### Note

adapted from GENECOUNTING

### Author(s)

Jing Hua Zhao

**See Also**

[gc.em](#), [LDk1](#)

**Examples**

```
## Not run:
# HLA data
data(hla)
hla.gc <- genecounting(hla[,3:8])
summary(hla.gc)
hla.gc$10
hla.gc$11

# ALDH2 data
data(aldh2)
control <- gc.control(handle.miss=1,assignment="ALDH2.out")
aldh2.gc <- genecounting(aldh2[,3:6],control=control)
summary(aldh2.gc)
aldh2.gc$10
aldh2.gc$11

# Chromosome X data
# assuming allelic data have been extracted in columns 3-13
# and column 3 is sex
filespec <- file.path(.path.package("gap"),"tests/mao.dat")
mao2 <- read.table(filespec)
dat <- mao2[,3:13]
loci <- c(12,9,6,5,3)
contr <- gc.control(xdata=TRUE,handle.miss=1)
mao.gc <- genecounting(dat,loci=loci,control=contr)
mao.gc$npusr
mao.gc$npdat

## End(Not run)
```

---

 gif

---

*Kinship coefficient and genetic index of familiarity*


---

**Description**

The genetic index of familiarity is defined as the mean kinship between all pairs of individuals in a set multiplied by 100,000. Formally, it is defined as

$$100,000 \times \frac{2}{n(n-1)} \sum_{i=1}^{n-1} \sum_{j=i+1}^n k_{ij}$$

where  $n$  is the number of individuals in the set and  $k_{ij}$  is the kinship coefficient between individuals  $i$  and  $j$ .

The scaling is purely for convenience of presentation.

**Usage**

```
gif(data,gifset)
```

**Arguments**

data	the trio data of a pedigree
gifset	a subgroup of pedigree members

**Value**

The returned value is a list containing:

gifval	the genetic index of familiarity
--------	----------------------------------

**References**

Gholami K, Thomas A (1994) A linear time algorithm for calculation of multiple pairwise kinship coefficients and genetic index of familiarity. *Comp Biomed Res* 27:342-350

**Note**

Adapted from gif.c, testable with -Dexecutable as standalone program, which can be use for any pair of individuals

**Author(s)**

Alun Thomas, Jing Hua Zhao

**See Also**

[pfc](#)

**Examples**

```
## Not run:
test<-c(
  5, 0, 0,
  1, 0, 0,
  9, 5, 1,
  6, 0, 0,
  10, 9, 6,
  15, 9, 6,
  21, 10, 15,
  3, 0, 0,
  18, 3, 15,
  23, 21, 18,
  2, 0, 0,
  4, 0, 0,
  7, 0, 0,
  8, 4, 7,
  11, 5, 8,
```

```

12,    9,    6,
13,    9,    6,
14,    5,    8,
16,   14,    6,
17,   10,    2,
19,    9,   11,
20,   10,   13,
22,   21,   20)
test<-matrix(test,ncol=3,byrow=TRUE)
gif(test,gifset=c(20,21,22))

# all individuals
gif(test,gifset=1:23)

## End(Not run)

```

h2

*Heritability estimation according to twin correlations***Description**

Heritability and variance estimation according to twin pair correlations.

**Usage**

```
h2(mzDat=NULL, dzDat=NULL, rmz=NULL, rdz=NULL, nmz=NULL, ndz=NULL, selV=NULL)
```

**Arguments**

mzDat	a data frame for monozygotic twins (MZ)
dzDat	a data frame for dizygotic twins (DZ)
rmz	correlation for MZ twins
rdz	correlation for DZ twins
nmz	sample size for MZ twins
ndz	sample size for DZ twins
selV	names of variables for twin and cotwin

**Details**

The example section shows how to obtain bootstrap 95%CI.

**Value**

The returned value is a matrix containing heritability and their variance estimations for "h2", "c2", "e2", "vh", "vc", "ve".

**References**

Keeping ES. Introduction to Statistical Inference, Dover Publications, Inc. 1995

**Author(s)**

Jing Hua Zhao

**Examples**

```
## Not run:

ACE_CI <- function(mzData,dzData,n.sim=5,selV=NULL,verbose=TRUE)
{
  ACER_twinData <- h2(mzDat=mzData,dzDat=dzData,selV=selV)
  print(ACER_twinData)

  nmz <- dim(mzData)[1]
  ndz <- dim(dzData)[1]
  a <- ar <- vector()
  set.seed(12345)
  for(i in 1:n.sim)
  {
    cat("\rRunning # ",i,"/", n.sim,"\r",sep="")
    sampled_mz <- sample(1:nmz, replace=TRUE)
    sampled_dz <- sample(1:ndz, replace=TRUE)
    mzDat <- mzData[sampled_mz,]
    dzDat <- dzData[sampled_dz,]
    ACER_i <- h2(mzDat=mzDat,dzDat=dzDat,selV=selV)
    if(verbose) print(ACER_i)
    ar <- rbind(ar,ACER_i)
  }
  cat("\n\nheritability according to correlations\n\n")
  ar <- as.data.frame(ar)
  m <- mean(ar,na.rm=TRUE)
  s <- sd(ar,na.rm=TRUE)
  allr <- data.frame(mean=m,sd=s,lc1=m-1.96*s,ucl=m+1.96*s)
  print(allr)
}

selVars <- c('bmi1','bmi2')

library(mvtnorm)
n.sim <- 500
cat ("\n\nThe first study\n\n")
mzm <- as.data.frame(rmvnorm(195, c(22.75,22.75), matrix(2.66^2*c(1, 0.67, 0.67, 1), 2)))
dzm <- as.data.frame(rmvnorm(130, c(23.44,23.44), matrix(2.75^2*c(1, 0.32, 0.32, 1), 2)))
mzw <- as.data.frame(rmvnorm(384, c(21.44,21.44), matrix(3.08^2*c(1, 0.72, 0.72, 1), 2)))
dzw <- as.data.frame(rmvnorm(243, c(21.72,21.72), matrix(3.12^2*c(1, 0.33, 0.33, 1), 2)))
names(mzm) <- names(dzm) <- names(mzw) <- names(dzw) <- c("bmi1","bmi2")
ACE_CI(mzm,dzm,n.sim,selV=selVars,verbose=FALSE)
ACE_CI(mzw,dzw,n.sim,selV=selVars,verbose=FALSE)

## End(Not run)
```

---

 hap *Haplotype reconstruction*


---

**Description**

Haplotype reconstruction using sorting and trimming algorithms

**Usage**

```
hap(id,data,nloci,loci=rep(2,nloci),names=paste("loci",1:nloci,sep=""),
    control=hap.control())
```

**Arguments**

id	a column of subject id
data	genotype table
nloci	number of loci
loci	number of alleles at all loci
names	locus names
control	is a function with the following arguments, <ol style="list-style-type: none"> <li>1. mb Maximum dynamic storage to be allocated, in Mb</li> <li>2. pr Prior (ie population) probability threshold</li> <li>3. po Posterior probability threshold</li> <li>4. to Log-likelihood convergence tolerance</li> <li>5. th Posterior probability threshold for output</li> <li>6. maxit Maximum EM iteration</li> <li>7. n Force numeric allele coding (1/2) on output (off)</li> <li>8. ss Tab-delimited spreadsheet file output (off)</li> <li>9. rs Random starting points for each EM iteration (off)</li> <li>10. rp Restart from random prior probabilities</li> <li>11. ro Loci added in random order (off)</li> <li>12. rv Loci added in reverse order (off)</li> <li>13. sd Set seed for random number generator (use date+time)</li> <li>14. mm Repeat final maximization multiple times</li> <li>15. mi Create multiple imputed datasets. If set &gt;0</li> <li>16. mc Number of MCMC steps between samples</li> <li>17. ds Starting value of Dirichlet prior parameter</li> <li>18. de Finishing value of Dirichlet prior parameter</li> <li>19. q Quiet operation (off)</li> <li>20. hapfile a file for haplotype frequencies</li> <li>21. assignfile a file for haplotype assignment</li> </ol>

## Details

The package can handle much larger number of multiallelic loci. For large sample size with relatively small number of multiallelic loci, genecounting should be used.

## Value

The returned value is a list containing:

ll	log-likelihood assuming linkage disequilibrium
converge	convergence status, 0=failed, 1=succeeded
niter	number of iterations

## References

Clayton DG (2001) SNPHAP. <http://www-gene.cimr.cam.ac.uk/clayton/software>

Zhao JH and W Qian (2003) Association analysis of unrelated individuals using polymorphic genetic markers. RSS 2003, Hassalt, Belgium

Zhao JH (2004). 2LD, GENECOUNTING and HAP: Computer programs for linkage disequilibrium analysis. Bioinformatics 20: 1325-1326

## Note

adapted from hap

## See Also

[genecounting](#)

## Examples

```
## Not run:
# 4 SNP example, to generate hap.out and assign.out alone
data(fsnps)
hap(id=fsnps[,1],data=fsnps[,3:10],nloci=4)
dir()
file.show("hap.out")
file.show("assign.out")

# to generate results of imputations
control <- hap.control(ss=1,mi=5,hapfile="h",assignfile="a")
hap(id=fsnps[,1],data=fsnps[,3:10],nloci=4,control=control)
dir()

## End(Not run)
```

---

hap.em *Gene counting for haplotype analysis*

---

### Description

Gene counting for haplotype analysis with missing data, adapted for hap.score

### Usage

```
hap.em(id, data, locus.label=NA, converge.eps=1e-06, maxiter=500, miss.val=0)
```

### Arguments

id	a vector of individual IDs
data	Matrix of alleles, such that each locus has a pair of adjacent columns of alleles, and the order of columns corresponds to the order of loci on a chromosome. If there are K loci, then $\text{ncol}(\text{data}) = 2 * K$ . Rows represent alleles for each subject.
locus.label	Vector of labels for loci, of length K (see definition of data matrix).
converge.eps	Convergence criterion, based on absolute change in log likelihood (lnlike).
maxiter	Maximum number of iterations of EM
miss.val	missing value

### Value

List with components:

converge	Indicator of convergence of the EM algorithm (1=converged, 0 = failed).
niter	Number of iterations completed in the EM algorithm.
locus.info	A list with a component for each locus. Each component is also a list, and the items of a locus- specific list are the locus name and a vector for the unique alleles for the locus.
locus.label	Vector of labels for loci, of length K (see definition of input values).
haplotype	Matrix of unique haplotypes. Each row represents a unique haplotype, and the number of columns is the number of loci.
hap.prob	Vector of mle's of haplotype probabilities. The ith element of hap.prob corresponds to the ith row of haplotype.
lnlike	Value of lnlike at last EM iteration (maximum lnlike if converged).
indx.subj	Vector for index of subjects, after expanding to all possible pairs of haplotypes for each person. If $\text{indx}=i$ , then i is the ith row of input matrix data. If the ith subject has n possible pairs of haplotypes that correspond to their marker phenotype, then i is repeated n times.
nreps	Vector for the count of haplotype pairs that map to each subject's marker genotypes.

hap1code	Vector of codes for each subject's first haplotype. The values in hap1code are the row numbers of the unique haplotypes in the returned matrix haplotype.
hap2code	Similar to hap1code, but for each subject's second haplotype.
post	Vector of posterior probabilities of pairs of haplotypes for a person, given thier marker phenotypes.

## References

See hap

## Note

Adapted from HAP

## Author(s)

Jing Hua Zhao

## See Also

[hap](#), [LDk1](#)

## Examples

```
## Not run:
data(hla)
hap.em(id=1:length(hla[,1]),data=hla[,3:8],locus.label=c("DQR","DQA","DQB"))

## End(Not run)
```

---

hap.score

*Score statistics for association of traits with haplotypes*

---

## Description

Compute score statistics to evaluate the association of a trait with haplotypes, when linkage phase is unknown and diploid marker phenotypes are observed among unrelated subjects. For now, only autosomal loci are considered. This package haplo.score which this function is based is greatly acknowledged.

## Usage

```
hap.score(y, geno, trait.type="gaussian", offset=NA, x.adj=NA, skip.haplo=0.005,
          locus.label=NA, miss.val=0, n.sim=0,
          method="gc", id=NA, handle.miss=0, mloci=NA, sexid=NA)
```

**Arguments**

y	Vector of trait values. For trait.type = "binomial", y must have values of 1 for event, 0 for no event.
geno	Matrix of alleles, such that each locus has a pair of adjacent columns of alleles, and the order of columns corresponds to the order of loci on a chromosome. If there are K loci, then ncol(geno) = 2*K. Rows represent alleles for each subject.
trait.type	Character string defining type of trait, with values of "gaussian", "binomial", "poisson", "ordinal".
offset	Vector of offset when trait.type = "poisson"
x.adj	Matrix of non-genetic covariates used to adjust the score statistics. Note that intercept should not be included, as it will be added in this function.
skip.haplo	Skip score statistics for haplotypes with frequencies < skip.haplo
locus.label	Vector of labels for loci, of length K (see definition of geno matrix).
miss.val	Vector of codes for missing values of alleles.
n.sim	Number of simulations for empirical p-values. If n.sim=0, no empirical p-values are computed.
method	method of haplotype frequency estimation, "gc" or "hap"
id	an added option which contains the individual IDs
handle.miss	flag to handle missing genotype data, 0=no, 1=yes
mloci	maximum number of loci/sites with missing data to be allowed in the analysis
sexid	flag to indicator sex for data from X chromosome, i=male, 2=female

**Details**

This is a version which substitutes haplo.em

**Value**

List with the following components:

score.global	Global statistic to test association of trait with haplotypes that have frequencies $\geq$ skip.haplo.
df	Degrees of freedom for score.global.
score.global.p	P-value of score.global based on chi-square distribution, with degrees of freedom equal to df.
score.global.p.sim	P-value of score.global based on simulations (set equal to NA when n.sim=0).
score.haplo	Vector of score statistics for individual haplotypes that have frequencies $\geq$ skip.haplo.
score.haplo.p	Vector of p-values for score.haplo, based on a chi-square distribution with 1 df.
score.haplo.p.sim	Vector of p-values for score.haplo, based on simulations (set equal to NA when n.sim=0).

score.max.p.sim	P-value of maximum score.haplo, based on simulations (set equal to NA when n.sim=0).
haplotype	Matrix of haplotypes analyzed. The ith row of haplotype corresponds to the ith item of score.haplo, score.haplo.p, and score.haplo.p.sim.
hap.prob	Vector of haplotype probabilities, corresponding to the haplotypes in the matrix haplotype.
locus.label	Vector of labels for loci, of length K (same as input argument).
n.sim	Number of simulations.
n.val.global	Number of valid simulated global statistics.
n.val.haplo	Number of valid simulated score statistics (score.haplo) for individual haplotypes.

## References

Schaid DJ, Rowland CM, Tines DE, Jacobson RM, Poland GA (2002) Score tests for association of traits with haplotypes when linkage phase is ambiguous. *Amer J Hum Genet* 70:425-34

## Examples

```
## Not run:
data(hla)
y<-hla[,2]
geno<-hla[,3:8]
# complete data
hap.score(y,geno,locus.label=c("DRB","DQA","DQB"))
# incomplete genotype data
hap.score(y,geno,locus.label=c("DRB","DQA","DQB"),handle.miss=1,mloci=1)
unlink("assign.dat")

### note the differences in p values in the following runs
data(aldh2)
# to subset the data since hap doesn't handle one allele missing
deleted<-c(40,239,256)
aldh2[deleted,]
aldh2<-aldh2[-deleted,]
y<-aldh2[,2]
geno<-aldh2[,3:18]
# only one missing locus
hap.score(y,geno,handle.miss=1,mloci=1,method="hap")
# up to seven missing loci and with 10,000 permutations
hap.score(y,geno,handle.miss=1,mloci=7,method="hap",n.sim=10000)

# hap.score takes considerably longer time and does not handle missing data
hap.score(y,geno,n.sim=10000)

## End(Not run)
```

---

hla	<i>The HLA data</i>
-----	---------------------

---

**Description**

This data set contains HLA markers DRB, DQA, DQB and phenotypes of 271 Schizophrenia patients ( $y=1$ ) and controls ( $y=0$ ). Genotypes for 3 HLA loci have prefixes name (e.g., "DQB") and a suffix for each of two alleles (".a1" and ".a2").

**Usage**

```
data(hla)
```

**Format**

A data frame containing 271 rows and 8 columns

**Source**

Dr Padraig Wright of Pfizer

---

htr	<i>Haplotype trend regression</i>
-----	-----------------------------------

---

**Description**

Haplotype trend regression (with permutation)

**Usage**

```
htr(y,x,n.sim=0)
```

**Arguments**

y	a vector of phenotype
x	a haplotype table
n.sim	the number of permutations

**Value**

The returned value is a list containing:

f	the F statistic for overall association
p	the p value for overall association
fv	the F statistics for individual haplotypes
pi	the p values for individual haplotypes

## References

Zaykin DV, Westfall PH, Young SS, Karnoub MA, Wagner MJ, Ehm MG (2002) Testing association of statistically inferred haplotypes with discrete and continuous traits in samples of unrelated individuals. *Hum. Hered.* 53:79-91

Xie R, Stram DO (2005). Asymptotic equivalence between two score tests for haplotype-specific risk in general linear models. *Genet. Epidemiol.* 29:186-170

## Note

adapted from emgi.cpp, a pseudorandom number seed will be added on

## Author(s)

Dimitri Zaykin, Jing Hua Zhao

## See Also

[hap.score](#)

## Examples

```
## Not run:
# 26-10-03
# this is now part of demo
test2<-read.table("test2.dat")
y<-test2[,1]
x<-test2[,-1]
y<-as.matrix(y)
x<-as.matrix(x)
htr.test2<-htr(y,x)
htr.test2
htr.test2<-htr(y,x,n.sim=10)
htr.test2

# 13-11-2003
data(apoeapoc)
apoeapoc.gc<-gc.em(apoeapoc[,5:8])
y<-apoeapoc$y
for(i in 1:length(y)) if(y[i]==2) y[i]<-1
htr(y,apoeapoc.gc$htrtable)

# 20-8-2008
# part of the example from user!2008 tutorial by Andrea Foulkes
# It may be used beyond the generalized linear model (GLM) framework
HaploEM <- haplo.em(Geno,locus.label=SNPnames)
HapMat <- HapDesign(HaploEM)
m1 <- lm(Trait~HapMat)
m2 <- lm(Trait~1)
anova(m2,m1)

## End(Not run)
```

---

hwe *Hardy-Weinberg equilibrium test for a multiallelic marker*

---

### Description

Hardy-Weinberg equilibrium test

### Usage

```
hwe(data, data.type="allele", yates.correct=FALSE, miss.val=0)
```

### Arguments

<code>data</code>	A rectangular data containing the genotype, or an array of genotype counts
<code>data.type</code>	An option taking values "allele", "genotype", "count" if data is alleles, genotype or genotype count
<code>yates.correct</code>	A flag indicating if Yates' correction is used for Pearson $\chi^2$ statistic
<code>miss.val</code>	A list of missing values

### Details

This function obtains Hardy-Weinberg equilibrium test statistics. It can handle data coded as allele numbers (default), genotype identifiers (by setting `data.type="genotype"`) and counts corresponding to individual genotypes (by setting `data.type="count"`) which requires that genotype counts for all  $n(n+1)$  possible genotypes, with  $n$  being the number of alleles.

For highly polymorphic markers when asymptotic results do not hold, please resort to `hwe.hardy`.

### Value

The returned value is a list containing:

<code>allele.freq</code>	Frequencies of alleles
<code>x2</code>	Pearson $\chi^2$
<code>p.x2</code>	p value for $\chi^2$
<code>lrt</code>	Log-likelihood ratio test statistic
<code>p.lrt</code>	p value for lrt
<code>df</code>	Degree(s) of freedom
<code>rho</code>	$\sqrt{\chi^2/N}$ the contingency table coefficient

### Author(s)

Jing Hua Zhao

### See Also

[hwe.hardy](#)

## Examples

```
## Not run:
a <- c(3,2,2)
a.out <- hwe(a,data.type="genotype")
a.out
a.out <- hwe(a,data.type="count")
a.out
require(haplo.stats)
data(hla)
hla.DQR <- hwe(hla[,3:4])
summary(hla.DQR)
# multiple markers
s <- vector()
for(i in seq(3,8,2))
{
  hwe_i <- hwe(hla[,i:(i+1)])
  s <- rbind(s,hwe_i)
}
s

## End(Not run)
```

---

hwe.cc

*A likelihood ratio test of population Hardy-Weinberg equilibrium for case-control studies*

---

## Description

A likelihood ratio test of population Hardy-Weinberg equilibrium for case-control studies

## Usage

```
hwe.cc(model, case, ctrl, k0, initial1, initial2)
```

## Arguments

model	model specification, dominant, recessive
case	a vector of genotype counts in cases
ctrl	a vector of genotype counts in controls
k0	prevalence of disease in the population
initial1	initial values for beta, gamma, and q
initial2	initial values for logit(p) and log(gamma)

## Details

This is a collection of utility functions. The null hypothesis declares that the proportions of genotypes are according to Hardy-Weinberg law, while under the alternative hypothesis, the expected genotype counts are according to the probabilities that particular genotypes are obtained conditional on the prevalence of disease in the population. In so doing, Hardy-Weinberg equilibrium is considered using both case and control samples but pending on the disease model such that 2-parameter multiplicative model is built on baseline genotype  $\alpha$ ,  $\alpha\beta$  and  $\alpha\gamma$ .

## Value

The returned value is a list with the following components.

Cox	statistics under a general model
t2par	under the null hypothesis
t3par	under the alternative hypothesis
lrt.stat	the log-likelihood ratio statistic
pval	the corresponding p value

## References

Yu C, Zhang S, Zhou C, Sile S. A likelihood ratio test of population Hardy-Weinberg equilibrium for case-control studies. *Genetic Epidemiology* 33:275-280, 2009

## Author(s)

Chang Yu, <http://biostat.mc.vanderbilt.edu/wiki/Main/ChangYu>, Li Wang, Jing Hua Zhao

## See Also

[hwe](#)

## Examples

```
## Not run:

### Saba Sile, email of Jan 26, 2007, data always in order of GG AG AA, p=Pr(G), q=1-p=Pr(A)
case=c(155,27,4)
ctrl=c(408,55,15)
k0=.2
initial1=c(1.0,0.94,0.0904)
initial2=c(logit(1-0.0904),log(0.94))
hwe.cc("recessive",case,ctrl,k0, initial1, initial2)

### John Phillips III, TGFb1 data codon 10: TT CT CC, CC is abnormal and increasing TGFb1 activity
case=c(29,78,13)
ctrl=c(17,28,6)
k0 <- 1e-5
initial1 <- c(2.45,2.45,0.34)
initial2 <- c(logit(1-0.34),log(2.45))
hwe.cc("dominant",case,ctrl,k0,initial1,initial2)
```

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

---

```
hwe.hardy          Hardy-Weinberg equilibrium test using MCMC
```

---

### Description

Hardy-Weinberg equilibrium test by MCMC

### Usage

```
hwe.hardy(a, alleles = 3, seed = 3000, sample = c(1000, 1000, 5000))
```

### Arguments

a	an array containing the genotype counts, as integer.
alleles	number of allele at the locus, greater than or equal to 3, as integer
seed	pseudo-random number seed, as integer.
sample	optional, parameters for MCMC containing number of chunks, size of a chunk and burn-in steps, as integer.

### Value

The returned value is a list containing:

method	Hardy-Weinberg equilibrium test using MCMC
data.name	name of used data if x is given
p.value	Monte Carlo p value
p.value.se	standard error of Monte Carlo p value
switches	percentage of switches (partial, full and altogether)

### References

Guo, S.-W. and E. A. Thompson (1992) Performing the exact test of Hardy-Weinberg proportion for multiple alleles. *Biometrics*. 48:361–372.

### Note

Adapted from HARDY, testable with -Dexecutable as standalone program

### Author(s)

Sun-Wei Guo, Jing Hua Zhao, Gregor Gorjanc

**Source**

<http://www.stat.washington.edu/thompson/Genepi/pangaea.shtml>,

**See Also**

[hwe](#), [HWE.test](#), [genotype](#)

**Examples**

```
## Not run:
# example 2 from hwe.doc:
a<-c(
  3,
  4, 2,
  2, 2, 2,
  3, 3, 2, 1,
  0, 1, 0, 0, 0,
  0, 0, 0, 0, 0, 1,
  0, 0, 1, 0, 0, 0, 0,
  0, 0, 0, 2, 1, 0, 0, 0)
ex2 <- hwe.hardy(a=a,alleles=8)

# example using HLA
data(hla)
x <- hla[,3:4]
y <- pgc(x,handle.miss=0,with.id=1)
n.alleles <- max(x,na.rm=TRUE)
z <- vector("numeric",n.alleles*(n.alleles+1)/2)
z[y$idsave] <- y$wt
hwe.hardy(a=z,alleles=n.alleles)

# with use of class 'genotype'
# this is to be fixed
library(genetics)
hlagen <- genotype(a1=x$DQR.a1, a2=x$DQR.a2,
                  alleles=sort(unique(c(x$DQR.a1, x$DQR.a2))))
hwe.hardy(hlagen)

# comparison with hwe
hwe(z,data.type="count")

# to create input file for HARDY
print.tri<-function (xx,n) {
  cat(n,"\n")
  for(i in 1:n) {
    for(j in 1:i) {
      cat(xx[i,j]," ")
    }
    cat("\n")
  }
  cat("100 170 1000\n")
}
```

```
xx<-matrix(0,n.alleles,n.alleles)
xxx<-lower.tri(xx,diag=TRUE)
xx[xxx]<-z
sink("z.dat")
print.tri(xx,n.alleles)
sink()
# now call as: hwe z.dat z.out

## End(Not run)
```

---

kin.morgan

*kinship matrix for simple pedigree*

---

### Description

kinship matrix according to Morgan v2.1

### Usage

```
kin.morgan(ped,verbose=FALSE)
```

### Arguments

ped	individual's id, father's id and mother's id
verbose	an option to print out the original pedigree

### Value

The returned value is a list containing:

kin	the kinship matrix in vector form
kin.matrix	the kinship matrix

### References

Morgan V2.1 <http://www.stat.washington.edu/thompson/Genepi/MORGAN/Morgan.shtml>

### Note

The input data is required to be sorted so that parents precede their children

### Author(s)

Morgan development team, Jing Hua Zhao

### See Also

[gif](#)

**Examples**

```
## Not run:
# Werner syndrome pedigree
werner<-c(
  1, 0, 0, 1,
  2, 0, 0, 2,
  3, 0, 0, 2,
  4, 1, 2, 1,
  5, 0, 0, 1,
  6, 1, 2, 2,
  7, 1, 2, 2,
  8, 0, 0, 1,
  9, 4, 3, 2,
  10, 5, 6, 1,
  11, 5, 6, 2,
  12, 8, 7, 1,
  13,10, 9, 2,
  14,12, 11, 1,
  15,14, 13, 1)
werner<-t(matrix(werner,nrow=4))
kin.morgan(werner[,1:3])

## End(Not run)
```

klem

*Haplotype frequency estimation based on a genotype table of two multiallelic markers*

**Description**

Haplotype frequency estimation using expectation-maximization algorithm based on a table of genotypes of two multiallelic markers.

**Usage**

```
klem(obs, k=2, l=2)
```

**Arguments**

obs	a table of genotype counts
k	number of alleles at marker 1
l	number of alleles at marker 2

**Details**

The dimension of the genotype table should be  $k*(k+1)/2 \times l*(l+1)/2$ .

Modified from 2ld.c.

**Value**

The returned value is a list containing:

h	haplotype Frequencies
l0	log-likelihood under linkage equilibrium
l1	log-likelihood under linkage disequilibrium

**Author(s)**

Jing Hua Zhao

**See Also**

[genecounting](#)

**Examples**

```
## Not run:
# an example with known genotype counts
z <- klem(obs=1:9)
# an example with imputed genotypes at SH2B1
cwd <- getwd()
cs.dir <- file.path(.path.package("gap"), "doc", "klem")
setwd(cs.dir)
dir()
source("SH2B1.R", echo=TRUE)
setwd(cwd)

## End(Not run)
```

---

LD22

*LD statistics for two diallelic markers*

---

**Description**

LD statistics for two SNPs.

It is possible to perform permutation test of  $r^2$  by re-ordering the genotype through R's sample function, obtaining the haplotype frequencies by [gc.em](#) or [genecounting](#), supplying the estimated haplotype frequencies to the current function and record x2, and comparing the observed x2 and that from the replicates.

**Usage**

LD22(h, n)

**Arguments**

h	a vector of haplotype frequencies
n	number of haplotypes

**Value**

The returned value is a list containing:

h	the original haplotype frequency vector
n	the number of haplotypes
D	the linkage disequilibrium parameter
VarD	the variance of D
Dmax	the maximum of D
VarDmax	the variance of Dmax
Dprime	the scaled disequilibrium parameter
VarDprime	the variance of Dprime
x2	the Chi-squared statistic
lor	the log(OR) statistic
vlor	the var[log(OR)] statistic

**References**

Zabetian CP, Buxbaum SG, Elston RC, Kohnke MD, Anderson GM, Gelernter J, Cubells JF. The structure of linkage disequilibrium at the DBH locus strongly influences the magnitude of association between diallelic markers and plasma dopamine beta-hydroxylase activity *Am J Hum Genet* 72: 1389-1400

Zapata C, Alvarez G, Carollo C (1997) Approximate variance of the standardized measure of genetic disequilibrium  $D'$ . *Am. J. Hum. Genet.* 61:771-774

**Note**

extracted from 2ld.c

**Author(s)**

Jing Hua Zhao

**See Also**

[LDk1](#)

**Examples**

```
## Not run:
h <- c(0.442356,0.291532,0.245794,0.020319)
n <- 481*2
t <- LD22(h,n)
t

## End(Not run)
```

LDk1

*LD statistics for two multiallelic markers***Description**

LD statistics for two multiallelic loci. For two diallelic makers, the familiar  $r^2$  has standard error  $seX2$ .

**Usage**

```
LDk1(n1=2,n2=2,h,n,optrho=2,verbose=FALSE)
```

**Arguments**

n1	number of alleles at marker 1
n2	number of alleles at marker 2
h	a vector of haplotype frequencies
n	number of haplotypes
optrho	type of contingency table association, 0=Pearson, 1=Tschuprow, 2=Cramer (default)
verbose	detailed output of individual statistics

**Value**

The returned value is a list containing:

n1	the number of alleles at marker 1
n2	the number of alleles at marker 2
h	the haplotype frequency vector
n	the number of haplotypes
Dp	D'
VarDp	variance of D'
Dijtable	table of $D_{ij}$
VarDijtable	table of variances for $D_{ij}$
Dmaxtable	table of $D_{max}$

Dijtable	table of Dij'
VarDijtable	table of variances for Dij'
X2table	table of Chi-squares (based on Dij)
ptable	table of p values
x2	the Chi-squared statistic
seX2	the standard error of x2/n
rho	the measure of association
seR	the standard error of rho
optrho	the method for calculating rho
klinfo	the Kullback-Leibler information

## References

- Bishop YMM, Fienberg SE, Holland PW (1975) Discrete Multivariate Analysis – Theory and Practice, The MIT press
- Cramer H (1946) Mathematical Methods of Statistics. Princeton Univ. Press
- Zapata C, Carollo C, Rodriquez S (2001) Sampling variance and distribution of the D' measure of overall gametic disequilibrium between multiallelic loci. Ann. Hum. Genet. 65: 395-406
- Zhao, JH (2004). 2LD, GENECOUNTING and HAP: Computer programs for linkage disequilibrium analysis. Bioinformatics 20:1325-1326

## Note

adapted from 2ld.c

## Author(s)

Jing Hua Zhao

## See Also

[LD22](#)

## Examples

```
## Not run:
# two examples in the C program 2LD:
# two SNPs as in 2by2.dat
# this can be compared with output from LD22

h <- c(0.442356,0.291532,0.245794,0.020319)
n <- 481*2
t <- LDkl(2,2,h,n)
t

# two multiallelic markers as in kbyl.dat
# the two-locus haplotype vector is in file "kbyl.dat"
```

```

filespec <- file.path(.path.package("gap"), "tests/kbyl.dat")
h <- scan(filespec, skip=1)
t <- LDkl(9,5,h,213*2, verbose=TRUE)

## End(Not run)

```

---

lukas

*An example pedigree*


---

### Description

A multi-generational pedigree containing individual, father, mother IDs and sex.

### Usage

```
data(lukas)
```

### Format

An example pedigree

### Source

Lukas Keller

---

makeped

*A function to prepare pedigrees in post-MAKEPED format*


---

### Description

Many computer programs for genetic data analysis requires pedigree data to be in the so-called "post-MAKEPED" format. This function performs this translation and allows for some inconsistencies to be detected.

The first four columns of the input file contains the following information:

pedigree ID, individual ID, father's ID, mother's ID, sex

Either father's or mother's id is set to 0 for founders, i.e. individuals with no parents. Numeric coding for sex is 0=unknown, 1=male, 2=female. These can be followed by satellite information such as disease phenotype and marker information.

The output file has extra information extracted from data above.

### Usage

```

makeped(pifile="pedfile.pre", pofile="pedfile.ped", auto.select=1,
        with.loop=0, loop.file=NA, auto.proband=1, proband.file=NA)

```

**Arguments**

<code>pifile</code>	input filename
<code>pofile</code>	output filename
<code>auto.select</code>	no loops in pedigrees and probands are selected automatically? 0=no, 1=yes
<code>with.loop</code>	input data with loops? 0=no, 1=yes
<code>loop.file</code>	filename containing pedigree id and an individual id for each loop, set if <code>with.loop=1</code>
<code>auto.proband</code>	probands are selected automatically? 0=no, 1=yes
<code>proband.file</code>	filename containing pedigree id and proband id, set if <code>auto.proband=0</code> (not implemented)

**Details**

Before invoking `makeped`, input file, loop file and proband file have to be prepared.

By default, `auto.select=1`, so translation proceeds without considering loops and proband statuses. If there are loops in the pedigrees, then set `auto.select=0`, `with.loop=1`, `loop.file="filespec"`.

There may be several versions of `makeped` available, but their differences with this port should be minor.

**Value**

All output will be written in `pofile`

**Note**

adapted from `makeped.c` by W Li and others

**Source**

<http://linkage.rockefeller.edu>

**Examples**

```
cwd <- getwd()
cs.dir <- file.path(.path.package("gap"), "tests")
setwd(cs.dir)
dir()
makeped("ped7.pre", "ped7.ped", 0, 1, "ped7.loop")
setwd(cwd)
```

---

mao

*A study of Parkinson's disease and MAO gene*

---

### Description

The markers are both with actual allele sizes and allele numbers. The dataset is distributed with the GENECOUNTING version 2.0 illustrating gene counting method involving chromosome X. A total of 183 patients and 157 controls (150 males, 190 females) were available, together with five markers in MAOA (monoamine oxidase A) region with alleles 12, 9, 6, 5, 3, and the first three markers were genotyped in all individuals while the fourth and fifth were genotyped for 294 and 304 individuals.

### Usage

```
data(mao)
```

### Format

A data frame

### Source

Dr Helen Latsoudis of Institute of Psychiatry, KCL

### References

Zhao JH (2004). 2LD, GENECOUNTING and HAP: computer programs for linkage disequilibrium analysis. *Bioinformatics* 20:1325-1326

---

masize

*Sample size calculation for mediation analysis*

---

### Description

The function computes sample size for regression problems where the goal is to assess mediation of the effects of a primary predictor by an intermediate variable or mediator.

Mediation has been thought of in terms of the proportion of effect explained, or the relative attenuation of  $b_1$ , the coefficient for the primary predictor  $X_1$ , when the mediator,  $X_2$ , is added to the model. The goal is to show that  $b_1^*$ , the coefficient for  $X_1$  in the reduced model (i.e., the model with only  $X_1$ , differs from  $b_1$ , its coefficient in the full model (i.e., the model with both  $X_1$  and the mediator  $X_2$ ). If  $X_1$  and  $X_2$  are correlated, then showing that  $b_2$ , the coefficient for  $X_2$ , differs from zero is equivalent to showing  $b_1^*$  differs from  $b_1$ . Thus the problem reduces to detecting an effect of  $X_2$ , controlling for  $X_1$ . In short, it amounts to the more familiar problem of inflating sample size to account for loss of precision due to adjustment for  $X_1$ .

The approach here is to approximate the expected information matrix from the regression model including both X1 and X2, to obtain the expected standard error of the estimate of b2, evaluated at the MLE. The sample size follows from comparing the Wald test statistic (i.e., the ratio of the estimate of b2 to its SE) to the standard normal distribution, with the expected value of the numerator and denominator of the statistic computed under the alternative hypothesis. This reflects the Wald test for the statistical significance of a coefficient implemented in most regression packages.

The function provides methods to calculate sample sizes for the mediation problem for linear, logistic, Poisson, and Cox regression models in four cases for each model:

CpCm	continuous primary predictor, continuous mediator
BpCm	binary primary predictor, continuous mediator
CpBm	continuous primary predictor, binary mediator
BpBm	binary primary predictor, binary mediator

The function is also generally applicable to the analogous problem of calculating sample size adequate to detect the effect of a primary predictor in the presence of confounding. Simply treat X2 as the primary predictor and consider X1 the confounder.

### Usage

```
masize(model,opts,alpha=0.025,gamma=0.2)
```

### Arguments

model	"lineari", "logisticj", "poissonk", "cox1", where i,j,k,l range from 1 to 4,5,9,9, respectively.
opts	A list specific to the model
b1	regression coefficient for the primary predictor X1
b2	regression coefficient for the mediator X2
rho	correlation between X1 and X2
sdx1, sdx2	standard deviations (SDs) of X1 and X2
f1, f2	prevalence of binary X1 and X2
sdy	residual SD of the outcome for the linear model
p	marginal prevalence of the binary outcome in the logistic model
m	marginal mean of the count outcome in a Poisson model
f	proportion of uncensored observations for the Cox model
fc	proportion of observations censored early
alpha	one-sided type-I error rate
gamma	type-II error rate
ns	number of observations to be simulated
seed	random number seed

For linear model, the arguments are b2, rho, sdx2, sdy, alpha, and gamma. For cases CpBm and BpBm, set  $sdx2 = \sqrt{f2(1 - f2)}$ . Three alternative functions are included for the linear model. These functions make it possible to supply other combinations of input parameters affecting mediation:

- b1\* coefficient for the primary predictor  
in the reduced model excluding the mediator (b1 star)
- b1 coefficient for the primary predictor  
in the full model including the mediator
- PTE proportion of the effect of the primary predictor  
explained by the mediator, defined as  $(b1*-b1)/b1*$

These alternative functions for the linear model require specification of an extra parameter, but are provided for convenience, along with two utility files for computing PTE and b1\* from the other parameters. The required arguments are explained in comments within the R code.

- alpha Type-I error rate, one-sided
- gamma Type-II error rate

## Details

For linear model, a single function, `linear`, implements the analytic solution for all four cases, based on Hsieh et al., is to inflate sample size by a variance inflation factor,  $1/(1 - rho^2)$ , where rho is the correlation of X1 and X2. This also turns out to be the analytic solution in cases CpCm and BpCm for the Poisson model, and underlies approximate solutions for the logistic and Cox models. An analytic solution is also given for cases CpBm and BpBm for the Poisson model. Since analytic solutions are not available for the logistic and Cox models, a simulation approach is used to obtain the expected information matrix instead.

For logistic model, the approximate solution due to Hsieh is implemented in the function `logistic.approx`, and can be used for all four cases. Arguments are `p`, `b2`, `rho`, `sdX2`, `alpha`, and `gamma`. For a binary mediator with prevalence `f2`, `sdX2` should be reset to  $\sqrt{f2(1 - f2)}$ . Simulating the information matrix of the logistic model provides somewhat more accurate sample size estimates than the Hsieh approximation. The functions for cases CpCm, BpCm, CpBm, and BpBm are respectively `logistic.ccs`, `logistic.bcs`, `logistic.cbs`, and `logistic.bbs`, as for the Poisson and Cox models. Arguments for these functions include `p`, `b1`, `sdX1` or `f1`, `b2`, `sdX2` or `f2`, `rho`, `alpha`, `gamma`, and `ns`. As in other functions, `sdX1`, `sdX2`, `alpha`, and `gamma` are set to the defaults listed above. These four functions call two utility functions, `getb0` (to calculate the intercept parameter from the others) and `antilogit`, which are supplied.

For Poisson model, The function implementing the approximate solution based on the variance inflation factor is `poisson.approx`, and can be used for all four cases. Arguments are `EY` (the marginal mean of the Poisson outcome), `b2`, `sdX2`, `rho`, `alpha` and `gamma`, with `sdX2`, `alpha` and `gamma` set to the usual defaults; use `sdX2 = \sqrt{f2(1 - f2)}` for a binary mediator with prevalence `f2` (cases CpBm and BpBm). For cases CpCm and BpCm (continuous mediators), the approximate formula is also the analytic solution. For these cases, we supply redundant functions `poisson.cc` and `poisson.bc`, with the same arguments and defaults as for `poisson.approx` (it's the same function). For the two cases with binary mediators, the functions are `poisson.cb` and `poisson.bb`. In addition to `m`, `b2`, `f2`, `rho`, `alpha`, and `gamma`, `b1` and `sdX1` or `f1` must be specified. Defaults are as usual. Functions using simulation for the Poisson model are available: `poisson.ccs`, `poisson.bcs`, `poisson.cbs`, and `poisson.bbs`. As in the logistic case, these require arguments `b1` and `sdX1` or `f1`. For this case, however, the analytic functions are faster, avoid simulation error, and should be used. We include these functions as templates that could be adapted to other joint predictor distributions.

For Cox model, the function implementing the approximate solution, using the variance inflation factor and derived by Schmoor et al., is `cox.approx`, and can be used for all four cases. Arguments are `b2`, `sdx2`, `rho`, `alpha`, `gamma`, and `f`. For binary X2 set  $sdx2 = \sqrt{f^2(1 - f^2)}$ . The approximation works very well for cases CpCm and BpCm (continuous mediators), but is a bit less accurate for cases CpBm and BpBm (binary mediators). We get some improvement for those cases using the simulation approach. This approach is implemented for all four, as functions `cox.ccs`, `cox.bcs`, `cox.cbs`, and `cox.bbs`. Arguments are `b1`, `sdx1` or `f1`, `b2`, `sdx2` or `f2`, `rho`, `alpha`, `gamma`, `f`, and `ns`, with defaults as described above. Slight variants of these functions, `cox.ccs2`, `cox.bcs2`, `cox.cbs2`, and `cox.bbs2`, make it possible to allow for early censoring of a fraction `fc` of observations; but in our experience this has virtually no effect, even with values of `fc` of 0.5. The default for `fc` is 0.

A summary of the arguments is as follows, noting that additional parameter `seed` can be supplied for simulation-based method.

model	arguments	description
linear1	b2, rho, sdx2, sdy	linear
linear2	b1star, PTE, rho, sdx1, sdy	lineara
linear3	b1star, b2, PTE, sdx1, sdx2, sdy	linearb
linear4	b1star, b1, b2, sdx1, sdx2, sdy	linearc
logistic1	p, b2, rho, sdx2	logistic.approx
logistic2	p, b1, b2, rho, sdx1, sdx2, ns	logistic.ccs
logistic3	p, b1, f1, b2, rho, sdx2, ns	logistic.bcs
logistic4	p, b1, b2, f2, rho, sdx1, ns	logistic.cbs
logistic5	p, b1, f1, b2, f2, rho, ns	logistic.bbs
poisson1	m, b2, rho, sdx2	poisson.approx
poisson2	m, b2, rho, sdx2	poisson.cc
poisson3	m, b2, rho, sdx2	poisson.bc
poisson4	m, b1, b2, f2, rho, sdx1	poisson.cb
poisson5	m, b1, f1, b2, f2, rho	poisson.bb
poisson6	m, b1, b2, rho, sdx1, sdx2, ns	poisson.ccs
poisson7	m, b1, f1, b2, rho, sdx2, ns	poisson.bcs
poisson8	m, b1, b2, f2, rho, sdx1, ns	poisson.cbs
poisson9	m, b1, f1, b2, f2, rho, ns	poisson.bbs
cox1	b2, rho, f, sdx2	cox.approx
cox2	b1, b2, rho, f, sdx1, sdx2, ns	cox.ccs
cox3	b1, f1, b2, rho, f, sdx2, ns	cox.bcs
cox4	b1, b2, f2, rho, f, sdx1, ns	cox.cbs
cox5	b1, f1, b2, f2, rho, f, ns	cox.bbs
cox6	b1, b2, rho, f, fc, sdx1, sdx2, ns	cox.ccs2
cox7	b1, f1, b2, rho, f, fc, sdx2, ns	cox.bcs2
cox8	b1, b2, f2, rho, f, fc, sdx1, ns	cox.cbs2
cox9	b1, f1, b2, f2, rho, f, fc, ns	cox.bbs2

**Value**

A short description of model (desc, b=binary, c=continuous, s=simulation) and sample size (n). In the case of Cox model, number of events (d) is also indicated.

**References**

Hsieh FY, Bloch DA, Larsen MD. A simple method of sample size calculation for linear and logistic regression. *Stat Med* 1998; 17:1623-34.

Schmoor C, Sauerbrer W, Schumacher M. Sample size considerations for the evaluation of prognostic factors in survival analysis. *Stat Med* 2000; 19:441-52.

Vittinghoff E, Sen S, McCulloch CE. Sample size calculations for evaluating mediation. *Stat Med* 2009; 28:541-57.

**Source**

<http://www.epibiostat.ucsf.edu/biostat/mediation/>

**See Also**

[ab](#)

**Examples**

```
## Not run:
## linear model
# CpCm
opts <- list(b2=0.5, rho=0.3, sdx2=1, sdy=1)
masize("linear1",opts)
# BpBm
opts <- list(b2=0.75, rho=0.3, f2=0.25, sdx2=sqrt(0.25*0.75), sdy=3)
masize("linear1",opts,gamma=0.1)

## logistic model
# CpBm
opts <- list(p=0.25, b2=log(0.5), rho=0.5, sdx2=0.5)
masize("logistic1",opts)
opts <- list(p=0.25, b1=log(1.5), sdx1=1, b2=log(0.5), f2=0.5, rho=0.5, ns=10000, seed=1234)
masize("logistic4",opts)
opts <- list(p=0.25, b1=log(1.5), sdx1=1, b2=log(0.5), f2=0.5, rho=0.5, ns=10000, seed=1234)
masize("logistic4",opts)
opts <- list(p=0.25, b1=log(1.5), sdx1=4.5, b2=log(0.5), f2=0.5, rho=0.5, ns=50000, seed=1234)
masize("logistic4",opts)

## Poisson model
# BpBm
opts <- list(m=0.5, b2=log(1.25), rho=0.3, sdx2=sqrt(0.25*0.75))
masize("poisson1",opts)
opts <- list(m=0.5, b1=log(1.4), f1=0.25, b2=log(1.25), f2=0.25, rho=0.3)
masize("poisson5",opts)
opts <- c(opts,ns=10000, seed=1234)
```

```

masize("poisson9",opts)

## Cox model
# BpBm
opts <- list(b2=log(1.5), rho=0.45, f=0.2, sdx2=sqrt(0.25*0.75))
masize("cox1",opts)
opts <- list(b1=log(2), f1=0.5, b2=log(1.5), f2=0.25, rho=0.45, f=0.2, seed=1234)
masize("cox5",c(opts, ns=10000))
masize("cox5",c(opts, ns=50000))

## End(Not run)

```

---

metap

*Meta-analysis of p values*


---

### Description

This function is the method of meta-analysis used in the Genetic Investigation of ANThropometric Traits (GIANT) consortium, which is based on normal approximation of p values and weighted by sample sizes from individual studies.

### Usage

```
metap(data, N, verbose="Y", prefixp="p", prefixn="n")
```

### Arguments

data	data frame
N	Number of studies
verbose	Control of detailed output
prefixp	Prefix of p value, with default value "p"
prefixn	Preifx of sample size, with default value "n"

### Value

x2	Fisher's chi-squared statistics
p	P values from Fisher's method according to chi-squared distribution with 2*N degree(s) of freedom
z	Combined z value
p1	One-sided p value
p2	Two-sided p value

### Author(s)

Jing Hua Zhao

**See Also**[metareg](#)**Examples**

```
## Not run:
s <- data.frame(p1=0.1^rep(8:2,each=7,times=1),n1=rep(32000,49),p2=0.1^rep(8:2,each=1,times=7),n2=rep(8000,49))
cbind(s,metap(s,2))

# Speliotes, Elizabeth K., M.D. [ESPELIOTES@PARTNERS.ORG]
# 22-2-2008 MRC-Epid JHZ

np <- 7
p <- 0.1^((np+1):2)
z <- qnorm(1-p/2)
n <- c(32000,8000)
n1 <- n[1]

s1 <- s2 <- vector("numeric")

for (i in 1:np)
{
  a <- z[i]
  for (j in 1:np)
  {
    b <- z[j]
    metaz1 <- (sqrt(n1)*a+sqrt(n[1])*b)/sqrt(n1+n[1])
    metap1 <- pnorm(-abs(metaz1))
    metaz2 <- (sqrt(n1)*a+sqrt(n[2])*b)/sqrt(n1+n[2])
    metap2 <- pnorm(-abs(metaz2))
    k <- (i-1)*np+j
    cat(k, "\t", p[i], "\t", p[j], "\t", metap1, metaz1, "\t", metap2, metaz2, "\n")
    s1[k] <- metap1
    s2[k] <- metap2
  }
}

q <- -log10(sort(p,decreasing=TRUE))
t1 <- matrix(-log10(sort(s1,decreasing=TRUE)),np,np)
t2 <- matrix(-log10(sort(s2,decreasing=TRUE)),np,np)

par(mfrow=c(1,2),bg="white",mar=c(4.2,3.8,0.2,0.2))
persp(q,q,t1)
persp(q,q,t2)

## End(Not run)
```

**Description**

Given  $k = n$  studies with  $b_1, \dots, b_N$  being  $\beta$ 's and  $se_1, \dots, se_N$  standard errors from regression, the fixed effects model uses inverse variance weighting such that  $w_1 = 1/se_1^2, \dots, w_N = 1/se_N^2$  and the combined  $\beta$  as the weighted average,  $\beta_f = (b_1 * w_1 + \dots + b_N * w_N)/w$ , with  $w = w_1 + \dots + w_N$  being the total weight, the se for this estimate is  $se_f = \sqrt{1/w}$ . A normal z-statistic is obtained as  $z_f = \beta_f/se_f$ , and the corresponding p value  $p_f = 2 * pnorm(-abs(z_f))$ . For the random effects model, denote  $q_w = w_1 * (b_1 - \beta_f)^2 + \dots + w_N * (b_N - \beta_f)^2$  and  $dl = \max(0, (q_w - (k - 1))/(w - (w_1^2 + \dots + w_N^2)/w))$ , corrected weights are obtained such that  $w_{1c} = 1/(1/w_1 + dl), \dots, w_{Nc} = 1/(1/w_N + dl)$ , totaling  $w_c = w_{1c} + \dots + w_{Nc}$ . The combined  $\beta$  and se are then  $\beta_r = (b_1 * w_{1c} + \dots + b_N * w_{Nc})/w_c$  and  $se_r = \sqrt{1/w_c}$ , leading to a z-statistic  $z_r = \beta_r/se_r$  and a p-value  $p_r = 2 * pnorm(-abs(z_r))$ . Moreover, a p-value testing for heterogeneity is  $p_{heter} = pchisq(q_w, k - 1, lower.tail = FALSE)$ .

**Usage**

```
metareg(data, N, verbose="Y", prefixb="b", prefixse="se")
```

**Arguments**

data	Data frame to be used
N	Number of studies
verbose	A control for screen output
prefixb	Prefix of estimate; default value is "b"
prefixse	Prefix of standard error; default value is "se" The function accepts a wide format data with estimates as $b_1, \dots, b_N$ and standard errors as $se_1, \dots, se_N$ . More generally, they can be specified by prefixes in the function argument.

**Value**

The returned value is a data frame with the following variables:

p_f	P value (fixed effects model)
p_r	P value (random effects model)
beta_f	regression coefficient
beta_r	regression coefficient
se_f	standard error
se_r	standard error
z_f	z value
z_r	z value
p_heter	heterogeneity test p value
i2	$I^2$ statistic
k	No of tests used
eps	smallest double-precision number

**References**

JPT Higgins, SG Thompson, JJ Deeks, DG Altman. Measuring inconsistency in meta-analyses. *BMJ* 327:557-60

**Note**

Adapted from a SAS macro

**Author(s)**

Shengxu Li, Jing Hua Zhao

**Examples**

```
## Not run:
abc <- data.frame(chromosome=1,rsn='abcd',startpos=1234,b1=1,se1=2,p1=0.1,b2=2,se2=6,p2=0,b3=3,se3=8,p3=0.5)
metareg(abc,3)
abc2 <- data.frame(b1=c(1,2),se1=c(2,4),b2=c(2,3),se2=c(4,6),b3=c(3,4),se3=c(6,8))
print(metareg(abc2,3))

## End(Not run)
```

---

mhtdata

*An example data for Manhattan plot*

---

**Description**

This example contains p values for a list of SNPs whose information regarding chromosome, position and reference sequence as with gene annotation is obtained separately.

**Usage**

```
data(mhtdata)
```

**Format**

A data frame

**Source**

Dr Tuomas Kilpelainen at the MRC Epidemiology Unit

**References**

None

mhtplot

*Manhattan plot of p values***Description**

To generate Manhattan plot of genomewide significance (p values). It could also be used for any random variable that is uniformly distributed. By default, a log10-transformation is applied. Note that with real chromosomal positions, it is also appropriate to plot and some but not all chromosomes.

It is possible to specify options such as xlab and ylim when the plot is requested for data in other context.

**Usage**

```
mhtplot(data, control=mht.control(), hcontrol=hmht.control(), ...)
```

**Arguments**

data	a data frame with three columns representing chromosome, position and p values
control	A control function named <code>mht.control()</code> with the following arguments, <ol style="list-style-type: none"> <li>1. <code>type</code>. a flag with value "p" or "l" indicating if points or lines are to be drawn.</li> <li>2. <code>usepos</code>. a flag to use real chromosomal positions as composed to ordinal positions with default value FALSE</li> <li>3. <code>logscale</code>. a flag to indicate if p value is to be log-transformed with default value TRUE</li> <li>4. <code>base</code>. the base of the logarithm with default value 10</li> <li>5. <code>cutoffs</code>. the cut-offs where horizontal line(s) are drawn with default value NULL</li> <li>6. <code>colors</code>. the color for different chromosome(s), and random if unspecified with default values NULL</li> <li>7. <code>labels</code>. labels for the ticks on x-axis with default value NULL</li> <li>8. <code>srt</code>. degree to which labels are rotated with default value of 45</li> <li>9. <code>gap</code>. gap between chromosomes with default value NULL</li> <li>10. <code>cex</code>. cex for the data points</li> <li>11. <code>yline</code>. Margin line position</li> <li>12. <code>xline</code>. Margin line position</li> </ol>
hcontrol	A control function named <code>hmht.control()</code> with the following arguments, <ol style="list-style-type: none"> <li>1. <code>data</code>. chunk of data to be highlighted with default value NULL</li> <li>2. <code>colors</code>. colors for annotated genes</li> <li>3. <code>yoffset</code>. offset above the data point showing most significant p value with default value 0.5</li> <li>4. <code>cex</code>. shrinkage factor for data points with default value 1.5</li> <li>5. <code>boxed</code>. if the label for the highlighted region with default value FALSE</li> </ol>
...	other options in compatible with the R plot function

**Value**

The plot is shown on or saved to the appropriate device.

**Author(s)**

Jing Hua Zhao

**See Also**

[qqunif](#)

**Examples**

```
## Not run:
# foo example
test <- matrix(c(1,1,4,1,1,6,1,10,3,2,1,5,2,2,6,2,4,8),byrow=TRUE,6)
mhtplot(test)
mhtplot(test,mht.control(logscale=FALSE))

# fake example with Affy500k data
affy <-c(40220, 41400, 33801, 32334, 32056, 31470, 25835, 27457, 22864, 28501, 26273,
        24954, 19188, 15721, 14356, 15309, 11281, 14881, 6399, 12400, 7125, 6207)
CM <- cumsum(affy)
n.markers <- sum(affy)
n.chr <- length(affy)
test <- data.frame(chr=rep(1:n.chr,affy),pos=1:n.markers,p=runif(n.markers))

# to reduce size of the plot
# bitmap("mhtplot.bmp",res=72*5)
oldpar <- par()
par(cex=0.6)
colors <- rep(c("blue","green"),11)
# other colors, e.g.
# colors <- c("red","blue","green","cyan","yellow","gray","magenta","red","blue","green",
#            "cyan","yellow","gray","magenta","red","blue","green","cyan","yellow","gray","magenta","red")
mhtplot(test,control=mht.control(colors=colors),pch=19,bg=colors)
title("A simulated example according to EPIC-Norfolk QCed SNPs")
# dev.off()
par(oldpar)

mhtplot(test,control=mht.control(usepos=TRUE,colors=colors,gap=10000),pch=19,bg=colors)
title("Real positions with a gap of 10000 bp between chromosomes")
box()

png("manhattan.png",height=3600,width=6000,res=600)
opar <- par()
par(cex=0.4)
ops <- mht.control(colors=rep(c("lightgray","lightblue"),11),srt=0,yline=2.5,xline=2)
mhtplot(mhtdata[,c("chr","pos","p")],ops,xlab="",ylab="")
axis(2,at=1:16)
title("An adaptable plot as .png")
par(opar)
```

```

dev.off()

data <- with(mhtdata,cbind(chr,pos,p))
glist <- c("IRS1","SPRY2","FTO","GRIK3","SNED1","HTR1A","MARCH3","WISP3","PPP1R3B",
          "RP1L1","FDFT1","SLC39A14","GFRA1","MC4R")
hdata <- subset(mhtdata,gene%in%glist)[c("chr","pos","p","gene")]
color <- rep(c("lightgray","gray"),11)
glen <- length(glist)
hcolor <- rep("red",glen)
par(las=2, xpd=TRUE, cex.axis=1.8, cex=0.4)
ops <- mht.control(colors=color,yline=1.5,xline=3,labels=paste("chr",1:22,sep=""),srt=270)
hops <- hmht.control(data=hdata,colors=hcolor)
mhtplot(data,ops,hops,pch=19)
axis(2,pos=2,at=1:16)
title("Manhattan plot with genes highlighted",cex.main=1.8)

mhtplot(data,mht.control(cutoffs=c(4,6,8,16)),pch=19)
title("Another plain Manhattan plot")

## End(Not run)

```

---

mia

*multiple imputation analysis for hap*


---

## Description

This command reads outputs from hap session that uses multiple imputations, i.e. -mi# option. To simplify matters it assumes -ss option is specified together with -mi option there.

This is a very naive version of MIANALYZE, but can produce results for PROC MIANALYZE of SAS

## Usage

```

mia(hapfile,assfile,miafile,so,ns,mi,allsnps,sas)

```

## Arguments

hapfile	hap haplotype output file name
assfile	hap assignment output file name
miafile	mia output file name
so	to generate results according to subject order
ns	do not sort in subject order
mi	number of multiple imputations used in hap
allsnps	all loci are SNPs
sas	produce SAS data step program

## Details

It simply extracts outputs from hap

## Value

The returned value is a list containing:

## References

Zhao JH and W Qian (2003) Association analysis of unrelated individuals using polymorphic genetic markers. RSS 2003, Hassalt, Belgium

Clayton DG (2001) SNP HAP. <http://www-gene.cimr.cam.ac.uk/clayton/software>

## Note

adapted from hap, in fact cline.c and cline.h are not used

## See Also

[hap](#)

## Examples

```
## Not run:
# 4 SNP example, to generate hap.out and assign.out alone
data(fsnps)
hap(id=fsnps[,1],data=fsnps[,3:10],nloci=4)

# to generate results of imputations
control <- hap.control(ss=1,mi=5)
hap(id=fsnps[,1],data=fsnps[,3:10],nloci=4,control=control)

# to extract information from the second run above
mia(so=1,ns=1,mi=5)
file.show("mia.out")

## commands to check out where the output files are as follows:
## Windows
# system("command.com")
## Unix
# system("csh")

## End(Not run)
```

---

`mtdt`*Transmission/disequilibrium test of a multiallelic marker*

---

**Description**

This function calculates transmission-disequilibrium statistics involving multiallelic marker. Inside the function are `tril` and `triu` used to obtain lower and upper triangular matrices.

**Usage**

```
mtdt(x, n.sim=0)
```

**Arguments**

<code>x</code>	the data table
<code>n.sim</code>	the number of simulations

**Value**

It returned list contains the following components:

<code>SE</code>	Spielman-Ewens Chi-square from the observed data
<code>ST</code>	Stuart or score Statistic from the observed data
<code>pSE</code>	the simulated p value
<code>sSE</code>	standard error of the simulated p value
<code>pST</code>	the simulated p value
<code>sST</code>	standard error of the simulated p value

**References**

Miller MB (1997) Genomic scanning and the transmission/disequilibrium test: analysis of error rates. *Genet. Epidemiol.* 14:851-856

Sham PC (1997) Transmission/disequilibrium tests for multiallelic loci. *Am. J. Hum. Genet.* 61:774-778

Spielman RS, Ewens WJ (1996) The TDT and other family-based tests for linkage disequilibrium and association. *Am. J. Hum. Genet.* 59:983-989

Zhao JH, Sham PC, Curtis D (1999) A program for the Monte Carlo evaluation of significance of the extended transmission/disequilibrium test. *Am. J. Hum. Genet.* 64:1484-1485

**Author(s)**

Mike Miller, Jing Hua Zhao

**See Also**

[bt](#)

**Examples**

```
## Not run:
# Copeman et al (1995) Nat Genet 9: 80-5

x <- matrix(c(0,0, 0, 2, 0,0, 0, 0, 0, 0, 0, 0, 0,
              0,0, 1, 3, 0,0, 0, 2, 3, 0, 0, 0,
              2,3,26,35, 7,0, 2,10,11, 3, 4, 1,
              2,3,22,26, 6,2, 4, 4,10, 2, 2, 0,
              0,1, 7,10, 2,0, 0, 2, 2, 1, 1, 0,
              0,0, 1, 4, 0,1, 0, 1, 0, 0, 0, 0,
              0,2, 5, 4, 1,1, 0, 0, 0, 2, 0, 0,
              0,0, 2, 6, 1,0, 2, 0, 2, 0, 0, 0,
              0,3, 6,19, 6,0, 0, 2, 5, 3, 0, 0,
              0,0, 3, 1, 1,0, 0, 0, 1, 0, 0, 0,
              0,0, 0, 2, 0,0, 0, 0, 0, 0, 0, 0,
              0,0, 1, 0, 0,0, 0, 0, 0, 0, 0, 0),nrow=12)

# See note to bt for the score test obtained by SAS

mtdt(x)

## End(Not run)
```

---

mtdt2	<i>Transmission/disequilibrium test of a multiallelic marker by Bradley-Terry model</i>
-------	---

---

**Description**

This function calculates transmission-disequilibrium statistics involving multiallelic marker according to Bradley-Terry model.

**Usage**

```
mtdt2(x, verbose=TRUE, n.sim=NULL, ...)
```

**Arguments**

x	the data table
verbose	To print out test statistics if TRUE
n.sim	Number of simulations
...	other options compatible with the BTm function

**Value**

It returned list contains the following components:

c2b	A data frame in four-column format showing transmitted vs nontransmitted counts
BTm	A fitted Bradley-Terry model object
X2	Allele-wise, genotype-wise and goodness-of-fit Chi-squared statistics
df	Degrees of freedom
p	P value
pn	Monte Carlo p values when n.sim is specified

**References**

- Firth, D. (2005). Bradley-terry models in R. *Journal of Statistical Software* 12(1):1-12
- Sham PC, Curtis D (1995) An extended transmission/disequilibrium test (TDT) for multi-allelic marker loci. *Ann. Hum. Genet.* 59:323-336
- Turner H, Firth D (2010) Bradley-Terry models in R: The BradleyTerry2 package. <http://cran.r-project.org/web/packages/BradleyTerry2/vignettes/BradleyTerry.pdf>.
- Zhao JH, Sham PC, Curtis D (1999) A program for the Monte Carlo evaluation of significance of the extended transmission/disequilibrium test. *Am. J. Hum. Genet.* 64:1484-1485

**Author(s)**

Jing Hua Zhao

**See Also**

[mtdt](#)

**Examples**

```
## Not run:
# Copeman et al (1995) Nat Genet 9: 80-5

x <- matrix(c(0,0, 0, 2, 0,0, 0, 0, 0, 0, 0, 0,
             0,0, 1, 3, 0,0, 0, 2, 3, 0, 0, 0,
             2,3,26,35, 7,0, 2,10,11, 3, 4, 1,
             2,3,22,26, 6,2, 4, 4,10, 2, 2, 0,
             0,1, 7,10, 2,0, 0, 2, 2, 1, 1, 0,
             0,0, 1, 4, 0,1, 0, 1, 0, 0, 0, 0,
             0,2, 5, 4, 1,1, 0, 0, 0, 2, 0, 0,
             0,0, 2, 6, 1,0, 2, 0, 2, 0, 0, 0,
             0,3, 6,19, 6,0, 0, 2, 5, 3, 0, 0,
             0,0, 3, 1, 1,0, 0, 0, 1, 0, 0, 0,
             0,0, 0, 2, 0,0, 0, 0, 0, 0, 0, 0,
             0,0, 1, 0, 0,0, 0, 0, 0, 0, 0, 0),nrow=12)

xx <- mtdt2(x,refcat="12")
```

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

---

```
muvar
```

*Means and variances under 1- and 2- locus (biallelic) QTL model*

---

### Description

Function `muvar()` gives means and variances under 1-locus and 2-locus QTL model (simple); in the latter case it gives results from different avenues. This function is included for experimental purpose and yet to be generalized.

### Usage

```
muvar(n.loci,y1,y12,p1,p2)
```

### Usage

```
muvar(n.loci=1,y1=c(0,1,1),p1=0.5)
muvar(n.loci=2,y12=c(1,1,1,1,1,0,0,0,0),p1=0.99,p2=0.9)
```

### Arguments

<code>n.loci</code>	number of loci, 1=single locus, 2=two loci
<code>y1</code>	the genotypic means of aa, Aa and AA
<code>p1</code>	the frequency of the lower allele, or the that for the first locus under a 2-locus model
<code>y12</code>	the genotypic means of aa, Aa and AA at the first locus and bb, Bb and BB at the second locus
<code>p2</code>	the frequency of the lower allele at the second locus

### Value

Currently it does not return any value except screen output; the results can be kept via R's `sink()` command or via modifying the C/R codes.

### References

Sham P (1998). *Statistics in Human Genetics*. Arnold

### Note

Adapted from an earlier C program written for the above book

### Author(s)

Jing Hua Zhao

**Examples**

```
## Not run:
# the default 1-locus model
muvar(n.loci=1,y1=c(0,1,1),p1=0.5)

# the default 2-locus model
muvar(n.loci=2,y12=c(1,1,1,1,1,0,0,0),p1=0.99,p2=0.9)

## End(Not run)
```

mvmeta

*Multivariate meta-analysis based on generalized least squares***Description**

This function accepts a data matrix of parameter estimates and their variance-covariance matrix from individual studies and obtain a generalized least squares (GLS) estimate and heterogeneity statistic.

For instance, this would be appropriate for combining linear correlation coefficients of single nucleotide polymorphisms (SNPs) for a given region.

**Usage**

```
mvmeta(b,V)
```

**Arguments**

b	the parameter estimates
V	the triangular variance-covariance matrix

**Value**

The returned value is a list containing:

d	the compact parameter estimates
Psi	the compact covariance-covariance matrix
X	the design matrix
beta	the pooled parameter estimates
cov.beta	the pooled variance-covariance matrix
X2	the Chi-squared statistic for heterogeneity
df	the degrees(s) of freedom
p	the p value

**References**

Hartung J, Knapp G, Sinha BK. Statistical Meta-analysis with Applications, Wiley 2008.

**Author(s)**

Jing Hua Zhao

**See Also**

[metareg](#)

**Examples**

```
## Not run:
# example 11.3 from Hartung et al.
#
b <- matrix(c(
  0.808, 1.308, 1.379, NA, NA,
  NA, 1.266, 1.828, 1.962, NA,
  NA, 1.835, NA, 2.568, NA,
  NA, 1.272, NA, NA, 2.038,
  1.171, 2.024, 2.423, 3.159, NA,
  0.681, NA, NA, NA, NA),ncol=5, byrow=TRUE)

psi1 <- psi2 <- psi3 <- psi4 <- psi5 <- psi6 <- matrix(0,5,5)

psi1[1,1] <- 0.0985
psi1[1,2] <- 0.0611
psi1[1,3] <- 0.0623
psi1[2,2] <- 0.1142
psi1[2,3] <- 0.0761
psi1[3,3] <- 0.1215

psi2[2,2] <- 0.0713
psi2[2,3] <- 0.0539
psi2[2,4] <- 0.0561
psi2[3,3] <- 0.0938
psi2[3,4] <- 0.0698
psi2[4,4] <- 0.0981

psi3[2,2] <- 0.1228
psi3[2,4] <- 0.1119
psi3[4,4] <- 0.1790

psi4[2,2] <- 0.0562
psi4[2,5] <- 0.0459
psi4[5,5] <- 0.0815

psi5[1,1] <- 0.0895
psi5[1,2] <- 0.0729
psi5[1,3] <- 0.0806
psi5[1,4] <- 0.0950
psi5[2,2] <- 0.1350
psi5[2,3] <- 0.1151
psi5[2,4] <- 0.1394
psi5[3,3] <- 0.1669
```

```

psi5[3,4] <- 0.1609
psi5[4,4] <- 0.2381

psi6[1,1] <- 0.0223

V <- rbind(psi1[upper.tri(psi1,diag=TRUE)],psi2[upper.tri(psi2,diag=TRUE)],
psi3[upper.tri(psi3,diag=TRUE)],psi4[upper.tri(psi4,diag=TRUE)],
psi5[upper.tri(psi5,diag=TRUE)],psi6[upper.tri(psi6,diag=TRUE)])

mvmeta(b,V)

## End(Not run)

```

---

nep499

*A study of Alzheimer's disease with eight SNPs and APOE*


---

### Description

This is a study of the neprilysin gene and sporadic Alzheimer's disease in Chinese. There are 257 cases and 242 controls, each with eight SNPs detecting through denaturing high-performance liquid chromatography (DHPLC).

### Usage

```
data(nep499)
```

### Format

A data frame

### Source

Shi J, Zhang S, Tang M, Ma C, Zhao J, Li T, Liu X, Sun Y, Guo Y, Han H, Ma Y, Zhao Z. Mutation Screening and Association Study of the Neprilysin Gene in Sporadic Alzheimer's Disease in Chinese Persons. *J Gerontol A: Bio Sci Med Sci* 60:301-306, 2005

---

pbsize

*Power for population-based association design*


---

### Description

This function implements Long et al. (1997) statistics for population-based association design. This is based on a contingency table test and accurate level of significance can be obtained by Fisher's exact test.

**Usage**

```
pbsize(kp, gamma=4.5, p=0.15, alpha=5e-8, beta=0.2)
```

**Arguments**

kp	population disease prevalence
gamma	genotype relative risk assuming multiplicative model
p	frequency of disease allele
alpha	type I error rate
beta	type II error rate

**Value**

The returned value is scalar containing the required sample size

**References**

Scott WK, Pericak-Vance MA, et al. (1997). Genetic analysis of complex diseases. *Science* 275: 1327.

Long AD, Grote MN, Langley CH (1997). Genetic analysis of complex traits. *Science* 275: 1328.

Rosner B (2000). *Fundamentals of Biostatistics*, 5th Edition, Duxbury.

Armitage P, Colton T (2005). *Encyclopedia of Biostatistics*, 2nd Edition, Wiley.

**Note**

extracted from rm.c

**Author(s)**

Jing Hua Zhao

**See Also**

[fbsize](#)

**Examples**

```
kp <- c(0.01,0.05,0.10,0.2)
models <- matrix(c(
  4.0, 0.01,
  4.0, 0.10,
  4.0, 0.50,
  4.0, 0.80,
  2.0, 0.01,
  2.0, 0.10,
  2.0, 0.50,
  2.0, 0.80,
  1.5, 0.01,
```

```

      1.5, 0.10,
      1.5, 0.50,
      1.5, 0.80), ncol=2, byrow=TRUE)
outfile <- "pbsize.txt"
cat("gamma", "p", "p1", "p5", "p10", "p20\n", sep="\t", file=outfile)
for(i in 1:dim(models)[1])
{
  g <- models[i,1]
  p <- models[i,2]
  n <- vector()
  for(k in kp) n <- c(n, ceiling(pbsize(k,g,p)))
  cat(models[i,1:2], n, sep="\t", file=outfile, append=TRUE)
  cat("\n", file=outfile, append=TRUE)
}
table5 <- read.table(outfile, header=TRUE, sep="\t")
unlink(outfile)

# Alzheimer's disease
g <- 4.5
p <- 0.15
alpha <- 5e-8
beta <- 0.2
z1alpha <- qnorm(1-alpha/2) # 5.45
z1beta <- qnorm(1-beta)
q <- 1-p
pi <- 0.065 # 0.07 and zbeta generate 163
k <- pi*(g*p+q)^2
s <- (1-pi*g^2)*p^2+(1-pi*g)*2*p*q+(1-pi)*q^2
# LGL formula
lambda <- pi*(g^2*p+q-(g*p+q)^2)/(1-pi*(g*p+q)^2)
# mine
lambda <- pi*p*q*(g-1)^2/(1-k)
n <- (z1alpha+z1beta)^2/lambda
cat("\nPopulation-based result: Kp =", k, "Kq =", s, "n =", ceiling(n), "\n")

```

---

pbsize2

*Power for case-control association design*

---

## Description

This is a revised version of [pbsize](#) which is appropriate for a case-control design under a range of disease models. Essentially, for given sample size(s), a proportion of which (fc) being cases, the function calculates power estimate for a given type I error (alpha), genotype relative risk (gamma), frequency of the risk allele (p), the prevalence of disease in the population (kp) and optionally a disease model (model). A major difference would be the consideration of case/control ascertainment in [pbsize](#).

Internally, the function obtains a baseline risk to make the disease model consistent with Kp as in [tscc](#) and should produce accurate power estimate. Note it provides power estimates for given sample size(s) only.

**Usage**

```
pbsize2(N,fc=0.5,alpha=0.05,gamma=4.5,p=0.15,kp=0.1,model="additive")
```

**Arguments**

N	The sample size
fc	The proportion of cases in the sample
alpha	Type I error rate
gamma	The genotype relative risk (GRR)
p	Frequency of the risk allele
kp	The prevalence of disease in the population
model	Disease model, i.e., "multiplicative", "additive", "dominant", "recessive", "overdominant"

**Value**

The returned value is the power for the specified design.

**Note**

Why is the comparison with `power.casectl` so bad?

**Author(s)**

Jing Hua Zhao

**See Also**

The design follows that of [pbsize](#).

**Examples**

```
## Not run:

# single calc
m <- c("multiplicative","recessive","dominant","additive","overdominant")
for(i in 1:5) print(pbsize2(N=50,alpha=5e-2,gamma=1.1,p=0.1,kp=0.1, model=m[i]))

# for a range of sample sizes
pbsize2(p=0.1, N=c(25,50,100,200,500), gamma=1.1, kp=.1, alpha=5e-2, model='r')

# create a power table
f <- function(p)
  pbsize2(p=p, N=seq(100,1000,by=100), gamma=1.1, kp=.1, alpha=5e-2, model='recessive')
m <- sapply( X=seq(0.1,0.9, by=0.1), f)
colnames(m) <- seq(0.1,0.9, by=0.1)
rownames(m) <- seq(100,1000,by=100)
print(round(m,2))

library(genetics)
```

```
m <- c("multiplicative","recessive","dominant","partialrecessive")
for(i in 1:4) print(power.casectrl(p=0.1, N=50, gamma=1.1, kp=.1, alpha=5e-2, minh=m[i]))
power.casectrl(p=0.1, N=c(25,50,100,200,500), gamma=1.1, kp=.1, alpha=5e-2, minh='r')
f <- function(p)
  power.casectrl(p=p, N=seq(100,1000,by=100), gamma=1.1, kp=.1, alpha=5e-2, minh='recessive')
m <- sapply( X=seq(0.1,0.9, by=0.1), f)
colnames(m) <- seq(0.1,0.9, by=0.1)
rownames(m) <- seq(100,1000,by=100)
print(round(m,2))

## End(Not run)
```

---

PD

*A study of Parkinson's disease and APOE, LRRK2, SNCA makers*

---

### **Description**

A study of Parkinson's disease and controls with APOE, LRRK2 markers rs10506151, rs10784486, rs1365763, rs1388598, rs1491938, rs1491941 and SNCA markers m770, int4 and SNCA. The column abc indicates if a subject is familial Parkinson's (+), sporadic (-), or controls (Control). Races involved are American Indians (AI), African American (B), and the rest are Caucasians. Diagnosis also included possible (POS), probable (PRO) and definite PDs. AON is the age at onset.

### **Usage**

data(PD)

### **Format**

A data frame

### **Source**

Prof Abbas Parsian at NIH

### **References**

Parsian et al. ASHG 2005, Toronto

pedtodot

*Converting pedigree(s) to dot file(s)***Description**

This function converts GAS or LINKAGE formatted pedigree(s) into .dot file for each pedigree to be used by dot in graphviz, which is a flexible package for graphics freely available from <http://www.graphviz.org>

Note that a single PostScript file is obtainable by specifying \*.dot to dot or neato.

```
dot -Tps <dot file> -o <ps file>
```

or

```
neato -Tps <dot file> -o <ps file>
```

However, to preserve the original order of pedigree(s) in the data, you can examine the examples at the end of this document.

Under Cygwin/Linux/Unix, the PostScript file can be converted to Portable Document Format (PDF) default to Acrobat.

```
ps2pdf <ps file>
```

Use ps2pdf12, ps2pdf13, or ps2pdf14 for appropriate versions of Acrobat according to information given on the headline of <ps file>.

**Usage**

```
pedtodot(pedfile,makeped=FALSE,sink=TRUE,page="B5",
         url="http://www.mrc-epid.cam.ac.uk/~jinghua.zhao/r-progs.htm",
         height=0.5,width=0.75,rotate=0,dir="none")
```

**Arguments**

pedfile	a pedigree file in GAS or LINKAGE format, note if individual's ID is character then it is necessary to specify as.is=T in the read.table command
makeped	a logical variable indicating if the pedigree file is post-makeped
sink	a logical variable indicating if .dot file(s) are created
page	a string indicating the page size, e.g, A4, A5, B5, Legal, Letter, Executive, "x,y", where x, y is the customized page size
url	Unified Resource Locator (URL) associated with the diagram(s)
height	the height of node(s)
width	the width of node(s)
rotate	if set to 90, the diagram is in landscape
dir	direction of edges, i.e., "none", "forward","back","both". This will be useful if the diagram is viewed by Ineato

## Details

We can extract the code below (or within pedtodot.Rd) to pedtodot and then use command:

```
sh pedtodot <pedigree file>
```

```
# Read a GAS or LINKAGE format pedigree, return a digraph in the dot language
# call dot to make pedigree drawing
#
AWK=/bin/gawk
DOTEXE=/usr/local/bin/dot
# cygwin
# AWK=/bin/gawk
# DOTEXE=c:/local/graphviz/bin/dot

for fil in $*
do
  for ped in `awk '!/^![#]/ {print $1}' $fil | sort -u`
  do
    echo "Pedigree $ped"
    $AWK -v ped=$ped '
BEGIN { shape["m"]="box,regular=1"
        shape["1"]="box,regular=1"
        shape["f"]="circle"
        shape["2"]="circle"
        shade["y"]="blue"
        shade["2"]="blue"
        shade["n"]="grey"
        shade["1"]="grey"
        shade["x"]="green"
        shade["0"]="green"
        }
!/^[!#]/ && $1==ped {
  sex[$2]=$5
  aff[$2]="x" ; if ($6 ~ /[012nyx]/) aff[$2]=$6
  if($3!="x" && $3!="0") {
    marriage[$3,$4]++
    child[$3,$4,marriage[$3,$4]]=$2
  }
}
END { print "digraph Ped_" ped " {"
      print "# page =\"8.2677165,11.692913\" ;"
      print "ratio =\"auto\" ;"
      print "mincross = 2.0 ;"
      print "label=\"Pedigree " ped "\" ;"
      print "rotate=90 ;"
      for(s in sex) {
        print "\" s \" [shape=" shape[sex[s]] " , " \
          " style=filled,color=" shade[aff[s]] " ] ;"
      }
}
```

```

for(m in marriage) {
  n=split(m,par,"\034")
  mating="\\" par[1] "x" par[2] "\"
  print mating "[shape=diamond,style=filled," \
    "label=\\"",height=.1,width=.1] ;"
  print "\" par[1] "\" -> " mating " [dir=none, weight=1] ;"
  print "\" par[2] "\" -> " mating " [dir=none, weight=1] ;"
  for(k=1;k<=marriage[par[1],par[2]];k++) {
    print mating " -> "\" child[par[1],par[2],k] "\" \
      " [dir=none, weight=2] ;"
  }
}
print "}"
}' $fil > $ped.dot
$DOTEXE -Tps $ped.dot -o $ped.ps
done
done
$DOTEXE -Tps *.dot -o *.ps

```

**Value**

For each pedigree, the function generates a .dot file to be used by dot. The collection of all pedigrees (\*.dot) can also be put together.

**Note**

This is based on the gawk script program pedtodot by David Duffy with minor changes

**Author(s)**

David Duffy, Jing Hua Zhao

**See Also**

package sem in CRAN and Rgraphviz in BioConductor <http://www.bioconductor.org>

**Examples**

```

## Not run:
# example as in R News and Bioinformatics (see also plot.pedigree in package kinship)
# it works from screen paste only
p1 <- scan(nlines=16,what=list(0,0,0,0,0,"",""))
1  2  3  2  2  7/7  7/10
2  0  0  1  1  -/-  -/-
3  0  0  2  2  7/9  3/10
4  2  3  2  2  7/9  3/7
5  2  3  2  1  7/7  7/10
6  2  3  1  1  7/7  7/10
7  2  3  2  1  7/7  7/10
8  0  0  1  1  -/-  -/-
9  8  4  1  1  7/9  3/10

```

```

10  0  0  2  1  -/-  -/-
11  2  10  2  1  7/7  7/7
12  2  10  2  2  6/7  7/7
13  0  0  1  1  -/-  -/-
14  13  11  1  1  7/8  7/8
15  0  0  1  1  -/-  -/-
16  15  12  2  1  6/6  7/7

p2 <- as.data.frame(p1)
names(p2) <-c("id","fid","mid","sex","aff","GABRB1","D4S1645")
p3 <- data.frame(pid=10081,p2)
attach(p3)
pedtodot(p3)
#
# Three examples of pedigree-drawing
# assuming pre-MakePed LINKAGE file in which IDs are characters
pre<-read.table("pheno.pre",as.is=TRUE)[,1:6]
pedtodot(pre)
dir()
# for post-MakePed LINKAGE file in which IDs are integers
ped <-read.table("pheno.ped")[,1:10]
pedtodot(ped,makeped=TRUE)
dir()
# for a single file with a list of pedigrees ordered data
sink("gaw14.dot")
pedtodot(ped,sink=FALSE)
sink()
file.show("gaw14.dot")
# more details
pedtodot(ped,sink=FALSE,page="B5",url="http://www.mrc-epid.cam.ac.uk/~jinghua.zhao/r-progs.htm")

# An example from Richard Mott and in the demo
filespec <- file.path(.path.package("gap"),"tests/ped.1.3.pre")
pre <- read.table(filespec,as.is=TRUE)
pre
pedtodot(pre,dir="forward")

## End(Not run)

```

**Description**

To calculate exact probability of familial clustering of disease

**Usage**

```
pfc(famdata,enum)
```

**Arguments**

famdata            collective information of sib size, number of affected sibs and their frequencies  
 enum                a switch taking value 1 if all possible tables are to be enumerated

**Value**

The returned value is a list containing (tailp, sump, nenum are only available if enum=1):

p                    the probability of familial clustering  
 stat                the deviances, chi-squares based on binomial and hypergeometric distributions,  
                       the degrees of freedom should take into account the number of marginals used  
 tailp                the exact statistical significance  
 sump                sum of the probabilities used for error checking  
 nenum                the total number of tables enumerated

**References**

Yu C, Zelterman D (2001) Exact inference for family disease clusters. *Commun Stat – Theory Meth* 30:2293-2305  
 Yu C, Zelterman D (2002) Statistical inference for familial disease clusters. *Biometrics* 58:481-491

**Note**

Adapted from family.for by Dani Zelterman, 25/7/03

**Author(s)**

Dani Zelterman, Jing Hua Zhao

**See Also**

[kin.morgan](#)

**Examples**

```
## Not run:
# IPF among 203 siblings of 100 COPD patients from Liang KY, SL Zeger, B Qaquish (1992)
# Multivariate regression analyses for categorical data (with discussion). J Roy Stat Soc
# B 54:3-40

# the degrees of freedom is 15
famtest<-c(
  1, 0, 36,
  1, 1, 12,
  2, 0, 15,
  2, 1, 7,
  2, 2, 1,
  3, 0, 5,
  3, 1, 7,
```

```

3, 2, 3,
3, 3, 2,
4, 0, 3,
4, 1, 3,
4, 2, 1,
6, 0, 1,
6, 2, 1,
6, 3, 1,
6, 4, 1,
6, 6, 1)
test<-t(matrix(famtest,nrow=3))
famp<-pfc(test)

## End(Not run)

```

pfc.sim

*Probability of familial clustering of disease***Description**

To calculate probability of familial clustering of disease using Monte Carlo simulation

**Usage**

```
pfc.sim(famdata,n.sim=1000000,n.loop=1)
```

**Arguments**

famdata	collective information of sib size, number of affected sibs and their frequencies
n.sim	number of simulations in a single Monte Carlo run
n.loop	total number of Monte Carlo runs

**Value**

The returned value is a list containing:

n.sim	a copy of the number of simulations in a single Monte Carlo run
n.loop	the total number of Monte Carlo runs
p	the observed p value
tailpl	accumulated probabilities at the lower tails
tailpu	simulated p values

**References**

Yu C and D Zelterman (2001) Exact inference for family disease clusters. *Commun Stat – Theory Meth* 30:2293-2305

**Note**

Adapted from runi.for from Change Yu, 5/6/4

**Author(s)**

Chang Yu, Dani Zelterman

**See Also**

[pfc](#)

**Examples**

```
## Not run:
# Li FP, Fraumeni JF Jr, Mulvihill JJ, Blattner WA, Dreyfus MG, Tucker MA, Miller RW
# A cancer family syndrome in twenty-four kindreds.
# Cancer Res. 1988 Sep 15;48(18):5358-62.

# family_size #_of_affected frequency

famtest<-c(
1, 0, 2,
1, 1, 0,
2, 0, 1,
2, 1, 4,
2, 2, 3,
3, 0, 0,
3, 1, 2,
3, 2, 1,
3, 3, 1,
4, 0, 0,
4, 1, 2,
5, 0, 0,
5, 1, 1,
6, 0, 0,
6, 1, 1,
7, 0, 0,
7, 1, 1,
8, 0, 0,
8, 1, 1,
8, 2, 1,
8, 3, 1,
9, 3, 1)

test<-matrix(famtest,byrow=T,ncol=3)

famp<-pfc.sim(test)

## End(Not run)
```

---

pgc

*Preparing weight for GENECOUNTING*

---

### Description

This function is a R port of the GENECOUNTING/PREPARE program which takes an array of genotype data and collapses individuals with the same multilocus genotype. This function can also be used to prepare for the genotype table in testing Hardy-Weinberg equilibrium.

### Usage

```
pgc(data,handle.miss=1,is.genotype=0,with.id=0)
```

### Arguments

<code>data</code>	the multilocus genotype data for a set of individuals
<code>handle.miss</code>	a flag to indicate if missing data is kept, 0 = no, 1 = yes
<code>is.genotype</code>	a flag to indicate if the data is already in the form of genotype identifiers
<code>with.id</code>	a flag to indicate if the unique multilocus genotype identifier is generated

### Value

The returned value is a list containing:

<code>cdata</code>	the collapsed genotype data
<code>wt</code>	the frequency weight
<code>obscom</code>	the observed number of combinations or genotypes
<code>idsave</code>	optional, available only if <code>with.id = 1</code>

### References

Zhao JH, Sham PC (2003). Generic number system and haplotype analysis. *Comp Prog Meth Biomed* 70:1-9

### Note

Built on `pgc.c`

### Author(s)

Jing Hua Zhao

### See Also

[genecounting,hwe.hardy](#)

**Examples**

```
## Not run:

data(hla)
x <- hla[,3:8]

# do not handle missing data
y<-pgc(x,handle.miss=0,with.id=1)
hla.gc<-genecounting(y$cdata,y$wt,handle.miss=0)

# handle missing but with multilocus genotype identifier
pgc(x,handle.miss=1,with.id=1)

# handle missing data with no identifier
pgc(x,handle.miss=1,with.id=0)

## End(Not run)
```

---

plot.hap.score

*Plot haplotype frequencies versus haplotype score statistics*

---

**Description**

Method function to plot a class of type hap.score

**Usage**

```
## S3 method for class 'hap.score'
plot(x, ...)
```

**Arguments**

x                    The object returned from hap.score (which has class hap.score).  
...                   Optional arguments

**Details**

This is a plot method function used to plot haplotype frequencies on the x-axis and haplotype-specific scores on the y-axis. Because hap.score is a class, the generic plot function can be used, which in turn calls this plot.hap.score function.

**Value**

Nothing is returned.

**References**

Schaid DJ, Rowland CM, Tines DE, Jacobson RM, Poland GA (2002) Score tests for association of traits with haplotypes when linkage phase is ambiguous. *Amer J Hum Genet* 70:425-34

**See Also**[hap.score](#)**Examples**

```
## Not run:
save <- hap.score(y, geno, trait.type = "gaussian")

# Example illustrating generic plot function:
plot(save)

# Example illustrating specific method plot function:
plot.hap.score(save)

## End(Not run)
```

---

print.hap.score	<i>Print a hap.score object</i>
-----------------	---------------------------------

---

**Description**

Method function to print a class of type hap.score

**Usage**

```
## S3 method for class 'hap.score'
print(x, ...)
```

**Arguments**

x	The object returned from hap.score (which has class hap.score).
...	Optional arguments.

**Details**

This is a print method function used to print information from hap.score class, with haplotype-specific information given in a table. Because hap.score is a class, the generic print function can be used, which in turn calls this print.hap.score function.

**Value**

Nothing is returned.

**References**

Schaid DJ, Rowland CM, Tines DE, Jacobson RM, Poland GA (2002) Score tests for association of traits with haplotypes when linkage phase is ambiguous. *Amer J Hum Genet* 70:425-34

**See Also**[hap.score](#)**Examples**

```
## Not run:
save <- hap.score(y, geno, trait.type = "gaussian")

# Example illustrating generic print function:
print(save)

# Example illustrating specific method print function:
print.hap.score(save)

## End(Not run)
```

qqfun

*Quantile-comparison plots***Description**

Plots empirical quantiles of a variable against theoretical quantiles of a comparison distribution.

**Usage**

```
qqfun(x, distribution="norm", ylab=deparse(substitute(x)),
      xlab=paste(distribution, "quantiles"), main=NULL, las=par("las"),
      envelope=.95, labels=FALSE, col=palette()[4], lcol=palette()[2],
      xlim=NULL, ylim=NULL, lwd=1, pch=1, bg=palette()[4], cex=.4,
      line=c("quartiles", "robust", "none"), ...)
```

**Arguments**

x	vector of numeric values.
distribution	root name of comparison distribution – e.g., norm for the normal distribution; t for the t-distribution.
ylab	label for vertical (empirical quantiles) axis.
xlab	label for horizontal (comparison quantiles) axis.
main	label for plot.
envelope	confidence level for point-wise confidence envelope, or FALSE for no envelope.
labels	vector of point labels for interactive point identification, or FALSE for no labels.
las	if 0, ticks labels are drawn parallel to the axis; set to 1 for horizontal labels (see <a href="#">par</a> ).
col	color for points; the default is the <i>fourth</i> entry in the current color palette (see <a href="#">palette</a> and <a href="#">par</a> ).

lcol	color for lines; the default is the <i>second</i> entry as above.
xlim	the x limits (x1, x2) of the plot. Note that $x1 > x2$ is allowed and leads to a reversed axis.
ylim	the y limits of the plot
pch	plotting character for points; default is 1 (a circle, see <a href="#">par</a> ).
bg	background color of points
cex	factor for expanding the size of plotted symbols; the default is .4.
lwd	line width; default is 1 (see <a href="#">par</a> ). Confidence envelopes are drawn at half this line width.
line	"quartiles" to pass a line through the quartile-pairs, or "robust" for a robust-regression line; the latter uses the <code>r1m</code> function in the MASS package. Specifying <code>line = "none"</code> suppresses the line.
...	arguments such as <code>df</code> to be passed to the appropriate quantile function.

### Details

Draws theoretical quantile-comparison plots for variables and for studentized residuals from a linear model. A comparison line is drawn on the plot either through the quartiles of the two distributions, or by robust regression.

Any distribution for which quantile and density functions exist in R (with prefixes `q` and `d`, respectively) may be used. Studentized residuals are plotted against the appropriate t-distribution.

This is adapted from `qq.plot` of package `car` with different values for points and lines, more options, more transparent code and examples in the current setting. Another similar but sophisticated function is `qqmath` of package `lattice`.

### Value

NULL. These functions are used only for their side effect (to make a graph).

### Author(s)

John Fox, Jing Hua Zhao

### References

Davison, A. C. (2003) *Statistical Models*. Cambridge University Press.

Leemis, L. M., J. T. Mcqueston (2008) *Univariate distribution relationships*. The American Statistician 62:45-53

### See Also

[qqnorm](#), [qqunif](#), [gcontrol2](#)

**Examples**

```
## Not run:
p <- runif(100)
alpha <- 1/log(10)
qqfun(p,dist="unif")
qqfun(-log10(p),dist="exp",rate=alpha,pch=21)

#library(car)
#qq.plot(p,dist="unif")
#qq.plot(-log10(p),dist="exp",rate=alpha)

#library(lattice)
#qqmath(~ -log10(p), distribution = function(p) qexp(p,rate=alpha))

## End(Not run)
```

---

qqunif

*Q-Q plot for uniformly distributed random variable*


---

**Description**

This function produces Q-Q plot for a random variable following uniform distribution with or without using log-scale. Note that the log-scale is by default for type "exp", which is a plot based on exponential order statistics. This appears to be more appropriate than the commonly used procedure whereby the expected value of uniform order statistics is directly log-transformed.

**Usage**

```
qqunif(u,type="unif",logscale=TRUE,base=10,
       col=palette()[4],lcol=palette()[2],ci=FALSE,alpha=0.05,...)
```

**Arguments**

u	a vector of uniformly distributed random variables
type	string option to specify distribution: "unif"=uniform, "exp"=exponential
logscale	to use logscale
base	the base of the log function
col	color for points
lcol	color for the diagonal line
ci	logical option to show confidence interval
alpha	1-confidence level, e.g., 0.05
...	other options as appropriate for the qqplot function

**Value**

The returned value is a list with components of a qqplot:

x	expected value for uniform order statistics or its $-\log(\text{base})$ counterpart
y	observed value or its $-\log(\text{base})$ counterpart

**References**

Balakrishnan N, Nevzorov VB. A Primer on Statistical Distributions. Wiley 2003.  
 Casella G, Berger RL. Statistical Inference, Second Edition. Duxbury 2002.  
 Davison AC. Statistical Models. Cambridge University Press 2003.

**Author(s)**

Jing Hua Zhao

**See Also**

[qqfun](#)

**Examples**

```
## Not run:
# Q-Q Plot for 1000 U(0,1) r.v., marking those <= 1e-5
u_obs <- runif(1000)
r <- qqunif(u_obs,pch=21,bg="blue",bty="n")
u_exp <- r$y
hits <- u_exp >= 2.30103
points(r$x[hits],u_exp[hits],pch=21,bg="green")

## End(Not run)
```

---

read.ms.output

*A utility function to read ms output*

---

**Description**

This function reads in the output of the program ms, a program to generate samples under a variety of neutral models.

The argument indicates either a file name or a vector of character strings, one string for each line of the output of ms. As with the second case, it is appropriate with `system(,intern=TRUE)`, see example below.

**Usage**

```
read.ms.output(msout,is.file=TRUE,xpose=TRUE,verbose=TRUE,
              outfile=NULL,outfileonly=FALSE)
```

**Arguments**

msout	an ms output
is.file	a flag indicating ms output as a system file or an R object
xpose	a flag to obtain the tranposed format as it is (when TRUE)
verbose	when TRUE, display on screen every 1000 for large nsam
outfile	to save the haplotypes in a tab-delimited ASCII file
outfileonly	to reset gametes to NA when nsam/nreps is very large and is useful with outfile

**Value**

The returned value is a list storing the results.

call	system call to ms
seed	random number seed to ms
nsam	number of copies of the locus in each sample
nreps	the number of independent samples to generate
segsites	a vector of the numbers of segregating sites
times	vectors of time to most recent ancestor (TMRCA) and total tree lengths
positions	positions of polymorphic sites on a scale of (0,1)
gametes	a list of haplotype arrays
probs	the probability of the specified number of segregating sites given the genealogical history of the sample and the value to -t option

**References**

- Hudson RR (2002) Generating samples under a Wright-Fisher neutral model. *Bioinformatics* 18:337-8,
- Press WH, SA Teukolsky, WT Vetterling, BP Flannery (1992). *Numerical Recipes in C*. Cambridge University Press, Cambridge.

**Author(s)**

D Davison, RR Hudson, JH Zhao

**Examples**

```
## Not run:

# Assuming ms is on the path

system("ms 5 4 -s 5 > ms.out")
msout1 <- read.ms.output("ms.out")

system("ms 50 4 -s 5 > ms.out")
msout2 <- read.ms.output("ms.out",outfile="out",outfileonly=TRUE)
```

```
msout <- system("ms 5 4 -s 5 -L", intern=TRUE)
msout3 <- read.ms.output(msout, FALSE)

## End(Not run)
```

---

s2k

*Statistics for 2 by K table*

---

### Description

This function calculates one-to-others and maximum accumulated chi-squared statistics for a 2 by K contingency table.

### Usage

```
s2k(y1, y2)
```

### Arguments

y1                    a vector containing the first row of a 2 by K contingency table  
y2                    a vector containing the second row of a 2 by K contingency table

### Value

The returned value is a list containing:

x2a                    the one-to-other chisquare  
x2b                    the maximum accumulated chisquare  
col1                   the column index for x2a  
col2                   the column index for x2b  
p                      the corresponding p value

### References

Hirotsu C, Aoki S, Inada T, Kitao Y (2001) An exact test for the association between the disease and alleles at highly polymorphic loci with particular interest in the haplotype analysis. *Biometrics* 57:769-778

### Note

The lengths of y1 and y2 should be the same

### Author(s)

Chihiro Hirotsu, Jing Hua Zhao

**Examples**

```
## Not run:
# an example from Mike Neale
# termed 'ugly' contingency table by Patrick Sullivan
y1 <- c(2,15,16,35,132,30,25,7,12,24,10,10,0)
y2 <- c(0, 6,31,49,120,27,15,8,14,25, 3, 9,3)

result <- s2k(y1,y2)

## End(Not run)
```

SNP

*Functions for single nucleotide polymorphisms (SNPs)***Description**

snp.PAR gives PAR for a particular SNP.

snp.ES gives the effect size estimate based on the linear regression coefficient and standard error. For logistic regression, we can have similar idea for  $\log(\text{OR})$  and  $\log(\text{SE}(\text{OR}))$ .

snp.HWE gives an exact Hardy-Weinberg Equilibrium (HWE) test, and -1 in the case of misspecification of genotype counts.

Eventually, this will be a set of functions specifically for single nucleotide polymorphisms (SNPs), which are biallelic markers. This is particularly relevant to the genomewide association studies (GWAS) using GeneChips and in line with the classic generalised single-locus model. snp.HWE is from Abecasis's website and yet to adapt for chromosome X.

Internally, snp.PAR calls for an internal function PARn, which calculates the the population attributable risk (PAR) given a set of frequencies and associate relative risks (RR). Other 2x2 table statistics familiar to epidemiologists can be added when necessary.

**Usage**

```
snp.ES(beta, SE, N)
snp.HWE(g)
snp.PAR(RR, MAF, unit=2)
```

**Arguments**

MAF	Minor allele frequency
RR	Relative risk
unit	Unit to exponentiate for homozygote
beta	Regression coefficient
SE	Standard error for beta
N	Sample size
g	Observed genotype vector

**Author(s)**

Jing Hua Zhao, Shengxu Li

tsc

*Power calculation for two-stage case-control design***Description**

This function gives power estimates for two-stage case-control design for genetic association.

The false positive rates are calculated as follows,

$$P(|z_1| > C_1)P(|z_2| > C_2, \text{sign}(z_1) = \text{sign}(z_2))$$

and

$$P(|z_1| > C_1)P(|z_j| > C_j | |z_1| > C_1)$$

for replication-based and joint analyses, respectively; where  $C_1$ ,  $C_2$ , and  $C_j$  are thresholds at stages 1, 2 replication and joint analysis,

$$z_1 = z(p_1, p_2, n_1, n_2, pi.samples)$$

$$z_2 = z(p_1, p_2, n_1, n_2, 1 - pi.samples)$$

$$z_j = \text{sqrt}(pi.samples) * z_1 + \text{sqrt}(1 - pi.samples) * z_2$$

**Usage**

```
tsc(model, GRR, p1, n1, n2, M, alpha.genome, pi.samples, pi.markers, K)
```

**Arguments**

model	any in c("multiplicative", "additive", "dominant", "recessive")
GRR	genotype relative risk
p1	the estimated risk allele frequency in cases
n1	total number of cases
n2	total number of controls
M	total number of markers
alpha.genome	false positive rate at genome level
pi.samples	sample% to be genotyped at stage 1
pi.markers	markers% to be selected (also used as the false positive rate at stage 1)
K	the population prevalence

**Value**

The returned value is a list containing a copy of the input plus output as follows,

model	any in c("multiplicative","additive","dominant","recessive")
GRR	genotype relative risk
p1	the estimated risk allele frequency in cases
pprime	expected risk allele frequency in cases
p	expected risk allele frequency in controls
n1	total number of cases
n2	total number of controls
M	total number of markers
alpha.genome	false positive rate at genome level
pi.samples	sample% to be genotyped at stage 1
pi.markers	markers% to be selected (also used as the false positive rate at stage 1)
K	the population prevalence
C	thresholds for no stage, stage 1, stage 2, joint analysis
power	power corresponding to C

**References**

Skol AD, Scott LJ, Abecasis GR, Boehkne M (2006). Joint analysis in more efficient than replication-based analysis for two-stage genome-wide association studies. *Nature Genetics* 38:209-213

**Note**

solve.skol is adapted from CaTS

**Author(s)**

Jing Hua Zhao

**Examples**

```
K <- 0.1
p1 <- 0.4
n1 <- 1000
n2 <- 1000
M <- 300000
alpha.genome <- 0.05
GRR <- 1.4
p1 <- 0.4
pi.samples <- 0.2
pi.markers <- 0.1

options(echo=FALSE)
cat("sample%,marker%,GRR,(thresholds x 4)(power estimates x 4)\n")
```

```

for(GRR in c(1.3,1.35,1.40)) {
  cat("\n")
  for(pi.samples in c(1.0,0.5,0.4,0.3,0.2)) {
    if(pi.samples==1.0) s <- 1.0
    else s <- c(0.1,0.05,0.01)
    for(pi.markers in s)
    {
      x <- tsc("multiplicative",GRR,p1,n1,n2,M,alpha.genome,pi.samples,pi.markers,K)
      l <- c(pi.samples,pi.markers,GRR,x$C,x$power)
      l <- sprintf("%.2f %.2f %.2f, %.2f %.2f %.2f %.2f, %.2f %.2f %.2f %.2f",
                  l[1],l[2],l[3],l[4],l[5],l[6],l[7],l[8],l[9],l[10],l[11])
      cat(l,"\n")
    }
    cat("\n")
  }
}
options(echo=TRUE)

```

whscore

*Whittemore-Halpern scores for allele-sharing***Description**

Allele sharing score statistics

**Usage**

whscore(allele, type)

**Arguments**

allele	a matrix of alleles of affected pedigree members
type	0 = pairs, 1 = all

**Value**

The returned value is the value of score statistic

**References**

- Kruglyak L, Daly MJ, Reeve-Daly MP, Lander ES (1996) Parametric and Nonparametric linkage analysis: a unified multipoint approach. *Am. J. Hum. Genet.* 58:1347-1363
- Whittemore AS, Halpern J (1994) A class of tests for linkage using affected pedigree members. *Biometrics* 50:118-127
- Whittemore AS, Halpern J (1994) Probability of gene identity by descent: computation and applications. *Biometrics* 50:109-117

**Note**

adapted from GENEHUNTER

**Author(s)**

Leonid Kruglyak, Jing Hua Zhao

**Examples**

```
## Not run:  
c<-matrix(c(1,1,1,2,2,2),ncol=2)  
whscore(c,type=1)  
whscore(c,type=2)  
  
## End(Not run)
```

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