Package 'StageWise'

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Title Two-stage analysis of multi-environment trials for genomic selection and GWAS

Version 1.08

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Description Fully efficient, two stage analysis of multi-environment trials, including directional dominance and multi-trait genomic selection

Depends R (>= 4.0)

License GPL-3

RoxygenNote 7.2.3

Encoding UTF-8

Imports Matrix (>= 1.5-0), ggplot2, methods, ggrepel, rlang, ggpubr, SpATS, spam, AGHmatrix, MASS, CVXR, ggforce

Suggests knitr, rmarkdown, asreml

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R topics documented:

`blup` *BLUP*

Description

BLUP

Usage

```
blup(data, geno = NULL, what, index.coeff = NULL, gwas.ncore = 0L)
```

Arguments

`data`	one object, or list of objects, of `class_prep` from `blup_prep`
`geno`	object of `class_geno` from `read_geno`
`what`	One of the following: AV, BV, GV, AM, DM. See Details.
`index.coeff`	named vector of index coefficients for the locations or traits
`gwas.ncore`	Integer indicating number of cores to use for GWAS (default is 0 for no GWAS).

Details

The argument `what` takes 5 possible values: "AV" (additive value), "BV" (breeding value), "GV" (genotypic value), "AM" (additive marker effect), and "DM" (dominance marker effect). "Values" refer to predictions for individuals, as opposed to markers. Predicted values include the average fixed effect of the environments, whereas predicted marker effects do not. Argument `index.coeff` is a named vector (matching the names of the locations or traits), and the values are interpreted for standardized traits.

When multiple objects of `class_prep` are used for `data`, they must be based on the same marker data and genetic model. Also, reliabilities are not computed.

Value

Data frame of BLUPs

`blup_prep` *Prepare data for BLUP*

Description

Prepare data for BLUP

Usage

```
blup_prep(data, vcov = NULL, geno = NULL, vars, mask = NULL, method = NULL)
```

Arguments

`data`	data frame of BLUEs from Stage 1
`vcov`	list of variance-covariance matrices for the BLUEs
`geno`	object of `class_geno` from `read_geno`
`vars`	object of `class_var` from `Stage2`
`mask`	(optional) data frame with possible columns "id","env","trait"
`method`	(optional) "MME", "Vinv", NULL (defaut). see Details

Details

The `method` argument can be used to control how the linear system is solved. "MME" leads to inversion of the MME coefficient matrix, while "Vinv" leads to inversion of the overall var-cov matrix for the response vector. If NULL, the software uses whichever method involves inverting the smaller matrix. If the number of random effects (m) is less than the number of BLUEs (n), "MME" is used.

For the multi-location model, if all of the environments for a location are masked, the average of the other locations is used when computed average fixed effects.

Value

Object of `class_prep`

class_geno-class *S4 class for marker genotype data*

Description

S4 class for marker genotype data

Slots

`ploidy` ploidy

`map` Marker map positions

`coeff` Coefficients of the marker effects (dim: indiv x marker)

`scale` Scaling factor between markers and indiv

`G` Additive relationship matrix (from markers and potentially also pedigree)

`eigen.G` list of eigenvalues and eigenvectors

class_genoD-class *S4 class for marker genotype data with dominance*

Description

S4 class for marker genotype data with dominance

Slots

`ploidy` ploidy

`map` Marker map positions

`coeff` Coefficients of the additive marker effects (dim: indiv x marker)

`scale` Scaling factor between markers and indiv for additive effects

`G` Additive relationship matrix (from markers and potentially also pedigree)

`eigen.G` list of eigenvalues and eigenvectors for G

`coeff.D` coefficients of the dominance marker effects (dim: indiv x marker)

`scale.D` Scaling factor between markers and indiv for dominance effects

`D` Dominance relationship matrix

`eigen.D` list of eigenvalues and eigenvectors for D

`Fg` genomic inbreeding coefficient (based on dominance)

class_prep-class *S4 class to prepare for blup*

Description

S4 class to prepare for blup

Slots

`id` genotype identifiers

`ploidy` ploidy

`var.u` variance of random effects

`var.uhat` variance of BLUPs

`avg.env` average fixed effect of the environments

`heterosis` regression coefficients for inbreeding

`fixed.marker` fixed marker effects

`B` var-cov matrix for fixed effects

`random` random effect estimates

`geno1.var` first var-cov matrix from `class_var`

`geno2.var` second var-cov matrix from `class_var`

`model` model from `class_var`

class_var-class *S4 class for variances*

Description

S4 class for variances

Slots

`geno1` first genetic effect

`geno2` second genetic effect

`model` 0=no markers, 1=add, 2=add+g.resid, 3=add+dom

`resid` residual

`diagG` average diagonal element of the G matrix

`diagD` average diagonal element of the D matrix

`vars` variances for reporting

`B` var-cov matrix of fixed effects for gain

`fix.eff.marker` names of fixed effect markers

corr *Trait correlations*

Description

Trait correlations

Usage

```
corr(vars, traits = NULL, effect = NULL)
```

Arguments

vars	object of class_var from Stage2
traits	pair of traits
effect	name of effect

Details

Use either the argument traits or effect, not both. Using traits leads to a partitioning of the total correlation between those two traits, based on path analysis, assuming no correlation between the effects of the Stage 2 model. Using effect displays the correlation between all traits for that effect. Use the summary command to see the names of the possible effects.

Value

matrix

dominance *Report dominance parameters*

Description

Report dominance parameters

Usage

```
dominance(params, digits = 2, index.coeff = NULL, gamma = 0)
```

Arguments

params	list returned by Stage2
digits	number of digits for rounding
index.coeff	merit index coefficients
gamma	contribution of non-additive values for genetic merit

Details

The dominance variance (Vd) and baseline heterosis (b) are quantified relative to additive variance (Va) and std. dev. (SDa), respectively. For single traits, the estimate and SE of the ratios are calculated based on the delta method (Rice 2007, p. 162-166). For a multi-trait model, the result is just the ratio of the estimates, with `index.coeff` specifying the coefficients of the standardized true values (see also `blup`) and `gamma` specifying the relative weight for non-additive to additive genetic merit (see also `gain`).

Value

data frame with estimates and SE

References

Rice JA (2007) Mathematical Statistics and Data Analysis, 3rd ed. Duxbury, Pacific Grove.

`gain` *Genetic gain*

Description

Genetic gain calculations

Usage

```
gain(
  input,
  merit = NULL,
  desired = NULL,
  restricted = NULL,
  traits = NULL,
  gamma = NULL,
  solver = "ECOS",
  ...
)
```

Arguments

`input`	either object of `class_prep` or quad.mat returned by this function
`merit`	named vector of merit coefficients, in genetic standard deviation units
`desired`	named vector of desired gains, in genetic standard deviation units
`restricted`	data frame of restricted traits, see Details
`traits`	optional vector with exactly 2 trait names, to plot elliptical response
`gamma`	contribution of non-additive values for genetic merit
`solver`	name of convex solver (default is "ECOS")

Details

Either `merit` or `desired` can be used, not both. The former specifies the relative contribution of each trait to genetic merit, while the latter specifies the relative desired gain in genetic standard deviation units. All traits must be specified. Optional argument `restricted` is a data frame with columns "trait" and "sign", where the options for sign are "=",">","<", representing equal to zero, non-negative, and non-positive. When `desired` is used, the `restricted` argument is ignored.

The argument `gamma` controls the definition of genetic merit. (See notation in the journal publication.) The default is NULL, which implies breeding values. For purely additive values, use gamma = 0. For total genotypic value, use gamma = 1.

Note that this function assumes a selection index of BLUPs, not phenotypes.

Value

List containing

quad.mat quadratic matrix for the ellipsoid

plot ellipse plot

table data frame with the response and index coefficients for all traits

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`gwas_threshold` *Compute GWAS discovery threshold*

Description

Compute GWAS discovery threshold

Usage

```
gwas_threshold(geno, alpha = 0.05, exclude.chrom = NULL, n.core = 1)
```

Arguments

`geno`	object of `class_geno`
`alpha`	genome-wide significance level
`exclude.chrom`	chromosomes to exclude
`n.core`	number of cores to use

Details

Uses a Bonferroni-type correction based on an effective number of markers that accounts for LD (Moskvina and Schmidt, 2008).

Value

-log10(p) threshold

References

Moskvina V, Schmidt KM (2008) On multiple-testing correction in genome-wide association studies. Genetic Epidemiology 32:567-573. doi:10.1002/gepi.20331

inbreeding *Genomic inbreeding coefficient*

Description

Genomic inbreeding coefficient

Usage

```
inbreeding(geno)
```

Arguments

geno	object of class_geno

Details

Under the additive model, the inbreeding coefficient comes from the diagonal elements of the G matrix according to F = (G-1)/(ploidy-1). For dominance, the inbreeding coefficient is the scaled row-sum of the dominance coefficient matrix.

Value

data frame with F[G] and (when dominance is present) F[D]

manhattan_plot *Create Manhattan plot*

Description

Create Manhattan plot

Usage

```
manhattan_plot(data, chrom = NULL, thresh = NULL, rotate.label = FALSE)
```

Arguments

data	data frame with columns for marker, chrom, position, and score
chrom	optional, to plot only one chromosome
thresh	optional, to include horizontal line at discovery threshold
rotate.label	TRUE/FALSE whether to rotate x-axis labels to be perpendicular

Details

Assumes position in bp

Value

ggplot2 object

predict *Predict individual values from marker effects*

Description

Predict individual values from marker effects

Arguments

object	object of class_geno
marker.effects	data frame with columns "marker" and "effect"

Details

Use the blup function with what="AM" or "DM" to generate the data frame for marker.effects.

Value

data frame with columns "id" and "value"

quantile *G matrix quantile*

Description

G matrix quantile

Arguments

x	object of class_geno
prob	probability

Details

Unlike the S3 method, prob must have length = 1

Value

data frame with the quantile of the G matrix coefficients for each id

read_geno *Read marker genotype data*

Description

Read marker genotype data

Usage

```
read_geno(
  filename,
  ploidy,
  map,
  min.minor.allele = 5,
  w = 1e-05,
  ped = NULL,
  dominance = FALSE
)
```

Arguments

filename	Name of CSV file with marker allele dosage
ploidy	2,4,6,etc. (even numbers)
map	TRUE/FALSE
min.minor.allele	threshold for marker filtering (see Details)
w	blending parameter (see Details)
ped	optional, pedigree data frame with 3 or 4 columns (see Details)
dominance	TRUE/FALSE whether to include dominance covariance (see Details)

Details

When map=TRUE, first three columns of the file are marker, chrom, position. When map=FALSE, the first column is marker. Subsequent columns contain the allele dosage for individuals/clones, coded 0,1,2,...ploidy (fractional values are allowed). The input file for diploids can also be coded using -1,0,1 (fractional values allowed). Additive coefficients are computed by subtracting the population mean from each marker, and the additive (genomic) relationship matrix is computed as G = tcrossprod(coeff)/scale. The scale parameter ensures the mean of the diagonal elements of G equals 1 under panmictic equilibrium. Missing genotype data is replaced with the population mean.

G can be blended with the pedigree relationship matrix (A) by providing a pedigree data frame in ped and blending parameter w. The blended relationship matrix is H = (1-w)G + wA. The first three columns of ped are id, parent1, parent2. Missing parents must be coded NA. An optional fourth column in binary (0/1) format can be used to indicate which ungenotyped individuals should be included in the H matrix, but this option cannot be combined with dominance. If there is no fourth column, only genotyped individuals are included. If a vector of w values is provided, the function returns a list of class_geno objects.

If the A matrix is not used, then G is blended with the identity matrix (times the mean diagonal of G) to improve numerical conditioning for matrix inversion. The default for w is 1e-5, which is

somewhat arbitrary and based on tests with the vignette dataset. The D matrix is also blended with the identity matrix using 1e-5 for numerical conditioning.

When `dominance=FALSE`, non-additive effects are captured using a residual genetic effect, with zero covariance. If `dominance=TRUE`, a (digenic) dominance covariance matrix is used instead.

The argument `min.minor.allele` specifies the minimum number of individuals that must contain the minor allele. Markers that do not meet this threshold are discarded.

Value

Variable of class `class_geno`.

`remove_spatialtrend` *Remove spatial trend*

Description

Removes spatial trend to prepare for multi-trait Stage 1

Usage

```
remove_spatialtrend(filename, traits, spline, effects = NULL)
```

Arguments

`filename`	Name of CSV input file
`traits`	trait names
`spline`	vector of variable names for 2D spline with SpATS
`effects`	data frame specifying other effects in the model (see Details)

Details

SpATS used to remove 2D spatial trend for each field experiment, labeled with column 'expt' in the input file. Genotype labels are in column 'id' and modeled as i.i.d random effect. Argument `effects` is used to specify other i.i.d. effects besides genotype and has three columns: name, fixed, factor. The "name" column is a string that must match a column in the input file. The fixed column is a logical variable to indicate whether the effect is fixed (TRUE) or random (FALSE). The factor column is a logical variable to indicate whether the effect is a factor (TRUE) or numeric (FALSE).

Argument `traits` is a character vector of trait names. Single-trait analyses are performed for each trait, and the results are combined in the output.

Value

Data frame with adjusted phenotypes

`Stage1` *Stage 1 analysis of multi-environment trials*

Description

Computes genotype BLUEs for each experiment

Usage

```
Stage1(
  filename,
  traits,
  effects = NULL,
  solver = "asreml",
  spline = NULL,
  silent = TRUE,
  workspace = c("500mb", "500mb"),
  max.iter = 30
)
```

Arguments

`filename`	Name of CSV file
`traits`	trait names (see Details)
`effects`	data frame specifying other effects in the model (see Details)
`solver`	one of the following: "asreml","spats"
`spline`	vector of variable names for 2D spline with SpATS
`silent`	TRUE/FALSE, whether to suppress REML output
`workspace`	memory limits for ASRreml-R
`max.iter`	maximum number of iterations for ASRreml-R

Details

The input file must have one column labeled "id" for the individuals and one labeled "env" for the environments. The data for each environment are analyzed independently with a linear mixed model. Although not used in Stage1, to include a genotype x location effect in `Stage2`, a column labeled "loc" should be present in the input file.

Argument `effects` is used to specify other i.i.d. effects besides genotype and has three columns: name, fixed, factor. The "name" column is a string that must match a column in the input file. The fixed column is a logical variable to indicate whether the effect is fixed (TRUE) or random (FALSE). The factor column is a logical variable to indicate whether the effect is a factor (TRUE) or numeric (FALSE).

Argument `solver` specifies which software to use for REML. Current options are "asreml" and "spats". For "spats", the argument `spline` must be a vector of length two, with the names of the x and y variables (respectively) for the 2D spline.

The heritability and residuals in the output are based on a random effects model for id.

Missing response values are omitted for single-trait analysis but retained for multi-trait analysis (unless both traits are missing), to allow for prediction in Stage 2.

Argument workspace is a vector of length two containing the workspace and pworkspace limits for ASReml-R, with default values of 500mb. If you get an error about insufficient memory, try increasing the appropriate value (workspace for variance estimation and pworkspace for BLUE computation).

For multiple traits, only "asreml" is supported, and only the BLUE model is run, so the returned object does not contain H2.

If the input file has a column "expt", this allows for the use of separate spatial models for multiple experiments within an environment (only for single trait): each experiment is first analyzed separately, and then the BLUEs from all experiments per env are jointly analyzed to compute a single BLUE per env. The estimation errors from each experiment are propagated into the multi-expt model using ASReml-R. The situation is different with multi-trait analysis, as all experiments are analyzed jointly per env, with a fixed effect for expt but a common residual model. Any additional cofactors (e.g., block) that are nested within expt need to be explicitly nested!

Value

List containing

blues data frame of BLUEs

vcov list of variance-covariance matrices for the BLUEs, one per experiment (env)

fit data frame with broad-sense H2 (plot basis) and/or AIC

resid For single trait, list of diagnostic plots and data frame of residuals. For multi-trait, list of resid var-cov matrices.

Stage2 *Stage 2 analysis of multi-environment trials*

Description

Stage 2 analysis of multi-environment trials

Usage

```
Stage2(
  data,
  vcov = NULL,
  geno = NULL,
  fix.eff.marker = NULL,
  silent = TRUE,
  workspace = "500mb",
  non.add = "g.resid",
  max.iter = 20,
  covariates = NULL,
  pairwise = FALSE
)
```

Arguments

`data`	data frame of BLUEs from Stage 1 (see Details)
`vcov`	named list of variance-covariance matrices for the BLUEs
`geno`	output from `read_geno`
`fix.eff.marker`	markers in `geno` to include as additive fixed effect covariates
`silent`	TRUE/FALSE, whether to suppress ASReml-R output
`workspace`	Memory limit for ASRreml-R variance estimation
`non.add`	one of the following: "none","g.resid","dom"
`max.iter`	maximum number of iterations for asreml
`covariates`	names of other covariates in `data`
`pairwise`	TRUE/FALSE should multi-trait analysis proceed pairwise

Details

Stage 2 of the two-stage approach described by Damesa et al. 2017, using ASReml-R for variance component estimation. The variable `data` has three mandatory column: id, env, BLUE. Optionally, `data` can have a column labeled "loc", which changes the main effect for genotype into a separable genotype-within-location effect, using a FA2 covariance model for the locations. Optionally, `data` can have a column labeled "trait", which uses an unstructured covariance model. The multi-location and multi-trait analyses cannot be combined. Missing data are allowed in the multi-trait but not the single-trait analysis. The argument `geno` is used to partition genetic values into additive and non-additive components. Any individuals in `data` that are not present in `geno` are discarded.

The argument `vcov` is used to partition the macro- and micro-environmental variation, which are called GxE and residual in the output. `vcov` is a named list of variance-covariance matrices for the BLUEs within each environment, with id for rownames (single trait) or id:trait. The order in `vcov` and `data` should match. Both `data` and `vcov` can be created using the function `Stage1`.

Because ASReml-R can only use relationship matrices defined in the global environment, this function creates and then removes global variables when either `vcov` or `geno` is used. By default, the workspace memory for ASReml-R is set at 500mb. If you get an error about insufficient memory, try increasing it. ASReml-R version 4.1.0.148 or later is required.

The `covariates` option is only available for single trait/loc analysis.

Argument `pairwise` was added in package version 1.04, which specifies that multi-trait analysis is performed as multiple bivariate analyses, which often converges better. The returned object is a list of the results from the bivariate analyses, as well as "vars" for all traits, which is needed for `blup_prep`.

Value

List containing

aic AIC

vars variance components for `blup_prep`, as variable of class `class_var`

params Estimates and SE for fixed effects and variance components

random Random effect predictions

loadings scaled loadings for the FA2 multi-loc model

References

Damesa et al. 2017. Agronomy Journal 109: 845-857. doi:10.2134/agronj2016.07.0395

summary.var *Displays variances and correlations*

Description

Displays variances and correlations

Arguments

object	object of class_var
digits	number of digits for rounding
index.coeff	merit index coefficients
gamma	contribution of non-additive values for genetic merit

Details

For a single trait, the 'var' output is a data frame with two columns of information for the various effects: the first is the variance and the second is the proportion of variance explained (PVE), excluding the environment effect. For multiple locations or traits, the 'cor' output is the correlation matrix for additive effects (does not include fixed effect markers). For multiple traits, the variance and PVE results are returned as separate data frames, unless index.coeff is used to create an index.

The index.coeff are the coefficients of the standardized true values (see also blup). The argument gamma is the relative weight for non-additive to additive genetic merit (see also gain).

Value

List output that varies depending on the situation (see Details)

uniplot *Uniplot for multi-location models*

Description

Displays scaled loadings of the FA2 model

Usage

```
uniplot(loadings, nudge = 0.1)
```

Arguments

loadings	scaled factor loadings, from Stage2.
nudge	distance to nudge labels

Details

The squared radius for each point is the proportion of genetic variance explained by the latent factors. For points on the unit circle, the cosine of the subtended angle equals the correlation.

Value

ggplot2 object

`wheat.data` *Genomic prediction from secondary traits in wheat*

Description

Canopy temperature (CT) measurements collected during grain fill; used for genomic prediction of grain yield (GY) in wheat. Data come from the drought and extreme drought environments of Rutkoski et al. (2016). The CT phenotype was dated 3/7/2014. Stage 1 BLUEs were computed using rep(trial) as a random effect.

Usage

```
data(wheat)
```

Format

wheat.geno is object of `class_geno`. wheat.blues and wheat.vcov are output from `Stage1`.

References

Rutkoski et al. (2016) G3 (Bethesa) 6:2799–2808. https://doi.org/10.1534/g3.116.032888

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