

# Package ‘gap’

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**Type** Package

**Title** Genetic Analysis Package

**Version** 1.5-2

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## Description

As first reported [Zhao, J. H. 2007. “gap: Genetic Analysis Package”. J Stat Soft 23(8):1-18. <[doi:10.18637/jss.v023.i08](https://doi.org/10.18637/jss.v023.i08)>], 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, statistics in linkage analysis, and association analysis involving genetic markers including haplotype analysis with or without environmental covariates. Over years, the package has been developed in-between many projects hence also in line with the name (gap).

**License** GPL (>= 2)

**URL** <https://github.com/jinghuazhao/R>

**BugReports** <https://github.com/jinghuazhao/R/issues>

**Depends** R (>= 2.10), gap.datasets

**Imports** dplyr, ggplot2, plotly, Rdpack

**Suggests** BradleyTerry2, DiagrammeR, DOT, MASS, Matrix, MCMCglmm, R2jags, bdsmatrix, bookdown, calibrate, circlize, coda, cowplot, coxme, foreign, forestplot, genetics, grid, haplo.stats, htmlwidgets, jsonlite, kinship2, knitr, lattice, magic, manhattanly, matrixStats, meta, metafor, nlme, pedigree, pedigreemm, plotrix, readr, reshape, rmarkdown, rmeta, rms, survival

**Enhances** shiny

**LazyData** Yes

**LazyLoad** Yes

**NeedsCompilation** yes

**Encoding** UTF-8

**VignetteBuilder** knitr

**Roxygen** list(markdown = TRUE)

**RoxygenNote** 7.2.3

**RdMacros** Rdpack

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a2g	<i>Allele-to-genotype conversion</i>
-----	--------------------------------------

---

## Description

Allele-to-genotype conversion

## Usage

a2g(a1, a2)

## Arguments

a1	first allele.
a2	second allele.

---

ab*Test/Power calculation for mediating effect*

---

**Description**

Test/Power calculation for mediating effect

**Usage**

```
ab(  
  type = "power",  
  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.

**Details**

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.

**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.

**Author(s)**

Jing Hua Zhao

## 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 (2008). "Common variation in the FTO gene alters diabetes-related metabolic traits to the extent expected given its effect on BMI." *Diabetes*, **57**(5), 1419-26. ISSN 0012-1797 (Print) 0012-1797, doi:10.2337/db071466.

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 <https://quantpsy.org/sobel/sobel.htm>

## 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)
```

---

AE3

*AE model using nuclear family trios*

---

## Description

AE model using nuclear family trios

## Usage

```
AE3(model, random, data, seed = 1234, n.sim = 50000, verbose = TRUE)
```

## Arguments

model	a linear mixed model formula, see example below.
random	random effect, see example below.
data	data to be analyzed.

seed	random number seed.
n.sim	number of simulations.
verbose	a flag for printing out results.

### Details

This function is adapted from example 7.1 of Rabe-Hesketh et al. (2008). It also provides heritability estimate and confidence intervals.

### Value

The returned value is a list containing:

- lme.result the linear mixed model result.
- h2 the heritability estimate.
- CL confidence intervals.

### Note

Adapted from f.mbf.R from the paper.

### Author(s)

Jing Hua Zhao

### References

Rabe-Hesketh S, Skrondal A, Gjessing HK (2008). “Biometrical modeling of twin and family data using standard mixed model software.” *Biometrics*, **64**(1), 280-8. ISSN 0006-341X (Print) 0006-341x, doi:[10.1111/j.15410420.2007.00803.x](https://doi.org/10.1111/j.15410420.2007.00803.x).

### Examples

```
## Not run:
require(gap.datasets)
AE3(bwt ~ male + first + midage + highage + birthyr,
    list(familyid = pdIdent(~var1 + var2 + var3 -1)), mfblong)

## End(Not run)
```

---

allele.recode

*Allele recoding*


---

### Description

Allele recoding

### Usage

```
allele.recode(a1, a2, miss.val = NA)
```

**Arguments**

a1	first allele.
a2	second allele.
miss.val	missing value.

---

asplot	<i>Regional association plot</i>
--------	----------------------------------

---

**Description**

Regional association plot

**Usage**

```
asplot(
  locus,
  map,
  genes,
  flanking = 1000,
  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 <sub>10</sub> (p).
pch	Plotting character for the SNPs to be highlighted, e.g., 21 and 23 refer to circle and diamond.

**Details**

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.

**Author(s)**

Paul de Bakker, Jing Hua Zhao, Shengxu Li



## References

Saxena R, Voight BF, Lyssenko V, Burt NP, de Bakker PI, Chen H, Roix JJ, Kathiresan S, Hirschhorn JN, Daly MJ, Hughes TE, Groop L, Altshuler D, Almgren P, Florez JC, Meyer J, Ardlie K, Bengtsson Boström K, Isomaa B, Lettre G, Lindblad U, Lyon HN, Melander O, Newton-Cheh C, Nilsson P, Orho-Melander M, Råstam L, Speliotes EK, Taskinen MR, Tuomi T, Guiducci C, Berglund A, Carlson J, Gianniny L, Hackett R, Hall L, Holmkvist J, Laurila E, Sjögren M, Sterner M, Surti A, Svensson M, Svensson M, Tewhey R, Blumenstiel B, Parkin M, Defelice M, Barry R, Brodeur W, Camarata J, Chia N, Fava M, Gibbons J, Handsaker B, Healy C, Nguyen K, Gates C, Sougnez C, Gage D, Nizzari M, Gabriel SB, Chirn GW, Ma Q, Parikh H, Richardson D, Ricke D, Purcell S (2007). "Genome-wide association analysis identifies loci for type 2 diabetes and triglyceride levels." *Science*, **316**(5829), 1331-6. ISSN 0036-8075, doi:10.1126/science.1142358.

## Examples

```
## Not run:
require(gap.datasets)
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
chr_pos <- GetSNPInfo(with(p, SNP))[c("chr", "chrpos")]
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))
# We have complaints; a possibility is to get around with
# https://ftp.ncbi.nlm.nih.gov/hapmap/
hit_LD <- subset(LD, SNPA==hit)
hit_LD <- within(hit_LD, {RSQR=r2})
info <- GetSNPInfo(p$SNP)
haldane <- function(x) 0.5*(1-exp(-2*x))
locus <- with(info, data.frame(CHR=chr, POS=chrpos, NAME=marker,
                             DIST=(chrpos-min(chrpos))/1000000,
                             THETA=haldane((chrpos-min(chrpos))/1000000)))
locus <- merge.data.frame(locus, hit_LD, by.x="NAME", by.y="SNPB", all=TRUE)
locus <- merge.data.frame(locus, p, by.x="NAME", by.y="SNP", all=TRUE)
locus <- subset(locus, !is.na(POS))
ann <- AnnotateSNPList(p$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)
ugenex <- unique(GENE)
ustart <- as.vector(as.table(by(START, GENE, min))[, ugenex])
ustop <- as.vector(as.table(by(STOP, GENE, max))[, ugenex])
ustrand <- as.vector(as.table(by(as.character(STRAND), GENE, max))[, ugenex])
detach(genes)
genes <- data.frame(START=ustart, STOP=ustop, STRAND=ustrand, GENE=ugenex)
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**

Obtain correlation coefficients and their variance-covariances

**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.

**Details**

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.

**Value**

The returned value is a list containing:

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

**Author(s)**

Jing Hua Zhao

**References**

- Elston RC (1975). "On the correlation between correlations." *Biometrika*, **62**(1), 133-140. ISSN 0006-3444, doi:[10.1093/biomet/62.1.133](https://doi.org/10.1093/biomet/62.1.133).
- Becker BJ (2000). "Multivariate meta-analysis." In Tinsley HE, Brown SD (eds.), *Handbook of Applied Multivariate Statistics and Mathematical Modeling*, chapter 17, 499-525. Academic Press, San Diego. ISBN 978-0126913606, <https://www.amazon.com/dp/0126913609/>.
- Casella G, Berger RL (2002). *Statistical Inference*, 2 edition. Duxbury. ISBN 978-0-534-24312-8, <https://www.amazon.com/dp/7111109457/>.

**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	<i>Bayesian false-discovery probability</i>
------	---

---

**Description**

Bayesian false-discovery probability

**Usage**

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

**Arguments**

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

**Details**

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  $RR_{hi}$ .

**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.

**Note**

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

**Author(s)**

Jon Wakefield, Jing Hua Zhao

**References**

Wakefield J (2007). "A Bayesian measure of the probability of false discovery in genetic epidemiology studies." *Am J Hum Genet*, **81**(2), 208-27. ISSN 0002-9297 (Print) 0002-9297, doi:10.1086/519024.

**See Also**

[FPRP](#)

**Examples**

```
## Not run:
# Example from BDFP.xls by Jon Wakefield and Stephanie Monnier
# Step 1 - Pre-set an BDFP-level threshold for noteworthiness: BDFP 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 discovery

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 BDFP

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

## End(Not run)
```

bt

*Bradley-Terry model for contingency table***Description**

Bradley-Terry model for contingency table

**Usage**

```
bt(x)
```

**Arguments**

x                      the data table.

**Details**

This function calculates statistics under Bradley-Terry model.

**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.

**Note**

Adapted from a SAS macro for data in the example section.

**Author(s)**

Jing Hua Zhao

## References

- Bradley RA, Terry ME (1952). “Rank analysis of incomplete block designs.” *Biometrika*, **39**, 324-335.
- Sham PC, Curtis D (1995). “An extended transmission/disequilibrium test (TDT) for multi-allele marker loci.” *Ann Hum Genet*, **59**(3), 323-36. ISSN 0003-4800 (Print) 0003-4800, doi:10.1111/j.14691809.1995.tb00751.x.
- Copeman JB, Cucca F, Hearne CM, Cornall RJ, Reed PW, Rønningen KS, Undlien DE, Nisticò 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**(1), 80-5. ISSN 1061-4036 (Print) 1061-4036, doi:10.1038/ng019580.

## See Also

[mtdt](#)

## Examples

```
## Not run:
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, 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

Power and sample size for case-cohort design

## Usage

```
ccsize(n, q, pD, p1, theta, alpha, beta = 0.2, power = FALSE, 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).
theta	log-hazard ratio for two groups.
alpha	type I error – significant level.
beta	type II error.
power	if specified, the power for which sample size is calculated.
verbose	error messages are explicitly printed out.

## Details

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.

## Value

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

## Note

Programmed for EPIC study. keywords misc

## Author(s)

Jing Hua Zhao

## References

Cai J, Zeng D (2004). "Sample size/power calculation for case-cohort studies." *Biometrics*, **60**(4), 1015-24. ISSN 0006-341X (Print) 0006-341x, doi:10.1111/j.0006341X.2004.00257.x.

## See Also

[pbsize](#)

## Examples

```
## Not run:
# 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)

    ## End(Not run)

```

**Description**

Chow's test for heterogeneity in two regressions

**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.

**Details**

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.

**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.

**Note**

adapted from chow.R.

**Author(s)**

Shigenobu Aoki, Jing Hua Zhao

## References

Chow GC (1960). “Tests of Equality Between Sets of Coefficients in Two Linear Regressions.” *Econometrica*, **28**(3), 591-605. ISSN 00129682, 14680262, doi:[10.2307/1910133](https://doi.org/10.2307/1910133).

## 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)
# from http://aoki2.si.gunma-u.ac.jp/R/

## End(Not run)
```

---

chr\_pos\_a1\_a2

*SNP id by chr:pos+a1/a2*

---

## Description

SNP id by chr:pos+a1/a2

**Usage**

```
chr_pos_a1_a2(
  chr,
  pos,
  a1,
  a2,
  prefix = "chr",
  seps = c(":", "_", "-"),
  uppercase = TRUE
)
```

**Arguments**

chr	Chromosome.
pos	Position.
a1	Allele 1.
a2	Allele 2.
prefix	Prefix of the identifier.
seps	Delimiters.
uppercase	A flag to return in upper case.

**Details**

This function generates unique identifiers for variants

**Value**

Identifier.

**Examples**

```
# rs12075
chr_pos_a1_a2(1, 159175354, "A", "G", prefix="chr", seps=c(":", "_", "-"), uppercase=TRUE)
```

---

ci2ms

*Effect size and standard error from confidence interval*


---

**Description**

Effect size and standard error from confidence interval

**Usage**

```
ci2ms(ci, logscale = TRUE, alpha = 0.05)
```

**Arguments**

ci	confidence interval (CI). The delimiter between lower and upper limit is either a hyphen (-) or en dash (–).
logscale	a flag indicating the confidence interval is based on a log-scale.
alpha	Type 1 error.

## Details

Effect size is a measure of strength of the relationship between two variables in a population or parameter estimate of that population. Without loss of generality, denote  $m$  and  $s$  to be the mean and standard deviation of a sample from  $N(\mu, \sigma^2)$ . Let  $z \sim N(0, 1)$  with cutoff point  $z_\alpha$ , confidence limits  $L, U$  in a CI are defined as follows,

$$L = m - z_\alpha s$$

$$U = m + z_\alpha s$$

$\Rightarrow U + L = 2m, U - L = 2z_\alpha s$ . Consequently,

$$m = \frac{U + L}{2}$$

$$s = \frac{U - L}{2z_\alpha}$$

Effect size in epidemiological studies on a binary outcome is typically reported as odds ratio from a logistic regression or hazard ratio from a Cox regression,  $L \equiv \log(L), U \equiv \log(U)$ .

## Value

Based on CI, the function provides a list containing estimates

- $m$  effect size ( $\log(\text{OR})$ )
- $s$  standard error
- direction a decrease/increase  $(-/+)$  sign such that  $\text{sign}(m) = -1, 0, 1$ , is labelled "-", "0", "+", respectively as in PhenoScanner.

## Examples

```
# rs3784099 and breast cancer recurrence/mortality
ms <- ci2ms("1.28-1.72")
print(ms)
# Vector input
ci2 <- c("1.28-1.72", "1.25-1.64")
ms2 <- ci2ms(ci2)
print(ms2)
```

---

```
circos.cis.vs.trans.plot
```

*circos plot of cis/trans classification*

---

## Description

circos plot of cis/trans classification

## Usage

```
circos.cis.vs.trans.plot(hits, panel, id, radius = 1e+06)
```

**Arguments**

hits	A text file as input data with variables named "CHR","BP","SNP","prot".
panel	Protein panel with prot(ein), uniprot (id) and "chr","start","end","gene".
id	Identifier.
radius	The flanking distance as cis.

**Details**

The function implements a circos plot at the early stage of SCALLOP-INF meta-analysis.

**Value**

None.

**Examples**

```
## Not run:
  circos.cis.vs.trans.plot(hits="INF1.clumped", panel=inf1, id="uniprot")

## End(Not run)
```

---

circos.cnvplot	<i>circos plot of CNVs.</i>
----------------	-----------------------------

---

**Description**

circos plot of CNVs.

**Usage**

```
circos.cnvplot(data)
```

**Arguments**

data	CNV data containing chromosome, start, end and freq.
------	--

**Details**

The function plots frequency of CNVs.

**Value**

None.

**Examples**

```
## Not run:
  circos.cnvplot(cnv)

## End(Not run)
```

---

<code>circos.mhtplot</code>	<i>circos Manhattan plot with gene annotation</i>
-----------------------------	---

---

### Description

circos Manhattan plot with gene annotation

### Usage

```
circos.mhtplot(data, glist)
```

### Arguments

<code>data</code>	Data to be used.
<code>glist</code>	A gene list.

### Details

The function generates circos Manhattan plot with gene annotation.

### Value

None.

### Examples

```
## Not run:
require(gap.datasets)
glist <- c("IRS1", "SPRY2", "FTO", "GRIK3", "SNED1", "HTR1A", "MARCH3", "WISP3",
           "PPP1R3B", "RP1L1", "FDFT1", "SLC39A14", "GFRA1", "MC4R")
circos.mhtplot(mhtdata, glist)

## End(Not run)
```

---

<code>circos.mhtplot2</code>	<i>Another circos Manhattan plot</i>
------------------------------	--------------------------------------

---

### Description

Another circos Manhattan plot

### Usage

```
circos.mhtplot2(dat, labs, species = "hg18", ticks = 0:3 * 10, y = 20)
```

**Arguments**

<code>dat</code>	Data to be plotted with variables chr, pos, log10p.
<code>labs</code>	Data on labels.
<code>species</code>	Genome build.
<code>ticks</code>	Tick positions.
<code>y</code>	Starting position of y-axis label.

**Details**

This is adapted from work for a recent publication. It enables a y-axis to the  $-\log_{10}(P)$  for association statistics

**Value**

There is no return value but a plot.

**Examples**

```
## Not run:
require(gap.datasets)
library(dplyr)
glist <- c("IRS1", "SPRY2", "FTO", "GRIK3", "SNED1", "HTR1A", "MARCH3", "WISP3",
           "PPP1R3B", "RP1L1", "FDFT1", "SLC39A14", "GFRA1", "MC4R")
testdat <- mhtdata[c("chr", "pos", "p", "gene", "start", "end")] %>%
  rename(log10p=p) %>%
  mutate(chr=paste0("chr", chr), log10p=-log10(log10p))
dat <- mutate(testdat, start=pos, end=pos) %>%
  select(chr, start, end, log10p)
labs <- subset(testdat, gene %in% glist) %>%
  group_by(gene, chr, start, end) %>%
  summarize() %>%
  mutate(cols="blue") %>%
  select(chr, start, end, gene, cols)
labs[2, "cols"] <- "red"
circos.mhtplot2(dat, labs, ticks=0:2*10)
# https://www.rapidtables.com/web/color/RGB_Color.html

## End(Not run)
```

---

cis.vs.trans.classification

*A cis/trans classifier*

---

**Description**

A cis/trans classifier

**Usage**

```
cis.vs.trans.classification(hits, panel, id, radius = 1e+06)
```



Arguments

hits	Data to be used, which contains prot, Chr, bp, id and/or other information such as SNPid.
panel	Panel data.
id	Identifier.
radius	The flanking distance for variants.

Details

The function classifies variants into cis/trans category according to a panel which contains id, chr, start, end, gene variables.

Value

The cis/trans classification.

Author(s)

James Peters

Examples

```

cis.vs.trans.classification(hits=jma.cojo, panel=inf1, id="uniprot")
## Not run:
INF <- Sys.getenv("INF")
f <- file.path(INF,"work","INF1.merge")
clumped <- read.delim(f,as.is=TRUE)
hits <- merge(clumped[c("CHR","POS","MarkerName","prot","log10p")],
              inf1[c("prot","uniprot")],by="prot")
names(hits) <- c("prot","Chr","bp","SNP","log10p","uniprot")
cistrans <- cis.vs.trans.classification(hits,inf1,"uniprot")
cis.vs.trans <- with(cistrans,data)
knitr::kable(with(cistrans,table),caption="Table 1. cis/trans classification")
with(cistrans,total)

## End(Not run)
```

---

cnvplot	<i>genomewide plot of CNVs</i>
---------	--------------------------------

---

Description

genomewide plot of CNVs

Usage

```
cnvplot(data)
```

Arguments

data	Data to be used.
------	------------------

## Details

The function generates a plot containing genomewide copy number variants (CNV) chr, start, end, freq(uencies).

## Value

None.

## Examples

```
knitr::kable(cnv,caption="A CNV dataset")
cnvplot(cnv)
```

---

comp.score	<i>score statistics for testing genetic linkage of quantitative trait</i>
------------	---

---

## Description

score statistics for testing genetic linkage of quantitative trait

## 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.

## Details

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.,  $w_k w_l$ ).

### Value

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

### Note

Adapt from score2.r.

### Author(s)

Yingwei Peng, Kai Wang

### 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**(6), 1347-63. ISSN 0002-9297 (Print) 0002-9297.

Kruglyak L, Lander ES (1998). "Faster multipoint linkage analysis using Fourier transforms." *J Comput Biol*, **5**(1), 1-7. ISSN 1066-5277 (Print) 1066-5277, doi:10.1089/cmb.1998.5.1.

Wang K (2005). "A likelihood approach for quantitative-trait-locus mapping with selected pedigrees." *Biometrics*, **61**(2), 465-73. ISSN 0006-341X (Print) 0006-341x, doi:10.1111/j.15410420.2005.031213.x.

### Examples

```
## Not run:
# 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(find.package("gap"), "tests/comp.score")
setwd(cs.dir)
dir()
# system("gh < gh.inp")
cs.default <- comp.score()
setwd(cwd)

## End(Not run)
```

---

cs	<i>Credible set</i>
----	---------------------

---

## Description

Credible set

## Usage

```
cs(tbl, b = "Effect", se = "StdErr", log_p = NULL, cutoff = 0.95)
```

## Arguments

tbl	Input data.
b	Effect size.
se	Standard error.
log_p	if not NULL it will be used to derive z-statistic
cutoff	Threshold for inclusion.

## Details

The function implements credible set as in fine-mapping.

## Value

Credible set.

## Examples

```
## Not run:
\preformatted{
  zcat METAL/4E.BP1-1.tbl.gz | \
  awk 'NR==1 || ($1==4 && $2 >= 187158034 - 1e6 && $2 < 187158034 + 1e6)' > 4E.BP1.z
}
tbl <- within(read.delim("4E.BP1.z"),{logp <- logp(Effect/StdErr)})
z <- cs(tbl)
l <- cs(tbl,log_p="logp")

## End(Not run)
```

---

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

---

**Description**

Effect-size plot

**Usage**

```
ESplot(ESdat, alpha = 0.05, fontsize = 12)
```

**Arguments**

ESdat	A data frame consisting of model id, parameter estimates and standard errors.
alpha	Type-I error rate used to construct 100(1-alpha) confidence interval.
fontsize	size of font.

**Details**

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

**Value**

A high resolution plot object.

**Author(s)**

Jing Hua Zhao

**Examples**

```
rs12075 <- data.frame(id=c("CCL2", "CCL7", "CCL8", "CCL11", "CCL13", "CXCL6", "Monocytes"),
                      b=c(0.1694, -0.0899, -0.0973, 0.0749, 0.189, 0.0816, 0.0338387),
                      se=c(0.0113, 0.013, 0.0116, 0.0114, 0.0114, 0.0115, 0.00713386))

ESplot(rs12075)

# The function replaces an older implementation.
within(data.frame(
  id=c("Basic model", "Adjusted", "Moderately adjusted", "Heavily adjusted", "Other"),
  b=log(c(4.5, 3.5, 2.5, 1.5, 1)),
  se=c(0.2, 0.1, 0.2, 0.3, 0.2)
), {
  lcl <- exp(b-1.96*se)
  ucl <- exp(b+1.96*se)
  x <- seq(-2, 8, length=length(id))
  y <- 1:length(id)
  plot(x, y, type="n", xlab="", ylab="", axes=FALSE)
  points((lcl+ucl)/2, y, pch=22, bg="black", cex=3)
  segments(lcl, y, ucl, y, lwd=3, lty="solid")
  axis(1, cex.axis=1.5, lwd=0.5)
  par(las=1)
  abline(v=1)
  axis(2, labels=id, at=y, lty="blank", hadj=0.2, cex.axis=1.5)
```

```
    title("A fictitious plot")
  })
```

fbsize

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

## Description

Sample size for family-based linkage and association design

## Usage

```
fbsize(
  gamma,
  p,
  alpha = c(1e-04, 1e-08, 1e-08),
  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.

## Details

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).

## 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.

**Note**

extracted from rm.c.

**Author(s)**

Jing Hua Zhao

**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.

**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$lambdas,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**

False-positive report probability

**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.

**Details**

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,  $\pi = P(H_0 = TRUE) = P(association)$ . Let  $T$ =test statistic, and  $P(T > z_\alpha | H_0 = TRUE) = P(rejecting H_0 | H_0 = TRUE) = \alpha$ ,  $P(T > z_\alpha | H_0 = FALSE) = P(rejecting H_0 | H_A = TRUE) = 1 - \beta$ . The joint probability of test and truth of hypothesis can be expressed by  $\alpha$ ,  $\beta$  and  $\pi$ .

Joint probability of significance of test and truth of hypothesis

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  $FNRP = \{1 + [(1 - \alpha) / \beta] [(1 - \pi) / \pi]\}^{-1}$ .



**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.

**Author(s)**

Jing Hua Zhao

**References**

Wacholder S, Chanock S, Garcia-Closas M, El Ghormli L, Rothman N (2004). "Assessing the probability that a positive report is false: an approach for molecular epidemiology studies." *J Natl Cancer Inst*, **96**(6), 434-42. ISSN 0027-8874 (Print) 0027-8874, doi:10.1093/jnci/djh075.

**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% confidence interval (CI) to obtain FPRP

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\
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)
```

---

g2a	<i>Conversion of a genotype identifier to alleles</i>
-----	---

---

**Description**

Conversion of a genotype identifier to alleles

**Usage**

```
g2a(g)
```

**Arguments**

g                      a genotype identifier.

---

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

---

**Description**

As is first reported, 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, statistics in linkage analysis, and association analysis involving genetic markers including haplotype analysis with or without environmental covariates. Over years, the package has been developed in-between many projects hence also in line with the name (gap).

**Details**

We have incorporated functions for a wide range of problems as shown below.

**ANALYSIS**

AE3	AE model using nuclear family trios
bt	Bradley-Terry model for contingency table
ccsize	Power and sample size for case-cohort design
cs	Credibel set
fbsize	Sample size for family-based linkage and association design
gc.em	Gene counting for haplotype analysis

gcontrol	genomic control
gcontrol2	genomic control based on p values
gcp	Permutation tests using GENECOUNTING
gc.lambda	Estimation of the genomic control inflation statistic (lambda)
genecounting	Gene counting for haplotype analysis
gif	Kinship coefficient and genetic index of familiarity
hap	Haplotype reconstruction
hap.em	Gene counting for haplotype analysis
hap.score	Score statistics for association of traits with haplotypes
htr	Haplotype trend regression
h2.jags	Heritability estimation based on genomic relationship matrix using JAGS
hwe	Hardy-Weinberg equilibrium test for a multiallelic marker
hwe.cc	A likelihood ratio test of population Hardy-Weinberg equilibrium
hwe.hardy	Hardy-Weinberg equilibrium test using MCMC
hwe.jags	Hardy-Weinberg equilibrium test for a multiallelic marker using JAGS
invnormal	inverse Normal transformation
kin.morgan	kinship matrix for simple pedigree
LD22	LD statistics for two diallelic markers
LDkl	LD statistics for two multiallelic markers
lambda1000	A standardized estimate of the genomic inflation scaling to a study of 1,000 cases and 1,000 controls
log10p	log10(p) for a standard normal deviate
log10pvalue	log10(p) for a P value including its scientific format
logp	log(p) for a normal deviate
masize	Sample size calculation for mediation analysis
MCMCgrm	Mixed modeling with genetic relationship matrices
mia	multiple imputation analysis for hap
mr	Mendelian randomization analysis
mtdt	Transmission/disequilibrium test of a multiallelic marker
mtdt2	Transmission/disequilibrium test of a multiallelic marker by Bradley-Terry model
mvmeta	Multivariate meta-analysis based on generalized least squares
pbsize	Power for population-based association design
pbsize2	Power for case-control association design
pfc	Probability of familial clustering of disease
pfc.sim	Probability of familial clustering of disease
pgc	Preparing weight for GENECOUNTING
print.hap.score	Print a hap.score object
s2k	Statistics for 2 by K table
sentinels	Sentinel identification from GWAS summary statistics
tsc	Power calculation for two-stage case-control design

## GRAPHICS

asplot	Regional association plot
ESplot	Effect-size plot
circos.cis.vs.trans.plot	circos plot of cis/trans classification
circos.cnvplot	circos plot of CNVs
circos.mhtplot	circos Manhattan plot with gene annotation
circos.mhtplot2	Another circos Manhattan plot
cnvplot	genomewide plot of CNVs
labelManhattan	Annotate Manhattan or Miami Plot

makeRLEplot	make relative log expression plot
METAL_forestplot	forest plot as R/meta's forest for METAL outputs
mhtplot	Manhattan plot
mhtplot2	Manhattan plot with annotations
mhtplot.trunc	truncated Manhattan plot
miamipLOT	Miami plot
miamipLOT2	Miami plot
mr_forestplot	Mendelian Randomization forest plot
pedtodot	Converting pedigree(s) to dot file(s)
pedtodot_verbatim	Pedigree-drawing with graphviz
plot.hap.score	Plot haplotype frequencies versus haplotype score statistics
qqfun	Quantile-comparison plots
qqunif	Q-Q plot for uniformly distributed random variable
qtl2dplot	2D QTL plot
qtl2dplotly	2D QTL plotly
qtl3dplotly	3D QTL plotly

## UTILITIES

SNP	Functions for single nucleotide polymorphisms (SNPs)
BFDP	Bayesian false-discovery probability
FPRP	False-positive report probability
ab	Test/Power calculation for mediating effect
b2r	Obtain correlation coefficients and their variance-covariances
chow.test	Chow's test for heterogeneity in two regressions
chr_pos_a1_a2	Form SNPID from chromosome, position and alleles
ci2ms	Effect size and standard error from confidence interval
cis.vs.trans.classification	a cis/trans classifier
comp.score	score statistics for testing genetic linkage of quantitative trait
GRM functions	ReadGRM, ReadGRMBin, ReadGRMPLINK, ReadGRMPCA, WriteGRM, WriteGRMBin, WriteGRMSAS
	handle genomic relationship matrix involving other software
get_b_se	Get b and se from AF, n, and z
get_pve_se	Get pve and its standard error from n, z
get_sdy	Get sd(y) from AF, n, b, se
h2G	A utility function for heritability
h2GE	A utility function for heritability involving gene-environment interaction
h2l	A utility function for converting observed heritability to its counterpart under liability threshold model
h2_mzdz	Heritability estimation according to twin correlations
klem	Haplotype frequency estimation based on a genotype table of two multiallelic markers
makeped	A function to prepare pedigrees in post-MAKEPED format
metap	Meta-analysis of p values
metareg	Fixed and random effects model for meta-analysis
muvar	Means and variances under 1- and 2- locus (diallelic) QTL model
qtlClassifier	A QTL cis/trans classifier
read.ms.output	A utility function to read ms output
revStrand	Allele on the reverse strand
runshinygap	Start shinygap
snptest_sample	A utility to generate SNPTEST sample file
whscore	Whittemore-Halpern scores for allele-sharing

weighted.median      Weighted median with interpolation

## Usage

Vignettes on package usage:

- Genetic Analysis Package. `vignette("gap")`.
- Shiny for Genetic Analysis Package (gap) Designs. `vignette("shinygap")`.
- JSS paper: Genetic Analysis Package. `vignette("jss")`.

## Author(s)

Jing Hua Zhao in collaboration with other colleagues and with help from Kurt Hornik, Brian Ripley, Uwe Liggs and Achim Zeileis

maintained by Jing Hua Zhao [jinghuazhao@hotmail.com](mailto:jinghuazhao@hotmail.com)

## References

Zhao JH (2007). "gap: genetic analysis package." *Journal of Statistical Software*, **23**(8), 1-18.  
[doi:10.18637/jss.v023.i08](https://doi.org/10.18637/jss.v023.i08).

## See Also

Useful links:

- <https://github.com/jinghuazhao/R>
- Report bugs at <https://github.com/jinghuazhao/R/issues>

---

gc.em

*Gene counting for haplotype analysis*

---

## Description

Gene counting for haplotype analysis

## 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 (lnlike).
<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> .

## Details

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

## 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  $i$ th element of `hap.prob` corresponds to the  $i$ th row of haplotype.
- `hap.prob.noLD` Similar to `hap.prob`, but assuming no linkage disequilibrium.
- `lnlike` Value of lnlike at last EM iteration (maximum lnlike if converged).
- `lr` Likelihood ratio statistic to test no linkage disequilibrium among all loci.
- `indx.subj` Vector for index of subjects, after expanding to all possible pairs of haplotypes for each person. If `indx=i`, then  $i$  is the  $i$ th row of input matrix data. If the  $i$ th 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.
- `htrtable` A table which can be used in haplotype trend regression.

## Note

Adapted from GENECOUNTING.

**Author(s)**

Jing Hua Zhao

**References**

Zhao JH, Lissarrague S, Essioux L, Sham PC (2002). "GENECOUNTING: haplotype analysis with missing genotypes." *Bioinformatics*, **18**(12), 1694-5. ISSN 1367-4803 (Print) 1367-4803, doi:10.1093/bioinformatics/18.12.1694.

Zhao JH, Sham PC (2003). "Generic number systems and haplotype analysis." *Comput Methods Programs Biomed*, **70**(1), 1-9. ISSN 0169-2607 (Print) 0169-2607, doi:10.1016/s01692607(01)00193-6.

**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)
```

gc.lambda

*Estimation of the genomic control inflation statistic (lambda)***Description**

Estimation of the genomic control inflation statistic (lambda)

**Usage**

```
gc.lambda(x, logscale = FALSE, z = FALSE)
```

**Arguments**

x                      A real vector (p or z).  
logscale                A logical variable such that x as -log10(p).  
z                        A flag to indicate x as a vector of z values.

**Value**

Estimate of inflation factor.

**Examples**

```

set.seed(12345)
p <- runif(100)
gc.lambda(p)
lp <- -log10(p)
gc.lambda(lp, logscale=TRUE)
z <- qnorm(p/2)
gc.lambda(z, z=TRUE)

```

gcontrol

*genomic control***Description**

genomic control

**Usage**

```

gcontrol(
  data,
  zeta = 1000,
  kappa = 4,
  tau2 = 1,
  epsilon = 0.01,
  ngib = 500,
  burn = 50,
  idum = 2348
)

```

**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.

**Details**

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 $\text{Normal}(\sqrt{\text{lambdahat}}\kappa, \text{lambdahat}*\tau^2)$
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.

## Value

The returned value is a list containing:

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

## Note

Adapted from gcontrol by Bobby Jones and Kathryn Roeder, use -Dexecutable for standalone program, function getnum in the original code needs \

## Author(s)

Bobby Jones, Jing Hua Zhao

## Source

<https://www.cmu.edu/dietrich/statistics-datascience/index.html>

## References

Devlin B, Roeder K (1999). "Genomic control for association studies." *Biometrics*, **55**(4), 997-1004. ISSN 0006-341X (Print) 0006-341x, doi:10.1111/j.0006341x.1999.00997.x.

## 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**

genomic control based on p values

**Usage**

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

**Arguments**

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

**Details**

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.

**Value**

A list containing:

- x the expected  $\chi^2$  statistics.
- y the observed  $\chi^2$  statistics.
- lambda the inflation factor.

**Author(s)**

Jing Hua Zhao

**References**

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

**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**

Permutation tests using GENECOUNTING

**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.

**Details**

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

**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.

**Note**

Built on gcp.c.

**Author(s)**

Jing Hua Zhao

**References**

Zhao JH, Curtis D, Sham PC (2000). "Model-free analysis and permutation tests for allelic associations." *Hum Hered*, **50**(2), 133-9. ISSN 0001-5652 (Print) 0001-5652, doi:10.1159/000022901.

Zhao JH (2004). "2LD. GENECOUNTING and HAP: computer programs for linkage disequilibrium analysis." *Bioinformatics*, **20**(8), 1325-6. ISSN 1367-4803 (Print) 1367-4803, doi:10.1093/bioinformatics/bth071.

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

**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

**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:

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

### Details

Gene counting for haplotype analysis with missing data.

### 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`.

### Note

adapted from GENECOUNTING.

### Author(s)

Jing Hua Zhao

## References

- Zhao JH, Lissarrague S, Essioux L, Sham PC (2002). "GENECOUNTING: haplotype analysis with missing genotypes." *Bioinformatics*, **18**(12), 1694-5. ISSN 1367-4803 (Print) 1367-4803, doi:10.1093/bioinformatics/18.12.1694.
- Zhao JH, Sham PC (2003). "Generic number systems and haplotype analysis." *Comput Methods Programs Biomed*, **70**(1), 1-9. ISSN 0169-2607 (Print) 0169-2607, doi:10.1016/s01692607(01)00193-6.
- Zhao JH (2004). "2LD. GENECOUNTING and HAP: computer programs for linkage disequilibrium analysis." *Bioinformatics*, **20**(8), 1325-6. ISSN 1367-4803 (Print) 1367-4803, doi:10.1093/bioinformatics/bth071.

## See Also

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

## Examples

```
## Not run:
require(gap.datasets)
# HLA data
data(hla)
hla.gc <- genecounting(hla[,3:8])
summary(hla.gc)
hla.gc$l0
hla.gc$l1

# 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$l0
aldh2.gc$l1

# Chromosome X data
# assuming allelic data have been extracted in columns 3-13
# and column 3 is sex
filespec <- system.file("tests/genecounting/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)
```

**Description**

Genotype recoding

**Usage**

```
geno.recode(geno, miss.val = 0)
```

**Arguments**

geno	genotype.
miss.val	missing value.

---

get_b_se	<i>Get b and se from AF, n, and z</i>
----------	---------------------------------------

---

**Description**

The function obtains effect size and its standard error.

**Usage**

```
get_b_se(f, n, z)
```

**Arguments**

f	Allele frequency.
n	Sample size.
z	z-statistics.

**Value**

b and se.

**Examples**

```
## Not run:
library(dplyr)
# eQTLGen
cis_pQTL <- merge(read.delim('eQTLGen.lz') %>%
  filter(GeneSymbol=="LTBR"),read.delim("eQTLGen.AF"),by="SNP") %>%
  mutate(data.frame(get_b_se AlleleB_all,NrSamples,Zscore)))
head(cis_pQTL,1)
      SNP   Pvalue SNPChr  SNPPos AssessedAllele OtherAllele Zscore
rs1003563 2.308e-06    12 6424577             A           G 4.7245
      Gene GeneSymbol GeneChr GenePos NrCohorts NrSamples      FDR
ENSG00000111321    LTBR     12 6492472      34    23991 0.006278872
BonferroniP hg19_chr hg19_pos AlleleA AlleleB allA_total allAB_total
      1      12 6424577      A      G      2574      8483
allB_total AlleleB_all      b      se
7859    0.6396966 0.04490488 0.009504684

## End(Not run)
```

---

get_pve_se	<i>Get pve and its standard error from n, z</i>
------------	---

---

**Description**

Get pve and its standard error from n, z

**Usage**

```
get_pve_se(n, z, correction = TRUE)
```

**Arguments**

n	Sample size.
z	z-statistic, i.e., b/se when they are available instead.
correction	if TRUE an correction based on t-statistic is applied.

**Details**

This function obtains proportion of explained variance of a continuous outcome.

**Value**

pve and its se.

---

get_sdy	<i>Get sd(y) from AF, n, b, se</i>
---------	------------------------------------

---

**Description**

Get sd(y) from AF, n, b, se

**Usage**

```
get_sdy(f, n, b, se, method = "mean", ...)
```

**Arguments**

f	Allele frequency.
n	Sample size.
b	effect size.
se	standard error.
method	method of averaging: "mean" or "median".
...	argument(s) passed to method

**Details**

This function obtains standard error of a continuous outcome.



**Value**

sd(y).

**Examples**

```
## Not run:
set.seed(1)
X1 <- matrix(rbinom(1200,1,0.4),ncol=2)
X2 <- matrix(rbinom(1000,1,0.6),ncol=2)
colnames(X1) <- colnames(X2) <- c("f1","f2")
Y1 <- rnorm(600,apply(X1,1,sum),2)
Y2 <- rnorm(500,2*apply(X2,1,sum),5)
summary(lm1 <- lm(Y1~f1+f2,data=as.data.frame(X1)))
summary(lm2 <- lm(Y2~f1+f2,data=as.data.frame(X2)))
b1 <- coef(lm1)
b2 <- coef(lm2)
v1 <- vcov(lm1)
v2 <- vcov(lm2)
require(coloc)
## Bayesian approach, esp. when only p values are available
abf <- coloc.abf(list(beta=b1, varbeta=diag(v1), N=nrow(X1), sdY=sd(Y1), type="quant"),
                  list(beta=b2, varbeta=diag(v2), N=nrow(X2), sdY=sd(Y2), type="quant"))

abf
# sdY
cat("sd(Y)=",sd(Y1),"==> Estimates:",sqrt(diag(var(X1)*b1[-1]^2+var(X1)*v1[-1,-1]*nrow(X1))),"\n")
for(k in 1:2)
{
  k1 <- k + 1
  cat("Based on b",k," sd(Y1) = ",sqrt(var(X1[,k1])*(b1[k1]^2+nrow(X1)*v1[k1,k1])), "\n", sep="")
}
cat("sd(Y)=",sd(Y2),"==> Estimates:",sqrt(diag(var(X2)*b2[-1]^2+var(X2)*v2[-1,-1]*nrow(X2))),"\n")
for(k in 1:2)
{
  k1 <- k + 1
  cat("Based on b",k," sd(Y2) = ",sqrt(var(X2[,k1])*(b2[k1]^2+nrow(X2)*v2[k1,k1])), "\n", sep="")
}
get_sdy(0.6396966,23991,0.04490488,0.009504684)

## End(Not run)
```

---

 gif

---

*Kinship coefficient and genetic index of familiarity*


---

**Description**

Kinship coefficient and genetic index of familiarity

**Usage**

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

**Arguments**

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

## Details

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 in (Gholami and Thomas 1994) 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.

## Value

The returned value is a list containing:

- gifval the genetic index of familiarity.

## 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

## References

Gholami K, Thomas A (1994). "A linear time algorithm for calculation of multiple pairwise kinship coefficients and the genetic index of familiarity." *Comput Biomed Res*, **27**(5), 342-50. ISSN 0010-4809 (Print) 0010-4809, doi:[10.1006/cbmr.1994.1026](https://doi.org/10.1006/cbmr.1994.1026).

## 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)

```

---

grid2d	<i>Two-dimensional grid</i>
--------	-----------------------------

---

## Description

This function build 2-d grids

## Usage

```

grid2d(
  chrlen,
  plot = TRUE,
  cex.labels = 0.6,
  xlab = "QTL position",
  ylab = "Gene position"
)

```

## Arguments

chrlen	Lengths of chromosomes; e.g., hg18, hg19 or hg38.
plot	A flag for plot.
cex.labels	A scaling factor for labels.
xlab	X-axis title.
ylab	Y-axis title.

## Value

A list with two variables:

- n Number of chromosomes.
- CM Cumulative lengths starting from 0.

---

h2.jags	<i>Heritability estimation based on genomic relationship matrix using JAGS</i>
---------	--

---

### Description

Heritability estimation based on genomic relationship matrix using JAGS

### Usage

```
h2.jags(
  y,
  x,
  G,
  eps = 1e-04,
  sigma.p = 0,
  sigma.r = 1,
  parms = c("b", "p", "r", "h2"),
  ...
)
```

### Arguments

y	outcome vector.
x	covariate matrix.
G	genomic relationship matrix.
eps	a positive diagonal perturbation to G.
sigma.p	initial parameter values.
sigma.r	initial parameter values.
parms	monitored parameters.
...	parameters passed to jags, e.g., n.chains, n.burnin, n.iter.

### Details

This function performs Bayesian heritability estimation using genomic relationship matrix.

### Value

The returned value is a fitted model from jags().

### Author(s)

Jing Hua Zhao keywords htest

### References

Zhao JH, Luan JA, Congdon P (2018). "Bayesian Linear Mixed Models with Polygenic Effects." *Journal of Statistical Software*, **85**(6), 1 - 27. doi:[10.18637/jss.v085.i06](https://doi.org/10.18637/jss.v085.i06).

## Examples

```
## Not run:
require(gap.datasets)
set.seed(1234567)
meyer <- within(meyer,{
  y[is.na(y)] <- rnorm(length(y[is.na(y)]),mean(y,na.rm=TRUE),sd(y,na.rm=TRUE))
  g1 <- ifelse(generation==1,1,0)
  g2 <- ifelse(generation==2,1,0)
  id <- animal
  animal <- ifelse(!is.na(animal),animal,0)
  dam <- ifelse(!is.na(dam),dam,0)
  sire <- ifelse(!is.na(sire),sire,0)
})
G <- kin.morgan(meyer)$kin.matrix*2
library(regress)
r <- regress(y~-1+g1+g2,~G,data=meyer)
r
with(r,h2G(sigma,sigma.cov))
eps <- 0.001
y <- with(meyer,y)
x <- with(meyer,cbind(g1,g2))
ex <- h2.jags(y,x,G,sigma.p=0.03,sigma.r=0.014)
print(ex)

## End(Not run)
```

---

h2G

*Heritability and its variance*


---

## Description

Heritability and its variance

## Usage

```
h2G(V, VCOV, verbose = TRUE)
```

## Arguments

V	Variance estimates.
VCOV	Variance-covariance matrix.
verbose	Detailed output.

## Value

A list of phenotypic variance/heritability estimates and their variances.

h2GE

*Heritability and its variance when there is an environment component***Description**

Heritability and its variance when there is an environment component

**Usage**

```
h2GE(V, VCOV, verbose = TRUE)
```

**Arguments**

V	Variance estimates.
VCOV	Variance-covariance matrix.
verbose	Detailed output.

**Value**

A list of phenotypic variance/heritability/GxE interaction estimates and their variances.

h2l

*Heritability under the liability threshold model***Description**

Heritability under the liability threshold model

**Usage**

```
h2l(K = 0.05, P = 0.5, h2, se, verbose = TRUE)
```

**Arguments**

K	Disease prevalence.
P	Phenotypic variance.
h2	Heritability estimate.
se	Standard error.
verbose	Detailed output.

**Value**

A list of the input heritability estimate/standard error and their counterpart under liability threshold model, the normal deviate..

---

h2\_mzdz*Heritability estimation according to twin correlations*

---

## Description

Heritability estimation according to twin correlations

## Usage

```
h2_mzdz(  
  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

Given MZ/DZ data or their correlations and sample sizes, it obtains heritability and variance estimates under an ACE model as in [doi:10.1038/s4156202301530](https://doi.org/10.1038/s4156202301530) and Keeping (1995).

## Value

A data.frame with variables h2, c2, e2, vh2, vc2, ve2.

## References

Elks CE, den Hoed M, Zhao JH, Sharp SJ, Wareham NJ, Loos RJ, Ong KK (2012). “Variability in the heritability of body mass index: a systematic review and meta-regression.” *Front Endocrinol (Lausanne)*, **3**, 29. ISSN 1664-2392, [doi:10.3389/fendo.2012.00029](https://doi.org/10.3389/fendo.2012.00029).

Keeping ES (1995). *Introduction to statistical inference*, Dover books on mathematics, Dover edition. Dover Publications, New York. ISBN 9780486685021.

## Examples

```
## Not run:
library(mvtnorm)
set.seed(12345)
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)))
selVars <- c('bmi1','bmi2')
names(mzm) <- names(dzm) <- names(mzw) <- names(dzw) <- selVars
ACE_CI <- function(mzData,dzData,n.sim=5,selV=NULL,verbose=TRUE)
{
  ACE_obs <- h2_mzdz(mzDat=mzData,dzDat=dzData,selV=selV)
  cat("\n\nheritability according to correlations\n\n")
  print(format(ACE_obs,digits=3),row.names=FALSE)
  nmz <- nrow(mzData)
  ndz <- nrow(dzData)
  r <- data.frame()
  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,]
    ACE_i <- h2_mzdz(mzDat=mzDat,dzDat=dzDat,selV=selV)
    if (verbose) print(ACE_i)
    r <- rbind(r,ACE_i)
  }
  m <- apply(r,2,mean,na.rm=TRUE)
  s <- apply(r,2,sd,na.rm=TRUE)
  allr <- data.frame(mean=m,sd=s,lcl=m-1.96*s,ucl=m+1.96*s)
  print(format(allr,digits=3))
}
ACE_CI(mzm,dzm,n.sim=500,selV=selVars,verbose=FALSE)
ACE_CI(mzw,dzw,n.sim=500,selV=selVars,verbose=FALSE)

## End(Not run)
```

---

hap

*Haplotype reconstruction*


---

## Description

Haplotype reconstruction

## Usage

```
hap(
```



```

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

```

### Arguments

<code>id</code>	a column of subject id.
<code>data</code>	genotype table.
<code>nloci</code>	number of loci.
<code>loci</code>	number of alleles at all loci.
<code>names</code>	locus names.
<code>control</code>	is a call to <code>hap.control()</code> .

### Details

Haplotype reconstruction using sorting and trimming algorithms.

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:

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

### Note

adapted from `hap`.

### References

Clayton DG (2001) SNPHAP. <https://github.com/chrlswallace/snphap>.

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

Zhao JH (2004). "2LD. GENECOUNTING and HAP: computer programs for linkage disequilibrium analysis." *Bioinformatics*, **20**(8), 1325-6. ISSN 1367-4803 (Print) 1367-4803, doi:[10.1093/bioinformatics/bth071](https://doi.org/10.1093/bioinformatics/bth071).

### See Also

[genecounting](#)

## Examples

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

# 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.control

*Control for haplotype reconstruction*


---

## Description

Control for haplotype reconstruction

## Usage

```
hap.control(
  mb = 0,
  pr = 0,
  po = 0.001,
  to = 0.001,
  th = 1,
  maxit = 100,
  n = 0,
  ss = 0,
  rs = 0,
  rp = 0,
  ro = 0,
  rv = 0,
  sd = 0,
  mm = 0,
  mi = 0,
  mc = 50,
  ds = 0.1,
  de = 0,
  q = 0,
  hapfile = "hap.out",
  assignfile = "assign.out"
)
```

**Arguments**

mb	Maximum dynamic storage to be allocated, in Mb.
pr	Prior (ie population) probability threshold.
po	Posterior probability threshold.
to	Log-likelihood convergence tolerance.
th	Posterior probability threshold for output.
maxit	Maximum EM iteration.
n	Force numeric allele coding (1/2) on output (off).
ss	Tab-delimited spreadsheet file output (off).
rs	Random starting points for each EM iteration (off).
rp	Restart from random prior probabilities.
ro	Loci added in random order (off).
rv	Loci added in reverse order (off).
sd	Set seed for random number generator (use date+time).
mm	Repeat final maximization multiple times.
mi	Create multiple imputed datasets. If set >0.
mc	Number of MCMC steps between samples.
ds	Starting value of Dirichlet prior parameter.
de	Finishing value of Dirichlet prior parameter.
q	Quiet operation (off).
hapfile	a file for haplotype frequencies.
assignfile	a file for haplotype assignment.

**Value**

A list containing the parameter specifications to the function.

---

hap.em

*Gene counting for haplotype analysis*


---

**Description**

Gene counting for haplotype analysis

**Usage**

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

**Arguments**

<code>id</code>	a vector of individual IDs.
<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 (lnlike).
<code>maxiter</code>	Maximum number of iterations of EM.
<code>miss.val</code>	missing value.

**Details**

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

**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  $i$ th element of `hap.prob` corresponds to the  $i$ th 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 `indx=i`, then  $i$  is the  $i$ th row of input matrix data. If the  $i$ th 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.

**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	<i>Score statistics for association of traits with haplotypes</i>
-----------	---

---

**Description**

Score statistics for association of traits with haplotypes

**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

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.

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 between traits and haplotypes when linkage phase is ambiguous." *Am J Hum Genet*, **70**(2), 425-34. ISSN 0002-9297 (Print) 0002-9297, doi:10.1086/338688.

**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)
```

hg18

*Chromosomal lengths for build 36***Description**

Data are used in other functions.

**Usage**

```
hg18
```

**Format**

A vector containing lengths of chromosomes.

**Details**

generated from GRCh.R.

---

hg19	<i>Chromosomal lengths for build 37</i>
------	---

---

**Description**

Data are used in other functions.

**Usage**

hg19

**Format**

A vector containing lengths of chromosomes.

---

hg38	<i>Chromosomal lengths for build 38</i>
------	---

---

**Description**

Data are used in other functions.

**Usage**

hg38

**Format**

A vector containing lengths of chromosomes.

---

hmht.control	<i>Controls for highlights</i>
--------------	--------------------------------

---

**Description**

Specification of highlights

**Usage**

```
hmht.control(  
  data = NULL,  
  colors = NULL,  
  yoffset = 0.25,  
  cex = 1.5,  
  boxed = FALSE  
)
```



**Arguments**

data	Data.
colors	Colors.
yoffset	Y offset.
cex	Scaling factor.
boxed	Label in box.

**Value**

A list as above.

---

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

---

**Description**

Haplotype trend regression

**Usage**

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

**Arguments**

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

**Details**

Haplotype trend regression (with permutation)

**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.

**Note**

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

**Author(s)**

Dimitri Zaykin, Jing Hua Zhao

## 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**(2), 79-91. ISSN 0001-5652 (Print) 0001-5652, doi:10.1159/000057986.

Xie R, Stram DO (2005). "Asymptotic equivalence between two score tests for haplotype-specific risk in general linear models." *Genetic Epidemiology*, **29**(2), 166-170. ISSN 0741-0395, doi:10.1002/gepi.20087.

## 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
require(gap.datasets)
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 for a multiallelic marker

**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**

Hardy-Weinberg equilibrium test.

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:

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

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

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.

**Author(s)**

Chang Yu, Li Wang, Jing Hua Zhao

**References**

Yu C, Zhang S, Zhou C, Sile S (2009). "A likelihood ratio test of population Hardy-Weinberg equilibrium for case-control studies." *Genet Epidemiol*, **33**(3), 275-80. ISSN 0741-0395 (Print) 0741-0395, doi:[10.1002/gepi.20381](https://doi.org/10.1002/gepi.20381).

**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 using 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.

**Details**

Hardy-Weinberg equilibrium test by MCMC

**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).

**Note**

Codes are commented for taking x a genotype object, as genotype to prepare a and alleles on the fly.

Adapted from HARDY, testable with -Dexecutable as standalone program.

keywords htest

**Author(s)**

Sun-Wei Guo, Jing Hua Zhao, Gregor Gorjanc

**Source**

<https://sites.stat.washington.edu/thompson/Genepi/pangaea.shtml>

**References**

Guo SW, Thompson EA (1992). "Performing the exact test of Hardy-Weinberg proportion for multiple alleles." *Biometrics*, **48**(2), 361-72. ISSN 0006-341X (Print) 0006-341x.

**See Also**

[hwe](#), [genetics::HWE.test](#), [genetics::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)

```

hwe.jags

*Hardy-Weinberg equilibrium test for a multiallelic marker using JAGS***Description**

Hardy-Weinberg equilibrium test for a multiallelic marker using JAGS

**Usage**

```
hwe.jags(
  k,
  n,
  delta = rep(1/k, k),
  lambda = 0,
  lambdamu = -1,
  lambdasd = 1,
  parms = c("p", "f", "q", "theta", "lambda"),
  ...
)
```

**Arguments**

k	number of alleles.
n	a vector of $k(k+1)/2$ genotype counts.
delta	initial parameter values.
lambda	initial parameter values.
lambdamu	initial parameter values.
lambdasd	initial parameter values.
parms	monitored parameters.
...	parameters passed to jags, e.g., n.chains, n.burnin, n.iter.

**Details**

Hardy-Weinberg equilibrium test.

This function performs Bayesian Hardy-Weinberg equilibrium test, which mirrors [hwe.hardy](#), another implementation for highly polymorphic markers when asymptotic results do not hold.

**Value**

The returned value is a fitted model from jags().

**Author(s)**

Jing Hua Zhao, Jon Wakefield

**References**

Wakefield J (2010). "Bayesian methods for examining Hardy-Weinberg equilibrium." *Biometrics*, **66**(1), 257-65. ISSN 0006-341X (Print) 0006-341x, doi:10.1111/j.15410420.2009.01267.x.



**See Also**[hwe.hardy](#)**Examples**

```
## Not run:
ex1 <- hwe.jags(4,c(5,6,1,7,11,2,8,19,26,15))
print(ex1)
ex2 <- hwe.jags(2,c(49,45,6))
print(ex2)
ex3 <- hwe.jags(4,c(0,3,1,5,18,1,3,7,5,2),lambda=0.5,lambdamu=-2.95,lambdasd=1.07)
print(ex3)
ex4 <- hwe.jags(9,c(1236,120,3,18,0,0,982,55,7,249,32,1,0,12,0,2582,132,20,1162,29,
1312,6,0,0,4,0,4,0,2,0,0,0,0,0,0,115,5,2,53,1,149,0,0,4),
delta=c(1,1,1,1,1,1,1,1,1),lambdamu=-4.65,lambdasd=0.21)
print(ex4)
ex5 <- hwe.jags(8,n=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))
print(ex5)

# Data and code according to the following URL,
# http://darwin.eeb.uconn.edu/eeb348-notes/testing-hardy-weinberg.pdf
hwe.jags.AB0 <- function(n,...)
{
  hwe <- function() {
    # likelihood
    pi[1] <- p.a*p.a + 2*p.a*p.o
    pi[2] <- 2*p.a*p.b
    pi[3] <- p.b*p.b + 2*p.b*p.o
    pi[4] <- p.o*p.o
    n[1:4] ~ dmulti(pi[],N)
    # priors
    a1 ~ dexp(1)
    b1 ~ dexp(1)
    o1 ~ dexp(1)
    p.a <- a1/(a1 + b1 + o1)
    p.b <- b1/(a1 + b1 + o1)
    p.o <- o1/(a1 + b1 + o1)
  }
  hwd <- function() {
    # likelihood
    pi[1] <- p.a*p.a + f*p.a*(1-p.a) + 2*p.a*p.o*(1-f)
    pi[2] <- 2*p.a*p.b*(1-f)
    pi[3] <- p.b*p.b + f*p.b*(1-p.b) + 2*p.b*p.o*(1-f)
    pi[4] <- p.o*p.o + f*p.o*(1-p.o)
    n[1:4] ~ dmulti(pi[],N)
    # priors
    a1 ~ dexp(1)
    b1 ~ dexp(1)
  }
}
```

```

o1 ~ dexp(1)
p.a <- a1/(a1 + b1 + o1)
p.b <- b1/(a1 + b1 + o1)
p.o <- o1/(a1 + b1 + o1)
f ~ dunif(0,1)
}
N <- sum(n)
AB0.hwe <- R2jags::jags(list(n=n,N=N),,c("pi","p.a","p.b","p.o"),hwe,...)
AB0.hwd <- R2jags::jags(list(n=n,N=N),,c("pi","p.a","p.b","p.o","f"),hwd,...)
invisible(list(hwe=AB0.hwe,hwd=AB0.hwd))
}
hwe.jags.AB0.results <- hwe.jags.AB0(n=c(862, 131, 365, 702))
hwe.jags.AB0.results

## End(Not run)

```

---

invnormal

*Inverse normal transformation*


---

## Description

Inverse normal transformation

## Usage

```
invnormal(x)
```

## Arguments

x                      Data with missing values.

## Value

Transformed value.

## Examples

```

x <- 1:10
z <- invnormal(x)
plot(z,x,type="b")

```

---

inv_chr_pos_a1_a2	<i>Retrieval of chr:pos+a1/a2 according to SNP id</i>
-------------------	---

---

**Description**

This function obtains information embedded in unique identifiers.

**Usage**

```
inv_chr_pos_a1_a2(chr_pos_a1_a2, prefix = "chr", seps = c(":", "_", "-"))
```

**Arguments**

chr_pos_a1_a2	SNP id.
prefix	Prefix of the identifier.
seps	Delimiters of fields.

**Value**

A data.frame with the following variables:

- chr Chromosome.
- pos Position.
- a1 Allele 1.
- a2 Allele 2.

**Examples**

```
# rs12075
inv_chr_pos_a1_a2("chr1:159175354_A_G", prefix="chr", seps=c(":", "_", "-"))
```

---

ixy	<i>Conversion of chrosome name from strings</i>
-----	---

---

**Description**

This function converts 1:22, X, Y back to 1:24.

**Usage**

```
ixy(x)
```

**Arguments**

x	Chromosome name in strings
---	----------------------------

**Value**

As indicated.

---

KCC	<i>Disease prevalences in cases and controls</i>
-----	--

---

**Description**

Disease prevalences in cases and controls

**Usage**

```
KCC(model, GRR, p1, K)
```

**Arguments**

model	disease model (one of "multiplicative", "additive", "recessive", "dominant", "overdominant").
GRR	genotype relative risk.
p1	disease allele frequency.
K	disease prevalence in the whole population.

**Details**

KCC calculates disease prevalences in cases and controls for a given genotype relative risk, allele frequency and prevalence of the disease in the whole population. It is used by tscc and pbsize2.

**Value**

A list of two elements:

- pprime prevalence in cases.
- p prevalence in controls.

---

kin.morgan	<i>kinship matrix for simple pedigree</i>
------------	---

---

**Description**

kinship matrix for simple pedigree

**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.

**Details**

kinship matrix according to Morgan v2.1.

**Value**

The returned value is a list containing:

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

**Note**

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

**Author(s)**

Morgan development team, Jing Hua Zhao

**References**

Morgan V2.1 <https://sites.stat.washington.edu/thompson/Genepi/MORGAN/Morgan.shtml>

**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.

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
source(file.path(find.package("gap"), "scripts", "SH2B1.R"), echo=TRUE)

## End(Not run)
```

labelManhattan

*Annotate Manhattan or Miami Plot***Description**

Annotate Manhattan or Miami Plot

**Usage**

```
labelManhattan(
  chr,
  pos,
  name,
  gwas,
  gwasChrLab = "chr",
  gwasPosLab = "pos",
  gwasPLab = "p",
  gwasZLab = "NULL",
  chrmaxpos,
  textPos = 4,
  angle = 0,
  miamiBottom = FALSE
)
```

**Arguments**

chr	A vector of chromosomes for the markers to be labelled.
pos	A vector of positions on the chromosome for the markers to be labelled. These must correspond to markers in the GWAS dataset used to make the manhattan plot.
name	A vector of labels to be added next to the points specified by chr and pos.
gwas	The same GWAS dataset used to plot the existing Manhattan or Miami plot to be annotated.
gwasChrLab	The name of the column in gwas containing chromosome number. Defaults to "chr".
gwasPosLab	The name of the column in gwas containing position. Defaults to "pos".
gwasPLab	The name of the column in gwas containing p-values. Defaults to "p".
gwasZLab	The name of the column in gwas containing z-values. Defaults to "NULL".
chrmaxpos	Data frame containing x coordinates for chromosome start positions, generated by <a href="#">labelManhattan</a> .
textPos	An integer or vector dictating where the label should be plotted relative to each point. Good for avoiding overlapping labels. Provide an integer to plot all points in the same relative position or use a vector to specify position for each label. Passed to the 'pos' option of <a href="#">graphics::text</a> . Defaults to '4'.
angle	An integer or vector dictating the plot angle of the label for each point. Provide an integer to plot all points in the same relative position or use a vector to specify position for each label. Passed to the 'srt' option of <a href="#">graphics::text</a> . Defaults to '0'.
miamiBottom	If 'TRUE', labels will be plotted on the lower region of a Miami plot. If 'FALSE', labels will be plotted on the upper region. Defaults to 'FALSE'.

**Details**

Add labels beside specified points on a Manhattan or Miami plot. Ideal for adding locus names to peaks. Currently only designed to work with [miamiplot2](#).

**Value**

Adds annotation to existing Manhattan or Miami plot

**Note**

Extended to handle extreme P values.

**Author(s)**

Jonathan Marten

**Examples**

```
## Not run:
labelManhattan(c(4,5,11,19),c(9994215,16717922,45538760,51699256),
               c("GENE1","GENE2","GENE3","GENE4"),
               gwas1,chrmaxpos=chrmaxpos)
labelManhattan(geneLabels$chr,geneLabel$pos,geneLabel$geneName,gwas1,chrmaxpos=chrmaxpos)

## End(Not run)
```

---

LD22

*LD statistics for two diallelic markers*


---

**Description**

LD statistics for two diallelic markers

**Usage**

```
LD22(h, n)
```

**Arguments**

h	a vector of haplotype frequencies.
n	number of haplotypes.

**Details**

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.



**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.

**Note**

extracted from 2ld.c, worked 28/6/03, tables are symmetric do not fix, see kbyl below

**Author(s)**

Jing Hua Zhao

**References**

Zabetian CP, Buxbaum SG, Elston RC, Köhnke MD, Anderson GM, Gelernter J, Cubells JF (2003). "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**(6), 1389-400. ISSN 0002-9297 (Print) 0002-9297, doi:10.1086/375499.

Zapata C, Alvarez G, Carollo C (1997). "Approximate variance of the standardized measure of gametic disequilibrium D'." *Am J Hum Genet*, **61**(3), 771-4. ISSN 0002-9297 (Print) 0002-9297, doi:10.1016/s00029297(07)643420.

**See Also**

[LDk1](#)

**Examples**

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

## End(Not run)
```

LDkl

*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**

```
LDkl(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 Dij.
- VarDijtable table of variances for Dij.
- Dmaxtable table of Dmax.
- Dijptable table of Dij'.
- VarDijptable 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.

**Note**

adapted from 2ld.c.

**Author(s)**

Jing Hua Zhao

**References**

Bishop YMM, Fienberg SE, Holland PW (1975). *Discrete multivariate analysis: theory and practice*. MIT Press, Cambridge, Mass. ISBN 9780262021135.

Cramer H (1946). *Mathematical Methods of Statistics*. Princeton Univ. Press.

Zapata C, Carollo C, Rodriguez S (2001). "Sampling variance and distribution of the D' measure of overall gametic disequilibrium between multiallelic loci." *Ann Hum Genet*, **65**(Pt 4), 395-406. ISSN 0003-4800 (Print) 0003-4800, doi:10.1017/s0003480001008697.

Zhao JH (2004). "2LD. GENECOUNTING and HAP: computer programs for linkage disequilibrium analysis." *Bioinformatics*, **20**(8), 1325-6. ISSN 1367-4803 (Print) 1367-4803, doi:10.1093/bioinformatics/bth071.

**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"
# The data is now available from 2ld in Haplotype-Analysis

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

## End(Not run)
```

---

log10p	<i>log10(p) for a normal deviate z</i>
--------	--

---

**Description**

log10(p) for a normal deviate z

**Usage**

log10p(z)

**Arguments**

z                      normal deviate.

**Value**

log10(P)

**Author(s)**

James Peters

**Examples**

log10p(100)

---

log10pvalue	<i>log10(p) for a P value including its scientific format</i>
-------------	---

---

**Description**

log10(p) for a P value including its scientific format

**Usage**

log10pvalue(p = NULL, base = NULL, exponent = NULL)

**Arguments**

p                      value.  
 base                  base part in scientific format.  
 exponent              exponent part in scientific format.

**Value**

log10(P)

**Examples**

log10pvalue(1e-323)  
 log10pvalue(base=1,exponent=-323)

---

logp	<i>log(p) for a normal deviate z</i>
------	--------------------------------------

---

**Description**

log(p) for a normal deviate z

**Usage**

logp(z)

**Arguments**

z                      normal deviate.

**Value**

log(P)

**Examples**

logp(100)

---

makeped	<i>A function to prepare pedigrees in post-MAKEPED format</i>
---------	---

---

**Description**

A function to prepare pedigrees in post-MAKEPED format

**Usage**

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

**Arguments**

pifile	input filename.
pofile	output filename.
auto.select	no loops in pedigrees and probands are selected automatically? 0=no, 1=yes.
with.loop	input data with loops? 0=no, 1=yes.
loop.file	filename containing pedigree id and an individual id for each loop, set if with.loop=1.

auto.proband	probands are selected automatically? 0=no, 1=yes.
proband.file	filename containing pedigree id and proband id, set if auto.proband=0 (not implemented).

### Details

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.

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.

### Note

adapted from makeped.c by W Li and others. keywords datagen

### Examples

```
## Not run:
cwd <- getwd()
cs.dir <- file.path(find.package("gap.examples"), "tests", "kinship")
setwd(cs.dir)
dir()
makeped("ped7.pre", "ped7.ped", 0, 1, "ped7.lop")
setwd(cwd)
# https://lab.rockefeller.edu/ott/

## End(Not run)
```

---

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.

### 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
sdv	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, sdv, 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 (b1star)
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

Mediation has been thought of in terms of the proportion of effect explained, or the relative attenuation of b1, the coefficient for the primary predictor X1, when the mediator, X2, is added to the model. The goal is to show that b1\*, the coefficient for X1 in the reduced model (i.e., the model with only X1, differs from b1, its coefficient in the full model (i.e., the model with both X1 and the mediator X2. If X1 and X2 are correlated, then showing that b2, the coefficient for X2, differs from zero is equivalent to showing b1\* differs from b1. Thus the problem reduces to detecting an effect of X2, controlling for X1. In short, it amounts to the more familiar problem of inflating sample size to account for loss of precision due to adjustment for X1.

The approach here is to approximate the expected information matrix from the regression model including both  $X_1$  and  $X_2$ , to obtain the expected standard error of the estimate of  $b_2$ , evaluated at the MLE. The sample size follows from comparing the Wald test statistic (i.e., the ratio of the estimate of  $b_2$  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  $X_2$  as the primary predictor and consider  $X_1$  the confounder.

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  $X_1$  and  $X_2$ . 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  $X_2$  set `sdX2 = sqrt(f2(1 - f2))`. 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`, `sd1` or `f1`, `b2`, `sd2` 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, sd2, sd1	linear
linear2	b1star, PTE, rho, sd1, sd1	lineara
linear3	b1star, b2, PTE, sd1, sd2, sd1	linearb
linear4	b1star, b1, b2, sd1, sd2, sd1	linearc
logistic1	p, b2, rho, sd2	logistic.approx
logistic2	p, b1, b2, rho, sd1, sd2, ns	logistic.ccs
logistic3	p, b1, f1, b2, rho, sd2, ns	logistic.bcs
logistic4	p, b1, b2, f2, rho, sd1, ns	logistic.cbs
logistic5	p, b1, f1, b2, f2, rho, ns	logistic.bbs
poisson1	m, b2, rho, sd2	poisson.approx
poisson2	m, b2, rho, sd2	poisson.cc
poisson3	m, b2, rho, sd2	poisson.bc
poisson4	m, b1, b2, f2, rho, sd1	poisson.cb
poisson5	m, b1, f1, b2, f2, rho	poisson.bb
poisson6	m, b1, b2, rho, sd1, sd2, ns	poisson.ccs
poisson7	m, b1, f1, b2, rho, sd2, ns	poisson.bcs
poisson8	m, b1, b2, f2, rho, sd1, ns	poisson.cbs
poisson9	m, b1, f1, b2, f2, rho, ns	poisson.bbs
cox1	b2, rho, f, sd2	cox.approx
cox2	b1, b2, rho, f, sd1, sd2, ns	cox.ccs
cox3	b1, f1, b2, rho, f, sd2, ns	cox.bcs
cox4	b1, b2, f2, rho, f, sd1, ns	cox.cbs
cox5	b1, f1, b2, f2, rho, f, ns	cox.bbs
cox6	b1, b2, rho, f, fc, sd1, sd2, ns	cox.ccs2
cox7	b1, f1, b2, rho, f, fc, sd2, ns	cox.bcs2
cox8	b1, b2, f2, rho, f, fc, sd1, 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 (1998). "A simple method of sample size calculation for linear and logistic regression." *Stat Med*, **17**(14), 1623-34. ISSN 0277-6715 (Print) 0277-6715, doi:10.1002/(sici)10970258(19980730)17:14<1623::aid-sim871>3.0.co;2s.

Schmoor C, Sauerbrei W, Schumacher M (2000). "Sample size considerations for the evaluation of prognostic factors in survival analysis." *Stat Med*, **19**(4), 441-52. ISSN 0277-6715 (Print) 0277-6715, doi:10.1002/(sici)10970258(20000229)19:4<441::aidsim349>3.0.co;2n.

Vittinghoff E, Sen S, McCulloch CE (2009). "Sample size calculations for evaluating mediation." *Stat Med*, **28**(4), 541-57. ISSN 0277-6715 (Print) 0277-6715, doi:10.1002/sim.3491.

## 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)
```

**Description**

Mixed modeling with genetic relationship matrices

**Usage**

```
MCMCgrm(
  model,
  prior,
  data,
  GRM,
  eps = 0,
  n.thin = 10,
  n.burnin = 3000,
  n.iter = 13000,
  ...
)
```

**Arguments**

<code>model</code>	statistical model.
<code>prior</code>	a list of priors for parameters in the model above.
<code>data</code>	a data.frame containing outcome and covariates.
<code>GRM</code>	a relationship matrix.
<code>eps</code>	a small number added to the diagonal of the a nonpositive definite GRM.
<code>n.thin</code>	thinning parameter in the MCMC.
<code>n.burnin</code>	the number of burn-in's.
<code>n.iter</code>	the number of iterations.
<code>...</code>	other options as appropriate for MCMCglmm.

**Details**

Mixed modeling with genomic relationship matrix. This is appropriate with relationship matrix derived from family structures or unrelated individuals based on whole genome data.

The function was created to address a number of issues involving mixed modelling with family data or population sample with whole genome data. First, the implementaiton will shed light on the uncertainty involved with polygenic effect in that posterior distributions can be obtained. Second, while the model can be used with the MCMCglmm package there is often issues with the specification of pedigree structures but this is less of a problem with genetic relationship matrices. We can use established algorithms to generate kinship or genomic relationship matrix as input to the MCMCglmm function. Third, it is more intuitive to specify function arguments in line with other packages such as R2OpenBUGS, R2jags or glmmBUGS. In addition, our experiences of tuning the model would help to reset the input and default values.

**Value**

The returned value is an object as generated by MCMCglmm.

**Author(s)**

Jing Hua Zhao

**References**

Hadfield JD (2010). "MCMC Methods for Multi-Response Generalized Linear Mixed Models: The MCMCglmm R Package." *Journal of Statistical Software*, **33**(2), 1 - 22. doi:[10.18637/jss.v033.i02](https://doi.org/10.18637/jss.v033.i02).

**Examples**

```
## Not run:
### with kinship

# library(kinship)
# fam <- with(l51,makefamid(id,fid,mid))
# s <-with(l51, makekinship(fam, id, fid, mid))
# K <- as.matrix(s)*2

### with gap

s <- kin.morgan(l51)
K <- with(s,kin.matrix*2)
prior <- list(R=list(V=1, nu=0.002), G=list(G1=list(V=1, nu=0.002)))
m <- MCMCgrm(qt~1,prior,l51,K)
save(m,file="l51.m")
pdf("l51.pdf")
plot(m)
dev.off()

# A real analysis on bats
## data
bianfu.GRM <- read.table("bianfu.GRM.txt", header = TRUE)
bianfu.GRM[1:5,1:6]
Data <- read.table(file = "PHONE.txt", header = TRUE,
                  colClasses=c(rep("factor",3),rep("numeric",7)))

## MCMCgrm
library("MCMCglmm")
GRM <- as.matrix(bianfu.GRM[, -1])
colnames(GRM) <- rownames(GRM) <- bianfu.GRM[,1]
library(gap)
names(Data)[1] <- "id"
prior <- list(G = list(G1 = list(V = 1, nu = 0.002)), R = list(V = 1, nu = 0.002))
model1.1 <- MCMCgrm(WEIGHT ~ 1, prior, Data, GRM, n.burnin=100, n.iter=1000, verbose=FALSE)
## an alternative
names(Data)[1] <- "animal"
N <- nrow(Data)
i <- rep(1:N, rep(N, N))
j <- rep(1:N, N)
s <- Matrix::spMatrix(N, N, i, j, as.vector(GRM))
Ginv <- Matrix::solve(s)
class(Ginv) <- "dgCMatrix"
rownames(Ginv) <- Ginv@Dimnames[[1]] <- with(Data, animal)
```

```

model1.2 <- MCMCglmm(WEIGHT ~ 1, random = ~ animal, data = Data,
  ginverse=list(animal=Ginv), prior = prior, burnin=100, nitt=1000, verbose=FALSE)
## without missing data
model1.3 <- MCMCglmm(Peak_Freq ~ WEIGHT, random = ~ animal,
  data=subset(Data,!is.na(Peak_Freq)&!is.na(WEIGHT)),
  ginverse=list(animal=Ginv), prior = prior, burnin=100, nitt=1000, verbose=FALSE)

## End(Not run)

```

---

METAL_forestplot	<i>forest plot as R/meta's forest for METAL outputs</i>
------------------	---

---

## Description

forest plot as R/meta's forest for METAL outputs

## Usage

```
METAL_forestplot(tbl, all, rsid, package = "meta", split = FALSE, ...)
```

## Arguments

<code>tbl</code>	Meta-analysis summary statistics.
<code>all</code>	statistics from all contributing studies.
<code>rsid</code>	SNPID-rsid mapping file.
<code>package</code>	style of plot as in meta, rmeta or forestplot.
<code>split</code>	when TRUE, individual prot-MarkerName.pdf will be generated.
<code>...</code>	Additional arguments to meta::forest.

## Details

This functions takes a meta-data from METAL (`tbl`) and data from contributing studies (`all`) for forest plot. It also takes a SNPID-rsid mapping (`rsid`) as contributing studies often involve discrepancies in rsid so it is appropriate to use SNPID, i.e., chr:pos\_A1\_A2 (A1<=A2).

The study-specific and total sample sizes (N) can be customised from METAL commands. By default, the input triplets each contain a MarkerName variable which is the unique SNP identifier (e.g., chr:pos:a1:a2) and the `tbl` argument has variables A1 and A2 as produced by METAL while the `all` argument has EFFECT\_ALLELE and REFERENCE\_ALLELE as with a study variable indicating study name. Another variable common the `tbl` and `all` is prot variable as the function was developed in a protein based meta-analysis. From these all information is in place for generation of a list of Forest plots through a batch run.

```

CUSTOMVARIABLE N
LABEL N as N
WEIGHTLABEL N

```

## Value

It will generate a forest plot specified by pdf for direction-adjusted effect sizes.

**Author(s)**

Jing Hua Zhao

**References**

Scharzer G. (2007). meta: An R package for meta-analysis. R News, 7:40-5, [https://cran.r-project.org/doc/Rnews/Rnews\\_2007-3.pdf](https://cran.r-project.org/doc/Rnews/Rnews_2007-3.pdf), <https://CRAN.R-project.org/package=meta>.

Willer CJ, Li Y, Abecasis GR (2010). "METAL: fast and efficient meta-analysis of genomewide association scans." *Bioinformatics*, **26**(17), 2190-1. ISSN 1367-4803 (Print) 1367-4803, [doi:10.1093/bioinformatics/btq340](https://doi.org/10.1093/bioinformatics/btq340).

**Examples**

```
## Not run:
require(gap.datasets)
data(OPG)
METAL_forestplot(OPGtbl,OPGall,OPGrsid,width=8.75,height=5,digits.TE=2,digits.se=2)

## End(Not run)
```

---

metap

---

*Meta-analysis of p values*


---

**Description**

Meta-analysis of p values

**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	Prefix of sample size, with default value "n".

**Details**

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.

**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)

```

metareg

*Fixed and random effects model for meta-analysis***Description**

Fixed and random effects model for meta-analysis

**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.

**Details**

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  $p_{heter} = pchisq(q_w, k - 1, lower.tail = FALSE)$ .

**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.

### Note

Adapted from a SAS macro, 23-7-2009 MRC-Epid JHZ

### Author(s)

Shengxu Li, Jing Hua Zhao

### References

Higgins JP, Thompson SG, Deeks JJ, Altman DG (2003). "Measuring inconsistency in meta-analyses." *BMJ*, **327**(7414), 557-60. ISSN 0959-8138 (Print) 0959-8138, doi:[10.1136/bmj.327.7414.557](https://doi.org/10.1136/bmj.327.7414.557).

### 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)
```

---

mht.control

*Controls for mhtplot*


---

### Description

Parameter specification through function

### Usage

```
mht.control(
  type = "p",
  usepos = FALSE,
  logscale = TRUE,
  base = 10,
  cutoffs = NULL,
```

```

    colors = NULL,
    labels = NULL,
    srt = 45,
    gap = NULL,
    cex = 0.4,
    yline = 3,
    xline = 3
  )

```

### Arguments

type	Type of plot.
usepos	A flag.
logscale	A flag for log-scale.
base	Base of log.
cutoffs	Cutoffs of P-value, etc.
colors	Colours for chromosomes.
labels	Labels for chromosomes.
srt	Rotation degrees.
gap	Gap between data points.
cex	Scaling factor of data points.
ylines	Vertical adjustment.
xlines	Horizontal adjustment.

### Value

A list as above.

---

mhtplot

*Manhattan plot*


---

### Description

Manhattan plot

### 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 mht.control() with the following arguments: <ul style="list-style-type: none"> <li>• type a flag with value "p" or "l" indicating if points or lines are to be drawn.</li> <li>• usepos a flag to use real chromosomal positions as composed to ordinal positions with default value FALSE.</li> </ul>

- logscale a flag to indicate if p value is to be log-transformed with default value TRUE.
  - base the base of the logarithm with default value 10.
  - cutoffs the cut-offs where horizontal line(s) are drawn with default value NULL.
  - colors the color for different chromosome(s), and random if unspecified with default values NULL.
  - labels labels for the ticks on x-axis with default value NULL.
  - srt degree to which labels are rotated with default value of 45.
  - gap gap between chromosomes with default value NULL.
  - cex cex for the data points.
  - yline Margin line position.
  - xline Margin line position.
- hcontrol A control function named hmht.control() with the following arguments:
- data. chunk of data to be highlighted with default value NULL.
  - colors. colors for annotated genes.
  - yoffset. offset above the data point showing most significant p value with default value 0.5.
  - cex shrinkage factor for data points with default value 1.5.
  - boxed if the label for the highlighted region with default value FALSE.
- ... other options in compatible with the R plot function.

## Details

To generate Manhattan plot, e.g., of genomewide significance (p values) and a 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.

## 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,srt=0)
title("A simulated example according to EPIC-Norfolk QCed SNPs")
axis(2)
axis(1,pos=0,labels=FALSE,tick=FALSE)
abline(0,0)
# 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)
require(gap.datasets)
mhtplot(mhtdata[,c("chr","pos","p")],ops,xlab="",ylab="",srt=0)
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)
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")

```

```
# Miami plot

test <- within(test, {pr=1-p})
miamiplot(test,chr="chr",bp="pos",p="p",pr="pr")

## End(Not run)
```

mhtplot.trunc

*Truncated Manhattan plot*

## Description

Truncated Manhattan plot

## Usage

```
mhtplot.trunc(
  x,
  chr = "CHR",
  bp = "BP",
  p = NULL,
  log10p = NULL,
  z = NULL,
  snp = "SNP",
  col = c("gray10", "gray60"),
  chrlabs = NULL,
  suggestiveline = -log10(1e-05),
  genomewideline = -log10(5e-08),
  highlight = NULL,
  annotatelog10P = NULL,
  annotateTop = FALSE,
  cex.mtext = 1.5,
  cex.text = 0.7,
  mtext.line = 2,
  y.ax.space = 5,
  y.brk1 = NULL,
  y.brk2 = NULL,
  trunc.yaxis = TRUE,
  cex.axis = 1.2,
  delta = 0.05,
  ...
)
```

## Arguments

x	A data.frame.
chr	Chromosome.
bp	Position.
p	p values, e.g., "1.23e-600".
log10p	log10(p).

<code>z</code>	z statistic, i.e., BETA/SE.
<code>snp</code>	SNP. Pending on the setup it could either of variant or gene ID(s).
<code>col</code>	Colours.
<code>chrlabs</code>	Chromosome labels, 1,2,...22,23,24,25.
<code>suggestiveline</code>	Suggestive line.
<code>genomewideline</code>	Genomewide line.
<code>highlight</code>	A list of SNPs to be highlighted.
<code>annotatelog10P</code>	Threshold of $-\log_{10}(P)$ to annotate.
<code>annotateTop</code>	Annotate top.
<code>cex.mtext</code>	axis label extension factor.
<code>cex.text</code>	SNP label extension factor.
<code>mtext.line</code>	position of the y lab.
<code>y.ax.space</code>	interval of ticks of the y axis.
<code>y.brk1</code>	lower $-\log_{10}(P)$ break point.
<code>y.brk2</code>	upper $-\log_{10}(P)$ break point.
<code>trunc.yaxis</code>	do not truncate y-axisx when FALSE.
<code>cex.axis</code>	extension factor for x-, y-axis.
<code>delta</code>	a value to enable column(s) of red points.
<code>...</code>	other options.

## Details

To generate truncated Manhattan plot, e.g., of genomewide significance (P values) or a random variable that is uniformly distributed.

The rationale of this function is to extend `mhtplot()` to handle extremely small p values as often seen from a protein GWAS. Optionally, the function also draws an ordinary Manhattan plot.

## Value

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

## Author(s)

James Peters, Jing Hua Zhao

## See Also

[mhtplot.](#)

## Examples

```
## Not run:
options(width=120)
require(gap.datasets)
mhtdata <- within(mhtdata, {z=qnorm(p/2, lower.tail=FALSE)})
mhtplot.trunc(mhtdata, chr = "chr", bp = "pos", z = "z", snp = "rsn",
              y.brk1=6, y.brk2=10, y.ax.space=1, mtext.line=2.5)
# https://portals.broadinstitute.org/collaboration/
```

```

# giant/images/c/c8/Meta-analysis_Locke_et_al%2BUKBiobank_2018_UPDATED.txt.gz
gz <- gzfile("work/Meta-analysis_Locke_et_al+UKBiobank_2018_UPDATED.txt.gz")
BMI <- within(read.delim(gz,as.is=TRUE), {Z <- BETA/SE})
print(subset(BMI[c("CHR","POS","SNP","P")],CHR!=16 & P<=1e-150))
library(Rmpfr)
print(within(subset(BMI, P==0, select=c(CHR,POS,SNP,Z)),
  {P <- format(2*pnorm(mpfr(abs(Z),100),lower.tail=FALSE));
    Pvalue <- pvalue(Z); log10P <- -log10p(Z)}}))
png("BMI.png", res=300, units="in", width=9, height=6)
par(oma=c(0,0,0,0), mar=c(5,6.5,1,1))
mhtplot.trunc(BMI, chr="CHR", bp="POS", z="Z", snp="SNP",
  suggestiveline=FALSE, genomewideline=-log10(1e-8),
  cex.mtext=1.2, cex.text=1.2,
  annotatelog10P=156, annotateTop = FALSE,
  highlight=c("rs13021737","rs17817449","rs6567160"),
  mtext.line=3, y.brk1=200, y.brk2=280, trunc.yaxis=TRUE,
  cex.axis=1.2, cex=0.5,
  y.ax.space=20,
  col = c("blue4", "skyblue")
)
dev.off()

## End(Not run)

```

mhtplot2

*Manhattan plot with annotations*

## Description

Manhattan plot with annotations

## Usage

```
mhtplot2(data, control = mht.control(), hcontrol = hmht.control(), ...)
```

## Arguments

- |         |  |
|---------|--|
| data    | a data frame with three columns representing chromosome, position and p values.  |
| control | <p>A control function named <code>mht.control()</code> with the following arguments:</p> <ul style="list-style-type: none"> <li>• <code>type</code> a flag with value "p" or "l" indicating if points or lines are to be drawn.</li> <li>• <code>usepos</code> a flag to use real chromosomal positions as composed to ordinal positions with default value FALSE.</li> <li>• <code>logscale</code> a flag to indicate if p value is to be log-transformed with default value TRUE.</li> <li>• <code>base</code> the base of the logarithm with default value 10.</li> <li>• <code>cutoffs</code> the cut-offs where horizontal line(s) are drawn with default value NULL.</li> <li>• <code>colors</code> the color for different chromosome(s), and random if unspecified with default values NULL.</li> <li>• <code>labels</code> labels for the ticks on x-axis with default value NULL.</li> </ul> |

- srt degree to which labels are rotated with default value of 45.
  - gap gap between chromosomes with default value NULL.
  - cex cex for the data points.
  - yline Margin line position.
  - xline Margin line position.
- hcontrol A control function named hmht.control() with the following arguments:
- data chunk of data to be highlighted with default value NULL.
  - colors colors for annotated genes.
  - yoffset offset above the data point showing most significant p value with default value 0.5.
  - cex shrinkage factor for data points with default value 1.5.
  - boxed if the label for the highlighted region with default value FALSE.
- ... other options in compatible with the R plot function.

### Details

To generate Manhattan plot with annotations. The function is generic and for instance could be used for genomewide p values or 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, ylim and font family when the plot is requested for data in other context.

To maintain back compatibility options as in [mhplot](#) are used. The positions of the horizontal labels are now in the middle rather than at the beginning of their bands in the plot.

### Value

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

### Author(s)

Jing Hua Zhao

### References

den Hoed M, Eijgelsheim M, Esko T, Brundel BJ, Peal DS, Evans DM, Nolte IM, Segrè AV, Holm H, Handsaker RE, Westra HJ, Johnson T, Isaacs A, Yang J, Lundby A, Zhao JH, Kim YJ, Go MJ, Almgren P, Bochud M, Boucher G, Cornelis MC, Gudbjartsson D, Hadley D, van der Harst P, Hayward C, den Heijer M, Igl W, Jackson AU, Kutalik Z, Luan J, Kemp JP, Kristiansson K, Ladenvall C, Lorentzon M, Montasser ME, Njajou OT, O'Reilly PF, Padmanabhan S, St Pourcain B, Rankinen T, Salo P, Tanaka T, Timpson NJ, Vitart V, Waite L, Wheeler W, Zhang W, Draisma HH, Feitosa MF, Kerr KF, Lind PA, Mihailov E, Onland-Moret NC, Song C, Weedon MN, Xie W, Yengo L, Absher D, Albert CM, Alonso A, Arking DE, de Bakker PI, Balkau B, Barlassina C, Benaglio P, Bis JC, Bouatia-Naji N, Brage S, Chanock SJ, Chines PS, Chung M, Darbar D, Dina C, Dörr M, Elliott P, Felix SB, Fischer K, Fuchsberger C, de Geus EJ, Goyette P, Gudnason V, Harris TB, Hartikainen AL, Havulinna AS, Heckbert SR, Hicks AA, Hofman A, Holewijn S, Hoogstra-Berends F, Hottenga JJ, Jensen MK, Johansson A, Junttila J, Kääb S, Kanon B, Ketkar S, Khaw KT, Knowles JW, Kooner AS, others (2013). "Identification of heart rate-associated loci and their effects on cardiac conduction and rhythm disorders." *Nat Genet*, **45**(6), 621-31. ISSN 1061-4036 (Print) 1061-4036, [doi:10.1038/ng.2610](https://doi.org/10.1038/ng.2610).



## Examples

```
## Not run:
The following example uses only chromosomes 14 and 20 of the Nat Genet paper.

mdata <- within(hr1420,{
  c1<-colour==1
  c2<-colour==2
  c3<-colour==3
  colour[c1] <- 62
  colour[c2] <- 73
  colour[c3] <- 552
})
mdata <- mdata[,c("CHR","POS","P","gene","colour")]
ops <- mht.control(colors=rep(c("lightgray","gray"),11),yline=1.5,xline=2,srt=0)
hops <- hmht.control(data=subset(mdata,!is.na(gene)))
v <- "Verdana"
ifelse(Sys.info()['sysname']=="Windows", windowsFonts(ffamily=windowsFont(v)),
  ffamily <- v)
tiff("mh.tiff", width=.03937*189, height=.03937*189/2, units="in", res=1200,
  compress="lzw")
par(las=2, xpd=TRUE, cex.axis=1.8, cex=0.4)
mhtplot2(with(mdata,cbind(CHR,POS,P,colour)),ops,hops,pch=19,
  ylab=expression(paste(plain("-"),log[10],plain("p-value"),sep=" ")),
  family="ffamily")
axis(2,pos=2,at=seq(0,25,5),family="ffamily",cex=0.5,cex.axis=1.1)
dev.off()

# To exemplify the use of chr, pos and p without gene annotation
# in response to query from Vallejo, Roger <Roger.Vallejo@ARS.USDA.GOV>
opar <- par()
par(cex=0.4)
ops <- mht.control(colors=rep(c("lightgray","lightblue"),11),srt=0,yline=2.5,xline=2)
mhtplot2(data.frame(mhtdata[,c("chr","pos","p")],gene=NA,color=NA),ops,xlab="",ylab="",srt=0)
axis(2,at=1:16)
title("data in mhtplot used by mhtplot2")
par(opar)

## End(Not run)
```

## Description

Multiple imputation analysis for hap

## Usage

```
mia(
  hapfile = "hap.out",
  assfile = "assign.out",
  miafile = "mia.out",
  so = 0,
```

```

    ns = 0,
    mi = 0,
    allsnps = 0,
    sas = 0
  )

```

### 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

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.

It simply extracts outputs from hap.

### Value

The returned value is a list.

### Note

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

### References

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

Clayton DG (2001) SNPHAP. <https://github.com/chrlswallace/snphap>.

### 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)

```

---

miamiplot

*Miami plot*


---

## Description

Miami plot

## Usage

```

miamiplot(
  x,
  chr = "CHR",
  bp = "BP",
  p = "P",
  pr = "PR",
  snp = "SNP",
  col = c("midnightblue", "chartreuse4"),
  col2 = c("royalblue1", "seagreen1"),
  ymax = NULL,
  highlight = NULL,
  highlight.add = NULL,
  pch = 19,
  cex = 0.75,
  cex.lab = 1,
  xlab = "Chromosome",
  ylab = "-log10(P) [y>0]; log10(P) [y<0]",
  lcols = c("red", "black"),
  lwds = c(5, 2),
  ltys = c(1, 2),
  main = "",
  ...
)

```

## Arguments

x                      Input data.

chr	Chromosome.
bp	Position.
p	P value.
pr	P value of the other GWAS.
snp	Marker.
col	Colors.
col2	Colors.
ymax	Max y.
highlight	Highlight flag.
highlight.add	Highlight meta-data.
pch	Symbol.
cex	cex.
cex.lab	cex for labels.
xlab	Label for x-axis.
ylab	Label for y-axis.
lcols	Colors.
lwds	lwd.
ltys	lty.
main	Main title.
...	Additional options.

### Details

The function allows for contrast of genomewide P values from two GWASs. It is conceptually simpler than at the first sight since it involves only one set of chromosomal positions.

### Value

None.

### Examples

```
## Not run:
mhtdata <- within(mhtdata,{pr=p})
miamiplot(mhtdata,chr="chr",bp="pos",p="p",pr="pr",snp="rsn")

## End(Not run)
```

miamiplot2

*Miami Plot***Description**

Miami Plot

**Usage**

```

miamiplot2(
  gwas1,
  gwas2,
  name1 = "GWAS 1",
  name2 = "GWAS 2",
  chr1 = "chr",
  chr2 = "chr",
  pos1 = "pos",
  pos2 = "pos",
  p1 = "p",
  p2 = "p",
  z1 = NULL,
  z2 = NULL,
  sug = 1e-05,
  sig = 5e-08,
  pcutoff = 0.1,
  topcols = c("green3", "darkgreen"),
  botcols = c("royalblue1", "navy"),
  yAxisInterval = 5
)

```

**Arguments**

gwas1	The first of two GWAS datasets to plot, in the upper region.
gwas2	The second of two GWAS datasets to plot, in the lower region.
name1	The name of the first dataset, plotted above the upper plot region. Defaults to "GWAS 1".
name2	The name of the second dataset, plotted below the lower plot region. Defaults to "GWAS 2".
chr1	The name of the column containing chromosome number in gwas1. Defaults to "chr".
chr2	The name of the column containing chromosome number in gwas2. Defaults to "chr".
pos1	The name of the column containing SNP position in gwas1. Defaults to "pos".
pos2	The name of the column containing SNP position in gwas2. Defaults to "pos".
p1	The name of the column containing p-values in gwas1. Defaults to "p".
p2	The name of the column containing p-values in gwas2. Defaults to "p".
z1	The name of the column containing z-values in gwas1. Defaults to "NULL".
z2	The name of the column containing z-values in gwas2. Defaults to "NULL".

sug	The threshold for suggestive significance, plotted as a light grey dashed line.
sig	The threshold for genome-wide significance, plotted as a dark grey dashed line.
pcutoff	The p-value threshold below which SNPs will be ignored. Defaults to 0.1. It is not recommended to set this higher as it will narrow the central gap between the two plot region where the chromosome number is plotted.
topcols	A vector of two colours to plot alternating chromosomes in for the upper plot. Defaults to green3 and darkgreen.
botcols	A vector of two colours to plot alternating chromosomes in for the lower plot. Defaults to royalblue1 and navy.
yAxisInterval	The interval between tick marks on the y-axis. Defaults to 5, 2 may be more suitable for plots with larger minimum p-values.

### Details

Creates a Miami plot to compare results from two genome-wide association analyses.

### Value

In addition to creating a Miami plot, the function returns a data frame containing x coordinates for chromosome start positions (required for [labelManhattan](#))

### Note

Extended to handle extreme P values.

### Author(s)

Jonathan Marten

### Examples

```
## Not run:
# miamiplot2(gwas1, gwas2)
# chrmaxpos <- miamiplot2(gwas1, gwas2)
gwas <- within(mhtdata[c("chr", "pos", "p")], {z=qnrm(p/2)})
chrmaxpos <- miamiplot2(gwas, gwas, name1="Batch 2", name2="Batch 1", z1="z", z2="z")
labelManhattan(chr=c(2,16), pos=c(226814165, 52373776), name=c("AnonymousGene", "FT0"),
               gwas, gwasZLab="z", chrmaxpos=chrmaxpos)

## End(Not run)
```

---

mr

Mendelian randomization analysis

---

### Description

Mendelian randomization analysis

### Usage

```
mr(data, X, Y, alpha = 0.05, other_plots = FALSE)
```

**Arguments**

data	Data to be used.
X	Exposure.
Y	Outcome.
alpha	type I error rate for confidence intervals.
other_plots	To add funnel and forest plots.

**Details**

The function initially intends to rework on GSMR outputs, but it would be appropriate for general use.

**Value**

The result and plots.

**Examples**

```
library(ggplot2)
library(gap)
mrdat <- '
rs188743906 0.6804 0.1104 0.00177 0.01660 NA NA
rs2289779 -0.0788 0.0134 0.00104 0.00261 -0.007543 0.0092258
rs117804300 -0.2281 0.0390 -0.00392 0.00855 0.109372 0.0362219
rs7033492 -0.0968 0.0147 -0.00585 0.00269 0.022793 0.0119903
rs10793962 0.2098 0.0212 0.00378 0.00536 -0.014567 0.0138196
rs635634 -0.2885 0.0153 -0.02040 0.00334 0.077157 0.0117123
rs176690 -0.0973 0.0142 0.00293 0.00306 -0.000007 0.0107781
rs147278971 -0.2336 0.0378 -0.01240 0.00792 0.079873 0.0397491
rs11562629 0.1155 0.0181 0.00960 0.00378 -0.010040 0.0151460
'

v <- c("SNP", "b.LIF.R", "SE.LIF.R", "b.FEV1", "SE.FEV1", "b.CAD", "SE.CAD")
mrdat <- setNames(as.data.frame(scan(file=textConnection(mrdat),
                                     what=list("",0,0,0,0,0,0))), v)

knitr::kable(mrdat,caption="Table 2. LIF.R and CAD/FEV1")
res <- mr(mrdat, "LIF.R", c("CAD","FEV1"), other_plots=TRUE)
s <- res$r[-1,]
colnames(s) <- res$r[1,]
r <- matrix(as.numeric(s[-1]),nrow(s),dimnames=list(res$r[-1,1],res$r[1,-1]))
p <- sapply(c("IVW","EGGER","WM","PWM"), function(x)
  format(2*pnorm(-abs(r[,paste0("b",x)]/r[,paste0("seb",x)])),digits=3,scientific=TRUE))
rp <- t(data.frame(round(r,3),p))
knitr::kable(rp,align="r",caption="Table 3. LIFR variant rs635634 and CAD/FEV1")
```

mr\_forestplot

*Mendelian Randomization forest plot***Description**

Mendelian Randomization forest plot

**Usage**

```
mr_forestplot(dat, sm = "", title = "", ...)
```

**Arguments**

<code>dat</code>	A data.frame with outcome id, effect size and standard error.
<code>sm</code>	Summary measure such as OR, RR, MD.
<code>title</code>	Title of the meta-analysis.
<code>...</code>	Other options for meta::forest().

**Details**

This is a wrapper of meta::forest() for multi-outcome Mendelian Randomization. It allows for the flexibility of both binary and continuous outcomes with and without summary level statistics.

**Examples**

```
## Not run:
tnfb <- '
      "multiple sclerosis" 0.69058600 0.059270400
      "systemic lupus erythematosus" 0.76687500 0.079000500
      "sclerosing cholangitis" 0.62671500 0.075954700
      "juvenile idiopathic arthritis" -1.17577000 0.160293000
      "psoriasis" 0.00582586 0.000800016
      "rheumatoid arthritis" -0.00378072 0.000625160
      "inflammatory bowel disease" -0.14334200 0.025272500
      "ankylosing spondylitis" -0.00316852 0.000626225
      "hypothyroidism" -0.00432054 0.000987324
      "allergic rhinitis" 0.00393075 0.000926002
      "IgA glomerulonephritis" -0.32696600 0.105262000
      "atopic eczema" -0.00204018 0.000678061
,
require(dplyr)
tnfb <- as.data.frame(scan(file=textConnection(tnfb),what=list("",0,0))) %>%
  setNames(c("outcome","Effect","StdErr")) %>%
  mutate(outcome=gsub("\\b(^[a-z])","\\U\\1",outcome,perl=TRUE))

# default output
mr_forestplot(tnfb, colgap.forest.left="0.05cm", fontsize=14, leftlabs=c("Outcome","b","SE"),
  common=FALSE, random=FALSE, print.I2=FALSE, print.pval.Q=FALSE, print.tau2=FALSE,
  spacing=1.6,digits.TE=2,digits.se=2)

# no summary level statistics
mr_forestplot(tnfb, colgap.forest.left="0.05cm", fontsize=14,
  leftcols="studlab", leftlabs="Outcome", plotwidth="3inch", sm="OR", rightlabs="ci",
  sortvar=tnfb[["Effect"]],
  common=FALSE, random=FALSE, print.I2=FALSE, print.pval.Q=FALSE, print.tau2=FALSE,
  backtransf=TRUE, spacing=1.6)

# with P values
mr_forestplot(tnfb,colgap.forest.left="0.05cm", fontsize=14,
  leftcols=c("studlab"), leftlabs=c("Outcome"),
  plotwidth="3inch", sm="OR", sortvar=tnfb[["Effect"]],
  rightcols=c("effect","ci","pval"), rightlabs=c("OR","95%CI","P"),
  digits=3, digits.pval=2, scientific.pval=TRUE,
  common=FALSE, random=FALSE, print.I2=FALSE, print.pval.Q=FALSE, print.tau2=FALSE,
  addrow=TRUE, backtransf=TRUE, spacing=1.6)
```



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

mtdt

*Transmission/disequilibrium test of a multiallelic marker*

## Description

Transmission/disequilibrium test of a multiallelic marker

## Usage

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

## Arguments

x	the data table.
n.sim	the number of simulations.

## Details

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

## Value

It returned list contains the following components:

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

## Author(s)

Mike Miller, Jing Hua Zhao

## References

Miller MB (1997). "Genomic scanning and the transmission/disequilibrium test: analysis of error rates." *Genet Epidemiol*, **14**(6), 851-6. ISSN 0741-0395 (Print) 0741-0395, doi:[10.1002/\(sici\)1098-2272\(1997\)14:6<854::aidgepi48>3.3.co;27](https://doi.org/10.1002/(sici)1098-2272(1997)14:6<854::aidgepi48>3.3.co;27).

Sham PC, Curtis D (1995). "An extended transmission/disequilibrium test (TDT) for multi-allele marker loci." *Ann Hum Genet*, **59**(3), 323-36. ISSN 0003-4800 (Print) 0003-4800, doi:[10.1111/j.14691809.1995.tb00751.x](https://doi.org/10.1111/j.14691809.1995.tb00751.x).

Spielman RS, Ewens WJ (1996). "The TDT and other family-based tests for linkage disequilibrium and association." *Am J Hum Genet*, **59**(5), 983-9. ISSN 0002-9297 (Print) 0002-9297.

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.

See Also

[bt](#)

Examples

```
## Not run:
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, 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

Transmission/disequilibrium test of a multiallelic marker by 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.

Details

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

**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.

**Author(s)**

Jing Hua Zhao keywords models keywords htest

**References**

Firth D (2005). “Bradley-Terry Models in R.” *Journal of Statistical Software*, **12**(1), 1 - 12. [doi:10.18637/jss.v012.i01](https://doi.org/10.18637/jss.v012.i01).

Turner H, Firth D (2010) Bradley-Terry models in R: The BradleyTerry2 package. <https://cran.r-project.org/web/packages/BradleyTerry2/vignettes/BradleyTerry.pdf>.

**See Also**

[mtdt](#)

**Examples**

```
## Not run:
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, 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**

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

**Usage**

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

**Arguments**

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

**Details**

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.

**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.

**Note**

Adapted from an earlier C program written for the above book.

**Author(s)**

Jing Hua Zhao

**References**

Sham P (1997). *Statistics in Human Genetics*. Wiley. ISBN 978-0470689288, <https://www.amazon.com/dp/0470689285/>.

## 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(1,1,1,1,1,0,0,0,0),p1=0.99,p2=0.9)

## End(Not run)
```

---

mvmeta

---

*Multivariate meta-analysis based on generalized least squares*


---

## Description

Multivariate meta-analysis based on generalized least squares

## Usage

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

## Arguments

b	the parameter estimates.
V	the triangular variance-covariance matrix.

## Details

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.

## 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.

**Author(s)**

Jing Hua Zhao

**References**

Hartung J, Knapp G, Sinha BK (2008). *Statistical Meta-analysis with Applications*. Wiley. ISBN 978-0-470-29089-7.

**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)

```

---

pbsize

---

*Power for population-based association design*


---

## Description

Power for population-based association design

## Usage

```
pbsize(kp, gamma = 4.5, p = 0.15, alpha = 5e-08, 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.

## Details

This function implements Scott 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.

## Value

The returned value is scalar containing the required sample size.

## Author(s)

Jing Hua Zhao extracted from rm.c.

## References

- Scott WK, Pericak-Vance MA, Haines JL (1997). "Genetic analysis of complex diseases." *Science*, **275**(5304), 1327; author reply 1329-30. ISSN 0036-8075 (Print) 0036-8075.
- Long AD, Grote MN, Langley CH (1997). Genetic analysis of complex traits. *Science* 275: 1328.
- Rosner B (2000). *Fundamentals of biostatistics*, 5 edition. Duxbury, Pacific Grove, CA. ISBN 9780534370688.
- Armitage P, Colton T (eds.) (2005). *Encyclopedia of biostatistics*, 2 edition. John Wiley, Chichester, West Sussex, England ; Hoboken, NJ. ISBN 9780470849071.

## 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**

Power for case-control association design

**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".

**Details**

This extends [pbsize](#) from a multiplicative model for a case-control design under a range of disease models. Essentially, for given sample sizes(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. It provides power estimates for given sample size(s) only.

**Value**

The returned value is the power for the specified design.

**See Also**

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

**Examples**

```
## Not run:
# single calculation
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]))

# a range of sample sizes
pbsize2(p=0.1, N=c(25,50,100,200,500), gamma=1.2, kp=.1, alpha=5e-2, model='r')

# a power table
m <- sapply(seq(0.1,0.9, by=0.1),
            function(x) pbsize2(p=x, N=seq(100,1000,by=100),
                                gamma=1.2, kp=.1, alpha=5e-2, model='recessive'))
colnames(m) <- seq(0.1,0.9, by=0.1)
rownames(m) <- seq(100,1000,by=100)
print(round(m,2))

## End(Not run)
```

---

pedtodot

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

---

**Description**

Converting pedigree(s) to dot file(s)

**Usage**

```
pedtodot(
  pedfile,
  makeped = FALSE,
  sink = TRUE,
  page = "B5",
  url = "https://jinghuazhao.github.io/",
  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

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.

Note that a single PostScript (PDF) file can be obtained by dot, fdp, or neato.

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

or

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

or

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

See relevant documentations for other formats.

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>.

Under Linux, you can also visualize the .dot file directly via command,

```
dotty <dot file> &
```

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

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

## 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 <https://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(0,0,0,0,0,0,"",""))
 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="https://jinghuazhao.github.io/")
```

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

## End(Not run)
```

---

pedtodot\_verbatim      *Pedigree-drawing with graphviz*

---

## Description

Pedigree-drawing with graphviz

## Usage

```
pedtodot_verbatim(f, run = FALSE, toDOT = FALSE, ...)
```

## Arguments

f	A data.frame containing pedigrees, each with pedigree id, individual id, father id, mother id, sex and affection status.
run	A flag to run dot/neato on the generated .dot file(s).
toDOT	A flag to generate script for DOT::dot().
...	Other flag(s) for DOT::dot().

## Details

Read a GAS or LINKAGE format pedigree, return a digraph in the dot language and optionally call dot/neato to make pedigree drawing.

This is a verbatim translation of the original pedtodot implemented in Bash/awk in contrast to pedtodot which was largely a mirror. To check independently, try `xsel -i < <(cat pedtodot_verbatim.R)` or `cat pedtodot_verbatim.R | xsel -i` and paste into an R session.

## Value

No value is returned but outputs in .dot, .pdf, and .svg.

## Note

Adapted from Bash/awk script by David Duffy

## Examples

```
## Not run:
# pedigree p3 in pedtodot
pedtodot_verbatim(p3,run=TRUE,toDOT=TRUE,return="verbatim")

## End(Not run)
```

pfc

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

Probability of familial clustering of disease

**Usage**

```
pfc(famdata, enum = 0)
```

**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.

**Details**

To calculate exact probability of familial clustering of disease

**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.

**Note**

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

**Author(s)**

Dani Zelberman, Jing Hua Zhao

**References**

Yu C, Zelberman D (2001). "Exact inference for family disease clusters." *Communications in Statistics - Theory and Methods*, **30**(11), 2293-2305. ISSN 0361-0926, doi:[10.1081/STA100107686](https://doi.org/10.1081/STA100107686).  
 Yu C, Zelberman D (2002). "Statistical inference for familial disease clusters." *Biometrics*, **58**(3), 481-91. ISSN 0006-341X (Print) 0006-341x, doi:[10.1111/j.0006341x.2002.00481.x](https://doi.org/10.1111/j.0006341x.2002.00481.x).

**See Also**

[kin.morgan](#)

## Examples

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

Probability of familial clustering of disease

## Usage

```
pfc.sim(famdata, n.sim = 1e+06, 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.

## Details

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

**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.

**Note**

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

**Author(s)**

Chang Yu, Dani Zelterman

**References**

Yu C, Zelterman D (2001). “Exact inference for family disease clusters.” *Communications in Statistics - Theory and Methods*, **30**(11), 2293-2305. ISSN 0361-0926, doi:[10.1081/STA100107686](https://doi.org/10.1081/STA100107686).

**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, 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**

Preparing weight for GENECOUNTING

**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.

**Details**

This function is a R port of the GENECOUNTING/PREPARE program which takes an array of genotyp 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.

**Value**

The returned value is a list containing:

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

**Note**

Built on `pgc.c`.

**Author(s)**

Jing Hua Zhao

## References

Zhao JH, Sham PC (2003). “Generic number systems and haplotype analysis.” *Comput Methods Programs Biomed*, **70**(1), 1-9. ISSN 0169-2607 (Print) 0169-2607, doi:10.1016/s01692607(01)00193-6.

## See Also

[genecounting](#), [hwe.hardy](#)

## Examples

```
## Not run:
require(gap.datasets)
data(hla)
x <- hla[,3:8]

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

# 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.

## Value

Nothing is returned.

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.

## 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.

## Value

Nothing is returned.

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.

## 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)
```

---

pvalue	<i>P value for a normal deviate</i>
--------	-------------------------------------

---

**Description**

P value for a normal deviate

**Usage**

```
pvalue(z, decimals = 2)
```

**Arguments**

z	normal deviate.
decimals	number of decimal places.

**Value**

P value as a string variable.

**Examples**

```
pvalue(-1.96)
```

qqfun

*Quantile-comparison plots***Description**

Quantile-comparison plots

**Usage**

```
qqfun(
  x,
  distribution = "norm",
  ylab = deparse(substitute(x)),
  xlab = paste(distribution, "quantiles"),
  main = NULL,
  las = par("las"),
  envelope = 0.95,
  labels = FALSE,
  col = palette()[4],
  lcol = palette()[2],
  xlim = NULL,
  ylim = NULL,
  lwd = 1,
  pch = 1,
  bg = palette()[4],
  cex = 0.4,
  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.
las	if 0, ticks labels are drawn parallel to the axis; set to 1 for horizontal labels (see <a href="#">graphics::par</a> ).
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.
col	color for points; the default is the <i>fourth</i> entry in the current color palette (see <a href="#">grDevices::palette</a> and <a href="#">graphics::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.

lwd	line width; default is 1 (see <code>graphics::par</code> ). Confidence envelopes are drawn at half this line width.
pch	plotting character for points; default is 1 (a circle, see <code>graphics::par</code> ).
bg	background color of points.
cex	factor for expanding the size of plotted symbols; the default is <code>1.4</code> .
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

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

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

### Value

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

### Author(s)

John Fox, Jing Hua Zhao

### References

- Davison AC (2003). *Statistical Models (Cambridge Series in Statistical and Probabilistic Mathematics)*. Cambridge University Press (2003-08-04). <https://www.amazon.com/dp/B01A0BLZKM/>.
- Leemis LM, McQueston JT (2008). "Univariate Distribution Relationships." *The American Statistician*, **62**(1), 45-53. ISSN 0003-1305, doi:10.1198/000313008X270448.

### See Also

`stats::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**

Q-Q plot for uniformly distributed random variable

**Usage**

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

**Arguments**

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

**Details**

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.

**Value**

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

- `x` expected value for uniform order statistics or its `-log(,base)` counterpart.
- `y` observed value or its `-log(,base)` counterpart.

**Author(s)**

Jing Hua Zhao

**References**

Balakrishnan N, Nevzorov VB (2003). *A Primer on Statistical Distributions*. Wiley, Hoboken, N.J. ISBN 9780471427988, <https://www.amazon.com/dp/B011SJAWXG/>.

Casella G, Berger RL (2002). *Statistical Inference*, 2 edition. Duxbury. ISBN 978-0-534-24312-8, <https://www.amazon.com/dp/7111109457/>.

Davison AC (2003). *Statistical Models (Cambridge Series in Statistical and Probabilistic Mathematics)*. Cambridge University Press (2003-08-04). <https://www.amazon.com/dp/B01A0BLZKM/>.

**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")
legend("topleft",sprintf("GC.lambda=\n"))

## End(Not run)
```

qtl2dplot

2D QTL plot

**Description**

2D QTL plot

**Usage**

```
qtl2dplot(
  d,
  chrLen = gap::hg19,
  snp_name = "SNP",
  snp_chr = "Chr",
  snp_pos = "bp",
  gene_chr = "p.chr",
  gene_start = "p.start",
  gene_end = "p.end",
  trait = "p.target.short",
  gene = "p.gene",
  TSS = FALSE,
```



```

    cis = "cis",
    value = "log10p",
    plot = TRUE,
    cex.labels = 0.6,
    cex.points = 0.6,
    xlab = "QTL position",
    ylab = "Gene position"
  )

```

### Arguments

d	Data to be used.
chrLen	lengths of chromosomes for specific build: hg18, hg19, hg38.
snp_name	variant name.
snp_chr	variant chromosome.
snp_pos	variant position.
gene_chr	gene chromosome.
gene_start	gene start position.
gene_end	gene end position.
trait	trait name.
gene	gene name.
TSS	to use TSS when TRUE.
cis	cis variant when TRUE.
value	A specific value to show.
plot	to plot when TRUE.
cex.labels	Axis label extension factor.
cex.points	Data point extension factor.
xlab	X-axis title.
ylab	Y-axis title.

### Details

This function is both used as its own for a 2d plot and/or generate data for a plotly counterpart.

### Value

positional information.

### Examples

```

## Not run:
INF <- Sys.getenv("INF")
d <- read.csv(file.path(INF, "work", "INF1.merge.cis.vs.trans"), as.is=TRUE)
r <- qtl2dplot(d)

## End(Not run)

```

qtl2dplotly

*2D QTL plotly***Description**

2D QTL plotly

**Usage**

```
qtl2dplotly(
  d,
  chrLen = gap::hg19,
  qtl.id = "SNPid:",
  qtl.prefix = "QTL:",
  qtl.gene = "Gene:",
  target.type = "Protein",
  TSS = FALSE,
  xlab = "QTL position",
  ylab = "Gene position",
  ...
)
```

**Arguments**

d	Data in qtl2dplot() format.
chrLen	Lengths of chromosomes for specific build: hg18, hg19, hg38.
qtl.id	QTL id.
qtl.prefix	QTL prefix.
qtl.gene	QTL gene.
target.type	Type of target, e.g., protein.
TSS	to use TSS when TRUE.
xlab	X-axis title.
ylab	Y-axis title.
...	Additional arguments, e.g., target, log10p, to qtl2dplot.

**Value**

A plotly figure.

**Examples**

```
## Not run:
INF <- Sys.getenv("INF")
d <- read.csv(file.path(INF, "work", "INF1.merge.cis.vs.trans"), as.is=TRUE)
r <- qtl2dplotly(d)
htmlwidgets::saveWidget(r, file=file.path(INF, "INF1.qtl2dplotly.html"))
r

## End(Not run)
```

qtl3dplotly

*3D QTL plot***Description**

3D QTL plot

**Usage**

```
qtl3dplotly(
  d,
  chrLen = gap::hg19,
  zmax = 300,
  qtl.id = "SNPid:",
  qtl.prefix = "QTL:",
  qtl.gene = "Gene:",
  target.type = "Protein",
  TSS = FALSE,
  xlab = "QTL position",
  ylab = "Gene position",
  ...
)
```

**Arguments**

d	Data in qtl2d() format.
chrLen	Lengths of chromosomes for specific build: hg18, hg19, hg38.
zmax	Maximum value (e.g., -log10p) to truncate, above which they would be set to this value.
qtl.id	QTL id.
qtl.prefix	QTL prefix.
qtl.gene	QTL target gene.
target.type	Type of target, e.g., protein.
TSS	to use TSS when TRUE.
xlab	X-axis title.
ylab	Y-axis title.
...	Additional arguments, e.g., to qtl2dplot().

**Value**

A plotly figure.

**Examples**

```
## Not run:
suppressMessages(library(dplyr))
INF <- Sys.getenv("INF")
d <- read.csv(file.path(INF, "work", "INF1.merge.cis.vs.trans"), as.is=TRUE) %>%
  mutate(log10p=-log10p)
```

```

r <- qtl3dplotly(d,zmax=300)
htmlwidgets::saveWidget(r,file=file.path(INF,"INF1.qtl3dplotly.html"))
r

## End(Not run)

```

---

qtlClassifier

*A QTL cis/trans classifier*


---

## Description

A QTL cis/trans classifier

## Usage

```
qtlClassifier(geneSNP, SNPPos, genePos, radius)
```

## Arguments

geneSNP	data.frame with columns on gene, SNP and biomarker (e.g., expression, protein).
SNPPos	data.frame containing SNP, chromosome and position.
genePos	data.frame containing gene, chromosome, start and end positions.
radius	flanking distance.

## Details

The function obtains QTL (simply called SNP here) cis/trans classification based on gene positions.

## Value

It returns a geneSNP-prefixed data.frame with the following columns:

- geneChrom gene chromosome.
- geneStart gene start.
- geneEnd gene end.
- SNPChrom pQTL chromosome.
- SNPPos pQTL position.
- Type cis/trans labels.

## Note

This is adapted from iBMQ/eqtlClassifier as an xQTL (x=e, p, me, ...) classifier.

## See Also

[cis.vs.trans.classification](#)

## Examples

```
## Not run:
merged <- read.delim("INF1.merge",as.is=TRUE)
hits <- merge(merged[c("CHR","POS","MarkerName","prot","log10p")],
             inf1[c("prot","uniprot")],by="prot")
names(hits) <- c("prot","Chr","bp","SNP","log10p","uniprot")

options(width=200)
geneSNP <- merge(hits[c("prot","SNP","log10p")],
                inf1[c("prot","gene")],by="prot")[c("gene","SNP","prot","log10p")]
SNPPos <- hits[c("SNP","Chr","bp")]
genePos <- inf1[c("gene","chr","start","end")]
cvt <- qtlClassifier(geneSNP,SNPPos,genePos,1e6)
cvt
cistrans <- cis.vs.trans.classification(hits,inf1,"uniprot")
cis.vs.trans <- with(cistrans,data)
cistrans.check <- merge(cvt[c("gene","SNP","Type")],cis.vs.trans[c("p.gene","SNP","cis.trans")],
                       by.x=c("gene","SNP"),by.y=c("p.gene","SNP"))
with(cistrans.check,table(Type,cis.trans))

## End(Not run)
```

---

read.ms.output

*A utility function to read ms output*


---

## Description

A utility function to read ms output

## 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.

## Details

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.

## 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.

## Author(s)

D Davison, RR Hudson, JH Zhao

## References

Hudson RR (2002). "Generating samples under a Wright-Fisher neutral model of genetic variation." *Bioinformatics*, **18**(2), 337-8. ISSN 1367-4803 (Print) 1367-4803, doi:[10.1093/bioinformatics/18.2.337](https://doi.org/10.1093/bioinformatics/18.2.337).

Press WH, SA Teukolsky, WT Vetterling, BP Flannery (1992). Numerical Recipes in C. Cambridge University Press, Cambridge.

## 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)
```

---

ReadGRM	<i>A function to read GRM file</i>
---------	------------------------------------

---

**Description**

A function to read GRM file

**Usage**

```
ReadGRM(prefix = 51)
```

**Arguments**

prefix	file root.
--------	------------

---

ReadGRMBin	<i>A function to read GRM binary files</i>
------------	--

---

**Description**

A function to read GRM binary files

**Usage**

```
ReadGRMBin(prefix, AllN = FALSE, size = 4)
```

**Arguments**

prefix	file root.
AllN	a logical variable.
size	size.

**Details**

Modified from GCTA documentation

---

revStrand	<i>Allele on the reverse strand</i>
-----------	-------------------------------------

---

**Description**

Allele on the reverse strand

**Usage**

```
revStrand(allele)
```

**Arguments**

allele            Allele to reverse.

**Details**

The function obtains allele on the reverse strand.

**Value**

Allele on the reverse strand.

**Examples**

```
## Not run:
alleles <- c("a","c","G","t")
reverse_strand(alleles)

## End(Not run)
```

---

runshinygap	<i>Start shinygap</i>
-------------	-----------------------

---

**Description**

Start shinygap

**Usage**

```
runshinygap(...)
```

**Arguments**

...            Additional arguments passed to the 'runApp' function from the 'shiny' package.

**Details**

This function starts the interactive 'shinygap' shiny web application that allows for flexible model specification.

The 'shiny' based web application allows for flexible model specification for the implemented study designs.



**Value**

These are design specific.

---

s2k	<i>Statistics for 2 by K table</i>
-----	------------------------------------

---

**Description**

Statistics for 2 by K 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. |

**Details**

This function calculates one-to-others and maximum accumulated chi-squared statistics for 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.

**Note**

The lengths of y1 and y2 should be the same.

**Author(s)**

Chihiro Hirotsu, Jing Hua Zhao

**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.

**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)
```

sentinels

*Sentinel identification from GWAS summary statistics***Description**

Sentinel identification from GWAS summary statistics

**Usage**

```
sentinels(
  p,
  pid,
  st,
  debug = FALSE,
  flanking = 1e+06,
  chr = "Chrom",
  pos = "End",
  b = "Effect",
  se = "StdErr",
  log_p = NULL,
  snp = "MarkerName",
  sep = ", "
)
```

**Arguments**

p	an object containing GWAS summary statistics.
pid	a phenotype (e.g., protein) name in pGWAS.
st	row number as in p.
debug	a flag to show the actual data.
flanking	the width of flanking region.
chr	Chromosome name.
pos	Position.
b	Effect size.
se	Standard error.
log_p	log(P).
snp	Marker name.
sep	field delimiter.

## Details

This function accepts an object containing GWAS summary statistics for signal identification as defined by flanking regions. As the associate P value could be extremely small, the effect size and its standard error are used.

A distance-based approach was consequently used and reframed as an algorithm here. It takes as input signals multiple correlated variants in particular region(s) which reach genomewide significance and output three types of sentinels in a region-based manner. For a given protein and a chromosome, the algorithm proceeds as follows:

### Algorithm sentinels

Step 1. for a particular collection of genomewide significant variants on a chromosome, the width of the region is calculated according to the start and end chromosomal positions and if it is smaller than the flanking distance, the variant with the smallest P value is taken as sentinel (I) otherwise goes to step 2.

Step 2. The variant at step 1 is only a candidate and a flanking region is generated. If such a region contains no variant the candidate is recorded as sentinel (II) and a new iteration starts from the variant next to the flanking region.

Step 3. When the flanking is possible at step 2 but the P value is still larger than the candidate at step 2, the candidate is again recorded as sentinel (III) but next iteration starts from the variant just after the variant at the end position; otherwise the variant is updated as a new candidate where the next iteration starts.

Note Type I signals are often seen from variants in strong LD at a cis region, type II results seen when a chromosome contains two trans signals, type III results seen if there are multiple trans signals.

Typically, input to the function are variants reaching certain level of significance and the function identifies minimum p value at the flanking interval; in the case of another variant in the flanking window has smaller p value it will be used instead.

For now key variables in p are "MarkerName", "End", "Effect", "StdErr", "P.value", where "End" is as in a bed file indicating marker position, and the function is set up such that row names are numbered as 1:nrow(p); see example below. When log\_p is specified, log(P) is used instead, which is appropriate with output from METAL with LOGPVALUE ON. In this case, the column named log(P) in the output is actually log<sub>10</sub>(P).

## Value

The function give screen output.

## Examples

```
## Not run:
## OPG as a positive control in our pGWAS
require(gap.datasets)
data(OPG)
p <- reshape::rename(OPGtbl1, c(Chromosome="Chrom", Position="End"))
chrs <- with(p, unique(Chrom))
for(chr in chrs)
{
  ps <- subset(p[c("Chrom", "End", "MarkerName", "Effect", "StdErr")], Chrom==chr)
  row.names(ps) <- 1:nrow(ps)
  sentinels(ps, "OPG", 1)
}
subset(OPGrsid, MarkerName=="chr8:120081031_C_T")
```

```

subset(OPGrsid,MarkerName=="chr17:26694861_A_G")
## log(P)
p <- within(p, {logp <- log(P.value)})
for(chr in chrs)
{
  ps <- subset(p[c("Chrom","End","MarkerName","logp")], Chrom==chr)
  row.names(ps) <- 1:nrow(ps)
  sentinels(ps, "OPG", 1, log_p="logp")
}
## to obtain variance explained
tbl <- within(OPGtbl, chi2n <- (Effect/StdErr)^2/N)
s <- with(tbl, aggregate(chi2n,list(prot),sum))
names(s) <- c("prot", "h2")
sd <- with(tbl, aggregate(chi2n,list(prot),sd))
names(sd) <- c("p1","sd")
m <- with(tbl, aggregate(chi2n,list(prot),length))
names(m) <- c("p2","m")
h2 <- cbind(s,sd,m)
ord <- with(h2, order(h2))
sink("h2.dat")
print(h2[ord, c("prot","h2","sd","m")], row.names=FALSE)
sink()
png("h2.png", res=300, units="in", width=12, height=8)
np <- nrow(h2)
with(h2[ord,], {
  plot(h2, cex=0.4, pch=16, xaxt="n", xlab="protein", ylab=expression(h^2))
  xtick <- seq(1, np, by=1)
  axis(side=1, at=xtick, labels = FALSE)
  text(x=xtick, par("usr")[3],labels = prot, srt = 75, pos = 1, xpd = TRUE, cex=0.5)
})
dev.off()
write.csv(tbl,file="INF1.csv",quote=FALSE,row.names=FALSE)

## End(Not run)

```

## Description

These are 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. snpHWE is from Abecasis's website and yet to be adapted for chromosome X.

## Usage

```
snpHWE(g)
```

```
PARn(p, RRlist)
```

```
snpPVE(beta, se, N)
```

```
snpPAR(RR, MAF, unit = 2)
```

**Arguments**

<code>g</code>	Observed genotype vector.
<code>p</code>	genotype frequencies.
<code>RRlist</code>	A list of RRs.
<code>beta</code>	Regression coefficient.
<code>se</code>	Standard error for beta.
<code>N</code>	Sample size.
<code>RR</code>	Relative risk.
<code>MAF</code>	Minor allele frequency.
<code>unit</code>	Unit to exponentiate for homozygote.

**Details**

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

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

snpPVE provides proportion of variance explained (PVE) estimate based on the linear regression coefficient and standard error. For logistic regression, we can have similar idea for log(OR) and log(SE(OR)).

**Author(s)**

Jing Hua Zhao, Shengxu Li

---

snptest\_sample

*A utility to generate SNPTEST sample file*

---

**Description**

A utility to generate SNPTEST sample file

**Usage**

```
snptest_sample(
  data,
  sample_file = "snptest.sample",
  ID_1 = "ID_1",
  ID_2 = "ID_2",
  missing = "missing",
  C = NULL,
  D = NULL,
  P = NULL
)
```

**Arguments**

data	Data to be used.
sample_file	Output filename.
ID_1	ID_1 as in the sample file.
ID_2	ID_2 as in the sample file.
missing	Missing data column.
C	Continuous variables.
D	Discrete variables.
P	Phenotypic variables.

**Value**

Output file in SNPTTEST's sample format.

**Examples**

```
## Not run:
d <- data.frame(ID_1=1, ID_2=1, missing=0, PC1=1, PC2=2, D1=1, P1=10)
snptest_sample(d, C=paste0("PC", 1:2), D=paste0("D", 1:1), P=paste0("P", 1:1))

## End(Not run)
```

tscc

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

Power calculation for two-stage case-control design

**Usage**

```
tscc(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.

## Details

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

The false positive rates are calculated as follows,

$$P(|z1| > C1)P(|z2| > C2, \text{sign}(z1) = \text{sign}(z2))$$

and

$$P(|z1| > C1)P(|zj| > Cj | |z1| > C1)$$

for replication-based and joint analyses, respectively; where C1, C2, and Cj are thresholds at stages 1, 2 replication and joint analysis,

$$z1 = z(p1, p2, n1, n2, pi.samples)$$

$$z2 = z(p1, p2, n1, n2, 1 - pi.samples)$$

$$zj = \text{sqrt}(pi.samples) * z1 + \text{sqrt}(1 - pi.samples) * z2$$

## 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.

## Note

solve.skol is adapted from CaTS.

## Author(s)

Jing Hua Zhao

## References

Skol AD, Scott LJ, Abecasis GR, Boehnke M (2006). "Joint analysis is more efficient than replication-based analysis for two-stage genome-wide association studies." *Nat Genet*, **38**(2), 209-13. ISSN 1061-4036 (Print) 1061-4036, doi:10.1038/ng1706.

**Examples**

```
## Not run:
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)

## End(Not run)
```

whscore

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

Whittemore-Halpern scores for allele-sharing

**Usage**

whscore(allele, type)

**Arguments**

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



**Details**

Allele sharing score statistics.

**Value**

The returned value is the value of score statistic.

**Note**

adapted from GENEHUNTER.

**Author(s)**

Leonid Kruglyak, Jing Hua Zhao

**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**(6), 1347-63. ISSN 0002-9297 (Print) 0002-9297.

Whittemore AS, Halpern J (1994). "A class of tests for linkage using affected pedigree members." *Biometrics*, **50**(1), 118-27. ISSN 0006-341X (Print) 0006-341x.

Whittemore AS, Halpern J (1994). "Probability of gene identity by descent: computation and applications." *Biometrics*, **50**(1), 109-17. ISSN 0006-341X (Print) 0006-341x.

**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)
```

---

WriteGRM

*A function to write GRM file*


---

**Description**

A function to write GRM file

**Usage**

```
WriteGRM(prefix = 51, id, N, GRM)
```

**Arguments**

prefix	file root.
id	id.
N	sample size.
GRM	a GRM.

---

WriteGRMBin	<i>A function to write GRM binary file</i>
-------------	--

---

**Description**

A function to write GRM binary file

**Usage**

```
WriteGRMBin(prefix, grm, N, id, size = 4)
```

**Arguments**

prefix	file root.
grm	a GRM.
N	Sample size.
id	id.
size	size.

---

xy	<i>Conversion of chromosome names to strings</i>
----	--

---

**Description**

Conversion of chromosome names to strings

**Usage**

```
xy(x)
```

**Arguments**

x	(alpha)numeric value indicating chromosome.
---	---

**Details**

This function converts x=1:24 to 1:22, X, Y

**Value**

As indicated.

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