Package 'pleioh2g'

October 28, 2025

Type Package

Title Estimation of Pleiotropic Heritability from Genome-Wide Association Studies (GWAS) Summary Statistics

Version 0.1.0

Description Provides tools to compute unbiased pleiotropic heritability estimates of complex diseases from genome-wide association studies (GWAS) summary statistics. We estimate pleiotropic heritability from GWAS summary statistics by estimating the proportion of variance explained from an estimated genetic correlation matrix (Bulik-Sullivan et al. 2015 <doi:10.1038/ng.3406>) and employing a Monte-Carlo bias correction procedure to account for sampling noise in genetic correlation estimates.

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Encoding UTF-8

LazyData true

Depends R (>= 2.10)

RoxygenNote 7.3.2

Imports data.table, dplyr, stats, rlang, mvtnorm, fs, arrow, checkmate, cli, gdata, glue, purrr, tibble, vroom

Suggests knitr, rmarkdown, testthat (>= 3.0.0)

Config/testthat/edition 3

VignetteBuilder knitr

Language en-US

NeedsCompilation no

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Repository CRAN

Date/Publication 2025-10-28 09:50:02 UTC

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`Cal_cor_pleiotropic_h2` *Compute a vector of pleioh2g for all diseases before correction This function computes pleioh2g for all diseases before correction in one go.*

Description

Compute a vector of pleioh2g for all diseases before correction This function computes pleioh2g for all diseases before correction in one go.

Usage

```
Cal_cor_pleiotropic_h2(rg_mat, h2g_T)
```

Arguments

rg_mat	genetic correlation matrix.
h2g_T	heritability vector for all diseases.

Value

pleioh2g vector

Examples

```
data(Results_full_rg_15D)
data(h2_vector_15D)
Cal_cor_pleiotropic_h2(Results_full_rg_15D,h2_vector_15D)
```

Cal_cor_pleiotropic_h2_corrected_single

Compute single pleioh2g for target disease after correction with referred disease index in the rg matrix and corrected ratio

---

Description

This function computes pleioh2g for the target disease after correction.

Usage

```
Cal_cor_pleiotropic_h2_corrected_single(
  rg_mat,
  h2g_T_single,
  corrected_weight_updated,
  plei_h2_idx
)
```

Arguments

rg_mat	genetic correlation matrix.
h2g_T_single	heritability for target diseases.
corrected_weight_updated	the ratio for correction
plei_h2_idx	index of the target disease in the rg_mat.

Value

pleioh2g value for the target disease after correction

Examples

```
data(Results_full_rg_15D)
data(h2_vector_15D)
plei_h2_idx<-1
h2g_T_single <- h2_vector_15D[plei_h2_idx]
corrected_weight_updated <- 0.78
Cal_cor_pleiotropic_h2_corrected_single(Results_full_rg_15D,h2g_T_single,
corrected_weight_updated,plei_h2_idx)
```

Cal_cor_pleiotropic_h2_single

Compute single pleioh2g for target disease before correction with referred disease index in the rg matrix

---

Description

This function computes pleioh2g for the target disease before correction.

Usage

```
Cal_cor_pleiotropic_h2_single(rg_mat, h2g_T_single, plei_h2_idx)
```

Arguments

rg_mat	genetic correlation matrix.
h2g_T_single	heritability for target diseases.
plei_h2_idx	index of the target disease in the rg_mat.

Value

pleioh2g value for the target disease before correction

Examples

```
data(Results_full_rg_15D)
data(h2_vector_15D)
plei_h2_idx<-1
h2g_T_single<-h2_vector_15D[plei_h2_idx]
Cal_cor_pleiotropic_h2_single(Results_full_rg_15D,h2g_T_single,plei_h2_idx)
```

Cal_cor_test_single *Compute inversed elements for the target disease in bias correction procedure with referred disease index in the rg matrix*

Description

This function inversed elements for the target disease in bias correction procedure.

Usage

```
Cal_cor_test_single(rg_mat, plei_h2_idx)
```

Arguments

rg_mat	genetic correlation matrix.
plei_h2_idx	index of the target disease in the rg_mat.

Value

inverse element value for the target disease used for bias correction

Examples

```
data(Results_full_rg_15D)
plei_h2_idx<-1
Cal_cor_test_single(Results_full_rg_15D,plei_h2_idx)
```

Cal_rg_h2g_alltraits *Compute rg + h2g*

Description

This function is used to compute rg + h2g using LDSC.

Usage

```
Cal_rg_h2g_alltraits(
  phenotype,
  munged_sumstats,
  ld_path,
  wld_path,
  sample_prev = NULL,
  population_prev = NULL
)
```

Arguments

phenotype	Vector of the phenotype name
munged_sumstats	All LDSC-munged GWAS .stat.gz
ld_path	Path to directory containing ld score files.
wld_path	Path to directory containing weight files.
sample_prev	Vector of sample prevalence, in the same order of input GWAS summary statistics.
population_prev	Vector of population prevalence, in the same order of input GWAS summary statistics.

Value

A named list containing LDSC-based heritability and genetic correlation estimates across all input phenotypes. The list includes the following elements:

- h2: Matrix of SNP-heritability estimates on the observed scale (rows = 1, columns = input phenotypes).
- h2Z: Matrix of corresponding heritability Z-scores.
- liah2: Matrix of heritability estimates on the liability scale.
- rg: Symmetric matrix of pairwise genetic correlations between traits.
- rgz: Matrix of Z-scores for the genetic correlation estimates.
- gcov: Symmetric matrix of genetic covariances between traits.

Each element corresponds to one LDSC-derived summary statistic, with trait names used as both row and column names.

Cal_rg_h2g_jk_alltraits

genomic-block jackknife and compute rg + h2g

Description

This function performs genomic-block jackknife and computes rg + h2g.

Usage

```
Cal_rg_h2g_jk_alltraits(
  n_block = 200,
  hmp3,
  phenotype,
  munged_sumstats,
  ld_path,
  wld_path,
  sample_prev = NULL,
  population_prev = NULL
)
```

Arguments

n_block	number of jackknife blocks.
hmp3	Directory for hapmap 3 snplist.
phenotype	Vector of the phenotype name
munged_sumstats	All LDSC-munged GWAS .stat.gz
ld_path	Path to directory containing ld score files.
wld_path	Path to directory containing weight files.
sample_prev	Vector of sample prevalence, in the same order of input GWAS summary statistics.
population_prev	Vector of population prevalence, in the same order of input GWAS summary statistics.

Value

A named list containing block jackknife estimates of SNP-heritability and genetic correlation across all input phenotypes. The list includes the following elements:

- h2array: A matrix of per-block SNP-heritability estimates on the observed scale. Rows correspond to jackknife blocks, and columns correspond to input phenotypes.
- liah2array: A matrix of per-block SNP-heritability estimates on the liability scale, with the same row and column structure as h2array.
- rgarray: A three-dimensional array of pairwise genetic correlation estimates. The first two dimensions represent phenotype pairs (rows and columns), and the third dimension indexes the jackknife blocks.
- gcovarray: A three-dimensional array of pairwise genetic covariance estimates, aligned in structure with rgarray.

Each element provides per-block estimates that can be used to compute standard errors or confidence intervals via the block jackknife method.

---

generate_proposal_sample_changea_cor

Generate samples based on sampling covariance matrix and rg matrix for target disease

---

Description

This function is used to generate samples based on sampling covariance matrix and rg matrix for target disease

Usage

```
generate_proposal_sample_changea_cor(
  Results_full_rg,
  Results_full_rg_array,
  plei_h2_idx,
  ratio_a
)
```

Arguments

Results_full_rg	genetic correlation matrix.
Results_full_rg_array	genetic correlation jackknife-block array.
plei_h2_idx	index of the target disease in the rg_mat.
ratio_a	corrected ratio.

Value

noisy_inversed_element for bias correction

Examples

```
data(Results_full_rg_15D)
data(Results_full_rg_array_15D)
plei_h2_idx<-1
ratio_a <- 0.75
generate_proposal_sample_changea_cor(Results_full_rg_15D,
 Results_full_rg_array_15D, plei_h2_idx, ratio_a)
```

---

h2_liability *Convert Heritability to Liability Scale*

Description

'h2_liability()' converts heritability estimates from the observed to liability scale.

Usage

```
h2_liability(h2, sample_prev, population_prev)
```

Arguments

h2	(numeric) Estimate of observed-scale heritability
sample_prev	(numeric) Proportion of cases in the current sample
population_prev	(numeric) Population prevalence of trait

Value

(numeric) Liability-scale heritability

Examples

```
h2_liability(0.28, 0.1, 0.05)
```

---

h2_vector_15D *h2 vector for 15 diseases*

Description

Example h2 vector used in the vignette and examples.

Usage

```
h2_vector_15D
```

Format

A numeric matrix.

Source

Internal simulation

---

h2_vector_mat_15D *h2 jk matrix for 15 diseases*

Description

Example h2 jk matrix used in the vignette and examples.

Usage

```
h2_vector_mat_15D
```

Format

A numeric matrix.

Source

Internal simulation

ldsc_h2 *Estimate heritability - refer to ldscr R package (https://github.com/mglev1n/ldscr)*

Description

'ldsc_h2()' uses ldscore regression to estimate the heritability of a trait from GWAS summary statistics and reference LD information.

Usage

```
ldsc_h2(
  munged_sumstats,
  sample_prev = NA,
  population_prev = NA,
  ld,
  wld,
  n_blocks = 200,
  chisq_max = NA,
  chr_filter = seq(1, 22, 1)
)
```

Arguments

munged_sumstats	Either a dataframe, or a path to a file containing munged summary statistics. Must contain at least columns named 'SNP' (rsid), 'A1' (effect allele), 'A2' (non-effect allele), 'N' (total sample size) and 'Z' (Z-score)
sample_prev	(numeric) For binary traits, this should be the prevalence of cases in the current sample, used for conversion from observed heritability to liability-scale heritability. The default is 'NA', which is appropriate for quantitative traits or estimating heritability on the observed scale.
population_prev	(numeric) For binary traits, this should be the population prevalence of the trait, used for conversion from observed heritability to liability-scale heritability. The default is 'NA', which is appropriate for quantitative traits or estimating heritability on the observed scale.
ld	(character) Path to directory containing ld score files, ending in '*.l2.ldscore.gz'.
wld	(character) Path to directory containing weight files.
n_blocks	(numeric) Number of blocks used to produce block jackknife standard errors. Default is '200'
chisq_max	(numeric) Maximum value of Z^2 for SNPs to be included in LD-score regression. Default is to set 'chisq_max' to the maximum of 80 and N*0.001.
chr_filter	(numeric vector) Chromosomes to include in analysis. Separating even/odd chromosomes may be useful for exploratory/confirmatory factor analysis.

Value

A [tibble][tibble::tibble-package] containing heritability information. If ‘sample_prev‘ and ‘population_prev‘ were provided, the heritability estimate will also be returned on the liability scale.

`ldsc_rg` *Estimate cross-trait genetic correlations (Robust Version) - refer to ldscr R package (https://github.com/mglev1n/ldscr)*

Description

‘ldsc_rg()‘ uses ldscore regression to estimate the pairwise genetic correlations between traits. The function relies on named lists of traits, sample prevalences, and population prevalences. The name of each trait should be consistent across each argument.

Usage

```
ldsc_rg(
  munged_sumstats,
  sample_prev = NA,
  population_prev = NA,
  ld,
  wld,
  n_blocks = 200,
  chisq_max = NA,
  chr_filter = seq(1, 22, 1)
)
```

Arguments

`munged_sumstats`
: (list) A named list of dataframes, or paths to files containing munged summary statistics. Each set of munged summary statistics contain at least columns named ‘SNP‘ (rsid), ‘A1‘ (effect allele), ‘A2‘ (non-effect allele), ‘N‘ (total sample size) and ‘Z‘ (Z-score)

`sample_prev`
: (list) A named list containing the prevalence of cases in the current sample, used for conversion from observed heritability to liability-scale heritability. The default is ‘NA‘, which is appropriate for quantitative traits or estimating heritability on the observed scale.

`population_prev`
: (list) A named list containing the population prevalence of the trait, used for conversion from observed heritability to liability-scale heritability. The default is ‘NA‘, which is appropriate for quantitative traits or estimating heritability on the observed scale.

`ld`
: (character) Path to directory containing ld score files, ending in ‘*.l2.ldscore.gz‘.

`wld`
: (character) Path to directory containing weight files.

n_blocks	(numeric) Number of blocks used to produce block jackknife standard errors. Default is '200'
chisq_max	(numeric) Maximum value of Z^2 for SNPs to be included in LD-score regression. Default is to set 'chisq_max' to the maximum of 80 and N*0.001.
chr_filter	(numeric vector) Chromosomes to include in analysis. Separating even/odd chromosomes may be useful for exploratory/confirmatory factor analysis.

Details

This function estimates the pairwise genetic correlations between an arbitrary number of traits. The function also estimates heritability for each individual trait. There is a [ggplot2::autoplot()] method for visualizing a heatmap of the results.

This version handles cases where traits have non-positive heritability estimates more gracefully by returning NA values for correlations involving such traits.

Value

A list of class 'ldscr_list' containing heritablilty and genetic correlation information - 'h2' = [tibble][tibble::tibble-package] containing heritability information for each trait. If 'sample_prev' and 'population_prev' were provided, the heritability estimates will also be returned on the liability scale. - 'rg' = [tibble][tibble::tibble-package] containing pairwise genetic correlations information. - 'raw' = A list of correlation/covariance matrices

---

make_weights *Internal Function to make weights - refer to ldscr R package (https://github.com/mglev1n/ldscr)*

Description

'make_weights()' Internal Function to make weights

Usage

```
make_weights(chi1, L2, wLD, N, M.tot)
```

Arguments

chi1	chi-square
L2	ld score
wLD	wld score
N	sample size
M.tot	Number of SNPs

Value

A numeric vector of initial LDSC weights for each SNP

`merge_sumstats` *Merging summary statistics with LD-score files - refer to ldscr R package (https://github.com/mglev1n/ldscr)*

Description

'merge_sumstats()' Merging summary statistics with LD-score files

Usage

```
merge_sumstats(sumstats_df, w, x, chr_filter)
```

Arguments

`sumstats_df`	dataframe of sumstat
`w`	wld score
`x`	ld score
`chr_filter`	(numeric vector) Chromosomes to include in analysis. Separating even/odd chromosomes may be useful for exploratory/confirmatory factor analysis.

Value

A tibble (data frame) containing the merged summary statistics and LD-score

`perform_analysis` *Internal function to perform LDSC heritability/covariance analysis - refer to ldscr R package (https://github.com/mglev1n/ldscr)*

Description

'perform_analysis()' Internal function to perform LDSC heritability/covariance analysis

Usage

```
perform_analysis(n.blocks, n.snps, weighted.LD, weighted.chi, N.bar, m)
```

Arguments

`n.blocks`	Number of blocks
`n.snps`	Number of SNPs
`weighted.LD`	wld score
`weighted.chi`	chi-square
`N.bar`	Average N after merging
`m`	Number of SNPs from LD data

Value

A list containing the results of the LDSC heritability/covariance analysis with the following elements:

- `reg.tot`: Estimated total heritability or covariance (regression coefficient scaled by `m`).
- `tot.se`: Standard error of the total heritability/covariance estimate, computed using a block jackknife.
- `intercept`: LDSC regression intercept.
- `intercept.se`: Standard error of the intercept, estimated via block jackknife.
- `pseudo.values`: Vector of pseudo-values from the block jackknife procedure, one per block.
- `N.bar`: Average sample size across SNPs after merging.

`pleiotropyh2_cor_computing_single` *Compute pleioh2g after bias correction for target disease*

Description

This function is used to compute pleioh2g after bias correction for target disease

Usage

```
pleiotropyh2_cor_computing_single(
  G,
  phenotype,
  h2_vector,
  h2_vector_mat,
  Results_full_rg,
  Results_full_rg_array,
  sample_rep
)
```

Arguments

`G`	index of target disease.
`phenotype`	Vector of the phenotype name
`h2_vector`	h2g vector for all traits - aligned as the order in phenotype file
`h2_vector_mat`	h2g array from jackknife-block estimates for all traits - aligned as the order in phenotype file
`Results_full_rg`	genetic correlation matrix. - aligned as the order in phenotype file
`Results_full_rg_array`	genetic correlation jackknife-block array. - aligned as the order in phenotype file
`sample_rep`	sampling times in bias correction

Value

A ‘list‘ containing the following elements: - ‘target_disease‘ (character): The value "401.1". - ‘target_disease_h2_est‘ (numeric): target disease h2g. - ‘target_disease_h2_se‘ (numeric): target disease h2g_se. - ‘selected_auxD‘ (character): auxiliary diseases. - ‘h2pleio_uncorr‘ (numeric): pre-correction pleiotropic heritability estimate. - ‘h2pleio_uncorr_se‘ (numeric): pre-correction pleiotropic heritability jackknife s.e. estimate. - ‘percentage_h2pleio_uncorr‘ (numeric): pre-correction percentage of pleiotropic heritability estimate. - ‘percentage_h2pleio_uncorr_se‘ (numeric): pre-correction percentage of pleiotropic heritability jackknife s.e. estimate. - ‘percentage_h2pleio_uncorr_jackknife‘ (numeric): vector of all pre-correction percentage of pleiotropic heritability jackknife estimates. - ‘h2pleio_corr‘ (numeric): post-correction pleiotropic heritability estimate. - ‘h2pleio_corr_se‘ (numeric): post-correction pleiotropic heritability jackknife s.e. estimate. - ‘percentage_h2pleio_corr‘ (numeric): post-correction percentage of pleiotropic heritability estimate. - ‘percentage_h2pleio_corr_se‘ (numeric): post-correction percentage of pleiotropic heritability jackknife s.e. estimate. - ‘corrected_weight‘ (numeric): corrected weight in bias correction.

Examples

```
G <- 1
data(Results_full_rg_15D)
data(Results_full_rg_array_15D)
data(h2_vector_15D)
data(h2_vector_mat_15D)
phenotype<-c("401.1","244.5","318","735.3","411.4",
"427.2","454.1","278.1","250.2","550.1","530.11",
"296.22","519.8","562.1","763")
sample_rep<-20
post_corrrresults_prune<-pleiotropyh2_cor_computing_single(G,phenotype,h2_vector_15D,
h2_vector_mat_15D,Results_full_rg_15D,Results_full_rg_array_15D, sample_rep)
```

---

pleiotropyh2_cor_computing_single_prune

Compute pleioh2g after bias correction for target disease

Description

This function is used to compute pleioh2g after bias correction for target disease

Usage

```
pleiotropyh2_cor_computing_single_prune(
  G,
  phenotype,
  h2_vector,
  h2_vector_mat,
  Results_full_rg,
  Results_full_rg_array,
  sample_rep
)
```

Arguments

G	index of target disease.
phenotype	Vector of the phenotype name
h2_vector	h2g vector for all traits - aligned as the order in phenotype file
h2_vector_mat	h2g array from jackknife-block estimates for all traits - aligned as the order in phenotype file
Results_full_rg	genetic correlation matrix. - aligned as the order in phenotype file
Results_full_rg_array	genetic correlation jackknife-block array. - aligned as the order in phenotype file
sample_rep	sampling times in bias correction

Value

A ‘list‘ containing the following elements: - ‘target_disease‘ (character): The value "401.1". - ‘target_disease_h2_est‘ (numeric): target disease h2g. - ‘target_disease_h2_se‘ (numeric): target disease h2g_se. - ‘selected_auxD‘ (character): auxiliary diseases. - ‘h2pleio_uncorr‘ (numeric): pre-correction pleiotropic heritability estimate. - ‘h2pleio_uncorr_se‘ (numeric): pre-correction pleiotropic heritability jackknife s.e. estimate. - ‘percentage_h2pleio_uncorr‘ (numeric): pre-correction percentage of pleiotropic heritability estimate. - ‘percentage_h2pleio_uncorr_se‘ (numeric): pre-correction percentage of pleiotropic heritability jackknife s.e. estimate. - ‘percentage_h2pleio_uncorr_jackknife‘ (numeric): vector of all pre-correction percentage of pleiotropic heritability jackknife estimates. - ‘h2pleio_corr‘ (numeric): post-correction pleiotropic heritability estimate. - ‘h2pleio_corr_se‘ (numeric): post-correction pleiotropic heritability jackknife s.e. estimate. - ‘percentage_h2pleio_corr‘ (numeric): post-correction percentage of pleiotropic heritability estimate. - ‘percentage_h2pleio_corr_se‘ (numeric): post-correction percentage of pleiotropic heritability jackknife s.e. estimate. - ‘corrected_weight‘ (numeric): corrected weight in bias correction.

Examples

```
G <- 1
data(Results_full_rg_15D)
data(Results_full_rg_array_15D)
data(h2_vector_15D)
data(h2_vector_mat_15D)
phenotype<-c("401.1","244.5","318","735.3","411.4",
"427.2","454.1","278.1","250.2","550.1","530.11",
"296.22","519.8","562.1","763")
sample_rep<-10
post_corrrresults_prune<-pleiotropyh2_cor_computing_single_prune(G,phenotype,h2_vector_15D,
h2_vector_mat_15D,Results_full_rg_15D,Results_full_rg_array_15D, sample_rep)
```

`pleiotropyh2_nocor_computing_single` *Compute pleioh2g before bias correction for target disease*

Description

This function is used to compute pleioh2g after bias correction for target disease

Usage

```
pleiotropyh2_nocor_computing_single(
  G,
  phenotype,
  h2_vector,
  h2_vector_mat,
  Results_full_rg,
  Results_full_rg_array
)
```

Arguments

`G`	index of target disease.
`phenotype`	Vector of the phenotype name
`h2_vector`	h2g vector for all traits - aligned as the order in phenotype file
`h2_vector_mat`	h2g array from jackknife-block estimates for all traits - aligned as the order in phenotype file
`Results_full_rg`	genetic correlation matrix.- aligned as the order in phenotype file
`Results_full_rg_array`	genetic correlation jackknife-block array.- aligned as the order in phenotype file

Value

A ‘list‘ containing the following elements: - ‘target_disease‘ (character): The value "401.1". - ‘target_disease_h2_est‘ (numeric): target disease h2g. - ‘target_disease_h2_se‘ (numeric): target disease h2g_se. - ‘selected_auxD‘ (character): auxiliary diseases. - ‘h2pleio_uncorr‘ (numeric): pre-correction pleiotropic heritability estimate. - ‘h2pleio_uncorr_se‘ (numeric): pre-correction pleiotropic heritability jackknife s.e. estimate. - ‘percentage_h2pleio_uncorr‘ (numeric): pre-correction percentage of pleiotropic heritability estimate. - ‘percentage_h2pleio_uncorr_se‘ (numeric): pre-correction percentage of pleiotropic heritability jackknife s.e. estimate. - ‘percentage_h2pleio_jackknife_uncorr‘ (numeric): vector of all pre-correction percentage of pleiotropic heritability jackknife estimates.

Examples

```
G <- 1
data(Results_full_rg_15D)
data(Results_full_rg_array_15D)
data(h2_vector_15D)
data(h2_vector_mat_15D)
phenotype<-c("401.1","244.5","318","735.3","411.4",
"427.2","454.1","278.1","250.2","550.1","530.11",
"296.22","519.8","562.1","763")
h2pleiobeforecorr<-pleiotropyh2_nocor_computing_single(G,phenotype,h2_vector_15D,
h2_vector_mat_15D,Results_full_rg_15D,Results_full_rg_array_15D)
```

Prune_disease_selection_DTrgzscore

Prune disease selection

Description

Prune disease selection

Usage

```
Prune_disease_selection_DTrgzscore(
  Target_disease,
  trait_name,
  Rg_mat,
  Rg_mat_z,
  rg_threshold
)
```

Arguments

Target_disease	trait_name of target disease
trait_name	trait_name of pre-prune rg_matrix
Rg_mat	pre-prune rg_matrix
Rg_mat_z	pre-prune rg z matrix
rg_threshold	rg_threshold

Value

Rg_mat_leave

Examples

```
trait_name<-c("401.1","244.5","318","735.3","411.4",
"427.2","454.1","278.1","250.2","550.1","530.11",
"296.22","519.8","562.1","763")
data("Results_full_rg_15D")
data("Rg_mat_z_15D")
Target_disease<-'401.1'
rg_threshold<-sqrt(0.3)
Rg_prune<-Prune_disease_selection_DTrgzscore(Target_disease, trait_name,
Results_full_rg_15D,Rg_mat_z_15D,rg_threshold)
```

`pruning_pleioh2g_wrapper` *Perform pruning in computing pleioh2g and correct bias*

Description

Perform pruning in computing pleioh2g and correct bias

Usage

```
pruning_pleioh2g_wrapper(
  G,
  phenotype,
  munged_sumstats,
  ld_path,
  wld_path,
  sample_prev = NULL,
  population_prev = NULL,
  n_block = 200,
  hmp3,
  sample_rep
)
```

Arguments

`G`	index of target disease.
`phenotype`	Vector of the phenotype name
`munged_sumstats`	All LDSC-munged GWAS .stat.gz
`ld_path`	Path to directory containing ld score files.
`wld_path`	Path to directory containing weight files.
`sample_prev`	Vector of sample prevalence, in the same order of input GWAS summary statistics.

population_prev	Vector of population prevalence, in the same order of input GWAS summary statistics.
n_block	number of jackknife blocks.
hmp3	Directory for hapmap 3 snplist.
sample_rep	sampling times in bias correction

Value

A ‘list‘ containing the following elements: - ‘target_disease‘ (character): The value "401.1". - ‘target_disease_h2_est‘ (numeric): target disease h2g. - ‘target_disease_h2_se‘ (numeric): target disease h2g_se. - ‘selected_auxD‘ (character): auxiliary diseases. - ‘h2pleio_uncorr‘ (numeric): pre-correction pleiotropic heritability estimate. - ‘h2pleio_uncorr_se‘ (numeric): pre-correction pleiotropic heritability jackknife s.e. estimate. - ‘percentage_h2pleio_uncorr‘ (numeric): pre-correction percentage of pleiotropic heritability estimate. - ‘percentage_h2pleio_uncorr_se‘ (numeric): pre-correction percentage of pleiotropic heritability jackknife s.e. estimate. - ‘percentage_h2pleio_uncorr_jackknife‘ (numeric): vector of all pre-correction percentage of pleiotropic heritability jackknife estimates. - ‘h2pleio_corr‘ (numeric): post-correction pleiotropic heritability estimate. - ‘h2pleio_corr_se‘ (numeric): post-correction pleiotropic heritability jackknife s.e. estimate. - ‘percentage_h2pleio_corr‘ (numeric): post-correction percentage of pleiotropic heritability estimate. - ‘percentage_h2pleio_corr_se‘ (numeric): post-correction percentage of pleiotropic heritability jackknife s.e. estimate. - ‘corrected_weight‘ (numeric): corrected weight in bias correction.

---

read_ld *Read ld from either internal or external file - refer to ldscr R package (https://github.com/mglev1n/ldscr)*

Description

‘read_ld()‘ Read ld from either internal or external file.

Usage

```
read_ld(ld)
```

Arguments

ld	(character) Path to directory containing ld score files, ending in ‘*.l2.ldscore.gz‘. Default is ‘NA‘, which will utilize the built-in ld score files from Pan-UK Biobank for the ancestry specified in ‘ancestry‘.

Value

A data frame (tibble) containing LD score information read from the specified directory. Each row corresponds to a SNP, and columns typically include:

- CHR: Chromosome number.

- SNP: SNP identifier (rsID).
- BP: Base pair position.
- L2: LD score value.
- M: Number of SNPs used in the LD score computation.

`read_m` *Read M from either internal or external file - refer to ldscr R package (https://github.com/mglev1n/ldscr)*

Description

'read_m()' Read M from either internal or external file

Usage

```
read_m(ld)
```

Arguments

`ld`	(character) Path to directory containing ld score files, ending in '*.l2.ldscore.gz'. Default is 'NA', which will utilize the built-in ld score files from Pan-UK Biobank for the ancestry specified in 'ancestry'.

Value

A data frame (tibble) containing SNP counts read from the specified M files.

`read_sumstats` *Read summary statistics from either internal or external file - refer to ldscr R package (https://github.com/mglev1n/ldscr)*

Description

'read_sumstats()' Read summary statistics from either internal or external file

Usage

```
read_sumstats(munged_sumstats, name)
```

Arguments

`munged_sumstats`	Either a dataframe, or a path to a file containing munged summary statistics. Must contain at least columns named 'SNP' (rsid), 'A1' (effect allele), 'A2' (non-effect allele), 'N' (total sample size) and 'Z' (Z-score)
`name`	trait name

Value

A data frame (tibble) containing GWAS summary statistics for the specified trait. The returned object will always contain at least the following columns:

- `SNP`: SNP identifier (rsID).
- `A1`: Effect allele.
- `A2`: Non-effect allele.
- `N`: Total sample size for the SNP.
- `Z`: Z-score of SNP-trait association.

`read_wld` *Read wld from either internal or external file - refer to ldscr R package (https://github.com/mglev1n/ldscr)*

Description

'read_wld()' Read wld from either internal or external file

Usage

```
read_wld(wld)
```

Arguments

`wld`	(character) Path to directory containing weight files. Default is 'NA', which will utilize the built-in weight files from Pan-UK Biobank for the ancestry specified in 'ancestry'.

Value

A data frame (tibble) containing LD weight information read from the specified directory. Each row corresponds to a SNP, and columns typically include:

- `CHR`: Chromosome number.
- `SNP`: SNP identifier (rsID).
- `BP`: Base pair position.
- `wLD`: Weight for LD regression.

Results_full_rg_15D *Genetic correlation matrix for 15 diseases*

Description

Example genetic correlation matrix used in the vignette and examples.

Usage

```
Results_full_rg_15D
```

Format

A numeric matrix.

Source

Internal simulation

Results_full_rg_array_15D *Jackknife array of genetic correlations (15 diseases)*

Description

Jackknife array of genetic correlations (15 diseases)

Usage

```
Results_full_rg_array_15D
```

Format

A 3-dim array.

Source

Internal simulation

Rg_mat_z_15D *Genetic correlation Z matrix for 15 diseases*

Description

Example genetic correlation Z matrix used in the vignette and examples.

Usage

```
Rg_mat_z_15D
```

Format

A numeric matrix.

Source

Internal simulation

sumstats_munged_example_input *Example munged dataframe - refer to ldscr R package (https://github.com/mglev1n/ldscr)*

Description

Example munged dataframe - refer to ldscr R package (https://github.com/mglev1n/ldscr)

Usage

```
sumstats_munged_example_input(example, dataframe = TRUE)
```

Arguments

example	(character) "401.1" which have been included as example traits.
dataframe	(logical) If 'TRUE' (default), return an example munged dataframe. If 'FALSE', return path to the file on disk.

Value

either a [tibble][tibble::tibble-package] containing a munged dataframe, or a path to the file on disk.

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