Package ‘statgenGWAS’

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Description

codeMarkers codes markers in a gData object and optionally performs imputation of missing values as well.

The function performs the following steps:

1. replace strings in naStrings by NA.
2. remove genotypes with a fraction of missing values higher than nMissGeno.
3. remove SNPs with a fraction of missing values higher than nMiss.
4. recode SNPs to numerical values.
5. remove SNPs with a minor allele frequency lower than MAF.
6. optionally remove duplicate SNPs.
7. optionally impute missing values.
8. repeat steps 5. and 6. if missing values are imputed.

Usage

codeMarkers(
  gData,
  refAll = "minor",
  nMissGeno = 1,
  nMiss = 1,
  MAF = NULL,
  removeDuplicates = TRUE,
```r
codeMarkers =
  keep = NULL,
  impute = TRUE,
  imputeType = c("random", "fixed", "beagle"),
  fixedValue = NULL,
  naStrings = NA,
  verbose = FALSE
)

Arguments

- **gData**: An object of class `gData` containing at least markers.
- **refAll**: A character string indicating the reference allele used when recoding markers. If "minor", then the recoding is done using the minor allele as reference allele. Alternatively a single character can be supplied as a reference allele for the whole set of SNPs, or a character vector with a reference allele per SNP.
- **nMissGeno**: A numerical value between 0 and 1. Genotypes with a fraction of missing values higher than `nMissGeno` will be removed. Genotypes with only missing values will always be removed.
- **nMiss**: A numerical value between 0 and 1. SNPs with a fraction of missing values higher than `nMiss` will be removed. SNPs with only missing values will always be removed.
- **MAF**: A numerical value between 0 and 1. SNPs with a Minor Allele Frequency (MAF) below this value will be removed.
- **removeDuplicates**: Should duplicate SNPs be removed?
- **keep**: A vector of SNPs that should never be removed in the whole process.
- **impute**: Should imputation of missing values be done?
- **imputeType**: A character string indicating what kind of imputation of values should be done.
  - fixed - missing values will be replaced by a given fixed value.
  - random - missing values will be replaced by a random value calculated using allele frequencies per SNP.
  - beagle - missing values will be imputed using beagle software. Beagle only accepts integers as map positions. If you use this option, please cite the original papers in your publication (see references).
- **fixedValue**: A numerical value used for replacing missing values in case `inputType` is fixed.
- **naStrings**: A character vector of strings to be treated as NA.
- **verbose**: Should a summary of the performed steps be printed?

Value

A copy of the input `gData` object with markers replaced by coded and imputed markers.

References

Examples

```r
## Create markers
markers <- matrix(c(
ncol = 10, byrow = TRUE, dimnames = list(paste0("IND", 1:10),
paste0("SNP", 1:10)))

## create object of class 'gData'.
gData <- createGData(geno = markers)

## Code markers by minor allele, no imputation.
gDataCoded1 <- codeMarkers(gData = gData, impute = FALSE)

## Code markers by reference alleles, impute missings by fixed value.
gDataCoded2 <- codeMarkers(gData = gData,
  refAll = rep(x = c("A", "B"), times = 5),
  impute = TRUE, imputeType = "fixed",
  fixedValue = 1)

## Code markers by minor allele, impute by random value.
gDataCoded3 <- codeMarkers(gData = gData, impute = TRUE,
  imputeType = "random")
```

Description

This dataset comes from the European Union project DROPS (DROught-tolerant yielding PlantS). A panel of 256 maize hybrids was grown with two water regimes (irrigated or rainfed), in seven fields in 2012 and 2013, respectively, spread along a climatic transect from western to eastern Europe, plus one site in Chile in 2013. This resulted in 28 experiments defined as the combination of one year, one site and one water regime, with two and three repetitions for rainfed and irrigated treatments, respectively. A detailed environmental characterisation was carried out, with hourly records of micrometeorological data and soil water status, and associated with precise measurement of phenology. Grain yield and its components were measured at the end of the experiment. The main purpose of this dataset consists in using the environmental characterisation to quantify the genetic variability of maize grain yield in response to the environmental drivers for genotype-by-environment interaction. For instance, allelic effects at QTLs identified over the field network.
are consistent within a scenario but largely differ between scenarios.

The data is split in three separate data.frames.

dropsMarkers This data.frame contains the 50K genotyping matrix coded in allelic dose (012) filtered and imputed. Genotyping of 41,722 loci on 246 parental lines were obtained using 50K Illumina Infinium HD arrays (Ganal et al., 2011). Genotype were coded in allelic dose with 0 for the minor allele, 1 for the heterozygote, and 2 for the major allele. Genotype were filtered (MAF>1%) and missing data imputed using Beagle v3. A data.frame with 246 rows and 41723 columns.

Ind name of the genotype
SYMN83 to PZE-110111485 coded QTLs

dropsMap This data.frame contains the description of the 41,722 loci genotyped by 50K Illumina Infinium Array on the 246 lines. A data.frame with 41722 rows and 5 columns.

SNP.names name of the SNP
Chromosome number of the B73 reference genome V2
Position position on the B73 reference genome V2 in centimorgan
allele1 first original allele (A, T, G or C)
allele2 second original allele (A, T, G or C)

dropsPheno This data.frame contains the genotypic means (Best Linear Unbiased Estimation, BLUEs), with one value per experiment (Location × year × water regime) per genotype. A data.frame with 6888 rows and 14 columns.

Experiment experiments ID described by the three first letters of the city’s name followed by the year of experiment and the water regime with W for watered and R for rain-fed.
parent1 identifier of donor dent line
Code_ID, Variety_ID, Accession_ID identifier of the genotype
gen.panel project in which the genetic material was generated
grain.yield genotypic mean for yield adjusted at 15% grain moisture, in ton per hectare (t ha-1)
grain.number genotypic mean for number of grain per square meter
grain.weight genotypic mean for individual grain weight in milligram (mg)
anthesis genotypic mean for male flowering (pollen shed), in thermal time cumulated since emergence (d20°C)
silking genotypic mean for female flowering (silking emergence), in thermal time cumulated since emergence (d20°C)
plant.height genotypic mean for plant height, from ground level to the base of the flag leaf (highest) leaf in centimeter (cm)
tassel.height genotypic mean for plant height including tassel, from ground level to the highest point of the tassel in centimeter (cm)
ear.height genotypic mean for ear insertion height, from ground level to ligule of the highest ear leaf in centimeter (cm)
Note

From the source data, the experiments from 2011 have been removed since these do not contain all genotypes. Also the experiment Gra13W has been removed.

Source

https://data.inra.fr/dataset.xhtml?persistentId=doi:10.15454/IASSTN

References


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gData  
S3 Class gData

Description

createGData creates an object of S3 class gData with genotypic and phenotypic data for usage in further analysis. All input to the function is optional, however at least one input should be provided. It is possible to provide an existing gData object as additional input in which case data is added to this object. Existing data will be overwritten with a warning.

Usage

```r
createGData(
  gData = NULL,
  geno = NULL,
  map = NULL,
  kin = NULL,
  pheno = NULL,
  covar = NULL
)
```

Arguments

gData  
An optional gData object to be modified. If NULL, a new gData object is created.

genox A matrix or data.frame with genotypes in the rows and markers in the columns. A matrix from the matrix in the base package may be provided as well as as matrix from the Matrix package. If no row names are provided, they are taken from pheno (if supplied and dimension matches). If no column names are provided, the row names from map are used (if supplied and dimension matches).
A data.frame with columns `chr` for chromosome and `pos` for position. Positions can be in base pair (bp) or centimorgan (cM). They should not be cumulative over the chromosomes. Other columns are ignored. Marker names should be in the row names. These should match the marker names in `geno` (if supplied).

A kinship matrix or list of kinship matrices with genotype in rows and columns. These matrices can be from the `matrix` class, as defined in the base package, or from the `dsyMatrix` class, the class of symmetric matrices in the Matrix package.

The genotypes should be identical to the genotypes in `geno`.

If a list of kinship matrices is provided these are supposed to be chromosome specific matrices. In that case their names should match the names of the chromosomes in `map`. If no names are provided, the number of matrices should match the number of chromosomes in `map` in which case default names are provided.

A data.frame or a list of data.frames with phenotypic data, with genotypes in the first column `genotype` and traits in the following columns. The trait columns should be numerical columns only. A list of data.frames can be used for replications, i.e. different trials.

A data.frame with extra covariates per genotype. Genotypes should be in the rows.

An object of class `gData` with the following components:

- `map`: a data.frame containing map data. Map is sorted by chromosome and position.
- `markers`: a sparse matrix from the Matrix package containing marker information in case of numerical genotypic data, a standard matrix otherwise.
- If `geno` is a three dimensional array, `markers` is a three dimensional array as well.
- `pheno`: a list of data.frames containing phenotypic data.
- `kinship`: a kinship matrix of class `dsyMatrix` from the Matrix package.
- `covar`: a data.frame with extra covariates.

Bart-Jan van Rossum

See Also

`summary.gData`

Examples

```r
set.seed(1234)
## Create genotypic data.
# Create genotypic data.
geno <- matrix(sample(x = c(0, 1, 2), size = 15, replace = TRUE), nrow = 3)
dimnames(geno) <- list(paste0("G", 1:3), paste0("M", 1:5))
```
## Construct map.
map <- data.frame(chr = c(1, 1, 2, 2, 2),
                  pos = 1:5,
                  row.names = paste0("M", 1:5))

## Compute kinship matrix.
kim <- kinship(X = geno, method = "IBS")

## Create phenotypic data.
pheno <- data.frame(paste0("G", 1:3),
                   matrix(rnorm(n = 12, mean = 50, sd = 5), nrow = 3),
                   stringsAsFactors = FALSE)
dimnames(pheno) = list(paste0("G", 1:3),
                        c("genotype", paste0("T", 1:4)))

## Combine all data in gData object.
gData <- createGData(geno = geno, map = map, kin = kin, pheno = pheno)
summary(gData)

## Construct covariate.
covar <- data.frame(C1 = c("a", "a", "b"), row.names = paste0("G", 1:3))

## Compute alternative kinship matrix.
kim2 <- kinship(X = geno, method = "astle")

## Add covariates to previously created gData object and overwrite
## current kinship matrix by newly computed one.
gData2 <- createGData(gData = gData, kin = kim2, covar = covar)

---

### kinship

Functions for calculating kinship matrices

#### Description

A collection of functions for calculating kinship matrices using different algorithms. The following algorithms are included: astle (Astle and Balding, 2009), Identity By State (IBS) and VanRaden (VanRaden, 2008) for marker matrices.

#### Usage

kinship(X, method = c("astle", "IBS", "vanRaden"), denominator = NULL)

#### Arguments

- **X**: An n x m marker matrix with genotypes in the rows (n) and markers in the columns (m).
- **method**: The method used for computing the kinship matrix.
- **denominator**: A numerical value. See details.
plot.GWAS

Value

An n x n kinship matrix.

Marker matrices

In all algorithms the input matrix $X$ is first cleaned, i.e. markers with a variance of 0 are excluded from the calculation of the kinship matrix. Then some form of scaling is done which differs per algorithm. This gives a scaled matrix $Z$. The matrix $ZZ^t/denominator$ is returned. By default the denominator is equal to the number of columns in $Z$ for astle and IBS and $2 \times p \times (1 - p)$ where $p = colSums(X)/(2 \times nrow(X))$ for vanRaden. This denominator can be overwritten by the user, e.g. when computing kinship matrices by splitting $X$ in smaller matrices and then adding the results together in the end.

References


Examples

```r
## Create example matrix.
M <- matrix(c(1, 1, 0, 0, 1, 1, 0, 0, 0, 1, 0, 1), nrow = 3)

## Compute kinship matrices using different methods.
kinship(M, method = "astle")
kinship(M, method = "IBS")
kinship(M, method = "vanRaden")

## Compute kinship matrix using astle and balding method with denominator 2.
kinship(M, method = "astle", denominator = 2)
```

plot.GWAS

Plot function for the class GWAS

Description

Creates a plot of an object of S3 class GWAS. The following types of plot can be made:

- a manhattan plot, i.e. a plot of LOD-scores per SNP
- a qq plot of observed LOD-scores versus expected LOD-scores
- a qtl plot of effect sizes and directions for multiple traits

Manhattan plots and qq plots are made for a single trait which should be indicated using the parameter trait. If the analysis was done for only one trait it is detected automatically. The qtl plot will plot all traits analysed.

See details for a detailed description of the plots and the plot options specific to the different plots.
## Usage

```r
## S3 method for class 'GWAS'
plot(
  x,
  ..., 
  plotType = c("manhattan", "qq", "qtl"),
  trial = NULL,
  trait = NULL,
  output = TRUE
)
```

### Arguments

- **x**: An object of class `GWAS`.
- **...**: further arguments to be passed on to the actual plotting functions.
- **plotType**: A character string indicating the type of plot to be made. One of "manhattan", "qq" and "qtl".
- **trial**: A character string or numeric index indicating for which trial the plot should be made. If `x` only contains results for one trial, `trial` may be `NULL`.
- **trait**: A character string indicating for which trait the results should be plotted. For type "qtl" all traits are plotted. If `x` only contains results for one trait, `trait` may be `NULL`.
- **output**: Should the plot be output to the current device? If `FALSE`, only a list of ggplot objects is invisibly returned.

### Manhattan Plot

A LOD-profile of all marker positions and corresponding LOD-scores is plotted. Significant markers are highlighted with red dots. By default these are taken from the result of the GWAS analysis however the LOD-threshold for significant parameters may be modified using the parameter `yThr`. The threshold is plotted as a horizontal line. If there are previously known marker effect, false positives and true negatives can also be marked.

### Extra parameter options:

- **xLab**: A character string, the x-axis label. Default = "Chromosomes"
- **yLab**: A character string, the y-axis label. Default = \(-\log_{10}(p)\)
- **effects**: A character vector, indicating which SNPs correspond to a real (known) effect. Used for determining true/false positives and false negatives. True positives are colored green, false positives orange and false negatives yellow.
- **colPalette**: A color palette used for plotting. Default coloring is done by chromosome, using black and grey.
- **yThr**: A numerical value for the LOD-threshold. The value from the GWAS analysis is used as default.
- **signLwd**: A numerical value giving the thickness of the points that are false/true positives/negatives. Default = 0.6
lod  A positive numerical value. For the SNPs with a LOD-value below this value, only 5% is plotted. The chance of a SNP being plotting is proportional to its LOD-score. This option can be useful when plotting a large number of SNPs. The 5% of SNPs plotted is selected randomly. For reproducible results use set.seed before calling the function.

chr  A vector of chromosomes to be plotted. By default, all chromosomes are plotted. Using this option allows restricting the plot to a subset of chromosomes.

QQ Plot

From the LOD-scores calculated in the GWAS analysis, a qq-plot is generated with observed LOD-scores versus expected LOD-scores. Code is adapted from Segura et al. (2012).

QTL Plot

A plot of effect sizes for the significant SNPs found in the GWAS analysis is created. Each horizontal line contains QTLs of one trait, phenotypic trait or trial. Optionally, vertical white lines can indicate chromosome subdivision, genes of interest, known QTL, etc. Circle diameters are proportional to the absolute value of allelic effect. Colors indicate the direction of the effect: green when the allele increases the trait value and blue when it decreases the value.

Extra parameter options:

normalize  Should the snpEffect be normalized? Default = FALSE

sortData  Should the data be sorted before plotting? Either FALSE, if no sorting should be done, or a character string indicating the data column to use for sorting. This should be a numerical column. Default = FALSE

binPositions  An optional data.frame containing at leasts two columns, chr(omosome) and pos(ition). Vertical lines are plotted at those positions. Default = NULL

printVertGrid  Should default vertical grid lines be plotted. Default = TRUE

yLab  A character string, the y-axis label. Default = "Traits"

yThr  A numerical value for the LOD-threshold. The value from the GWAS analysis is used as default.

chr  A vector of chromosomes to be plotted. By default all chromosomes are plotted. Using this option this can be restricted to a subset of chromosomes.

exportPptx  Should the plot be exported to a .pptx file? Default = FALSE

pptxName  A character string, the name of the .pptx file to which the plot is exported. Ignored if exportPptx = FALSE.

References


runSingleTraitGwas

Description
runSingleTraitGwas performs a single-trait Genome Wide Association Study (GWAS) on phenotypic and genotypic data contained in a gData object. A covariance matrix is computed using the EMMA algorithm (Kang et al., 2008) or the Newton-Raphson algorithm (Tunnicliffe, 1989) in the sommer package. Then a Generalized Least Squares (GLS) method is used for estimating the marker effects and corresponding p-values. This is done using either one kinship matrix for all chromosomes or different chromosome-specific kinship matrices for each chromosome. Significant SNPs are selected based on a user defined threshold.

Usage
runSingleTraitGwas(
  gData, 
  traits = NULL, 
  trials = NULL, 
  covar = NULL, 
  snpCov = NULL, 
  kin = NULL, 
  kinshipMethod = c("astle", "IBS", "vanRaden"), 
  remlAlgo = c("EMMA", "NR"), 
  GLSMethod = c("single", "multi"), 
  useMAF = TRUE, 
  MAF = 0.01, 
  MAC = 10, 
  genomicControl = FALSE, 
  thrType = c("bonf", "fixed", "small"), 
  alpha = 0.05, 
  LODThr = 4, 
  nSnpLOD = 10, 
  sizeInclRegion = 0, 
  minR2 = 0.5, 
  nCores = NULL)

Arguments
- **gData**: An object of class gData containing at least map, markers and pheno.
- **traits**: A vector of traits on which to run GWAS. These can be either numeric indices or character names of columns in pheno. If NULL, GWAS is run on all traits.
- **trials**: A vector of trials on which to run GWAS. These can be either numeric indices or character names of list items in pheno. If NULL, GWAS is run for all trials. GWAS is run for the selected trials in sequential order.
covar  An optional vector of covariates taken into account when running GWAS. These can be either numeric indices or character names of columns in covar in gData. If NULL no covariates are used.

snpCov  An optional character vector of snps to be included as covariates.

kin  An optional kinship matrix or list of kinship matrices. These matrices can be from the matrix class as defined in the base package or from the dsysMatrix class, the class of symmetric matrices in the Matrix package. If GLSMethod = "single" then one matrix should be provided, if GLSMethod = "multi", a list of chromosome specific matrices of length equal to the number of chromosomes in map in gData. If NULL then matrix kinship in gData is used. If both kin is provided and gData contains a matrix kinship then kin is used.

kinshipMethod An optional character indicating the method used for calculating the kinship matrix(ce). Currently "aste" (Astle and Balding, 2009), "IBS" and "vanRaden" (vanRaden, 2008) are supported. If a kinship matrix is supplied either in gData or in parameter kin, kinshipMethod is ignored.

remlAlgo  A character string indicating the algorithm used to estimate the variance components. Either EMMA, for the EMMA algorithm, or NR, for the Newton-Raphson algorithm.

GLSMethod  A character string indicating the method used to estimate the marker effects. Either single for using a single kinship matrix, or multi for using chromosome specific kinship matrices.

useMAF  Should the minor allele frequency be used for selecting SNPs for the analysis. If FALSE, the minor allele count is used instead.

MAF  The minor allele frequency (MAF) threshold used in GWAS. A numerical value between 0 and 1. SNPs with MAF below this value are not taken into account in the analysis, i.e. p-values and effect sizes are put to missing (NA). Ignored if useMAF is FALSE.

MAC  A numerical value. SNPs with minor allele count below this value are not taken into account for the analysis, i.e. p-values and effect sizes are set to missing (NA). Ignored if useMAF is TRUE.

genomicControl  Should genomic control correction as in Devlin and Roeder (1999) be applied?

thrType  A character string indicating the type of threshold used for the selection of candidate loci. Either bonf for using the Bonferroni threshold, a LOD-threshold of \(-log10(\alpha/p)\), where p is the number of markers and alpha can be specified in alpha, fixed for a self-chosen fixed LOD-threshold, specified in LODThr or small, the LOD-threshold is chosen such as the SNPs with the nSnpLOD smallest p-values are selected. nSnpLOD can be specified.

alpha  A numerical value used for calculating the LOD-threshold for thrType = "bonf".

LODThr  A numerical value used as a LOD-threshold when thrType = "fixed".

nSnpLOD  A numerical value indicating the number of SNPs with the smallest p-values that are selected when thrType = "small".

sizeInclRegion  An integer. Should the results for SNPs close to significant SNPs be included? If so, the size of the region in centimorgan or base pairs. Otherwise 0.
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**minR2**
A numerical value between 0 and 1. Restricts the SNPs included in the region close to significant SNPs to only those SNPs that are in sufficient Linkage Disequilibrium (LD) with the significant SNP, where LD is measured in terms of $R^2$. If for example `sizeInclRegion = 200000` and `minR2 = 0.5`, then for every significant SNP also those SNPs whose LD ($R^2$) with the significant SNP is at least 0.5 AND which are at most 200000 away from this significant SNP are included. Ignored if `sizeInclRegion = 0`.

**nCores**
A numerical value indicating the number of cores to be used by the parallel part of the algorithm. If NULL the number of cores used will be equal to the number of cores available on the machine - 1.

**Value**
An object of class `GWAS`.

**References**


Segura et al. (2012) An efficient multi-locus mixed-model approach for genome-wide association studies in structured populations. Nature Genetics 44 (7): 825–30. [https://doi.org/10.1038/ng.2314](https://doi.org/10.1038/ng.2314).


**See Also**

`GWAS`, `kinship`, `dropsData`
Examples

## Create a gData object Using the data from the DROPS project.
## See the included vignette for a more extensive description on the steps.
data(dropsMarkers)
data(dropsMap)
data(dropsPheno)
## Add genotypes as row names of dropsMarkers and drop Ind column.ownames(dropsMarkers) <- dropsMarkers["Ind"]
dropsMarkers <- dropsMarkers[rownames(dropsMarkers) != "Ind"]
## Add genotypes as row names of dropsMap.ownames(dropsMap) <- dropsMap["SNP.names"]
## Rename Chromosome and Position columns.
colnames(dropsMap)[match(c("Chromosome", "Position"),
    colnames(dropsMap))] <- c("chr", "pos")
## Convert phenotypic data to a list.
dropsPhenoList <- split(x = dropsPheno, f = dropsPheno["Experiment"])
## Rename Variety.ID to genotype and select relevant columns.
dropsPhenoList <- lapply(X = dropsPhenoList, FUN = function(trial) {
colnames(trial)[colnames(trial) == "Variety.ID"] <- "genotype"
    trial <- trial[c("genotype", "grain.yield", "grain.number", "seed.size",
        "anthesis", "silking", "plant.height", "tassel.height",
        "ear.height")]
return(trial)
})
gDataDrops <- createGData(geno = dropsMarkers, map = dropsMap,
    pheno = dropsPhenoList)

## Run single trait GWAS for trait 'grain.yield' for trial Mur13W.
GWASDrops <- runSingleTraitGwas(gData = gDataDrops,
    trials = "Mur13W",
    traits = "grain.yield")

## Run single trait GWAS for trait 'grain.yield' for trial Mur13W.
## Use chromosome specific kinship matrices calculated using vanRaden method.
GWASDropsMult <- runSingleTraitGwas(gData = gDataDrops,
    trials = "Mur13W",
    traits = "grain.yield",
    kinshipMethod = "vanRaden",
    GLSMethod = "multi")

---

summary.gData  

**Summary function for the class gData**

**Description**

Gives a summary for an object of S3 class gData.
Usage

```r
## S3 method for class 'gData'
summary(object, ..., trials = NULL)
```

Arguments

- **object**: An object of class `gData`.
- **...**: Not used.
- **trials**: A vector of trials to include in the summary. These can be either numeric indices or character names of list items in `pheno`. If `NULL`, all trials are included.

Value

A list with a most four components:

- **mapSum**: A list with number of markers and number of chromosomes in the map.
- **markerSum**: A list with number of markers, number of genotypes and the distribution of the values within the markers.
- **phenoSum**: A list of data.frames, one per trial with a summary of all traits within the trial.
- **covarSum**: A list of data.frames, one per trial with a summary of all covariates within the trial.

All components are only present in the output if the corresponding content is present in the `gData` object.

---

### summary.GWAS

*Summary function for the class GWAS*

Description

Gives a summary for an object of S3 class `GWAS`.

Usage

```r
## S3 method for class 'GWAS'
summary(object, ..., trials = NULL)
```

Arguments

- **object**: An object of class `GWAS`.
- **...**: Not used.
- **trials**: A vector of strings or numeric indices indicating for which trials the summary should be made. If `NULL`, a summary is made for all trials.
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