Package 'lmem.qtler'

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Type Package

Title Linear Mixed Effects Models for QTL Mapping for Multienvironment and Multitrait Analysis

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Description Performs QTL mapping analysis for balanced and for multi-environment and multi-trait analysis using mixed models. Balanced population, single trait, single environment QTL mapping is performed through marker-regression (Haley and Knott (1992) <DOI:10.1038/hdy.1992.131>, Martinez and Curnow (1992) <DOI:10.1007/BF00222330>, while multi-environment and multi-trait QTL mapping is performed through linear mixed models. These functions could use any of the following populations: double haploid, F2, recombinant inbred lines, back-cross, and 4-way crosses. Performs a Single Marker Analysis, a Single Interval Mapping, or a Composite Interval Mapping analysis, and then constructs a final model with all of the relevant QTL.

License GPL-3

Depends R (>= 2.10)

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VignetteBuilder knitr

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grDevices, stats

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DHpop_geno

Name of the file containing genotypic (marker scores) information.

Description

For this example, a doubled haploid population of 200 individuals was developed by crossing a short line (parent A), with a tall line (parent B). The 200 doubled haploid lines were evaluated in a field trial and the plant height measured in cm (the data is in the file DHpop_pheno.txt). The population was also genotyped by SNPs, and the data is presented in the file DHpop_geno.txt. The map location of each of the markers is in the file DHpop_map.txt.

Usage

DHpop_geno

Format

A data frame 202 genotypes (200 lines + 2 parents) and 130 markers.

DHpop_map

Description

For this example, a doubled haploid population of 200 individuals was developed by crossing a short line (parent A), with a tall line (parent B). The 200 doubled haploid lines were evaluated in a field trial and the plant height measured in cm (the data is in the file DHpop_pheno.txt). The population was also genotyped by SNPs, and the data is presented in the file DHpop_geno.txt. The map location of each of the markers is in the file DHpop_map.txt.

Usage

DHpop_map

Format

A data frame 130 row (markers) and 3 column.Column 1 gives the marker names, column 2 the chromosome on which the marker has been mapped, and column 3 indicates the position of the marker within the chromosome.

DHpop_pheno

Name of the file containing genotypic (marker scores) information.

Description

For this example, a doubled haploid population of 200 individuals was developed by crossing a short line (parent A), with a tall line (parent B). The 200 doubled haploid lines were evaluated in a field trial and the plant height measured in cm (the data is in the file DHpop_pheno). The population was also genotyped by SNPs, and the data is presented in the file DHpop_geno The map location of each of the markers is in the file DHpop_map.

Usage

DHpop_pheno

Format

A data frame 200 genotypes and 1 variable.

mq.diagnostics

Description

Performs molecular markers quality diagnostic of an object of class cross created by the qtl.cross function, including summary description for marker distribution and coverage, evaluating the map quality, the presence of identical individuals, visualizing marker alleles and missing marker scores for all individuals across the genome, the pairwise number of alleles shared by each pair of individuals, the pairwise recombination fraction among each pair of markers, and a test for segregation distortion for each marker in linkage analysis.

Usage

```
mq.diagnostics(crossobj, I.threshold = 0.1, estmarker = FALSE,
I.quant = FALSE, p.val = 0.01, na.cutoff = 0.1)
```

Arguments

crossobj	An object of class = cross obtained from the qtl.cross function from this package, or the read.cross function from r/qtl package (Broman and Sen, 2009). This file contains phenotypic means, genotypic marker score, and genetic map.
I.threshold	Threshold for proportion of allelic differences below which individuals are marked as too similar, pairs that differ more than (1-threshold) are marked as exceptioally different. Default is set to 10 per cent (I.threshold = 0.1).
estmarker	Logical value indicating whether a new marker map should be estimated and plotted. If estmarker=TRUE, this is passed onto r/qtl (Broman and Sen, 2009) and performs est.map function. This uses the Lander-Green algorithm (i.e., the hidden Markov model technology) to re-estimate the genetic map for an experimental cross. Default is set to FALSE.
I.quant	Threshold indicating the quantile to identify the most similar individuas. Default is set to FALSE.
p.val	Significance level for the chi-square test for segregation distortion. The default is set to p<0.01. No multiple comparison correction is performed here.
na.cutoff	Proportion of missing data above which individuals and markers are reported . Default is set to 10 per cent (na.cutoff = 0.1).

Details

Performs plots in the work directory.

Value

The following reports are written to mq_reports:

1) mq_summary_markers, reports on missing data and segregation distortion.

mq.diagnostics

2) mq_problems_markers, reports on duplicate or outlier genotypes.

Additionally, several diagnostic plots are performed:

1) mq_markermap_plot, this figure shows the position of all markers across the genome (equivalent R/qtl: plot.map) (Broman and Sen 2009).

2) mq_genotype_plot, this figure shows marker alleles for all individuals across thegenome (equivalent to r/qtl: geno.image) (Broman and Sen 2009).

3) mq_missinggenotype_plot, this figure highlights missing marker scores for all individuals across the genome (equivalent to r/qtl: plot.missing) (Broman and Sen 2009).

4) mq_comparegenotypes_plot, this figure represents the pairwise number of alleles shared by each pair of individuals (equivalent to r/qtl: comparegeno) (Broman and Sen 2009).

5) mq_cf_plot, this figure represents the pairwise recombination fraction among each pair of markers (equivalent to r/qtl: plot.rf). (Broman and Sen 2009).

6) mq_genotypic_distortion_plot, this figure represents the -log(p-values) of the test for segregation distortion for each marker represented by its chromosome and position.

7) mq_identical_genotypes_plot, this figure is the histogram of the proportion of shared alleles among each pair of individuals.

8) mq_estmarkermap_plot, this figure is a comparison between the map provided by the user and the map estimated with the est.map function. Will print only if estmarker=TRUE (equivalent to r/qtl: est.map,plot.map) (Broman and Sen 2009)

Note

Performs marker quality daignostics for QTL and GWAS analyses

Author(s)

Lucia Gutierrez

References

Broman KW, Sen S (2009) A Guide to QTL Mapping with R/qtl. Springer, NewYork Hayes PM, Liu BH, Knapp SJ, Chen F, Jones B, Blake T, Franckowiak JD, Rasmusson DC, Sorrells M, Ullrich SE, Wesenberg DM, Kleinhofs A (1993) Quantitative trait locus effects and environmental interaction in a sample of North American barley germplasm. Theor Appl Genet 87:392-401

See Also

qtl.cross

Examples

```
## Not run:
data (SxM_geno)
data (SxM_map)
data (SxM_pheno)
```

P.data <- SxM_pheno

pq.diagnostics *Performs phenotypic data quality diagnostics.*

Description

Performs phenotypic data quality diagnostic of an object of class cross created by the qtl.cross function, including summary descriptive diagnostics, correlation across traits, and distribution of traits.

Usage

```
pq.diagnostics (crossobj, boxplot = TRUE, qqplot = FALSE,
scatterplot = TRUE,heatplot = TRUE)
```

Arguments

crossobj	An object of class = cross obtained from the qtl.cross function from this package, or the read.cross function from r/qtl package (Broman and Sen, 2009). This file contains phenotypic means, genotypic marker score, and genetic map.
boxplot	Indicates whether a boxplot should be performed. TRUE/FALSE term. TRUE is set as default.
qqplot	Indicates whether a qqplot should be performed. TRUE/FALSE term. FALSE is set as default.
scatterplot	Indicates whether a scatterplot should be performed. TRUE/FALSE term. TRUE is set as default.
heatplot	Indicates whether a phenotypic heatplot should be performed. TRUE is set as default.

Details

Performs reports in the work directory.

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pq.diagnostics

Value

It returns: Boxplot, Scatterplot, QQplot, Heatplot

Note

Could be performed for QTL analysis in order to analyze the phenotypic data quality.

Author(s)

Lucia Gutierrez

References

Broman KW, Sen S (2009) A Guide to QTL Mapping with R/qtl. Springer, NewYork. Comadran J, Thomas W, van Eeuwijk F, Ceccarelli S, Grando S, Stanca A, Pecchioni N, Akar T, Al-Yassin A, Benbelkacem A, Ouabbou H, Bort J, Romagosa I, Hackett C, Russell J (2009) Patterns of genetic diversity and linkage disequilibrium in a highly structured Hordeum vulgare association-mapping population for the Mediterranean basin. Theor Appl Genet 119:175-187 Milne et al., (2010) Flap-jack - graphical genotype visualization. Bioinformatics 26(24), 3133-3134.

See Also

qtl.cross

Examples

```
## Not run:
data (SxM_geno)
data (SxM_map)
data (SxM_pheno)
P.data <- SxM_pheno
G.data <- SxM_geno
map.data <- SxM_map
cross.data <- qtl.cross (P.data, G.data, map.data,
cross='dh', heterozygotes = FALSE)
summary (cross.data)
jittermap (cross.data)
Pheno Quality
pq.diagnostics (crossobj=cross.data)
## End(Not run)
```

qtl.analysis

Description

Performs a balanced population QTL mapping analysis through marker-regression (Haley and Knott 1992; Martinez and Curnow 1992). This function could use any of the following populations: double haploid, F2, recombinant inbred lines, back-cross, and 4-way crosses. Performs a Single Marker Analysis, a Single Interval Mapping, or a Composite Interval Mapping analysis, and then constructs a final model with of relevant QTL. This function is for single environment single trait QTL mapping.

Usage

Arguments

crossobj	An object of class = cross obtained from the qtl.cross function from this package, or the read.cross function from r/qtl package (Broman and Sen, 2009).This file contains phenotypic means, genotypic marker score, and genetic map data.
trait	Column name for the phenotypic trait to be analyzed.
step	Maximum distance (in cM) between positions at which the genotype probabil- ities are calculated, though for step = 0, probabilities are calculated only at the marker locations.
method	"SIM" or "CIM" for simple interval (SIM) or composite interval mapping (CIM).
threshold	Threshold cut-of for multi-comparison correction. Value could be either a set threshold or "Li&Ji". If a fixed threshold is desired, a numerical value representing the alpha level should be indicated. If the threshold is set to "Li&Ji", the threshold is estimated through a bonferroni correction based on the effective number of markers (Li and Ji, 2005). The effective number of markers is calculated based on a singular value decomposition of the molecular marker matrix and the Tracy-Widom statistic (Li and Ji, 2005).
distance	To avoid co-linearity, nearby markers are not allowed in the same model. This is the minimum distance within which two markers are allowed to stay in the model.
cofactors	Vector of genetic predictors to be used as cofactors.
window.size	To avoid co-linearity, marker cofactors close to the markers being tested are not allowed in the model. This is the minimum distance to allow a co-factor when testing for a specific marker. Given the resolution of common QTL studies, it is recommended to use a large window.size (i.e. 50 cM). The default is set to 50 cM.

qtl.analysis

Details

"SIM" or "CIM" could be perform.

Value

A list of two elements: all, a data-frame containing the markers, map positions, and p-values from the marker-trait test for association for all markers in the data-set; and selected, a data-frame containing selected markers (i.e. putative QTL, selected based on their p-value), their map position, and the p-values from the marker-trait test for association. This is also written as a report to qtl_reports. A profile-plot is created showing the -log(p-value) against the map position.

Note

For multi-trait or multi-environment see qtl.memq

Author(s)

Lucia Gutierrez

References

Broman KW, Sen S (2009) A Guide to QTL Mapping with R/qtl. Springer, New York Haley CS, Knott SA (1992) A simple regression method for mapping quantitative trait loci in line crosses using flanking markers. Heredity, 69: 315-324 Li J, Ji L (2005) Adjusting multiple testing in multilocus analyses using the eigenvalues of a correlation matrix. Heredity, 95: 221-227. Martinez O, Curnow RN (1992) Estimating the locations and the sizes of the effects of quantitative trait loci using flanking markers. Theoretical and Applied Genetics 85(4): 480-488

See Also

qtl.cross mq.diagnostics and pq.diagnostics

Examples

qtl.cross

```
window.size=30)
## End(Not run)
# QTL_SIM
QTL.result <- qtl.analysis ( crossobj=cross.data, step=5,
method='SIM',trait="height", threshold="Li&Ji",
distance=30,cofactors=NULL,window.size=30)
# QTL CIM
cofactors <- as.vector (QTL.result$selected$marker)
QTL.result <- qtl.analysis ( crossobj=cross.data, step=5,
method='CIM', trait="height", threshold="Li&Ji", distance=30,
cofactors=cofactors, window.size=30)</pre>
```

qtl.cross

Read genomic data to perform QTL analyses.

Description

This function reads genomic data and is similar to the read.cross function from r/qtl package (Broman and Sen, 2009) but allows importing data from a flapjack format (Milne et al., 2010). The files required include a file containing phenotypic information (P.data), a file containing genotypic information (G.data), and a file containing map information (map.data) for all markers.

Usage

Arguments

P.data	Name of the file containing phenotypic information. Each row represents the individuals while each column represents the phenotypic traits. The first column should be labeled as 'genotype' and should contain identification name for each individual. The name of each trait should also be included.
G.data	Name of the file containing genotypic (marker scores) information. Each row represents the individuals while each column represents the markers. Headers for markers should be included, but not for genotypes. The first column contains the names of the genotypes. The first row contains the names of the markers. The marker genotypes are coded by two characters corresponding to the alleles using a separator between alleles (by default a slash /). If a single character is given, the genotype is assumed to be homozygous. Missing values are indicated by default with '-'. In the example below, the two alleles have been called 1 and 2 because it is useful to link alleles to their origin, i.e. parent 1 or parent 2. Therefore, 1 corresponds to homozygous for allele 1 (synonymous to 1/1),

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	1/2 corresponds to heterozygous, and 2 corresponds to homozygous for allele 2 (synonymous to 2/2). In the case of partially informative markers (e.g. dominant markers) genotypes are coded as 1/- or 2/-, depending on whether the dominant allele originated from parent 1 or parent 2.
map.data	Name of the file containing marker map information (i.e. linkage group and po- sition within linkage group). The file is a text tab delimited file. Each row rep- resents markers. The file consists of three columns. Column 1 gives the marker names, column 2 the chromosome on which the marker has been mapped, and column 3 indicates the position of the marker within the chromosome.
cross	The type of population studied. The type of population studied. Options are: F2 (f2), doubled haploids (dh), backcross (bc), recombinant inbred lines from selfing (riself, ri4self, or ri8self depending on the number of parents used), recombinant inbred lines from sib-mating (risib, ri4sib, or ri8sib depending on the number of parents used), segregating F1 cross-pollinated populations (cp),
heterozygotes	It indicates whether there are heterozygotes or not in the association mapping population. FALSE is set as default.
sep	To define the espace between the data.

Details

The function creates an intermediate file called 'temp.csv' and then uses the read.cross from r/qtl to read it. The output object is an object of class=cross, the same as the one produced by the function read.cross in r/qtl (Broman and Sen, 2009)

Value

Creates an object of class cross to be used in QTL analysis. The components are the same as r/qtl (Broman and Sen, 2009): geno This is a list with elements corresponding to chromosomes.names (geno) contains the names of the chromosomes. Each chromosome is itself a list, and is given class A or X according to whether it is autosomal or the X chromosome. There are two components for each chromosome: data, a matrix whose rows are individuals and whose columns are markers, and map, either a vector of marker positions (in cM) or a matrix of dim (2 x n.mar) where the rows correspond to marker positions in female and male genetic distance, respectively. The genotype data gets converted into numeric codes, as follows. The genotype data for a backcross is coded as NA = missing, 1 = AA, 2 = AB. For an F2 intercross, the coding is NA = missing, 1 = AA, 2 = AB, 3 = BB, 4 = not BB (i.e. AA or AB; D in Mapmaker/qtl), 5 = not AA (i.e. AB or BB; C in Mapmaker/qtl). For a 4-way cross, the mother and father are assumed to have genotypes AB and CD, respectively. The genotype data for the progeny is assumed to be phase-known, with the following coding scheme: NA = missing, 1 = AC, 2 = BC, 3 = AD, 4 = BD, 5 = A = AC or AD, 6 = B = BC or BD, 7 = C = AC or BC, 8 = D = AD or BD, 9 = AC or BD, 10 = AD or BC, 11 = not AC, 12 = not BC, 13 = not AD, 14 = not BD. pheno a data.frame of size (n.ind x n.phe) containing the phenotypes. If a phenotype with the name genotype is included, these identifiers will be used in top.errorlod, plotErrorlod, and plotGeno as identifiers for the individual.

Note

All functions in this package uses cross data style.

Author(s)

Lucia Gutierrez.

References

Broman KW, Sen S (2009) A Guide to QTL Mapping with R/qtl. Springer, NewYork Comadran J, Thomas W, van Eeuwijk F, Ceccarelli S, Grando S, Stanca A, Pecchioni N, Akar T, Al-Yassin A, Benbelkacem A, Ouabbou H, Bort J, Romagosa I, Hackett C, Russell J (2009) Patterns of genetic diversity and linkage disequilibrium in a highly structured Hordeum vulgare association-mapping population for the Mediterranean basin. Theor Appl Genet 119:175-187 Milne et al., (2010) Flapjack - graphical genotype visualization. Bioinformatics 26(24), 3133-3134.

See Also

qtl.analysis, qtl.memq

Examples

```
data (SxM_geno)
data (SxM_map)
data (SxM_pheno)
P.data <- SxM_pheno
G.data <- SxM_geno
map.data <- SxM_map
cross.data <- qtl.cross (P.data, G.data, map.data,
cross='dh', heterozygotes = FALSE)
summary (cross.data)</pre>
```

qtl.memq

Performs Multi-Environment (or Multi-Trait) Multi-QTL analysis for balanced populations.

Description

Mixed models have been used in balanced populations to detect QTL-by-environment (QEI) effects while modeling the variance-covariance matrix. This function performs a multi-environment (or multi-trait) multi-QTL biparental analysis modeling the correlations across environments (traits).

Usage

qtl.memq

Arguments

crossobj	An object of class = cross obtained from the qtl.cross function from this package, or the read.cross function from r/qtl package (Broman and Sen, 2009).This file contains phenotypic means, genotypic marker score, and genetic map data.
P.data	The name of the file containing the phenotypic information in a long format.
env.label	vector with the names of the environment (or traits) to select for the QTL analysis.
trait	name for the phenotypic trait to be analyzed.
step	Maximum distance (in cM) between positions at which the genotype probabil- ities are calculated, though for step = 0, probabilities are calculated only at the marker locations.
method	'SIM' or 'CIM' for simple interval (SIM) or composite interval mapping (CIM).
threshold	options are: Li&Ji (Li and Ji, 2005), FDR (Benjamini and Hochberg, 1995), and set alpha levels (p.values).
distance	To avoid co-linearity, nearby markers are not allowed in the same model. This is the minimum distance within which two markers are allowed to stay in the model.
cofactors	Vector of genetic predictors to be used as cofactors
window.size	To avoid co-linearity, marker cofactors close to the markers being tested are not allowed in the model. This is the minimum distance to allow a co-factor when testing for a specific marker. Given the resolution of common QTL studies, it is recommended to use a large window.size (i.e. 50 cM). The default is set to 50 cM.

Details

'SIM' or 'CIM' could be perform.

Value

The function returns a data.frame with the final QTL indicating the locus names, chromosome, position, p.values tested and QTL effects that are printed to qtl_memq_reports.

Note

For single trait and single environment see qtl.analysis

Author(s)

Lucia Gutierrez

References

Hayes PM, Liu BH, Knapp SJ, Chen F, Jones B, Blake T, Franckowiak JD, Rasmusson DC, Sorrells M, Ullrich SE, Wesenberg DM, Kleinhofs A (1993) Quantitative trait locus effects and environmental interaction in a sample of North American barley germplasm. Theor Appl Genet 87:392-401.

Malosetti, M., C.G. van der Linden, B. Vosman, and F. a van Eeuwijk. 2007a. A mixed-model approach to association mapping using pedigree information with an illustration of resistance to Phytophthora infestans in potato. Genetics 175(2): 879-89. Malosetti, M., J.M. Ribaut, M. Vargas, J. Crossa, and F. a. Eeuwijk. 2007b. A multi-trait multi-environment QTL mixed model with an application to drought and nitrogen stress trials in maize (Zea mays L.). Euphytica 161(1-2): 241-257.

See Also

qtl.analysis

Examples

```
## Not run:
data (SxM_geno)
data (SxM_map)
data (SxMxE_pheno)
P.data <- SxMxE_pheno
G.data <- SxM_geno
map.data <- SxM_map</pre>
cross.data <- qtl.cross (P.data, G.data, map.data, cross='dh',</pre>
                         heterozygotes=FALSE)
summary (cross.data)
## Pheno Quality
pq.diagnostics (crossobj=cross.data, boxplot =FALSE)
## Marker Quality
mq.diagnostics (crossobj=cross.data,I.threshold=0.1,
             p.val=0.01,na.cutoff=0.1)
# QTL_SIM
QTL.result <- gtl.memg (crossobj = cross.data, P.data = P.data,
                         env.label = c('ID91','ID92','MAN92','MTd91',
                         'MTd92', 'MTi91', 'MTi92', 'SKs92', 'WA91', 'WA92'),
                         trait = 'yield', step = 10, method = 'SIM',
                         threshold = 'Li&Ji', distance = 50, cofactors = NULL,
                         window.size = 50)
## QTL_CIM
QTL.result <- qtl.memq (crossobj = cross.data, P.data = P.data,
                        env.label = c('ID91','ID92','MAN92','MTd91','MTd92',
                        'MTi91', 'MTi92', 'SKs92', 'WA91', 'WA92'),
                        trait = 'yield', step = 10, method = 'CIM',
                        threshold = 'Li&Ji', distance = 50,
                        cofactors = QTL.result$selected$marker, window.size = 50)
```

End(Not run)

SxMxE_pheno

Description

The data is the well-known Steptoe x Morex doubled haploid population developed in the early 90s by the North American Barley Mapping Project. The objective was to improve in the understanding of the genetic basis of agronomic and malting quality traits in barley. The population consists of 150 doubled haploids lines; of which 148 have been genotyped by SNP markers (we use here 794 SNP markers). The population was extensively evaluated for several agronomic and malting quality traits (Hayes et al. 1993) in many locations and years (US and Canada). In this example we use information on yield in ten of those trials.

Usage

SxMxE_pheno

Format

A data frame 148 genotypes and 10 enviroment.

Source

Hayes et al. 1993

SxM_geno

Name of the file containing genotypic (marker scores) information.

Description

The data is the well-known Steptoe x Morex doubled haploid population developed in the early 90s by the North American Barley Mapping Project. The objective was to improve in the understanding of the genetic basis of agronomic and malting quality traits in barley. The population consists of 150 doubled haploids lines; of which 148 have been genotyped by SNP markers (we use here 794 SNP markers). The population was extensively evaluated for several agronomic and malting quality traits (Hayes et al. 1993) in many locations and years (US and Canada). In this example we use information on yield and heading date in one of those trials.

Usage

SxM_geno

Format

A data frame 150 genotypes and 794 markers.

Source

Hayes et al. 1993

SxM_map

Name of the file containing genotypic (marker scores) information.

Description

The data is the well-known Steptoe x Morex doubled haploid population developed in the early 90s by the North American Barley Mapping Project. The objective was to improve in the understanding of the genetic basis of agronomic and malting quality traits in barley. The population consists of 150 doubled haploids lines; of which 148 have been genotyped by SNP markers (we use here 794 SNP markers). The population was extensively evaluated for several agronomic and malting quality traits (Hayes et al. 1993) in many locations and years (US and Canada). In this example we use information on yield and heading date in one of those trials.

Usage

SxM_map

Format

A data frame 794 row (markers) and 3 column.Column 1 gives the marker names, column 2 the chromosome on which the marker has been mapped, and column 3 indicates the position of the marker within the chromosome.

Source

Hayes et al. 1993

SxM_pheno

Name of the file containing phenotypic information.

Description

The data is the well-known Steptoe x Morex doubled haploid population developed in the early 90s by the North American Barley Mapping Project. The objective was to improve in the understanding of the genetic basis of agronomic and malting quality traits in barley. The population consists of 150 doubled haploids lines; of which 148 have been genotyped by SNP markers (we use here 794 SNP markers). The population was extensively evaluated for several agronomic and malting quality traits (Hayes et al. 1993) in many locations and years (US and Canada). In this example we use information on yield and heading date in one of those trials.

Usage

SxM_pheno

SxM_pheno

Format

A data frame 150 genotypes and 2 variables.

Source

Hayes et al. 1993

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