Package 'SIP'

December 9, 2025

Type Package

Title Single-Iteration Permutation for Large-Scale Biobank Data

Version 0.1.0

Description A single, phenome-wide permutation of large-scale biobank data. When a large number of phenotypes are analyzed in parallel, a single permutation across all phenotypes followed by genetic association analyses of the permuted data enables estimation of false discovery rates (FDRs) across the phenome. These FDR estimates provide a significance criterion for interpreting genetic associations in a biobank context. For the basic permutation of unrelated samples, this package takes a sample-by-variable file with ID, genotypic covariates, phenotypic covariates, and phenotypes as input. For data with related samples, it also takes a file with sample pair-wise identity-by-descent information.
The function outputs a permuted sample-by-variable file ready for genome-wide association analysis. See Annis et al. (2021) <doi:10.21203/rs.3.rs-873449/v1> for details.

URL https://github.com/acannis/SIP

BugReports https://github.com/acannis/SIP/issues

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Encoding UTF-8

LazyData true

Depends R (>= 3.5)

Imports stats, data.table, ggplot2

RoxygenNote 7.3.3

Suggests testthat (>= 3.0.0)

Config/testthat/edition 3

NeedsCompilation no

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Repository CRAN

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Contents

`get_fixed` *This function subsets the sample-by-variable dataframe to the "fixed" (i.e., non-permuted) data. This subset should include ID variables, sex, and genotypic covariates.*

Description

This function subsets the sample-by-variable dataframe to the "fixed" (i.e., non-permuted) data. This subset should include ID variables, sex, and genotypic covariates.

Usage

```
get_fixed(df, id.var = id.var, sex.var = sex.var, geno.vars = geno.vars)
```

Arguments

`df`	Data frame
`id.var`, `sex.var`	String
`geno.vars`	Character vector

Value

Data frame

`get_pairPerm` *This function samples individuals by pairs for permuting phenotype vectors in the paired-permutation function (sipPair.R)*

Description

This function samples individuals by pairs for permuting phenotype vectors in the paired-permutation function (sipPair.R)

Usage

```
get_pairPerm(deglst, rid.vars = rid.vars, ibd.var = ibd.var, seed = seed)
```

Arguments

`deglst`	List of data frames
`rid.vars`	Character vector
`ibd.var`	String
`seed`	Number

Value

Data frame

`get_pairPermDF` *This function recombines the fixed data and permuted data in the paired-permutation function (sipPair.R) into a permuted sample-by-variable data frame.*

Description

This function recombines the fixed data and permuted data in the paired-permutation function (sipPair.R) into a permuted sample-by-variable data frame.

Usage

```
get_pairPermDF(fix.df, perm.df, perm.map, id.var = id.var)
```

Arguments

`fix.df`, `perm.df`, `perm.map`	Data frames
`id.var`	String

Value

Data frame

`get_permDF` *This function recombines the fixed data and permuted data into a permuted sample-by-variable data frame.*

Description

This function recombines the fixed data and permuted data into a permuted sample-by-variable data frame.

Usage

```
get_permDF(fix.df, perm.df, perm.idx)
```

Arguments

`fix.df`, `perm.df`	Data frames
`perm.idx`	Numeric vector

Value

Data frame

`get_permIdx` *This function samples indices for permuting phenotype vectors in the basic permutation function (sip.R) and for permuting leftover unpaired individuals in the paired-permutation function (sipPair.R).*

Description

This function samples indices for permuting phenotype vectors in the basic permutation function (sip.R) and for permuting leftover unpaired individuals in the paired-permutation function (sipPair.R).

Usage

```
get_permIdx(df, seed = seed)
```

Arguments

`df`	Data frame
`seed`	Number

Value

Numeric vector

`get_permute` *This function subsets the sample-by-variable data frame to the permutable data. This subset should include phenotypes and phenotypic covariates.*

Description

This function subsets the sample-by-variable data frame to the permutable data. This subset should include phenotypes and phenotypic covariates.

Usage

```
get_permute(df, id.var = id.var, pheno.vars = pheno.vars)
```

Arguments

`df`	Data frame
`id.var`	String
`pheno.vars`	Character vector

Value

Data frame

`get_relCat` *This function infers relatedness categories in the paired-permutation function (sip_pair.R) prior to permutation.*

Description

This function infers relatedness categories in the paired-permutation function (sip_pair.R) prior to permutation.

Usage

```
get_relCat(pairs, rid.vars = rid.vars, ibd.var = ibd.var)
```

Arguments

`pairs`	Data frame
`rid.vars`	Character vector
`ibd.var`	String

Value

List of data frames

`get_relPairs` *This function pairs individuals in the paired-permutation function (sip_pair.R) into the most highly-related pairs possible.*

Description

This function pairs individuals in the paired-permutation function (sip_pair.R) into the most highly-related pairs possible.

Usage

```
get_relPairs(
  df,
  id.var = id.var,
  rel.df = rel.df,
  rid.vars = rid.vars,
  ibd.var = ibd.var
)
```

Arguments

`df`, `rel.df`	Data frames
`id.var`, `ibd.var`	Strings
`rid.vars`	Character vector

Value

Data frame

`get_sexDF` *This function divides the sample-by-variable data frame into males and females prior to permutation within sexes.*

Description

This function divides the sample-by-variable data frame into males and females prior to permutation within sexes.

Usage

```
get_sexDF(df = df, sex.var = sex.var, sex.val = sex.val)
```

Arguments

df	Data frame
sex.var	String
sex.val	String or integer

Value

Data frame

`get_singSamp` *This function checks for uneven numbers of individuals within relatedness category and creates a data set for permuting single samples that will not be pair permuted (sip_pair.R).*

Description

This function checks for uneven numbers of individuals within relatedness category and creates a data set for permuting single samples that will not be pair permuted (sip_pair.R).

Usage

```
get_singSamp(df, deglst, id.var = id.var)
```

Arguments

df	Data frame
deglst	List of data frames
id.var	String

Value

Data frame

`order_permDF` *This function reorders the permuted sample-by-variable data frame to match the ID order of the primary sample-by-variable data frame.*

Description

This function reorders the permuted sample-by-variable data frame to match the ID order of the primary sample-by-variable data frame.

Usage

```
order_permDF(df = df, perm = perm, id.var = id.var)
```

Arguments

`df`, `perm`	Data frames
`id.var`	String

Value

Data frame

`phenotype_IBD_correlation` *Phenotype-IBD correlation*

Description

This function first calculates the correlation between phenotypes for sample pairs. Then it calculates the correlation between the phenotype correlation and identity-by-descent for the sample pairs. (N.B., Please omit missing values before running this function.)

Usage

```
phenotype_IBD_correlation(
  df = NULL,
  rel.df = NULL,
  id.var = NULL,
  rid.vars = NULL,
  ibd.var = NULL,
  pheno.vars = NULL
)
```

Arguments

df, rel.df	Data frame
id.var, ibd.var	Strings
pheno.vars, rid.vars	Character vectors

Details

The function requires the following inputs:

1) A sample-by-variable data frame with sample ID and phenotypes. Columns should include an individual ID variable and phenotype names.

2) A string identifying the ID variable name (e.g., id.var="ID").

3) A vector of phenotype names. (e.g., pheno.vars=c("PHENO1","PHENO2",...)).

4) A relatedness data frame containing identity-by-descent (IBD) for pairs of individuals in the sample-by-variable data frame Column names should include two ID variables and an IBD variable.

5) A vector of the 2 ID variable names in the relatedness data frame. (e.g., rid.vars=c("ID1","ID2")).

6) A string identifying the IBD variable name (e.g., ibd.var="PropIBD").

Value

Correlation

Examples

```
phenotype_IBD_correlation(df = sipPair_exampleData,
rel.df = sipPair_relatednessData, id.var = "IID",
rid.vars = c("IID1","IID2"), ibd.var = "PropIBD",
pheno.vars = paste0("PHENO",1:300))

phenotype_IBD_correlation(df = sipPair_exampleData[
sipPair_exampleData$IID %in% unlist(sipPair_relatednessData[1:100,c("IID1",
"IID2")]),], rel.df = sipPair_relatednessData[1:100,], id.var = "IID",
rid.vars = c("IID1","IID2"), ibd.var = "PropIBD",
pheno.vars = paste0("PHENO",1:300))
```

---

plot_phenotype_correlations

Phenotype correlation plot

Description

This function returns a plot showing correlation between phenotypes. (N.B., please omit missing values before running this function.)

Usage

```
plot_phenotype_correlations(df = NULL, pheno.vars = NULL)
```

Arguments

df	Data frame
pheno.vars	Character vector

Details

The function requires the following inputs:

1) A sample-by-variable data frame with phenotypes. Column names should include phenotype names.

2) A vector of phenotype names. (e.g., pheno.vars=c("PHENO1","PHENO2",...)).

Value

Plot

Examples

```
plot_phenotype_correlations(df = sip_exampleData,
pheno.vars = paste0("PHENO",1:500))
```

---

sip *Single-iteration permutation for large-scale biobank data*

Description

This function performs the basic permutation for permuting phenotype vectors in biobank data.

Usage

```
sip(
  df = NULL,
  id.var = NULL,
  sex.var = NULL,
  male.val = NULL,
  female.val = NULL,
  geno.vars = NULL,
  within.sex = TRUE,
  seed = NULL
)
```

Arguments

`df`	Data frame
`id.var`, `sex.var`	Strings
`male.val`, `female.val`	Strings or integers
`geno.vars`	Character vectors
`within.sex`	Boolean, defaults to TRUE
`seed`	Number

Details

The function requires the following inputs:

1) A sample-by-variable dataframe with phenotypes and covariates. Column names should include an ID variable, sex variable, genotypic covariate names, phenotypic covariate names, and phenotype names. (N.B. a secondary ID variable can be included in the genotypic covariate names.)

2) A string identifying the ID variable name (e.g., id.var="ID").

3) A vector of genotypic covariates (e.g., geno.vars=c("ID2","Batch","PC1","PC2",...)).

4) Optional: within.sex = FALSE. Default is within.sex = TRUE and will permute males and females separately.

5) If within.sex = TRUE (the default), a string identifying the sex variable name (e.g., sex.var="Inferred_Sex").

6) If within.sex = TRUE (the default), male and female values in the sex vector (e.g., male.val=1, female.val=2).

7) Optional: a seed for sampling. If a seed is not provided, one will be chosen randomly during the sampling process (e.g., seed=123).

8) N.B. Any column names not specified in (2)-(6) are assumed to be phenotypes or phenotypic covariates.

Value

Data frame

Examples

```
sip(df = sip_exampleData, id.var = "IID", sex.var = "SEX", male.val = 1,
female.val = 2, geno.vars = c("FID","ANCESTRY","BATCH",paste0("PC",1:4)))
```

`sipPair_exampleData` *Single-iteration paired permutation phenotype and covariate data*

Description

A sample-by-variable data frame with IDs, covariates, and phenotypes as column names.

Usage

```
sipPair_exampleData
```

Format

A data frame with 10,000 rows and 309 variables:

FID Family ID.

IID Individual ID.

BATCH Genotyping batch.

SEX Sample biological sex.

AGE Sample age.

PC1 Genetic principal component 1.

PC2 Genetic principal component 2.

PC3 Genetic principal component 3.

PC4 Genetic principal component 4.

PHENO1 Simulated phenotype 1.

PHENO2 Simulated phenotype 2.

PHENO3 Simulated phenotype 3.

PHENO4 Simulated phenotype 4.

PHENO5 Simulated phenotype 5.

PHENO6 Simulated phenotype 6.

PHENO7 Simulated phenotype 7.

PHENO8 Simulated phenotype 8.

PHENO9 Simulated phenotype 9.

PHENO10 Simulated phenotype 10.

PHENO11 Simulated phenotype 11.

PHENO12 Simulated phenotype 12.

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PHENO300 Simulated phenotype 300.

Source

<https://doi.org/10.21203/rs.3.rs-873449/v1>

sipPair_relatednessData *Single-iteration paired permutation relatedness data*

Description

A sample-by-variable data frame with IDs and identity-by-descent data between samples.

Usage

```
sipPair_relatednessData
```

Format

A data frame with 9886 rows and 4 variables:

IID1 Individual ID for one sample.

IID2 Iindividual ID for a second sample.

PropIBD Identity-by-descent proportion of genome shared between the two samples.

Source

<https://doi.org/10.21203/rs.3.rs-873449/v1>

sip_exampleData *Single-iteration permutation phenotype and covariate data*

Description

A sample-by-variable data frame with IDs, covariates, and phenotypes as column names.

Usage

```
sip_exampleData
```

Format

A data frame with 10,000 rows and 511 variables:

FID Family ID.

IID Individual ID.

ANCESTRY Sample ancestry.

SEX Sample biological sex.

AGE Sample age.

BATCH Genotyping batch.

STUDY Study contributing sample data.

PC1 Genetic principal component 1.

PC2 Genetic principal component 2.

PC3 Genetic principal component 3.

PC4 Genetic principal component 4.

PHENO1 Simulated phenotype 1.

PHENO2 Simulated phenotype 2.

PHENO3 Simulated phenotype 3.

PHENO4 Simulated phenotype 4.

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Source

<https://doi.org/10.21203/rs.3.rs-873449/v1>

`sip_pair` *Single-iteration paired permutation for large-scale biobank data with relatedness*

Description

This function performs paired permutation for permuting phenotype vectors among related individuals in biobank data.

Usage

```
sip_pair(
  df = NULL,
  id.var = NULL,
  sex.var = NULL,
  male.val = NULL,
  female.val = NULL,
  geno.vars = NULL,
  within.sex = TRUE,
  seed = NULL,
  rel.df = NULL,
  rid.vars = NULL,
  ibd.var = NULL
)
```

Arguments

`df`, `rel.df`	Data frame
`id.var`, `sex.var`, `ibd.var`	Strings
`male.val`, `female.val`	Strings or integers
`geno.vars`, `rid.vars`	Character vectors
`within.sex`	Boolean, defaults to TRUE
`seed`	Number

Details

The function requires the following inputs:

1) A sample-by-variable data frame with phenotypes and covariates. Column names should include an ID variable, sex variable, genotypic covariate names, phenotypic covariate names, and phenotype names. (N.B. a secondary ID variable can be included in the genotypic covariate names.)

2) A string identifying the ID variable name (e.g., id.var="ID").

3) A vector of genotypic covariates (e.g., geno.vars=c("ID2","Batch","PC1","PC2",...)).

4) A relatedness data frame containing identity-by-descent (IBD) for pairs of individuals in the sample-by-variable data frame. Column names should include two ID variables and an IBD variable.

5) A vector of the 2 ID variable names in the relatedness data frame. (e.g., rid.vars=c("ID1","ID2")).

6) A string identifying the IBD variable name (e.g., ibd.var="PropIBD").

7) Optional: within.sex = FALSE. Default is within.sex = TRUE and will permute males and females separately.

8) If within.sex = TRUE (the default), a string identifying the sex variable name (e.g., sex.var="Inferred_Sex").

9) If within.sex = TRUE (the default), male and female values in the sex vector (e.g., male.val=1, female.val=2).

10) Optional: a seed for sampling. If a seed is not provided, one will be chosen randomly during the sampling process (e.g., seed=123).

11) N.B. Any column names not specified in (2)-(9) are assumed to be phenotypes or phenotypic covariates.

Value

Data frame

Examples

```
sip_pair(df = sipPair_exampleData, id.var = "IID",
sex.var = "SEX", male.val = "M", female.val = "F",
geno.vars = c("FID","BATCH",paste0("PC",1:4)),
rel.df = sipPair_relatednessData, rid.vars=c("IID1","IID2"),
ibd.var="PropIBD")
```

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