

# Package ‘chopsticks’

December 1, 2025

**Title** The 'snp.matrix' and 'X.snp.matrix' Classes  
**Version** 1.76.0  
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**Author** Hin-Tak Leung <htl10@users.sourceforge.net>  
**Description** Implements classes and methods for large-scale SNP association studies  
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|--------------|-----------|

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|                   |                                                |
|-------------------|------------------------------------------------|
| snpMatrix-package | <i>The snp.matrix and X.snp.matrix classes</i> |
|-------------------|------------------------------------------------|

---

## Description

Implements classes and some basic methods for large-scale SNP association studies

## Details

Package: snpMatrix  
 Version: 1.2.4  
 Date: 2008-03-17  
 Depends: R(>= 2.3.0), survival, methods  
 Suggests: hexbin  
 Enhances: genetics  
 License: GNU General Public Licence (GPLv3)  
 URL: <http://www-gene.cimr.cam.ac.uk/clayton/software/>

Collate: ld.with.R ss.R contingency.table.R glm\\_test.R ibs.stats.R indata.R ld.snp.R ld.with.R.eml.R misc.R outdata.R  
 LazyLoad: yes  
 biocViews: Microarray, SNPsAndGeneticVariability  
 Packaged: Mon Mar 17 11:46:30 2008; david  
 Built: R 2.7.0; i686-pc-linux-gnu; 2008-03-17 11:47:01; unix

## Index:

|                    |                                                                                |
|--------------------|--------------------------------------------------------------------------------|
| X.snp-class        | Class "X.snp"                                                                  |
| X.snp.matrix-class | Class "X.snp.matrix"                                                           |
| epsout.ld.snp      | Function to write an eps file directly to visualize LD                         |
| for.exercise       | Data for exercise in use of the snpMatrix package                              |
| genotype-class     | snpMatrix-internal                                                             |
| glm.test.control   | Set up control object for GLM tests                                            |
| ibs.stats          | function to calculate the identity-by-state stats of a group of samples        |
| ibsCount           | Count alleles identical by state                                               |
| ibsDist            | Distance matrix based on identity by state (IBS)                               |
| ld.snp             | Function to calculate pairwise D', $r^2$                                       |
| ld.with            | function to calculate the LD measures of specific SNPs against other SNPs      |
| pair.result.ld.snp | Function to calculate the pairwise D', $r^2$ , LOD of a pair of specified SNPs |
| plot.snp.dprime    | Function to draw the pairwise D' in a eps file                                 |
| qq.chisq           | Quantile-quantile plot for chi-squared tests                                   |
| read.HapMap.data   | function to import HapMap genotype data as snp.matrix                          |
| read.pedfile.info  | function to read the accompanying info file of a LINKAGE ped file              |
| read.snps.chiamo   | Read genotype data from the output of Chiamo                                   |
| read.snps.long     | Read SNP data in long format                                                   |
| read.snps.long.old | Read SNP input data in "long" format (old version)                             |
| read.snps.pedfile  | Read genotype data from a LINKAGE "pedfile"                                    |
| read.wtccc.signals | read normalized signals in the WTCCC signal file format                        |
| row.summary        | Summarize rows of a snp matrix                                                 |
| single.snp.tests   | 1-df and 2-df tests for genetic associations with SNPs                         |
| snp-class          | Class "snp"                                                                    |
| snp.cbind          | Bind together two or more snp.matrix objects                                   |
| snp.cor            | Correlations with columns of a snp.matrix                                      |
| snp.dprime-class   | Class "snp.dprime" for Results of LD calculation                               |
| snp.lhs.tests      | Score tests with SNP genotypes as dependent variable                           |
| snp.matrix-class   | Class "snp.matrix"                                                             |
| snp.pre            | Pre- or post-multiply a snp.matrix object by a                                 |

|                   |                                                                      |
|-------------------|----------------------------------------------------------------------|
|                   | general matrix                                                       |
| snp.rhs.tests     | Score tests with SNP genotypes as independent variable               |
| snpMatrix-package | The snp.matrix and X.snp.matrix classes                              |
| testdata          | Test data for the snpMatrix package                                  |
| write.snp.matrix  | Write a snp.matrix object as a text file                             |
| wtccc.sample.list | read the sample list from the header of the WTCCC signal file format |
| xxt               | X.X-transpose for a normalised snp.matrix                            |

Further information is available in the following vignettes:

snpMatrix-vignette    snpMatrix (source, pdf)

### Author(s)

David Clayton <david.clayton@cimr.cam.ac.uk> and Hin-Tak Leung <htl10@users.sourceforge.net>

Maintainer: David Clayton <david.clayton@cimr.cam.ac.uk>

---

epsout.ld.snp

*Function to write an eps file directly to visualize LD*

---

### Description

epsout.ld.snp takes an object of snp.matrix class and a given snp range and depth, draw a eps file to visualize the LD in the same color scheme as haploview's default view. It was the first prototype of this bunch of software. Also, it does not keep any pair-wise data in memory at all, and maybe more suitable where the actual pair-wise LD data is not needed.

### Usage

```
epsout.ld.snp(snpdata, filename, start, end, depth, do.notes=FALSE)
```

### Arguments

|          |                                                                                        |
|----------|----------------------------------------------------------------------------------------|
| snpdata  | An object of snp.matrix class with M samples of N snps                                 |
| filename | The file name of the output, preferably ending with ".eps", but this rule not enforced |
| start    | The index of the start of the range of interest. Should be between 1 and (N-1)         |
| end      | The index of the end of the range of interest. Should be between 2 and N.              |
| depth    | The depth or lag of pair-wise calculation. Should be between 1 and N-1                 |
| do.notes | Boolean for whether to generate pdf annotation-related code                            |

### Details

The functionality of this routine has since been split into a two-stage processes involving `ld.snp` which generates a `snp.dprime` object which contains the result of the pairwise LD calculation, and `plot.snp.dprime` (or the `plot` method of a `snp.dprime` object) which does the drawing.

**Value**

return nothing

**Author(s)**

Hin-Tak Leung <ht110@users.sourceforge.net>

**References**

Clayton, D.G. and Leung, Hin-Tak (2007) An R package for analysis of whole-genome association studies. *Human Heredity* **64**:45-51.  
GSL (GNU Scientific Library) <http://www.gnu.org/software/gsl/>  
The postscript language reference manual: <http://www.adobe.com/products/postscript/pdfs/PLRM.pdf>  
The pdf specification: <http://partners.adobe.com/public/developer/en/pdf/PDFReference16.pdf>

**See Also**

[snp.dprime-class](#), [ld.snp](#), [plot.snp.dprime](#)

**Examples**

```
#  
data(testdata)  
epsout.ld.snp(Autosomes, start=1, end=500, depth=50, filename="test.eps")
```

---

for.exercise

*Data for exercise in use of the snpMatrix package*

---

**Description**

These data have been created artificially from publicly available datasets. The SNPs have been selected from those genotyped by the International HapMap Project (<http://www.hapmap.org>) to represent the typical density found on a whole genome association chip, (the Affymetrix 500K platform, [http://www.affymetrix.com/support/technical/sample\\_data/500k\\_hapmap\\_genotype\\_data.affx](http://www.affymetrix.com/support/technical/sample_data/500k_hapmap_genotype_data.affx) for a moderately sized chromosome (chromosome 10). A study of 500 cases and 500 controls has been simulated allowing for recombination using beta software from Su and Marchini (<http://www.stats.ox.ac.uk/~marchini/software/gwas/hapgen.html>). Re-sampling of cases was weighted in such a way as to simulate three “causal” locus on this chromosome, with multiplicative effects of 1.3, 1.4 and 1.5 for each copy of the risk allele.

**Usage**

```
data(for.exercise)
```

## Format

There are three data objects in the dataset:

- `snps.10` An object of class "snp.matrix" containing a matrix of SNP genotype calls. Rows of the matrix correspond to subjects and columns correspond to SNPs.
- `snp.support` A conventional R data frame containing information about the SNPs typed (the chromosome position and the nucleotides corresponding to the two alleles of the SNP).
- `subject.support` A conventional R dataframe containing information about the study subjects. There are two variables; `cc` gives case/control status (1=case), and `stratum` gives ethnicity.

## Source

The data were obtained from the diabetes and inflammation laboratory (see <http://www-gene.cimr.cam.ac.uk/todd>)

## References

<http://www-gene.cimr.cam.ac.uk/clayton>

## Examples

```
data(for.exercise)
snps.10
summary(summary(snps.10))
summary(snp.support)
summary(subject.support)
```

---

|                               |                                            |
|-------------------------------|--------------------------------------------|
| <code>glm.test.control</code> | <i>Set up control object for GLM tests</i> |
|-------------------------------|--------------------------------------------|

---

## Description

To carry out a score test for a GLM, we first fit a "base" model using the standard iteratively reweighted least squares (IRLS) algorithm and then carry out a score test for addition of further terms. This function sets various control parameters for this.

## Usage

```
glm.test.control(maxit, epsilon, R2Max)
```

## Arguments

|                      |                                           |
|----------------------|-------------------------------------------|
| <code>maxit</code>   | Maximum number of IRLS steps              |
| <code>epsilon</code> | Convergence threshold for IRLS algorithm  |
| <code>R2Max</code>   | R-squared limit for aliasing of new terms |

## Details

Sometimes (although not always), an iterative scheme is necessary to fit the "base" generalized linear model (GLM) before carrying out a score test for effect of adding new term(s). The `maxit` parameter sets the maximum number of iterations to be carried out, while the `epsilon` parameter sets the criterion for determining convergence. After fitting the base model, the new terms are added, but terms judged to be "aliased" are omitted. The method for determining aliasing is as follows (denoting the "design" matrix for the additional terms by  $Z$ ):

1. Step 1 Regress each column of  $Z$  on the base model matrix, using the final GLM weights from the base model fit, and replace  $Z$  with the residuals from these regressions.
2. Step 2 Consider each column of the new  $Z$  matrix in turn, regressing it on the *previous* columns (again using the weights from the base model fit). If the proportion of the weighted sum of squares "explained" by this regression exceeds `R2Max`, the term is dropped and not included in the test,

The aim of this procedure to avoid wasting degrees of freedom on columns so strongly aliased that there is little power to detect their effect.

## Value

Returns the parameters as a list in the expected order

## Author(s)

David Clayton <david.clayton@cimr.cam.ac.uk>

## See Also

[snp.lhs.tests](#), [snp.rhs.tests](#)

---

ibs.stats

*function to calculate the identity-by-state stats of a group of samples*

---

## Description

Given a [snp.matrix-class](#) or a [X.snp.matrix-class](#) object with  $N \times S$  samples, calculates some statistics about the relatedness of every pair of samples within.

## Usage

```
ibs.stats(x)
```

## Arguments

`x` a [snp.matrix-class](#) or a [X.snp.matrix-class](#) object containing  $N \times S$  samples

## Details

No-calls are excluded from consideration here.

Value

A data.frame containing  $N(N-1)/2$  rows, where the row names are the sample name pairs separated by a comma, and the columns are:

|          |                                                                                 |
|----------|---------------------------------------------------------------------------------|
| Count    | count of identical calls, excluding no-calls                                    |
| Fraction | fraction of identical calls compared to actual calls being made in both samples |

Warning

In some applications, it may be preferable to subset a (random) selection of SNPs first - the calculation time increases as  $N(N-1)M/2$ . Typically for  $N = 800$  samples and  $M = 3000$  SNPs, the calculation time is about 1 minute. A full GWA scan could take hours, and quite unnecessary for simple applications such as checking for duplicate or related samples.

Note

This is mostly written to find mislabelled and/or duplicate samples.

Illumina indexes their SNPs in alphabetical order so the mitochondria SNPs comes first - for most purpose it is undesirable to use these SNPs for IBS purposes.

TODO: Worst-case S4 subsetting seems to make 2 copies of a large object, so one might want to subset before `rbind()`, etc; a future version of this routine may contain a built-in subsetting facility to work around that limitation.

Author(s)

Hin-Tak Leung <htl10@users.sourceforge.net>

Examples

```
data(testdata)
result <- ibs.stats(Autosomes[11:20,])
summary(result)
```

---

|          |                                         |
|----------|-----------------------------------------|
| ibsCount | <i>Count alleles identical by state</i> |
|----------|-----------------------------------------|

---

Description

This function counts, for all pairs of subjects and across all SNPs, the total number of alleles which are identical by state (IBS)

Usage

```
ibsCount(snp)
```

Arguments

|     |                                                         |
|-----|---------------------------------------------------------|
| snp | An input object of class "snp.matrix" or "X.snp.matrix" |
|-----|---------------------------------------------------------|

## Details

For each pair of subjects the function counts the total number of alleles which are IBS. For autosomal SNPs, each locus contributes 4 comparisons, since each subject carries two copies. For SNPs on the X chromosome, the number of comparisons is also 4 for female:female comparisons, but is 2 for female:male and 1 for male:male comparisons.

## Value

If there are  $N$  rows in the input matrix, the function returns an  $N*N$  matrix. The upper triangle contains the total number of comparisons and the lower triangle contains the number of these which are IBS. The diagonal contains the number of valid calls for each subject.

## Note

In genome-wide studies, the SNP data will usually be held as a series of objects (of class "snp.matrix" or "X.snp.matrix"), one per chromosome. Note that the matrices produced by applying the `ibsCount` function to each object in turn can be added to yield the genome-wide result.

## Author(s)

David Clayton <david.clayton@cimr.cam.ac.uk>

## See Also

[ibsDist](#) which calculates a distance matrix based on proportion of alleles which are IBS

## Examples

```
data(testdata)
ibs.A <- ibsCount(Autosomes[,1:100])
ibs.X <- ibsCount(Xchromosome)
```

---

ibsDist

*Distance matrix based on identity by state (IBS)*

---

## Description

Expresses a matrix of IBS counts (see [ibsCount](#)) as a distance matrix. The distance between two samples is returned as the proportion of allele comparisons which are *not* IBS.

## Usage

```
ibsDist(counts)
```

## Arguments

counts                      A matrix of IBS counts as produced by the function [ibsCount](#)

## Value

An object of class "dist" (see [dist](#))

**Author(s)**

David Clayton <david.clayton@cimr.cam.ac.uk>

**See Also**

[ibsCount](#), [dist](#)

**Examples**

```
data(testdata)
ibs <- ibsCount(Xchromosome)
distance <- ibsDist(ibs)
```

---

ld.snp

---

*Function to calculate pairwise  $D'$ ,  $r^2$* 


---

**Description**

ld.snp takes an object of snp.matrix class and suitable range and depth and calculation the pair-wise  $D'$ ,  $r^2$ , LOD and return the result as a [snp.dprime](#) object.

**Usage**

```
ld.snp(snpdata, depth = 100, start = 1, end = dim(snpdata)[2], signed.r=FALSE)
```

**Arguments**

|          |                                                                                                                                                    |
|----------|----------------------------------------------------------------------------------------------------------------------------------------------------|
| snpdata  | An object of snp.matrix class with M samples of N snps                                                                                             |
| depth    | The depth or lag of pair-wise calculation. Should be between 1 and N-1; default 100. Using 0 (an invalid value) is the same as picking the maximum |
| start    | The index of the start of the range of interest. Should be between 1 and (N-1); default 1                                                          |
| end      | The index of the end of the range of interest. Should be between 2 and N. default N.                                                               |
| signed.r | Boolean for whether to returned signed $r$ values instead of $r^2$                                                                                 |

**Details**

The cubic equation and quadratic equation solver code is borrowed from GSL (GNU Scientific Library).

**Value**

return a [snp.dprime](#) object, which is a list of 3 named matrices dprime, rsq2 (or r depending on the input), lod, and an attribute snp.names for the list of snps involved. (Note that if  $x$  snps are involved, the row numbers of the 3 matrices are  $(x-1)$ ). Only one of rsq2 or r is present.

|        |            |
|--------|------------|
| dprime | $D'$       |
| rsq2   | $r^2$      |
| r      | signed $r$ |

lod                      Log of Odd's

All the matrices are defined such that the  $(n, m)$ th entry is the pair-wise value between the  $(n)$ th snp and the  $(n+m)$ th snp. Hence the lower right triangles are always filled with zeros. (See example section for the actual layout)

Invalid values are represented by an out-of-range value - currently we use -1 for  $D'$ ,  $r^2$  (both of which are between 0 and 1), and -2 for  $r$  (valid values are between -1 and +1). lod is set to zero in most of these invalid cases. (lod can be any value so it is not indicative).

## Note

The output `snp.dprime` object is suitable for input to `plot.snp.dprime` for drawing.

The speed of "ld.snp" LD calculation, on a single-processor opteron 2.2GHz box:

unsigned  $r^2$ , 13191 snps, depth 100 = 36.4 s (~ 1.3 mil pairs)

signed  $r$ , 13191 snps, depth 100 = 40.94s (~ 1.3 mil pairs)

signed  $r$ , 13191 snps, depth 1500 = 582s (~ 18.5 mil pairs)

For depth=1500, it uses 500MB just for the three matrices. So I actually cannot do the full depth at ~13,000; full depth should be under 50 minutes for 87 mil pairs, even in the signed-r version.

The LD code can be ran outside of R - mainly for debugging:

```
gcc -DWITHOUT_R -o /tmp/hello pairwise_linkage.c solve_cubic.c \
    solve_quadratic.c -lm
```

When used in this form, it takes 9 numbers:

```
$/tmp/hello 4 0 0 0 30 0 0 0 23
case 3                      <- internal code for which cases it falls in
root count 1                <- how many roots
trying 1.000000
p = 1.000000
4        0        0        6.333333        0.000000        0.000000
0        30        0        0.000000        25.333333        0.000000
0        0        23        0.000000        0.000000        25.333333
57 8 38.000000 38 38
8 0 0 46 30, 38 38 76 76
0.333333 0.000000 0.000000 0.666667
d' = 1.000000 , r2 = 1.000000, lod= 22.482643
```

## Author(s)

Hin-Tak Leung <ht110@users.sourceforge.net>

## References

Clayton, D.G. and Leung, Hin-Tak (2007) An R package for analysis of whole-genome association studies. *Human Heredity* **64**:45-51.

GSL (GNU Scientific Library) <http://www.gnu.org/software/gsl/>

**See Also**

[snp.dprime-class](#), [plot.snp.dprime](#), [ld.with](#)

**Examples**

```
# LD stats between 500 SNPs at a depth of 50
data(testdata)
ldinfo <- ld.snp(Autosomes, start=1, end=500, depth=50)
```

---

|         |                                                                                  |
|---------|----------------------------------------------------------------------------------|
| ld.with | <i>function to calculate the LD measures of specific SNPs against other SNPs</i> |
|---------|----------------------------------------------------------------------------------|

---

**Description**

This function calculates the LD measures ( $r^2$ ,  $D'$ , LOD) of specific SNPs against other SNPs.

**Usage**

```
ld.with(data, snps, include.itself = as.logical(length(snps) - 1), signed.r = NULL)
```

**Arguments**

|                |                                                                                                                                                          |
|----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------|
| data           | either a <a href="#">snp.dprime-class</a> object or a <a href="#">snp.matrix-class</a> object                                                            |
| snps           | A list of snps, some of which are found in data                                                                                                          |
| include.itself | Whether to include LD measures of SNPs against itself - it is FALSE for one SNP, since in that case, the result is known and trivial; but otherwise TRUE |
| signed.r       | Logical, whether to output signed r or $r^2$                                                                                                             |

**Details**

Not all combinations of the `include.itself` and `signed.r` make sense, nor fully operational.

**Value**

The returned value is somewhat similar to a [snp.dprime](#) object, but not the same. It is a list of 3 named matrices `dprime`, `rsq2` (or `r` depending on the input), `lod`.

**Warning**

Because this is really two functions rolled into one, depending on the class of data, not all combinations of the `include.itself` and `signed.r` make sense, nor fully operational.

Also, the two versions have slightly different idea about invalid values, e.g. the LOD value for a SNPs against itself, or  $r^2$  for two monomorphic snps (such as one against itself).

**Note**

The `ld.with` function started its life as an extractor function to take the output of `ld.snp`, a [snp.dprime-class](#) object, to rearrange it in a more convenient form to focus on the LD's against specific SNPs, but then evolved to take a [snp.matrix-class](#) object alternatively and perform the same task directly and more efficiently.

**Author(s)**

Hin-Tak Leung <htl10@users.sourceforge.net>

**See Also**

[ld.snp](#), [snp.dprime-class](#)

**Examples**

```
data(testdata)
snps10 <- Autosomes[1:10,1:10]
obj.snp.dprime <- ld.snp(snps10)

# result1 and result2 should be almost identical
# except where noted in the warning section above:
result1 <- ld.with(obj.snp.dprime, colnames(snps10))
result2 <- ld.with(snps10, colnames(snps10))
```

---

|                    |                                                                                                              |
|--------------------|--------------------------------------------------------------------------------------------------------------|
| pair.result.ld.snp | <i>Function to calculate the pairwise <math>D'</math>, <math>r^2</math>, LOD of a pair of specified SNPs</i> |
|--------------------|--------------------------------------------------------------------------------------------------------------|

---

**Description**

pair.result.ld.snp.Rd calculates the pairwise  $D'$ ,  $r^2$ , LOD of a pair of specified SNPs in a snp.matrix object. This is used mainly for debugging.

**Usage**

```
pair.result.ld.snp(snpdata, loc.snpA, loc.snpB)
```

**Arguments**

|          |                                                        |
|----------|--------------------------------------------------------|
| snpdata  | An object of snp.matrix class with M samples of N snps |
| loc.snpA | index of the first snp; should be between 1 and N      |
| loc.snpB | index of the second snp; should be between 1 and N     |

**Value**

Returns nothing. Results are displayed in stdout/console.

**Note**

Not really recommended for daily usage; the result isn't saved anywhere and this routine is primarily for debugging the details and correctness of the calculation.

**Author(s)**

Hin-Tak Leung <htl10@users.sourceforge.net>

## References

Clayton, D.G. and Leung, Hin-Tak (2007) An R package for analysis of whole-genome association studies. *Human Heredity* **64**:45-51.  
 GSL (GNU Scientific Library) <http://www.gnu.org/software/gsl/>

## See Also

[snp.matrix-class](#)

## Examples

```
data(testdata)
pair.result.ld.snp(Autosomes, 1, 2)
```

---

|                 |                                                       |
|-----------------|-------------------------------------------------------|
| plot.snp.dprime | <i>Function to draw the pairwise D' in a eps file</i> |
|-----------------|-------------------------------------------------------|

---

## Description

plot.snp.dprime takes a [snp.dprime](#) object and draw an eps file to visualize the pairwise D',  $r^2$  and LOD.

## Usage

```
## S3 method for class 'snp.dprime'
plot(x, filename, scheme = "standard", do.notes = FALSE,
     metric=NULL, ...)
```

## Arguments

|          |                                                                                                                                                        |
|----------|--------------------------------------------------------------------------------------------------------------------------------------------------------|
| x        | An object of class <a href="#">snp.dprime</a>                                                                                                          |
| filename | The output file name, preferably ending with ".eps" (not enforced)                                                                                     |
| scheme   | The colour scheme used. Valid values are "standard" for the Haploview default, and "rsq" for grayscale $r^2$ . More may come later                     |
| do.notes | Boolean for whether to generate pdf annotation-related code                                                                                            |
| metric   | An integer vector, detailing the chromosome position of the SNP, to draw a scaled metric of the location of the SNP. If NULL, no metric would be drawn |
| ...      | place holder                                                                                                                                           |

## Details

Annotation is a little used pdf features where certain part of a pdf file are hot spots where one can get pop-up balloons containing extra information, which doesn't appear in print. This is written to imitate the extra information one can get from right-clicking in Haploview's GUI.

## Value

return nothing. Write a file as a result. And if do.notes is specified, Will also suggest user to execute `ps2pdf -dEPSCrop <filename>` to get a suitable pdf.

**Note**

Unfortunately, there are two problems with annotations: only Acrobat Reader (out of all the pdf viewers, e.g. xpdf, kpdf, evince, various ghostscript based viewers) implements the feature, and a few thousand annotations can really make Acrobat Reader crawl.

Also, Acrobat Reader has an implementation limit of 200 inches of the widest dimension of a document. This translates to 1200 snps in the current implementation of the drawing code, hence a warning is emitted that pdf written this way is not viewable by Acrobat Reader.(but viewable by xpdf, etc). A work around is possible based on LaTeX pdfpage, or eps can be included with scaling in another document, to stay inside 200 inches.

In the future, one might want to put some additional scaling code to fit the whole drawing within an A4, for example.

There is a Google Summer of code <http://code.google.com/soc/> 2006 project to improve kpdf's annotation support. <http://wiki.kde.org/tiki-index.php?page=KDE%20Google%20SoC%202006%20ideas#id60851> I am involved.

**Author(s)**

Hin-Tak Leung <htl10@users.sourceforge.net>

**References**

Clayton, D.G. and Leung, Hin-Tak (2007) An R package for analysis of whole-genome association studies. *Human Heredity* **64**:45-51.

GSL (GNU Scientific Library) <http://www.gnu.org/software/gsl/>

The postscript language reference manual: <http://www.adobe.com/products/postscript/pdfs/PLRM.pdf>

The pdf specification: <http://partners.adobe.com/public/developer/en/pdf/PDFReference16.pdf>

**See Also**

[snp.dprime-class](#)

**Examples**

```
data(testdata)
# As for ld.snp example ...
data(testdata)
ldinfo <- ld.snp(Autosomes, start=1, end=500, depth=50)
# Now plot to an eps file
plot.snp.dprime(ldinfo, filename="test.eps")
```

**Description**

This function plots ranked observed chi-squared test statistics against the corresponding expected order statistics. It also estimates an inflation (or deflation) factor, lambda, by the ratio of the trimmed means of observed and expected values. This is useful for inspecting the results of whole-genome association studies for overdispersion due to population substructure and other sources of bias or confounding.

**Usage**

```
qq.chisq(x, df=1, x.max, main="QQ plot",
  sub=paste("Expected distribution: chi-squared (",df," df)", sep=""),
  xlab="Expected", ylab="Observed",
  conc=c(0.025, 0.975), overdisp=FALSE, trim=0.5,
  slope.one=FALSE, slope.lambda=FALSE,
  thin=c(0.25,50), oor.pch=24, col.shade="gray", ...)
```

**Arguments**

|                           |                                                                                                                                                                     |
|---------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <code>x</code>            | A vector of observed chi-squared test values                                                                                                                        |
| <code>df</code>           | The degrees of freedom for the tests                                                                                                                                |
| <code>x.max</code>        | If present, truncate the observed value (Y) axis here                                                                                                               |
| <code>main</code>         | The main heading                                                                                                                                                    |
| <code>sub</code>          | The subheading                                                                                                                                                      |
| <code>xlab</code>         | x-axis label (default "Expected")                                                                                                                                   |
| <code>ylab</code>         | y-axis label (default "Observed")                                                                                                                                   |
| <code>conc</code>         | Lower and upper probability bounds for concentration band for the plot. Set this to NA to suppress this                                                             |
| <code>overdisp</code>     | If TRUE, an overdispersion factor, lambda, will be estimated and used in calculating concentration band                                                             |
| <code>trim</code>         | Quantile point for trimmed mean calculations for estimation of lambda. Default is to trim at the median                                                             |
| <code>slope.one</code>    | Is a line of slope one to be superimposed?                                                                                                                          |
| <code>slope.lambda</code> | Is a line of slope lambda to be superimposed?                                                                                                                       |
| <code>thin</code>         | A pair of numbers indicating how points will be thinned before plotting (see Details). If NA, no thinning will be carried out                                       |
| <code>oor.pch</code>      | Observed values greater than <code>x.max</code> are plotted at <code>x.max</code> . This argument sets the plotting symbol to be used for out-of-range observations |
| <code>col.shade</code>    | The colour with which the concentration band will be filled                                                                                                         |
| <code>...</code>          | Further graphical parameter settings to be passed to <code>points()</code>                                                                                          |

**Details**

To reduce plotting time and the size of plot files, the smallest observed and expected points are thinned so that only a reduced number of (approximately equally spaced) points are plotted. The precise behaviour is controlled by the parameter `thin`, whose value should be a pair of numbers. The first number must lie between 0 and 1 and sets the proportion of the X axis over which thinning is to be applied. The second number should be an integer and sets the maximum number of points to be plotted in this section.

The "concentration band" for the plot is shown in grey. This region is defined by upper and lower probability bounds for each order statistic. The default is to use the 2.5 Note that this is not a simultaneous confidence region; the probability that the plot will stray outside the band at some point exceeds 95

When required, the dispersion factor is estimated by the ratio of the observed trimmed mean to its expected value under the chi-squared assumption.

**Value**

The function returns the number of tests, the number of values omitted from the plot (greater than `x.max`), and the estimated dispersion factor, `lambda`.

**Note**

All tests must have the same number of degrees of freedom. If this is not the case, I suggest transforming to p-values and then plotting  $-2\log(p)$  as chi-squared on 2 df.

**Author(s)**

David Clayton <david.clayton@cimr.cam.ac.uk>

**References**

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

**See Also**

[single.snp.tests](#), [snp.lhs.tests](#), [snp.rhs.tests](#)

**Examples**

```
## See example the single.snp.tests() function
```

---

|                  |                                                              |
|------------------|--------------------------------------------------------------|
| read.HapMap.data | <i>function to import HapMap genotype data as snp.matrix</i> |
|------------------|--------------------------------------------------------------|

---

**Description**

Given a URL for HapMap genotype data, `read.HapMap.data`, download and convert the genotype data into a `snp.matrix` class object, and saving snp support information into an associated `data.frame`.

**Usage**

```
read.HapMap.data(url, verbose=FALSE, save=NULL, ...)
```

**Arguments**

|                      |                                                                                                                                                 |
|----------------------|-------------------------------------------------------------------------------------------------------------------------------------------------|
| <code>url</code>     | URL for HapMap data. Web data is to be specified with prefix "http://", ftp data with prefix "ftp://", and local file as "file://"              |
| <code>verbose</code> | Where the <code>dnSNPalleles</code> annotation is ambiguous, output more details information about how/why assignment is made. See Notes below. |
| <code>save</code>    | filename to save the download - if unspecified, a temporary file will be created but removed afterwards.                                        |
| <code>...</code>     | Place-holder for further switches - currently ignored.                                                                                          |

## Details

During the conversion, if the dbSNPAlleles entry is exactly of the form "X/Y", where X, Y = A or C or G or T, then it is used directly for assigning allele 1 and allele 2.

However, about 1 in 1000 entries are more complicated e.g. may involving deletion, e.g. "-/A/G" or "-/A/AGT/G/T". Some heuristics are used in such cases, in which the observed genotypes in the specific snp of the current batch are examined in two passes. The first time to see which bases are present, excluding "N".

If more than 2 bases are observed in the batch specified in the url, the routine aborts, but so far this possibility has not arisen in tests. If there is exactly two, then allele 1 and 2 are assigned in alphabetical order (dbSNPAlleles entries seems to be always in dictionary order, so the assignment made should agree with a shorten version of the dbSNPAlleles entry). Likewise, if only "A" or "T" is observed, then we know automatically it is the first (assigned as "A/.") or the last allele (assigned as ".T") of a hypothetical pair, without looking at the dbSNPAlleles entry. For other observed cases of 1 base, the routine goes further and look at the dnSNPAlleles entry and see if it begins with "-/X/" or ends with "/X", as a single base, and compare it with the single base observed to see if it should be allele 1 (same as the beginning, or different from the end) and allele 2 (same as the end, or different from the beginning). If no decision can be made for a particular snp entry, the routine aborts with an appropriate message. (For zero observed bases, assignment is " ./.", and of course, all observed genotypes of that snp are therefore converted to the equivalent of NA.)

(This heuristics does not cover all grounds, but practically it seems to work. See Notes below.)

## Value

Returns a list containing these two items when successful, otherwise returns NULL:

|             |                                                                                                                                                                                                                                             |
|-------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| snp.data    | A snp.matrix-class object containing the snp data                                                                                                                                                                                           |
| snp.support | A data.frame, containing the dbSNPAlleles, Chromosome, Position, Strand entries from the hapmap genotype file, together with the actual Assignment used for allele 1 and allele 2 during the conversion (See Details above and Note below). |

## Note

Using both "file://" for url and save duplicates the file. (i.e. by default, the routine make a copy of the url in any case, but tidy up afterwards if run without save).

Sometimes the assignment may not be unique e.g. dnSNPAlleles entry "A/C/T" and only "C" is observed - this can be assigned "A/C" or "C/T". (currently it does the former). One needs to be especially careful when joining two sets of snp data and it is imperative to compare the assignment supplementary data to see they are compatible. (e.g. for an "A/C/T" entry, one data set may have "C" only and thus have assignment "A/C" and have all of it assigned Allele 2 homozygotes, whereas another data set contains both "C" and "T" and thus the first set needs to be modified before joining).

A typical run, chromosome 1 for CEU, contains about ~400,000 snps and ~100 samples, and the snp.matrix object is about ~60MB (40 million bytes for snps plus overhead) and similiar for the support data (i.e. ~ 2x), takes about 30 seconds, and at peak memory usage requires ~ 4x . The actual download is ~20MB, which is compressed from ~200MB.

## Author(s)

Hin-Tak Leung <ht110@users.sourceforge.net>

## References

<http://www.hapmap.org/genotypes>

## See Also

[snp.matrix-class](#)

## Examples

```
## Not run:

## ** Please be aware that the HapMap project generates new builds from
## ** time to time and the build number in the URL changes.

> library(snpMatrix)
> testurl <- paste0("http://www.hapmap.org/genotypes/latest/fwd_strand/",
  "non-redundant/genotypes_chr1_CEU_r21_nr_fwd.txt.gz")
> result1 <- read.HapMap.data(testurl)
> sum1 <- summary(result1$snp.data)

> head(sum1[is.finite(sum1$z.HWE),], n=10)
      Calls Call.rate      MAF      P.AA      P.AB      P.BB      z.HWE
rs1933024      87 0.9666667 0.005747126 0.0000000 0.01149425 0.9885057 0.05391549
rs11497407      89 0.9888889 0.005617978 0.0000000 0.01123596 0.9887640 0.05329933
rs12565286      88 0.9777778 0.056818182 0.0000000 0.11363636 0.8863636 0.56511033
rs11804171      83 0.9222222 0.030120482 0.0000000 0.06024096 0.9397590 0.28293272
rs2977656      90 1.0000000 0.005555556 0.9888889 0.01111111 0.0000000 0.05299907
rs12138618      89 0.9888889 0.050561798 0.0000000 0.10112360 0.8988764 0.50240136
rs3094315      88 0.9777778 0.136363636 0.7272727 0.27272727 0.0000000 1.48118392
rs17160906      89 0.9888889 0.106741573 0.0000000 0.21348315 0.7865169 1.12733108
rs2519016      85 0.9444444 0.047058824 0.0000000 0.09411765 0.9058824 0.45528615
rs12562034      90 1.0000000 0.088888889 0.0000000 0.17777778 0.8222222 0.92554468

## ** Please be aware that the HapMap project generates new builds from
## ** to time and the build number in the URL changes.

## This URL is broken up into two to fit the width of
## the paper. There is no need in actual usage:
> testurl2 <- paste0("http://www.hapmap.org/genotypes/latest/",
  "fwd_strand/non-redundant/genotypes_chr1_JPT_r21_nr_fwd.txt.gz")
> result2 <- read.HapMap.data(testurl2)

> head(result2$snp.support)
      dbSNPalleles Assignment Chromosome Position Strand
rs10399749      C/T      C/T      chr1      45162      +
rs2949420      A/T      A/T      chr1      45257      +
rs4030303      A/G      A/G      chr1      72434      +
rs4030300      A/C      A/C      chr1      72515      +
rs3855952      A/G      A/G      chr1      77689      +
rs940550       C/T      C/T      chr1      78032      +

## End(Not run)
```

---

|                   |                                                                          |
|-------------------|--------------------------------------------------------------------------|
| read.pedfile.info | <i>function to read the accompanying info file of a LINKAGE ped file</i> |
|-------------------|--------------------------------------------------------------------------|

---

## Description

This function read the accompanying info file of a LINKAGE ped file, for the SNP names, position and chromosome.

## Usage

```
read.pedfile.info(file)
```

## Arguments

|      |              |
|------|--------------|
| file | An info file |
|------|--------------|

## Details

One such info file is the one accompanying the sample ped file of Haploview.

## Value

A data frame with columns "snp.names", "position", "chromosome".

## Note

This is used internally by [read.snps.pedfile](#) to read an accompanying info file.

## Author(s)

Hin-Tak Leung <htl10@users.sourceforge.net>

## References

See the documentation and description of ped files in Haploview (<http://www.broad.mit.edu/mpg/haploview/>)

## See Also

[read.snps.pedfile](#)

---

|                  |                                                                         |
|------------------|-------------------------------------------------------------------------|
| read.pedfile.map | <i>function to read the accompanying map file of a LINKAGE ped file</i> |
|------------------|-------------------------------------------------------------------------|

---

## Description

This function read the accompanying map file of a LINKAGE ped file, for the SNP names, position and chromosome.

## Usage

```
read.pedfile.map(file)
```

## Arguments

|      |                  |
|------|------------------|
| file | A Plink map file |
|------|------------------|

## Details

One such map file is the one accompanying the sample ped file of Haploview.

## Value

A data frame with columns "snp.names", "position", "chromosome".

## Note

This is used internally by [read.snps.pedfile](#) to read an accompanying map file.

## Author(s)

Hin-Tak Leung <htl10@users.sourceforge.net>

## References

See the documentation and description of ped files in Haploview (<http://www.broad.mit.edu/mpg/haploview/>)

## See Also

[read.snps.pedfile](#)

---

|                  |                                                     |
|------------------|-----------------------------------------------------|
| read.snps.chiamo | <i>Read genotype data from the output of Chiamo</i> |
|------------------|-----------------------------------------------------|

---

## Description

This function reads data from the raw output of Chiamo

## Usage

```
read.snps.chiamo(filename, sample.list, threshold)
```

## Arguments

|             |                                                                                                                                                                    |
|-------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| filename    | List of file names of output from Chiamo ; the outcome is the concatenation from runs of Chiamo, e.g. on blocks of SNPs, which is often done for practical reasons |
| sample.list | A character vector giving the sample list                                                                                                                          |
| threshold   | Cut-off for the posterior probability for a no-call                                                                                                                |

## Details

The raw output of Chiamo consists of the first 5 columns of [read.wtccc.signals](#), followed by triplets of posterior probabilities of calling A-A, A-B, or B-B.

The sample list can typically be obtained using [wtccc.sample.list](#), from one of the (smaller) signal files, which are the inputs to Chiamo.

## Value

The result is a list of two items:

|             |                                                                                  |
|-------------|----------------------------------------------------------------------------------|
| snp.data    | The genotype data as a <a href="#">snp.matrix-class</a> object.                  |
| snp.support | The information from the first 5 columns of <a href="#">read.wtccc.signals</a> . |

## Author(s)

Hin-Tak Leung <htl10@users.sourceforge.net>

## References

To obtain a copy of the Chiamo software please email Jonathan L. Marchini <marchini@stats.ox.ac.uk>.

## See Also

[wtccc.sample.list](#), [read.wtccc.signals](#)

## Examples

```
#
```

---

|                |                                     |
|----------------|-------------------------------------|
| read.snps.long | <i>Read SNP data in long format</i> |
|----------------|-------------------------------------|

---

## Description

Reads SNP data when organized in free format as one call per line. Other than the one call per line requirement, there is considerable flexibility. Multiple input files can be read, the input fields can be in any order on the line, and irrelevant fields can be skipped. The samples and SNPs to be read must be pre-specified, and define rows and columns of an output object of class "snp.matrix".

## Usage

```
read.snps.long(files, sample.id = NULL, snp.id = NULL, female = NULL,
               fields = c(sample = 1, snp = 2, genotype = 3, confidence = 4),
               codes = c("0", "1", "2"), threshold = 0.9, lower = TRUE,
               sep = " ", comment = "#", skip = 0, simplify = c(FALSE,FALSE),
               verbose = FALSE, every = 1000)
```

## Arguments

|           |                                                                                                                                                                                                                                                                                                                                                                                                      |
|-----------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| files     | A character vector giving the names of the input files                                                                                                                                                                                                                                                                                                                                               |
| sample.id | A character vector giving the identifiers of the samples to be read                                                                                                                                                                                                                                                                                                                                  |
| snp.id    | A character vector giving the names of the SNPs to be read                                                                                                                                                                                                                                                                                                                                           |
| female    | If the SNPs are on the X chromosome and the data are to be read as such, this logical vector (of the same length as sample.id should specify whether each sample was from a female subject                                                                                                                                                                                                           |
| fields    | A integer vector with named elements specifying the positions of the required fields in the input record. The fields are identified by the names sample and snp for the sample and SNP identifier fields, confidence for a call confidence score (if present) and either genotype if genotype calls occur as a single field, or allele1 and allele2 if the two alleles are coded in different fields |
| codes     | Either the single string "nucleotide" denoting that coding in terms of nucleotides (A, C, G or T, case insensitive), or a character vector giving genotype or allele codes (see below)                                                                                                                                                                                                               |
| threshold | A numerical value for the calling threshold on the confidence score                                                                                                                                                                                                                                                                                                                                  |
| lower     | If TRUE, then threshold represents a lower bound. Otherwise it is an upper bound                                                                                                                                                                                                                                                                                                                     |
| sep       | The delimiting character separating fields in the input record                                                                                                                                                                                                                                                                                                                                       |
| comment   | A character denoting that any remaining input on a line is to be ignored                                                                                                                                                                                                                                                                                                                             |
| skip      | An integer value specifying how many lines are to be skipped at the beginning of each data file                                                                                                                                                                                                                                                                                                      |
| simplify  | If TRUE, sample and SNP identifying strings will be shortened by removal of any common leading or trailing sequences when they are used as row and column names of the output snp.matrix                                                                                                                                                                                                             |
| verbose   | If TRUE, a progress report is generated as every every lines of data are read                                                                                                                                                                                                                                                                                                                        |
| every     | See verbose                                                                                                                                                                                                                                                                                                                                                                                          |



## Arguments

|           |                                                                                                                                                                                                                                                                                                                                           |
|-----------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| file      | Name of file containing the input data. Input files which have been compressed by the gzip utility are recognized                                                                                                                                                                                                                         |
| chip.id   | Array of type "character" containing (unique) identifiers for the chips, samples, or subjects for which calls are to be read. Other samples in the input data will be ignored                                                                                                                                                             |
| snp.id    | Array of type "character" containing (unique) identifiers of the SNPs for which data will be read. Again, further SNPs in the input data will be ignored                                                                                                                                                                                  |
| codes     | For autosomal SNPs, an array of length 3 giving the codes for the three genotypes, in the order homozygous(AA), heterozygous(AB), homozygous(BB). For X SNPs, an additional two codes for the male genotypes (AY and BY) must be supplied. All other codes will be treated as "no call". The default codes are "0", "1", "2" [, "0", "2"] |
| female    | If the data to be read refer to SNPs on the X chromosome, this argument must be supplied and should indicate whether each row of data refers to a female (TRUE) or to a male (FALSE). The output object will then be of class "X.snp.matrix".                                                                                             |
| conf      | Confidence score. See details                                                                                                                                                                                                                                                                                                             |
| drop      | If TRUE, any rows or columns without genotype calls will be dropped from the output matrix. Otherwise the full matrix, with rows and columns defined by the chip.id and snp.id arguments, will be returned                                                                                                                                |
| threshold | Acceptance threshold for confidence score                                                                                                                                                                                                                                                                                                 |
| sorted    | Is input file already sorted into the correct order (see details)?                                                                                                                                                                                                                                                                        |
| progress  | If TRUE, progress will be reported to the standard output stream                                                                                                                                                                                                                                                                          |

## Details

Data are assumed to be input with one line per call, in free format:

```
<chip-id> <snp-id> <code for genotype call> [<confidence>] ...
```

Currently, any fields following the first three (or four) are ignored. If the argument sorted is TRUE, the file is assumed to be sorted with *snp-id* as primary key and *chip-id* as secondary key using the current locale. The rows and columns of the returned matrix will also be ordered in this manner. If sorted is set to FALSE, then an algorithm which avoids this assumption is used. The rows and columns of the returned matrix will then be in the same order as the input chip\_id and snp\_id vectors. Calls in which both id fields match elements in the chip.id and snp.id arguments are read in, after (optionally) checking that the level of confidence achieves a given threshold. Confidence level checking is controlled by the conf argument. conf=0 indicates that no confidence score is present and no checking is done. conf>0 indicates that calls with scores *above* threshold are accepted, while conf<0 indicates that only calls with scores *below* threshold should be accepted.

The routine is case-sensitive and it is important that the <chip-id> and <snp-id> match the cases of chip.id and snp.id exactly.

## Value

An object of class snp.matrix.

**Note**

If more than one instance of any combination of chip\_id element and snp\_id element passes the confidence threshold, the called to be used is decided by the following rules:

1. 1Any call trumps "no-call"
2. 2In the event of call conflict, "no-call" is returned

Use of sorted=TRUE is usually discouraged since the alternative algorithm is safer and, usually, not appreciably slower. However, if the input file is to be read multiple times and there is a reasonably close correspondence between cells of the matrix to be returned and lines of the input file, the sorted option can be faster.

This function has been replaced by the more flexible function [read.snps.long](#).

**Author(s)**

David Clayton <david.clayton@cimr.cam.ac.uk> and Hin-Tak Leung

**References**

<http://www-gene.cimr.cam.ac.uk/clayton>

**See Also**

[snp.matrix-class](#), [X.snp.matrix-class](#)

---

|                   |                                                    |
|-------------------|----------------------------------------------------|
| read.snps.pedfile | <i>Read genotype data from a LINKAGE "pedfile"</i> |
|-------------------|----------------------------------------------------|

---

**Description**

This function reads data arranged as a LINKAGE "pedfile" with some restrictions and returns a list of three objects: a data frame containing the initial 6 fields giving pedigree structure, sex and disease status, a vector or a data frame containing snp assignment and possibly other snp information, and an object of class "snp.matrix" or "X.snp.matrix" containing the genotype data

**Usage**

```
read.snps.pedfile(file, snp.names=NULL, assign=NULL, missing=NULL, X=FALSE, sep=".", low.mem = FALSE)
```

**Arguments**

|           |                                                                                                                                                                                                                                                                             |
|-----------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| file      | The file name for the input pedfile                                                                                                                                                                                                                                         |
| snp.names | A character vector giving the SNP names. If an accompanying map file or an info file is present, it will be read and the information used for the SNP names, and also the information merged with the result. If absent, the SNPs will be named numerically ("1", "2", ...) |
| assign    | A list of named mappings for which letter maps to which Allele; planned for the future, not currently used                                                                                                                                                                  |
| missing   | Meant to be a single character giving the code recorded for alleles of missing genotypes ; not used in the current code                                                                                                                                                     |

|         |                                                                                                                                                                                                                                                |
|---------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| X       | If TRUE the pedfile is assumed to describe loci on the X chromosome                                                                                                                                                                            |
| sep     | The character separating the family and member identifiers in the constructed row names; not used                                                                                                                                              |
| low.mem | Switch over to input with a routine which requires less memory to run, but takes a little longer. This option also has the disadvantage that assignment of A/B genotype is somewhat non-deterministic and depends the listed order of samples. |

### Details

Input variables are assumed to take the usual codes, with the restriction that the family (or pedigree) identifiers will be held as strings, but identifiers for members within families must be coded as integers. Genotype should be coded as pairs of single character allele codes (which can be alphameric or numeric), from either 'A', 'C', 'G', 'T' or '1', '2', '3', '4', with 'N', '-' and '0' denoting a missing; everything else is considered invalid and would invalidate the whole snp; also more than 2 alleles also cause the snp to be marked invalid.

Row names of the output objects are constructed by concatenation of the pedigree and member identifiers, "Family", "Individual" joined by ".", e.g. "Family.Adams.Individual.0".

### Value

|                 |                                                             |
|-----------------|-------------------------------------------------------------|
| snp             | The output "snp.matrix" or "X.snp.matrix"                   |
| subject.support | A data frame containing the first six fields of the pedfile |

### Author(s)

Hin-Tak Leung

### See Also

[snp.matrix-class](#), [X.snp.matrix-class](#), [read.snps.long](#), [read.HapMap.data](#), [read.pedfile.info](#), [read.pedfile.map](#)

---

|                    |                                                                |
|--------------------|----------------------------------------------------------------|
| read.wtccc.signals | <i>read normalized signals in the WTCCC signal file format</i> |
|--------------------|----------------------------------------------------------------|

---

### Description

read.wtccc.signals takes a file and a list of snp ids (either Affymetrix ProbeSet IDs or rs numbers), and extract the entries into a form suitable for plotting and further analysis

### Usage

```
read.wtccc.signals(file, snp.list)
```

### Arguments

|          |                                                                                                                       |
|----------|-----------------------------------------------------------------------------------------------------------------------|
| file     | file contains the signals. There is no need to gunzip.                                                                |
| snp.list | A list of snp id's. Some Affymetrix SNPs don't have rsnumbers both rsnumbers and Affymetrix ProbeSet IDs are accepted |

## Details

Do not specify both rs number and Affymetrix Probe Set ID in the input; one of them is enough.

The signal file is formatted as follows, with the first 5 columns being the Affymetrix Probe Set ID, rs number, chromosome position, AlleleA and AlleleB. The rest of the header containing the sample id appended with "\\_A" and "\\_B".

| AFFYID        | RSID       | pos      | AlleleA | AlleleB | 12999A2_A | 12999A2_B | ... |
|---------------|------------|----------|---------|---------|-----------|-----------|-----|
| SNP_A-4295769 | rs915677   | 14433758 | C       | T       | 0.318183  | 0.002809  |     |
| SNP_A-1781681 | rs9617528  | 14441016 | A       | G       | 1.540461  | 0.468571  |     |
| SNP_A-1928576 | rs11705026 | 14490036 | G       | T       | 0.179653  | 2.261650  |     |

The routine matches the input list against the first and the 2nd column.

(some early signal files, have the first "AFFYID" missing - this routine can cope with that also)

## Value

The routine returns a list of named matrices, one for each input SNP (NULL if the SNP is not found); the row names are sample IDs and columns are "A", "B" signals.

## Note

TODO: There is a built-in limit to the input line buffer (65535) which should be sufficient for 2000 samples and 30 characters each. May want to seek backwards, re-read and dynamically expand if the buffer is too small.

## Author(s)

Hin-Tak Leung <htl10@users.sourceforge.net>

## References

<http://www.wtccc.org.uk>

## Examples

```
## Not run:
answer <-
  read.wtccc.signals("NBS_22_signals.txt.gz", c("SNP_A-4284341", "rs4239845"))
> summary(answer)
              Length Class  Mode
SNP_A-4284341 2970    -none- numeric
rs4239845     2970    -none- numeric

> head(a$"SNP_A-4284341")
      A      B
12999A2 1.446261 0.831480
12999A3 1.500956 0.551987
12999A4 1.283652 0.722847
12999A5 1.549140 0.604957
12999A6 1.213645 0.966151
12999A8 1.439892 0.509547
>

## End(Not run)
```

---

|             |                                       |
|-------------|---------------------------------------|
| row.summary | <i>Summarize rows of a snp matrix</i> |
|-------------|---------------------------------------|

---

**Description**

This function calculates call rates and heterozygosity for each row of a an object of class "snp.matrix"

**Usage**

```
row.summary(object)
```

**Arguments**

object                      genotype data as a `snp.matrix-class` or `X.snp.matrix-class` object

**Value**

A data frame with rows corresponding to rows of the input object and with columns/elements:

Call.rate                  Proportion of SNPs called

Heterozygosity          Proportion of called SNPs which are heterozygous

**Note**

The current version does not deal with the X chromosome differently, so that males are counted as homozygous

**Author(s)**

David Clayton <david.clayton@cimr.cam.ac.uk>

**Examples**

```
data(testdata)
rs <- row.summary(Autosomes)
summary(rs)
rs <- row.summary(Xchromosome)
summary(rs)
```

---

|                  |                                                               |
|------------------|---------------------------------------------------------------|
| single.snp.tests | <i>1-df and 2-df tests for genetic associations with SNPs</i> |
|------------------|---------------------------------------------------------------|

---

**Description**

This function carries out tests for association between phenotype and a series of single nucleotide polymorphisms (SNPs), within strata defined by a possibly confounding factor. SNPs are considered one at a time and both 1-df and 2-df tests are calculated. For a binary phenotype, the 1-df test is the Cochran-Armitage test (or, when stratified, the Mantel-extension test).

**Usage**

```
single.snp.tests(phenotype, stratum, data = sys.parent(), snp.data, subset, snp.subset)
```

**Arguments**

|            |                                                                                                                                                                                                                                                                                                                                              |
|------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| phenotype  | A vector containing the values of the phenotype                                                                                                                                                                                                                                                                                              |
| stratum    | Optionally, a factor defining strata for the analysis                                                                                                                                                                                                                                                                                        |
| data       | A dataframe containing the phenotype and stratum data. The row names of this are linked with the row names of the snps argument to establish correspondence of phenotype and genotype data. If this argument is not supplied, phenotype and stratum are evaluated in the calling environment and should be in the same order as rows of snps |
| snp.data   | An object of class "snp.matrix" containing the SNP genotypes to be tested                                                                                                                                                                                                                                                                    |
| subset     | A vector or expression describing the subset of subjects to be used in the analysis. This is evaluated in the same environment as the phenotype and stratum arguments                                                                                                                                                                        |
| snp.subset | A vector describing the subset of SNPs to be considered. Default action is to test all SNPs.                                                                                                                                                                                                                                                 |

**Details**

Formally, the test statistics are score tests for generalized linear models with canonical link. That is, they are inner products between genotype indicators and the deviations of phenotypes from their stratum means. Variances (and covariances) are those of the permutation distribution obtained by randomly permuting phenotype within stratum.

The subset argument can either be a logical vector of length equal to the length of the vector of phenotypes, an integer vector specifying positions in the data frame, or a character vector containing names of the selected rows in the data frame. Similarly, the snp.subset argument can be a logical, integer, or character vector.

**Value**

|                           |                                                             |
|---------------------------|-------------------------------------------------------------|
| A dataframe, with columns |                                                             |
| chi2.1df                  | Cochran-Armitage type test for additive genetic component   |
| chi2.2df                  | Chi-squared test for both additive and dominance components |
| N                         | The number of valid data points used                        |

**Note**

The behaviour of this function for objects of class `X.snp.matrix` is as described by Clayton (2008). Males are treated as homozygous females and corrected variance estimates are used.

**Author(s)**

David Clayton <david.clayton@cimr.cam.ac.uk>

**References**

Clayton (2008) Testing for association on the X chromosome *Biostatistics* (In press)

**See Also**

[snp.lhs.tests](#), [snp.rhs.tests](#)

**Examples**

```
data(testdata)
results <- single.snp.tests(cc, stratum=region, data=subject.data,
                           snp.data=Autosomes, snp.subset=1:10)
summary(results)
# QQ plot - see help(qq.chisq)
qq.chisq(results$chi2.1df)
qq.chisq(results$chi2.2df)
```

---

|           |                    |
|-----------|--------------------|
| snp-class | <i>Class "snp"</i> |
|-----------|--------------------|

---

**Description**

Compact representation of data concerning single nucleotide polymorphisms (SNPs)

**Objects from the Class**

Objects can be created by calls of the form `new("snp", ...)` or by subset selection from an object of class "snp.matrix". Holds one row or column of an object of class "snp.matrix"

**Slots**

**.Data:** The genotype data coded as 0, 1, 2, or 3

**Methods**

**coerce** signature(from = "snp", to = "character"): map to codes "A/A", "A/B", "B/B", or ""

**coerce** signature(from = "snp", to = "numeric"): map to codes 0, 1, 2, or NA

**coerce** signature(from = "snp", to = "genotype"): maps a single SNP to an object of class "genotype". See the "genetics" package.

**show** signature(object = "snp"): shows character representation of the object

**is.na** signature(x = "snp"): returns a logical vector of missing call indicators

**Author(s)**

David Clayton <david.clayton@cimr.cam.ac.uk>

**References**

<http://www-gene.cimr.cam.ac.uk/clayton>

**See Also**

[snp.matrix-class](#), [X.snp.matrix-class](#), [X.snp-class](#)

**Examples**

```
## data(testdata)
## s <- autosomes[,1]
## class(s)
## s
```

snp.cbind

*Bind together two or more snp.matrix objects***Description**

These functions bind together two or more objects of class "snp.matrix" or "X.snp.matrix".

**Usage**

```
snp.cbind(...)
snp.rbind(...)
```

**Arguments**

...                      Objects of class "snp.matrix" or "X.snp.matrix".

**Details**

These functions reproduce the action of the standard functions [cbind](#) and [rbind](#). These are constrained to work by recursive calls to the generic functions [cbind2](#) and [rbind2](#) which take just two arguments. This is somewhat inefficient in both time and memory use when binding more than two objects, so the functions `snp.cbind` and `snp.rbind`, which take multiple arguments, are also supplied.

When matrices are bound together by column, row names must be identical, column names must not be duplicated and, for objects of class `X.snp.matrix` the contents of the Female slot must match. When matrices are bound by row, column names must be identical. and duplications of row names generate warnings.

**Value**

A new matrix, of the same type as the input matrices.

**Author(s)**

David Clayton <david.clayton@cimr.cam.ac.uk>

**See Also**

[cbind](#), [rbind](#)

## Examples

```
data(testdata)
# subsetting ( Autosomes[c(1:9,11:19,21:29),] ) is quicker. this is just for illustrating
# rbind and cbind
first <- Autosomes[1:9,]
second <- Autosomes[11:19,]
third <- Autosomes[21:29,]
result1 <- rbind(first, second, third)
result2 <- snp.rbind(first, second, third)
all.equal(result1, result2)

result3 <- Autosomes[c(1:9,11:19,21:29),]
all.equal(result1, result3)

first <- Autosomes[,1:9]
second <- Autosomes[,11:19]
third <- Autosomes[,21:29]
result1 <- cbind(first, second, third)
result2 <- snp.cbind(first, second, third)
all.equal(result1, result2)

result3 <- Autosomes[,c(1:9,11:19,21:29)]
all.equal(result1, result3)

first <- Xchromosome[1:9,]
second <- Xchromosome[11:19,]
third <- Xchromosome[21:29,]
result1 <- rbind(first, second, third)
result2 <- snp.rbind(first, second, third)
all.equal(result1, result2)

result3 <- Xchromosome[c(1:9,11:19,21:29),]
all.equal(result1, result3)

first <- Xchromosome[,1:9]
second <- Xchromosome[,11:19]
third <- Xchromosome[,21:29]
result1 <- cbind(first, second, third)
result2 <- snp.cbind(first, second, third)
all.equal(result1, result2)

result3 <- Xchromosome[,c(1:9,11:19,21:29)]
all.equal(result1, result3)
```

## Description

This function calculates Pearson correlation coefficients between columns of a `snp.matrix` and columns of an ordinary matrix. The two matrices must have the same number of rows. All valid pairs are used in the computation of each correlation coefficient.

**Usage**

```
snp.cor(x, y)
```

**Arguments**

`x`                    An  $N$  by  $M$  snp.matrix  
`y`                    An  $N$  by  $P$  general matrix

**Details**

This can be used together with [xxt](#) and [eigen](#) to calculate standardized loadings in the principal components

**Value**

An  $M$  by  $P$  matrix of correlation coefficients

**Note**

This version cannot handle X chromosomes

**Author(s)**

David Clayton <david.clayton@cimr.cam.ac.uk>

**See Also**

[xxt](#)

**Examples**

```
# make a snp.matrix with a small number of rows
data(testdata)
small <- Autosomes[1:100,]
# Calculate the X.X-transpose matrix
xx <- xxt(small, correct.for.missing=TRUE)
# Calculate the principal components
pc <- eigen(xx, symmetric=TRUE)$vectors
# Calculate the loadings in first 10 components,
# for example to plot against chromosome position
loadings <- snp.cor(small, pc[,1:10])
```

---

snp.dprime-class

---

*Class "snp.dprime" for Results of LD calculation*


---

**Description**

The snp.dprime class encapsulates results returned by [ld.snp](#) (— routine to calculate  $D'$ ,  $r^2$  and LOD of a [snp.matrix-class](#) object, given a range and a depth) and is based on a list of three named matrices.

The lower right triangle of the snp.dprime object returned by [ld.snp](#) always consists zeros. This is deliberate. The associated plotting routine would not normally access those elements either.

**Value**

The snp.dprime class is a list of 3 named matrices dprime, rsq2 or r, lod, and an attribute snp.names for the list of snps involved. (Note that if  $x$  snps are involved, the row numbers of the 3 matrices are  $(x-1)$ ). Only one of r or rsq2 is present.

```
dprime      D'
rsq2         $r^2$ 
r           signed  $r^2$ 
lod         Log of Odds
attr(*, class) "snp.dprime"
attr(*, snp.names)
              character vectors of the snp names involved
```

All the matrices are defined such that the  $(n, m)$ th entry is the pair-wise value between the  $n$ th snp and the  $(n+m)$ th snp. Hence the lower right triangles are always filled with zeros.

Invalid values are represented by an out-of-range value - currently we use -1 for  $D'$ ,  $r^2$  (both of which are between 0 and 1), and -2 for  $r$  (valid values are between -1 and +1). lod is set to zero in most of these invalid cases. (lod can be any value so it is not indicative).

**Methods**

See [plot.snp.dprime](#).

**Note**

TODO: Need a subsetting operator.

TODO: an assemble operator

**Author(s)**

Hin-Tak Leung <htl10@users.sourceforge.net>

**Source**

~~ reference to a publication or URL from which the data were obtained ~~

**References**

~~ possibly secondary sources and usages ~~

**Examples**

```
data(testdata)
snps20.20 <- Autosomes[11:20,11:20]
obj.snp.dprime <- ld.snp(snps20.20)
class(obj.snp.dprime)
summary(obj.snp.dprime)
## Not run:
# The following isn't executable-as-is example, so these illustrations
# are commented out to stop R CMD check from complaining:

> d<- ld.snp(all, 3, 10, 15)
```

```

rows = 48, cols = 132
... Done
> d
$dprime
      [,1] [,2] [,3]
[1,]    1    1    1
[2,]    1    1    1
[3,]    1    1    1
[4,]    1    1    0
[5,]    1    0    0

$rsq2
      [,1]      [,2]      [,3]
[1,] 1.0000000 0.9323467 1.0000000
[2,] 0.9285714 1.0000000 0.1540670
[3,] 0.9357278 0.1854481 0.9357278
[4,] 0.1694915 1.0000000 0.0000000
[5,] 0.1694915 0.0000000 0.0000000

$lod
      [,1]      [,2]      [,3]
[1,] 16.793677 11.909686 16.407120
[2,] 10.625650 15.117962  2.042668
[3,] 12.589586  2.144780 12.589586
[4,]  2.706318 16.781859  0.000000
[5,]  2.706318  0.000000  0.000000

attr("class")
[1] "snp.dprime"
attr("snp.names")
[1] "dil118" "dil119" "dil5904" "dil121" "dil5905" "dil5906"

## End(Not run)

```

---

snp.lhs.tests

---

*Score tests with SNP genotypes as dependent variable*


---

## Description

Under the assumption of Hardy-Weinberg equilibrium, a SNP genotype is a binomial variate with two trials for an autosomal SNP or with one or two trials (depending on sex) for a SNP on the X chromosome. With each SNP in an input "snp.matrix" as dependent variable, this function first fits a "base" logistic regression model and then carries out a score test for the addition of further term(s). The Hardy-Weinberg assumption can be relaxed by use of a "robust" option.

## Usage

```

snp.lhs.tests(snp.data, base.formula, add.formula, subset, snp.subset,
              data = sys.parent(), robust = FALSE,
              control=glm.test.control(maxit=20, epsilon=1.e-4, R2Max=0.98))

```

## Arguments

|              |                                                                                                                                                                                |
|--------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| snp.data     | The SNP data, as an object of class "snp.matrix" or "X.snp.matrix"                                                                                                             |
| base.formula | A formula object describing the base model, with dependent variable omitted                                                                                                    |
| add.formula  | A formula object describing the additional terms to be tested, also with dependent variable omitted                                                                            |
| subset       | An array describing the subset of observations to be considered                                                                                                                |
| snp.subset   | An array describing the subset of SNPs to be considered. Default action is to test all SNPs.                                                                                   |
| data         | The data frame in which base.formula, add.formula and subset are to be evaluated                                                                                               |
| robust       | If TRUE, a test which does not assume Hardy-Weinberg equilibrium will be used                                                                                                  |
| control      | An object giving parameters for the IRLS algorithm fitting of the base model and for the acceptable aliasing amongst new terms to be tested. See <code>glm.test.control</code> |

## Details

The tests used are asymptotic chi-squared tests based on the vector of first and second derivatives of the log-likelihood with respect to the parameters of the additional model. The "robust" form is a generalized score test in the sense discussed by Boos(1992). If a data argument is supplied, the snp.data and data objects are aligned by rowname. Otherwise all variables in the model formulae are assumed to be stored in the same order as the columns of the snp.data object.

## Value

A data frame containing, for each SNP,

|             |                                                                                                                                  |
|-------------|----------------------------------------------------------------------------------------------------------------------------------|
| Chi.squared | The value of the chi-squared test statistic                                                                                      |
| Df          | The corresponding degrees of freedom                                                                                             |
| Df.residual | The residual degrees of freedom for the base model; <i>i.e.</i> the number of observations minus the number of parameters fitted |

For the logistic model, the base model can, in some circumstances, lead to perfect prediction of some observations (*i.e.* fitted probabilities of 0 or 1). These observations are ignored in subsequent calculations; in particular they are not counted in the residual degrees of freedom.

## Note

A factor (or several factors) may be included as arguments to the function `strata(...)` in the base.formula. This fits all interactions of the factors so included, but leads to faster computation than fitting these in the normal way. Additionally, a `cluster(...)` call may be included in the base model formula. This identifies clusters of potentially correlated observations (e.g. for members of the same family); in this case, an appropriate robust estimate of the variance of the score test is used.

## Author(s)

David Clayton <david.clayton@cimr.cam.ac.uk>

## References

Boos, Dennis D. (1992) On generalized score tests. *The American Statistician*, **46**:327-333.

**See Also**

[glm.test.control](#), [snp.rhs.tests](#), [single.snp.tests](#), [snp.matrix-class](#), [X.snp.matrix-class](#)

**Examples**

```
data(testdata)
library(survival)
slt1 <- snp.lhs.tests(Autosomes[,1:10], ~cc, ~region, data=subject.data)
print(slt1)
slt2 <- snp.lhs.tests(Autosomes[,1:10], ~strata(region), ~cc,
                     data=subject.data)
print(slt2)
```

---

|                  |                    |
|------------------|--------------------|
| snp.matrix-class | Class "snp.matrix" |
|------------------|--------------------|

---

**Description**

This class defines objects holding large arrays of single nucleotide polymorphism (SNP) genotypes generated using array technologies.

**Objects from the Class**

Objects can be created by calls of the form `new("snp.matrix", x)` where `x` is a matrix with storage mode "raw". Chips (usually corresponding to samples or subjects) define rows of the matrix while polymorphisms (loci) define columns. Rows and columns will usually have names which can be used to link the data to further data concerning samples and SNPs

**Slots**

**.Data:** Object of class "matrix" and storage mode raw Internally, missing data are coded 00 and SNP genotypes are coded 01, 02 or 03.

**Extends**

Class "matrix", from data part. Class "structure", by class "matrix". Class "array", by class "matrix". Class "vector", by class "matrix", with explicit coerce. Class "vector", by class "matrix", with explicit coerce.

**Methods**

**[ ]** signature(`x = "snp.matrix"`): subset operations. Currently rather slow owing to excessive copying.

**cbind2** signature(`x = "snp.matrix"`, `y = "snp.matrix"`): S4 generic function to provide `cbind()` for two or more matrices together by column. Row names must match and column names must not coincide. If the matrices are of the derived class [X.snp.matrix-class](#), the Female slot values must also agree

**coerce** signature(`from = "snp.matrix"`, `to = "numeric"`): map to codes 0, 1, 2, or NA

**coerce** signature(`from = "snp.matrix"`, `to = "character"`): map to codes "A/A", "A/B", "B/B", ""

**coerce** signature(from = "matrix", to = "snp.matrix"): maps numeric matrix (coded 0, 1, 2 or NA) to a snp.matrix

**coerce** signature(from = "snp.matrix", to = "X.snp.matrix"): maps a snp.matrix to an X.snp.matrix. Sex is inferred from the genotype data since males should not be heterozygous at any locus. After inferring sex, heterozygous calls for males are set to NA

**is.na** signature(x = "snp.matrix"): returns a logical matrix indicating whether each element is NA

**rbind2** signature(x = "snp.matrix", y = "snp.matrix"): S4 generic function to provide rbind() for two or more matrices by row. Column names must match and duplicated row names prompt warnings

**show** signature(object = "snp.matrix"): shows the size of the matrix (since most objects will be too large to show in full)

**summary** signature(object = "snp.matrix"): calculate call rates, allele frequencies, genotype frequencies, and z-tests for Hardy-Weinberg equilibrium. Results are returned as a dataframe with column names Calls, Call.rate, MAF, P.AA, P.AB, P.BB, and z.HWE

**is.na** signature(x = "snp.matrix"): returns a logical matrix of missing call indicators

**show** signature(object = "snp.matrix"): ...

**summary** signature(object = "snp.matrix"): ...

### Note

This class requires at least version 2.3 of R

### Author(s)

David Clayton <david.clayton@cimr.cam.ac.uk>

### References

<http://www-gene.cimr.cam.ac.uk/clayton>

### See Also

[snp-class](#), [X.snp-class](#), [X.snp.matrix-class](#)

### Examples

```
data(testdata)
summary(summary(Autosomes))

# Just making it up - 3-10 will be made into NA during conversion
snps.class<-new("snp.matrix", matrix(1:10))
snps.class
if(!isS4(snps.class)) stop("constructor is not working")

pretend.X <- as(Autosomes, 'X.snp.matrix')
if(!isS4(pretend.X)) stop("coersion to derived class is not S4")
if(class(pretend.X) != 'X.snp.matrix') stop("coersion to derived class is not working")

pretend.A <- as(Xchromosome, 'snp.matrix')
if(!isS4(pretend.A)) stop("coersion to base class is not S4")
if(class(pretend.A) != 'snp.matrix') stop("coersion to base class is not working")
```

snp.pre

*Pre- or post-multiply a snp.matrix object by a general matrix***Description**

These functions first standardize the input `snp.matrix` in the same way as does the function `xxt`. The standardized matrix is then either pre-multiplied (`snp.pre`) or post-multiplied (`snp.post`) by a general matrix. Allele frequencies for standardizing the input `snp.matrix` may be supplied but, otherwise, are calculated from the input `snp.matrix`

**Usage**

```
snp.pre(snp, mat, frequency=NULL)
snp.post(snp, mat, frequency=NULL)
```

**Arguments**

|                        |                                                                                                                                                                                                                                                     |
|------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <code>snp</code>       | An object of class "snp.matrix" or "X.snp.matrix"                                                                                                                                                                                                   |
| <code>mat</code>       | A general (numeric) matrix                                                                                                                                                                                                                          |
| <code>frequency</code> | A numeric vector giving the allele (relative) frequencies to be used for standardizing the columns of <code>snp</code> . If <code>NULL</code> , allele frequencies will be calculated internally. Frequencies should refer to the second (B) allele |

**Details**

The two matrices must be conformant, as with standard matrix multiplication. The main use envisaged for these functions is the calculation of factor loadings in principal component analyses of large scale SNP data, and the application of these loadings to other datasets. The use of externally supplied allele frequencies for standardizing the input `snp.matrix` is required when applying loadings calculated from one dataset to a different dataset

**Value**

The resulting matrix product

**Author(s)**

David Clayton <david.clayton@cimr.cam.ac.uk>

**See Also**

`xxt`

**Examples**

```
##--
##-- Calculate first two principal components and their loading, and verify
##--
# Make a snp.matrix with a small number of rows
data(testdata)
small <- Autosomes[1:20,]
# Calculate the X.X-transpose matrix
```

```

xx <- xxt(small, correct.for.missing=FALSE)
# Calculate the first two principal components and corresponding eigenvalues
eigvv <- eigen(xx, symmetric=TRUE)
pc <- eigvv$vectors[,1:2]
ev <- eigvv$values[1:2]
# Calculate loadings for first two principal components
Dinv <- diag(1/sqrt(ev))
loadings <- snp.pre(small, Dinv %*% t(pc))
# Now apply loadings back to recalculate the principal components
pc.again <- snp.post(small, t(loadings) %*% Dinv)
print(cbind(pc, pc.again))

```

snp.rhs.tests

*Score tests with SNP genotypes as independent variable*

## Description

This function fits a generalized linear model with phenotype as dependent variable and, optionally, one or more potential confounders of a phenotype-genotype association as independent variable. A series of SNPs (or small groups of SNPs) are then tested for additional association with phenotype. In order to protect against misspecification of the variance function, "robust" tests may be selected.

## Usage

```

snp.rhs.tests(formula, family = "binomial", link, weights, subset,
              data = parent.frame(), snp.data, tests=NULL, robust = FALSE,
              control = glm.test.control(maxit=20, epsilon=1e-4, R2Max=0.98),
              allow.missing = 0.01)

```

## Arguments

|               |                                                                                                                                                                                                                                                                                                                      |
|---------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| formula       | The base model formula, with phenotype as dependent variable                                                                                                                                                                                                                                                         |
| family        | A string defining the generalized linear model family. This currently should (partially) match one of "binomial", "Poisson", "Gaussian" or "gamma" (case-insensitive)                                                                                                                                                |
| link          | A string defining the link function for the GLM. This currently should (partially) match one of "logit", "log", "identity" or "inverse". The default action is to use the "canonical" link for the family selected                                                                                                   |
| data          | The dataframe in which the base model is to be fitted                                                                                                                                                                                                                                                                |
| snp.data      | An object of class "snp.matrix" or "X.snp.matrix" containing the SNP data                                                                                                                                                                                                                                            |
| tests         | Either a vector of column names or numbers for the SNPs to be tested, or a list of short vectors defining groups of SNPs to be tested (again by name or number). The default action is to carry out <i>all</i> single SNP tests, but <a href="#">single.snp.tests</a> will often achieve the same result much faster |
| weights       | "Prior" weights in the generalized linear model                                                                                                                                                                                                                                                                      |
| subset        | Array defining the subset of rows of data to use                                                                                                                                                                                                                                                                     |
| robust        | If TRUE, robust tests will be carried out                                                                                                                                                                                                                                                                            |
| control       | An object giving parameters for the IRLS algorithm fitting of the base model and for the acceptable aliasing amongst new terms to be tested. See <a href="#">codeglm.test.control</a>                                                                                                                                |
| allow.missing | The maximum proportion of SNP genotype that can be missing before it becomes necessary to refit the base model                                                                                                                                                                                                       |

## Details

The tests used are asymptotic chi-squared tests based on the vector of first and second derivatives of the log-likelihood with respect to the parameters of the additional model. The "robust" form is a generalized score test in the sense discussed by Boos(1992). The "base" model is first fitted, and a score test is performed for addition of one or more SNP genotypes to the model. Homozygous SNP genotypes are coded 0 or 2 and heterozygous genotypes are coded 1. For SNPs on the X chromosome, males are coded as homozygous females. For X SNPs, it will often be appropriate to include sex of subject in the base model (this is not done automatically).

If a data argument is supplied, the `snp.data` and `data` objects are aligned by rowname. Otherwise all variables in the model formulae are assumed to be stored in the same order as the columns of the `snp.data` object.

## Value

A data frame containing, for each SNP,

|                          |                                                                                                                                  |
|--------------------------|----------------------------------------------------------------------------------------------------------------------------------|
| <code>Chi.squared</code> | The value of the chi-squared test statistic                                                                                      |
| <code>Df</code>          | The corresponding degrees of freedom                                                                                             |
| <code>Df.residual</code> | The residual degrees of freedom for the base model; <i>i.e.</i> the number of observations minus the number of parameters fitted |

For the binomial family model, the base model can, in some circumstances, lead to perfect prediction of some observations (*i.e.* fitted probabilities of 0 or 1). These observations are ignored in subsequent calculations; in particular they are not counted in the residual degrees of freedom. Similarly for Poisson means fitted exactly to zero.

## Note

A factor (or several factors) may be included as arguments to the function `strata(...)` in the formula. This fits all interactions of the factors so included, but leads to faster computation than fitting these in the normal way. Additionally, a `cluster(...)` call may be included in the base model formula. This identifies clusters of potentially correlated observations (e.g. for members of the same family); in this case, an appropriate robust estimate of the variance of the score test is used.

## Author(s)

David Clayton <david.clayton@cimr.cam.ac.uk>

## References

Boos, Dennis D. (1992) On generalized score tests. *The American Statistician*, **46**:327-333.

## See Also

[single.snp.tests](#), [snp.lhs.tests](#), [snp.matrix-class](#), [X.snp.matrix-class](#)

## Examples

```
data(testdata)
library(survival) # strata
slt3 <- snp.rhs.tests(cc~strata(region), family="binomial",
  data=subject.data, snp.data = Autosomes, tests=1:10)
print(slt3)
```

---

|                    |                           |
|--------------------|---------------------------|
| snpMatrix-internal | <i>snpMatrix-internal</i> |
|--------------------|---------------------------|

---

### Description

All the dirty details that doesn't belong elsewhere. At the moment just for hiding references to the genotype-class and haplotype-class class which is in the genetics package.

---

|          |                                            |
|----------|--------------------------------------------|
| testdata | <i>Test data for the snpMatrix package</i> |
|----------|--------------------------------------------|

---

### Description

This dataset comprises several data frames from a fictional (and unrealistically small) study. The dataset started off as real data from a screen of non-synonymous SNPs for association with type 1 diabetes, but the original identifiers have been removed and a random case/control status has been generated.

### Usage

```
data(testdata)
```

### Format

There are five data objects in the dataset:

- AutosomesAn object of class "snp.matrix" containing genotype calls for 400 subjects at 9445 autosomal SNPs
- XchromosomeAn object of class "X.snp.matrix" containing genotype calls for 400 subjects at 155 SNPs on the X chromosome
- AsnpsA dataframe containing information about the autosomal SNPs. Here it contains only one variable, chromosome, indicating the chromosomes on which the SNPs are located
- XsnpsA dataframe containing information about the X chromosome SNPs. Here it is empty and is only included for completeness
- subject.dataA dataframe containing information about the subjects from whom each row of SNP data was obtained. Here it contains:
  - ccCase-control status
  - sexSex
  - regionGeographical region of residence

### Source

The data were obtained from the diabetes and inflammation laboratory (see <http://www-gene.cimr.cam.ac.uk/todd>)

### References

<http://www-gene.cimr.cam.ac.uk/clayton>

**Examples**

```
data(testdata)
Autosomes
Xchromosome
summary(Asnps)
summary(Xsnps)
summary(subject.data)
summary(summary(Autosomes))
summary(summary(Xchromosome))
```

---

|                  |                                                 |
|------------------|-------------------------------------------------|
| write.snp.matrix | <i>Write a snp.matrix object as a text file</i> |
|------------------|-------------------------------------------------|

---

**Description**

This function is closely modelled on `write.table`. It writes an object of class `snp.matrix` as a text file with one line for each row of the matrix. Genotypes are written in numerical form, *i.e.* as 0, 1 or 2 (where 1 denotes heterozygous).

**Usage**

```
write.snp.matrix(x, file, append = FALSE, quote = TRUE, sep = " ", eol = "\n", na = "NA", row.names = T)
```

**Arguments**

|                        |                                                                                        |
|------------------------|----------------------------------------------------------------------------------------|
| <code>x</code>         | The object to be written                                                               |
| <code>file</code>      | The name of the output file                                                            |
| <code>append</code>    | If TRUE, the output is appended to the designated file. Otherwise a new file is opened |
| <code>quote</code>     | If TRUE, row and column names will be enclosed in quotes                               |
| <code>sep</code>       | The string separating entries within a line                                            |
| <code>eol</code>       | The string terminating each line                                                       |
| <code>na</code>        | The string written for missing genotypes                                               |
| <code>row.names</code> | If TRUE, each row will commence with the row name                                      |
| <code>col.names</code> | If TRUE, the first line will contain all the column names                              |

**Value**

A numeric vector giving the dimensions of the matrix written

**Author(s)**

David Clayton <david.clayton@cimr.cam.ac.uk>

**See Also**

[write.table](#), [snp.matrix-class](#), [X.snp.matrix-class](#)

---

|                   |                                                                             |
|-------------------|-----------------------------------------------------------------------------|
| wtccc.sample.list | <i>read the sample list from the header of the WTCCC signal file format</i> |
|-------------------|-----------------------------------------------------------------------------|

---

## Description

This is a convenience function for constructing the sample list from the header of a WTCCC signal file.

## Usage

```
wtccc.sample.list(infile)
```

## Arguments

|        |                                                                                                                                   |
|--------|-----------------------------------------------------------------------------------------------------------------------------------|
| infile | One of the signal files in a set of 23 (it is advisable to use the smaller ones such as number 22, although it shouldn't matter). |
|--------|-----------------------------------------------------------------------------------------------------------------------------------|

## Details

The header of a WTCCC signal file is like this:

```
AFFYID RSID pos AlleleA AlleleB 12999A2_A 12999A2_B ...
```

The first 5 fields are discarded. There after, every other token is retained, with the "\_A" or "\_B" part removed to give the sample list.

See also [read.wtccc.signals](#) for more details.

## Value

The value returned is a character vector contain the sample names or the plate-well names as appropriate.

## Author(s)

Hin-Tak Leung <ht110@users.sourceforge.net>

## References

<http://www.wtccc.org.uk>

## See Also

[read.wtccc.signals](#)

X.snp-class

Class "X.snp"

**Description**

Compact representation of data concerning single nucleotide polymorphisms (SNPs) on the X chromosome

**Objects from the Class**

Objects can be created by calls of the form `new("snp", ..., Female=...)` or by subset selection from an object of class "X.snp.matrix". Holds one row or column of an object of class "X.snp.matrix"

**Slots**

**.Data:** The genotype data coded as 0, 1, 2, or 3. For males are coded as homozygous females  
**Female:** A logical array giving the sex of the sample(s)

**Extends**

Class "snp", directly. Class "raw", by class "snp". Class "vector", by class "snp".

**Methods**

**coerce** signature(from = "X.snp", to = "character"): map to codes "A/A", "A/B", "B/B", "A/Y", "B/Y", or ""

**coerce** signature(from = "X.snp", to = "numeric"): map to codes 0, 1, 2, or NA

**coerce** signature(from = "X.snp", to = "genotype"): Yet to be implemented

**show** signature(object = "X.snp"): shows character representation of the object

**Author(s)**

David Clayton <david.clayton@cimr.cam.ac.uk>

**References**

<http://www-gene.cimr.cam.ac.uk/clayton>

**See Also**

[X.snp.matrix-class](#), [snp.matrix-class](#), [snp-class](#)

**Examples**

```
data(testdata)
s <- Xchromosome[,1]
class(s)
s
```

---

X.snp.matrix-class      *Class "X.snp.matrix"*


---

## Description

This class extends the `snp.matrix-class` to deal with SNPs on the X chromosome.

## Objects from the Class

Objects can be created by calls of the form `new("X.snp.matrix", x, Female)`. Such objects have an additional slot to objects of class `"snp.matrix"` consisting of a logical array of the same length as the number of rows. This array indicates whether the sample corresponding to that row came from a female (TRUE) or a male (FALSE).

## Slots

**.Data:** Object of class `"matrix"` and storage mode `"raw"`  
**Female:** Object of class `"logical"` indicating sex of samples

## Extends

Class `"snp.matrix"`, directly, with explicit coerce. Class `"matrix"`, by class `"snp.matrix"`. Class `"structure"`, by class `"snp.matrix"`. Class `"array"`, by class `"snp.matrix"`. Class `"vector"`, by class `"snp.matrix"`, with explicit coerce. Class `"vector"`, by class `"snp.matrix"`, with explicit coerce.

## Methods

**[ ]** signature(`x = "X.snp.matrix"`): subset operations. Currently rather slow owing to excessive copying

**[<-** signature(`x = "X.snp.matrix"`): subset assignment operation to replace part of an object

**coerce** signature(`from = "X.snp.matrix"`, `to = "character"`): map to codes 0, 1, 2, or NA

**coerce** signature(`from = "snp.matrix"`, `to = "X.snp.matrix"`): maps a `snp.matrix` to an `X.snp.matrix`. Sex is inferred from the genotype data since males should not be heterozygous at any locus. After inferring sex, heterozygous calls for males are set to NA

**show** signature(`object = "X.snp.matrix"`): map to codes "A/A", "A/B", "B/B", "A/Y", "B/Y" or ""

**summary** signature(`object = "X.snp.matrix"`): calculate call rates, allele frequencies, genotype frequencies, and chi-square tests for Hardy-Weinberg equilibrium. Genotype frequencies are calculated for males and females separately and Hardy-Weinberg equilibrium tests use only the female data. Allele frequencies are calculated using data from both males and females. Results are returned as a dataframe with column names `Calls`, `Call.rate`, `MAF`, `P.AA`, `P.AB`, `P.BB`, `P.AY`, `P.BY`, and `z.HWE`

## Author(s)

David Clayton <david.clayton@cimr.cam.ac.uk>

## References

<http://www-gene.cimr.cam.ac.uk/clayton>

**See Also**

[X.snp-class](#), [snp.matrix-class](#), [snp-class](#)

**Examples**

```
data(testdata)
summary(summary(Xchromosome))
```

---

|     |                                                  |
|-----|--------------------------------------------------|
| xxt | <i>X.X-transpose for a normalised snp.matrix</i> |
|-----|--------------------------------------------------|

---

**Description**

The input `snp.matrix` is first normalised by subtracting the mean from each call and dividing by the expected standard deviation under Hardy-Weinberg equilibrium. It is then post-multiplied by its transpose. This is a preliminary step in the computation of principal components.

**Usage**

```
xxt(snps, correct.for.missing = FALSE, lower.only = FALSE)
```

**Arguments**

|                                  |                                                                                                                                                                                       |
|----------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <code>snps</code>                | The input matrix, of type " <code>snp.matrix</code> "                                                                                                                                 |
| <code>correct.for.missing</code> | If TRUE, an attempt is made to correct for the effect of missing data by use of inverse probability weights. Otherwise, missing observations are scored zero in the normalised matrix |
| <code>lower.only</code>          | If TRUE, only the lower triangle of the result is returned and the upper triangle is filled with zeros. Otherwise, the complete symmetric matrix is returned                          |

**Details**

This computation forms the first step of the calculation of principal components for genome-wide SNP data. As pointed out by Price et al. (2006), when the data matrix has more rows than columns it is most efficient to calculate the eigenvectors of  $X.X$ -transpose, where  $X$  is a `snp.matrix` whose columns have been normalised to zero mean and unit variance. For autosomes, the genotypes are given codes 0, 1 or 2 after subtraction of the mean,  $2p$ , are divided by the standard deviation  $\sqrt{2p(1-p)}$  ( $p$  is the estimated allele frequency). For SNPs on the X chromosome in male subjects, genotypes are coded 0 or 2. Then the mean is still  $2p$ , but the standard deviation is  $2\sqrt{p(1-p)}$ .

Missing observations present some difficulty. Price et al. (2006) recommended replacing missing observations by their means, this being equivalent to replacement by zeros in the normalised matrix. However this results in a biased estimate of the complete data result. Optionally this bias can be corrected by inverse probability weighting. We assume that the probability that any one call is missing is small, and can be predicted by a multiplicative model with row (subject) and column (locus) effects. The estimated probability of a missing value in a given row and column is then given by  $m = RC/T$ , where  $R$  is the row total number of no-calls,  $C$  is the column total of no-calls, and  $T$  is the overall total number of no-calls. Non-missing contributions to  $X.X$ -transpose are then weighted by  $w = 1/(1 - m)$  for contributions to the diagonal elements, and products of the relevant pairs of weights for contributions to off-diagonal elements.

**Value**

A square matrix containing either the complete  $X.X$ -transpose matrix, or just its lower triangle

**Warning**

The correction for missing observations can result in an output matrix which is not positive semi-definite. This should not matter in the application for which it is intended

**Note**

In genome-wide studies, the SNP data will usually be held as a series of objects (of class "snp.matrix" or "X.snp.matrix"), one per chromosome. Note that the  $X.X$ -transpose matrices produced by applying the xxt function to each object in turn can be added to yield the genome-wide result.

**Author(s)**

David Clayton <david.clayton@cimr.cam.ac.uk>

**References**

Price et al. (2006) Principal components analysis corrects for stratification in genome-wide association studies. *Nature Genetics*, **38**:904-9

**Examples**

```
# make a snp.matrix with a small number of rows
data(testdata)
small <- Autosomes[1:100,]
# Calculate the X.X-transpose matrix
xx <- xxt(small, correct.for.missing=TRUE)
# Calculate the principal components
pc <- eigen(xx, symmetric=TRUE)$vectors
```

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