Package 'martini'

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Type Package

Title GWAS Incorporating Networks

Version 1.29.0

Description martini deals with the low power inherent to GWAS studies by using prior knowledge represented as a network. SNPs are the vertices of the network, and the edges represent biological relationships between them (genomic adjacency, belonging to the same gene, physical interaction between protein products). The network is scanned using SConES, which looks for groups of SNPs maximally associated with the phenotype, that form a close subnetwork.

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LazyData TRUE

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Contents

`arrange_covars` *Prepare covariates for* `scones`

Description

Prepares de covariates data.frame for the functions used in `scones`, like `single_snp_association` or `score_folds` .

Usage

```
arrange_covars(gwas, covars)
```

Arguments

`gwas`	A SnpMatrix object with the GWAS information.
`covars`	A data frame with the covariates. It must contain a column 'sample' containing the sample IDs, and an additional columns for each covariate.

Value

The covars data.frame, with the rows in the same order as gwas.

`calculateE` *Calculate the environmental component of the phenotype*

Description

Calculates the environmental component of the phenotype using the variance in the genetic component.

Usage

```
calculateE(G, h2)
```

Arguments

`G`	The genetic component of the phenotype.
`h2`	The heritability.

Value

A vector with the environmental component of each sample.

`calculateG` *Calculate the genetic component of the phenotype*

Description

Calculates the genetic component of the phenotype from a genotype.

Usage

```
calculateG(effectSize, X, model)
```

Arguments

`effectSize`	A vector with the effect size of each SNP.
`X`	Genotypes in a numeric matrix, where each row is a sample and each column a SNP.
`model`	Genetic model to assume.

Value

A vector with the genetic component of each sample.

`check_installed` *Check package is installed*

Description

Checks if a package is installed, launches an error if it is not.

Usage

```
check_installed(pkgs, fn = "This function")
```

Arguments

`pkgs`	Character vector with the names of the packages.
`fn`	Function calling the check.

Value

The package is loaded into the namespace.

Examples

```
martini:::check_installed(c("martini"))
## Not run: martini:::check_installed("martinid")
```

`connect_biomart` *Open a biomaRt connection*

Description

Opens a biomaRt connection for the relevant species.

Usage

```
connect_biomart(organism)
```

Arguments

`organism`	String containing the ensembl species name (e.g. hsapiens for human)

`get_adjacency` *Compute Laplacian matrix*

Description

Compute Laplacian matrix

Usage

```
get_adjacency(gwas, net)
```

Arguments

`gwas`	A SnpMatrix object with the GWAS information.
`net`	An igraph network that connects the SNPs.

Value

A Laplacian matrix.

`get_GI_network` *Get gene-interaction network.*

Description

Creates a network of SNPs where each SNP is connected as in the GM network and, in addition, to all the other SNPs pertaining to any interactor of the gene it is mapped to. Corresponds to the gene-interaction (GI) network described by Azencott et al.

Usage

```
get_GI_network(
  gwas,
  organism = 9606,
  snpMapping = snp2ensembl(gwas, organism),
  ppi = get_gxg("biogrid", organism, flush),
  col_ppi = c("gene1", "gene2"),
  col_genes = c("snp", "gene"),
  flush = FALSE
)
```

Arguments

`gwas`	A SnpMatrix object with the GWAS information.
`organism`	Tax ID of the studied organism. The default is 9606 (human).
`snpMapping`	A data.frame informing how SNPs map to genes. It contains minimum two columns: SNP id and a gene it maps to. Each row corresponds to one gene-SNP mapping. Unless column names are specified using `col_genes`, involved columns must be named `'snp'` and `'gene'`.
`ppi`	A data.frame describing protein-protein interactions with at least two colums. Gene ids must be the contained in snpMapping. Unless column names are specified using `col_ppi`, involved columns must be named `gene1` and `gene2`.
`col_ppi`	Optional, length-2 character vector with the names of the two columns involving the protein-protein interactions.
`col_genes`	Optional, length-2 character vector with the names of the two columns involving the SNP-gene mapping. The first element is the column of the SNP, and the second is the column of the gene.
`flush`	Remove cached results? Boolean value.

Value

An igraph network of the GI network of the SNPs.

References

Azencott, C. A., Grimm, D., Sugiyama, M., Kawahara, Y., & Borgwardt, K. M. (2013). Efficient network-guided multi-locus association mapping with graph cuts. Bioinformatics, 29(13), 171-179. `https://doi.org/10.1093/bioinformatics/btt238`

Examples

```
get_GI_network(minigwas, snpMapping = minisnpMapping, ppi = minippi)
```

`get_GM_network` *Get gene membership network.*

Description

Creates a network of SNPs where each SNP is connected as in the GS network and, in addition, to all the other SNPs pertaining to the same gene. Corresponds to the gene membership (GM) network described by Azencott et al.

Usage

```
get_GM_network(
  gwas,
  organism = 9606,
  snpMapping = snp2ensembl(gwas, organism),
  col_genes = c("snp", "gene")
)
```

Arguments

`gwas`	A SnpMatrix object with the GWAS information.
`organism`	Tax ID of the studied organism. The default is 9606 (human).
`snpMapping`	A data.frame informing how SNPs map to genes. It contains minimum two columns: SNP id and a gene it maps to. Each row corresponds to one gene-SNP mapping. Unless column names are specified using `col_genes`, involved columns must be named `'snp'` and `'gene'`.
`col_genes`	Optional, length-2 character vector with the names of the two columns involving the SNP-gene mapping. The first element is the column of the SNP, and the second is the column of the gene.

Value

An igraph network of the GM network of the SNPs.

References

Azencott, C. A., Grimm, D., Sugiyama, M., Kawahara, Y., & Borgwardt, K. M. (2013). Efficient network-guided multi-locus association mapping with graph cuts. Bioinformatics, 29(13), 171-179. `https://doi.org/10.1093/bioinformatics/btt238`

Examples

```
get_GM_network(minigwas, snpMapping = minisnpMapping)
```

`get_grid` *Parse* `scones.cv` *settings*

Description

Creates a list composed by all `scones.cv` settings, with the values provided by the user, or the default ones if none is provided.

Usage

```
get_grid(c = numeric(), etas = numeric(), lambdas = numeric())
```

Arguments

`c`	Numeric vector with the association scores of the SNPs. Specify it to automatically an appropriate range of etas and lambas.
`etas`	Numeric vector with the etas to explore in the grid search. If ommited, it's automatically created based on the association scores.
`lambdas`	Numeric vector with the lambdas to explore in the grid search. If ommited, it's automatically created based on the association scores.

Value

A list of `scones.cv` settings.

Examples

```
martini:::get_grid(etas = c(1,2,3), lambdas = c(4,5,6))
martini:::get_grid(c = c(1,10,100))
```

`get_GS_network` *Get genomic sequence network*

Description

Creates a network of SNPs where each SNP is connected to its adjacent SNPs in the genome sequence. Corresponds to the genomic sequence (GS) network described by Azencott et al.

Usage

```
get_GS_network(gwas)
```

Arguments

`gwas`	A SnpMatrix object with the GWAS information.

Value

An igraph network of the GS network of the SNPs.

References

Azencott, C. A., Grimm, D., Sugiyama, M., Kawahara, Y., & Borgwardt, K. M. (2013). Efficient network-guided multi-locus association mapping with graph cuts. Bioinformatics, 29(13), 171-179. https://doi.org/10.1093/bioinformatics/btt238

Examples

```
get_GS_network(minigwas)
```

`get_gxg` *Get gene interactions*

Description

Wrapper for the different functions to get gene-gene interactions. Supports cached results.

Usage

```
get_gxg(db, organism, flush)
```

Arguments

`db`	String containing the database to obtain the gene-gene interactions from. Possible values: 'biogrid', 'string'.
`organism`	Tax ID of the studied organism. The default is 9606 (human).
`flush`	Remove cached results? Boolean value.

Value

A data.frame with two columns with pairs of interacting proteins.

`get_gxg_biogrid` *Get BioGRID protein-protein interactions.*

Description

Get all protein-protein interactions for an organism from BioGRID.

Usage

```
get_gxg_biogrid(organism = 9606)
```

Arguments

`organism`	Tax ID of the studied organism. The default is 9606 (human).

Value

A data.frame with two columns with pairs of interacting proteins.

Examples

```
# download dog interactions
## Not run: martini:::get_gxg_biogrid(9615)
```

`get_gxg_string` *Get STRING protein-protein interactions.*

Description

Get all protein-protein interactions for an organism from STRING. It uses a score cut-off of 400.

Usage

```
get_gxg_string(organism = 9606)
```

Arguments

`organism`	Tax ID of the studied organism. The default is 9606 (human).

Value

A data.frame with two columns with pairs of interacting proteins.

Examples

```
# download frog interactions
## Not run: martini:::get_gxg_string(8364)
```

`get_snp_modules` *Return groups of interconnected SNPs.*

Description

Find modules composed by interconnected SNPs.

Usage

```
get_snp_modules(gwas, net)
```

Arguments

`gwas`	A SnpMatrix object with the GWAS information.
`net`	An igraph network that connects the SNPs.

Value

A list with the modules of selected SNPs.

Examples

```
## Not run:
gi <- get_GI_network(minigwas, snpMapping = minisnpMapping, ppi = minippi)
cones <- search_cones(minigwas, gi)
martini:::get_snp_modules(cones, gi)

## End(Not run)
```

`group_snps` *Groups nearby SNPs*

Description

Groups SNPs closer than a specifiec threshold of distance.

Usage

```
group_snps(bed, chr_col, pos_col, threshold)
```

Arguments

`bed`	data.frame containing at least two properties (chromosome and position) of a set of SNPs.
`chr_col`	Name of the column containing the SNP chromosome.
`pos_col`	Name of the column containing the SNP position.
`threshold`	Maximum distance to group two SNPs group.

Value

A data.frame in bed format, with the same dimensions as the original, but with the groups.

`gwas2bed` *Converts a MAP data.frame to a BED data.frame*

Description

Takes a map file and:

- column 1: Used as the chromosome column in the BED file.
- column 4: Used as start and end in the BED data.frame (as we work with SNPs).

Usage

```
gwas2bed(gwas)
```

Arguments

`gwas`	A SnpMatrix object with the GWAS information.

Value

A BED data.frame.

`is_coherent` *Check inner coherence of GWAS dataset*

Description

Checks that the different data structures have the SNPs in the same order.

Usage

```
is_coherent(gwas)
```

Arguments

`gwas`	A SnpMatrix object with the GWAS information.

Value

TRUE if the GWAS dataset is coherent. Else, raises an error.

Examples

```
martini:::is_coherent(minigwas)
```

`ldweight_edges` *Include linkage disequilibrium information in the network.*

Description

Include linkage disequilibrium information in the SNP network. The weight of the edges will be lower the higher the linkage is.

Usage

```
ldweight_edges(net, ld, method = "inverse")
```

Arguments

`net`	A SNP network.
`ld`	A `dsCMatrix` or `dgCMatrix` containing linkage disequilibrium measures, like the output of `ld`.
`method`	How to incorporate linkage-disequilibrium values into the network.

Value

An copy of net where the edges weighted according to linkage disequilibrium.

Examples

```
ld <- snpStats::ld(minigwas[['genotypes']], depth = 2, stats = "R.squared")
# don't weight edges for which LD cannot be calculated
ld[is.na(ld)] <- 0
gi <- get_GI_network(minigwas, snpMapping = minisnpMapping, ppi = minippi)
ldGi <- ldweight_edges(gi, ld)
```

`maxflow` *Maxflow algorithm*

Description

Run the maxflow algorithm.

Usage

```
maxflow(A, As, At)
```

Arguments

`A`	A sparse matrix with the connectivity.
`As`	A vector containing the edges to the source.
`At`	A vector containing the edges to the sink.

Value

A list with vector indicating if the feature was selected and the objective score.

`mget_gxg_biogrid` *Memoised version of get_gxg_biogrid*

Description

Get all protein-protein interactions for an organism from BioGRID.

Usage

```
mget_gxg_biogrid(organism = 9606)
```

Arguments

`organism`	Tax ID of the studied organism. The default is 9606 (human).

Value

A data.frame with two columns with pairs of interacting proteins.

Examples

```
# download dog interactions
## Not run: martini:::get_gxg_biogrid(9615)
```

`mget_gxg_string` *Memoised version of get_gxg_stringdb*

Description

Get all protein-protein interactions for an organism from STRING. It uses a score cut-off of 400.

Usage

```
mget_gxg_string(organism = 9606)
```

Arguments

`organism`	Tax ID of the studied organism. The default is 9606 (human).

Value

A data.frame with two columns with pairs of interacting proteins.

Examples

```
# download frog interactions
## Not run: martini:::get_gxg_string(8364)
```

`mincut` *Run min-cut algorithm*

Description

Run min-cut algorithm

Usage

```
mincut(gwas, net, covars, eta, lambda, score, sigmod, family, link)
```

Value

A copy of the `SnpMatrix$map` `data.frame`, with the following additions:

- c: contains the univariate association score for every single SNP.
- selected: logical vector indicating if the SNP was selected by SConES or not.
- module: integer with the number of the module the SNP belongs to.

`mincut.cv` *Run the cross-validated min-cut algorithm*

Description

Run the cross-validated min-cut algorithm

Usage

```
mincut.cv(
  gwas,
  net,
  covars,
  etas,
  lambdas,
  criterion,
  score,
  sigmod,
  family,
  link,
  max_prop_snp
)
```

Arguments

`gwas`	A SnpMatrix object with the GWAS information.
`net`	An igraph network that connects the SNPs.
`covars`	A data frame with the covariates. It must contain a column 'sample' containing the sample IDs, and an additional columns for each covariate.
`family`	A string defining the generalized linear model family. This should match one of "binomial", "poisson", "gaussian" or "gamma". See snp.rhs.tests for details.
`link`	A string defining the link function for the GLM. This should match one of "logit", "log", "identity" or "inverse". See snp.rhs.tests for details.

`mincut_c` *Min-cut algorithm*

Description

Run the mincut algorithm.

Usage

```
mincut_c(c, eta, lambda, W)
```

Arguments

`c`	A vector with the association of each SNP with the phenotype.
`eta`	A numeric with the value of the eta parameter.
`lambda`	A numeric with the value of the eta parameter.
`W`	A sparse matrix with the connectivity.

Value

A list with vector indicating if the feature was selected and the objective score.

`minigwas` *Description of the minigwas dataset.*

Description

Small GWAS example.

Format

A list with 3 items:

genotypes Genotype and phenotype information.

fam Simulated network.

map Result of runing `find_cones` with gwas and net.

Examples

```
data(minigwas)

# access different elements
minigwas[["genotypes"]]
minigwas[["map"]]
minigwas[["fam"]]
```

`minippi` *PPIs for the minigwas dataset.*

Description

data.frame describing pairs of proteins that interact for minigwas.

Examples

```
data(minippi)

head(minippi)
```

`minisnpMapping` *Genes for the minigwas dataset.*

Description

data.frame that maps SNPs from minigwas to their gene.

Examples

```
data(minisnpMapping)

head(minisnpMapping)
```

`organism_id2name` *Tax id to ensembl species name*

Description

Converts taxid to ensembl species name e.g. human databases are hsapiens_*

Usage

```
organism_id2name(id)
```

Arguments

`organism`	Tax ID of the studied organism. The default is 9606 (human).

`permute_snpMatrix` *Permute samples*

Description

Compute a permutation of the samples of a snpMatrix object. Useful to make sure that the folds are not stratified by phenotype.

Usage

```
permute_snpMatrix(gwas)
```

Arguments

`gwas`	A SnpMatrix object with the GWAS information.

`plot_ideogram` *Ideogram of SConES results.*

Description

Create a circular ideogram of the a network results using the circlize package (Gu et al., 2014).

Usage

```
plot_ideogram(gwas, net, covars = data.frame(), genome = "hg19")
```

Arguments

`gwas`	A SnpMatrix object with the GWAS information.
`net`	An igraph network that connects the SNPs.
`covars`	A data frame with the covariates. It must contain a column 'sample' containing the sample IDs, and an additional columns for each covariate.
`genome`	Abbreviations of the genome to use: hg19 for human (default), mm10 for mouse, etc.

Value

A circular ideogram, including the manhattan plot, and the interactions between the selected SNPs.

References

Gu, Z., Gu, L., Eils, R., Schlesner, M., & Brors, B. (2014). circlize Implements and enhances circular visualization in R. Bioinformatics (Oxford, England), 30(19), 2811-2. `https://doi.org/10.1093/bioinformatics/btu393`

`sanitize_map` *Check map*

Description

Check that map is a proper data.frame.

Usage

```
sanitize_map(gwas)
```

Arguments

`gwas`	A SnpMatrix object with the GWAS information.

`sanitize_snpMapping` *Check snpMapping*

Description

Check that snpMapping is a proper data.frame.

Usage

```
sanitize_snpMapping(snpMapping, col_genes)
```

Arguments

`snpMapping`	data.frame containing the correspondence between SNPs and genes.
`col_genes`	Length 2 character vector containing the colnames containing the SNP and the gene ids, respectively.

`scones` *Find connected explanatory SNPs*

Description

Finds the SNPs maximally associated with a phenotype while being connected in an underlying network.

Usage

```
scones(
  gwas,
  net,
  eta,
  lambda,
  covars = data.frame(),
  score = c("chi2", "glm", "r2"),
  family = c("binomial", "poisson", "gaussian", "gamma"),
  link = c("logit", "log", "identity", "inverse")
)
```

Arguments

`gwas`	A SnpMatrix object with the GWAS information.
`net`	An igraph network that connects the SNPs.
`eta`	Value of the eta parameter.
`lambda`	Value of the lambda parameter.
`covars`	A data frame with the covariates. It must contain a column 'sample' containing the sample IDs, and an additional columns for each covariate.
`score`	Association score to measure association between genotype and phenotype. Possible values: chi2 (default), glm.

`family`	A string defining the generalized linear model family. This should match one of "binomial", "poisson", "gaussian" or "gamma". See snp.rhs.tests for details.
`link`	A string defining the link function for the GLM. This should match one of "logit", "log", "identity" or "inverse". See snp.rhs.tests for details.

Value

A copy of the `SnpMatrix$map` `data.frame`, with the following additions:

- c: contains the univariate association score for every single SNP.
- selected: logical vector indicating if the SNP was selected by SConES or not.
- module: integer with the number of the module the SNP belongs to.

References

Azencott, C. A., Grimm, D., Sugiyama, M., Kawahara, Y., & Borgwardt, K. M. (2013). Efficient network-guided multi-locus association mapping with graph cuts. Bioinformatics, 29(13), 171-179. `https://doi.org/10.1093/bioinformatics/btt238`

Examples

```
gi <- get_GI_network(minigwas, snpMapping = minisnpMapping, ppi = minippi)
scones(minigwas, gi, 10, 1)
```

`scones.cv` *Find connected explanatory SNPs.*

Description

Finds the SNPs maximally associated with a phenotype while being connected in an underlying network. Select the hyperparameters by cross-validation.

Usage

```
scones.cv(
  gwas,
  net,
  covars = data.frame(),
  score = c("chi2", "glm", "r2"),
  criterion = c("stability", "bic", "aic", "aicc", "global_clustering",
    "local_clustering"),
  etas = numeric(),
  lambdas = numeric(),
  family = c("binomial", "poisson", "gaussian", "gamma"),
  link = c("logit", "log", "identity", "inverse"),
  max_prop_snp = 0.5
)
```

Arguments

`gwas`	A SnpMatrix object with the GWAS information.
`net`	An igraph network that connects the SNPs.
`covars`	A data frame with the covariates. It must contain a column 'sample' containing the sample IDs, and an additional columns for each covariate.
`score`	Association score to measure association between genotype and phenotype. Possible values: chi2 (default), glm.
`criterion`	String with the function to measure the quality of a split.
`etas`	Numeric vector with the etas to explore in the grid search. If ommited, it's automatically created based on the association scores.
`lambdas`	Numeric vector with the lambdas to explore in the grid search. If ommited, it's automatically created based on the association scores.
`family`	A string defining the generalized linear model family. This should match one of "binomial", "poisson", "gaussian" or "gamma". See snp.rhs.tests for details.
`link`	A string defining the link function for the GLM. This should match one of "logit", "log", "identity" or "inverse". See snp.rhs.tests for details.
`max_prop_snp`	Maximum proportion of SNPs accepted in the model (between 0 and 1). Larger solutions will be discarded.

Value

A copy of the `SnpMatrix$map` `data.frame`, with the following additions:

- c: contains the univariate association score for every single SNP.
- selected: logical vector indicating if the SNP was selected by SConES or not.
- module: integer with the number of the module the SNP belongs to.

References

Azencott, C. A., Grimm, D., Sugiyama, M., Kawahara, Y., & Borgwardt, K. M. (2013). Efficient network-guided multi-locus association mapping with graph cuts. Bioinformatics, 29(13), 171-179. `https://doi.org/10.1093/bioinformatics/btt238`

Examples

```
gi <- get_GI_network(minigwas, snpMapping = minisnpMapping, ppi = minippi)
scones.cv(minigwas, gi)
scones.cv(minigwas, gi, score = "glm")
```

`scones.cv_` *Find connected explanatory features*

Description

Finds the features maximally associated with a phenotype while being connected in an underlying network. Select the hyperparameters by cross-validation.

Usage

```
scones.cv_(X, y, featnames, net)
```

Arguments

`X`	n x d design matrix
`y`	Vector of length n with the outcomes
`featnames`	Vector of length d with the feature names
`net`	An igraph network that connects the SNPs.

Value

A copy of the `SnpMatrix$map` `data.frame`, with the following additions:

- c: contains the univariate association score for every single SNP.
- selected: logical vector indicating if the SNP was selected by SConES or not.
- module: integer with the number of the module the SNP belongs to.

Examples

```
X <- as(minigwas[['genotypes']], 'numeric')
X <- X + matrix(rnorm(2500, sd = 0.1), nrow(X), ncol(X))
gi <- get_GI_network(minigwas, snpMapping = minisnpMapping, ppi = minippi)
scones.cv_(X, minigwas[['fam']]$affected, minigwas[['map']]$snp, gi)
```

`scones_` *Find connected explanatory features*

Description

Finds the features maximally associated with a phenotype while being connected in an underlying network.

Usage

```
scones_(X, y, featnames, net, eta, lambda)
```

Arguments

`X`	n x d design matrix
`y`	Vector of length n with the outcomes
`featnames`	Vector of length d with the feature names
`net`	An igraph network that connects the SNPs.
`eta`	Value of the eta parameter.
`lambda`	Value of the lambda parameter.

Value

A copy of the `SnpMatrix$map` `data.frame`, with the following additions:

- c: contains the univariate association score for every single SNP.
- selected: logical vector indicating if the SNP was selected by SConES or not.
- module: integer with the number of the module the SNP belongs to.

Examples

```
X <- as(minigwas[['genotypes']], 'numeric')
X <- X + matrix(rnorm(2500, sd = 0.1), nrow(X), ncol(X))
gi <- get_GI_network(minigwas, snpMapping = minisnpMapping, ppi = minippi)
scones_(X, minigwas[['fam']]$affected, minigwas[['map']]$snp, gi, 10, 1)
```

`score_fold` *Score the solutions of a k-fold*

Description

Take the k-solutions for a combination of hyperparameters, and assign a score to it (the larger, the better).

Usage

```
score_fold(gwas, covars, net, selected, criterion, max_prop_snp)
```

Arguments

`gwas`	A SnpMatrix object with the GWAS information.
`covars`	A data frame with the covariates. It must contain a column 'sample' containing the sample IDs, and an additional columns for each covariate.
`net`	An igraph network that connects the SNPs.
`criterion`	String with the function to measure the quality of a split.
`max_prop_snp`	Maximum proportion of SNPs accepted in the model (between 0 and 1). Larger solutions will be discarded.

`search_cones` *Find connected explanatory SNPs.*

Description

Finds the SNPs maximally associated with a phenotype while being connected in an underlying network (Azencott et al., 2013).

Usage

```
search_cones(
  gwas,
  net,
  encoding = "additive",
  sigmod = FALSE,
  covars = data.frame(),
  associationScore = c("chi2", "glm"),
  modelScore = c("stability", "bic", "aic", "aicc", "global_clustering",
    "local_clustering"),
  etas = numeric(),
  lambdas = numeric()
)
```

Arguments

`gwas`	A SnpMatrix object with the GWAS information.
`net`	An igraph network that connects the SNPs.
`encoding`	SNP encoding (unused argument).
`sigmod`	Boolean. If TRUE, use the Sigmod variant of SConES, meant to prioritize tightly connected clusters of SNPs.
`covars`	A data frame with the covariates. It must contain a column 'sample' containing the sample IDs, and an additional columns for each covariate.
`associationScore`	Association score to measure association between genotype and phenotype.
`modelScore`	String with the function to measure the quality of a split.
`etas`	Numeric vector with the etas to explore in the grid search. If ommited, it's automatically created based on the association scores.
`lambdas`	Numeric vector with the lambdas to explore in the grid search. If ommited, it's automatically created based on the association scores.

Value

A copy of the `SnpMatrix$map` `data.frame`, with the following additions:

- c: contains the univariate association score for every single SNP.
- selected: logical vector indicating if the SNP was selected by SConES or not.
- module: integer with the number of the module the SNP belongs to.

References

Azencott, C. A., Grimm, D., Sugiyama, M., Kawahara, Y., & Borgwardt, K. M. (2013). Efficient network-guided multi-locus association mapping with graph cuts. Bioinformatics, 29(13), 171-179. https://doi.org/10.1093/bioinformatics/btt238

Examples

```
## Not run: gi <- get_GI_network(minigwas, snpMapping = minisnpMapping, ppi = minippi)
search_cones(minigwas, gi)
search_cones(minigwas, gi, encoding = "recessive")
search_cones(minigwas, gi, associationScore = "skat")
## End(Not run)
```

`sigmod` *Find connected explanatory SNPs*

Description

Finds the SNPs maximally associated with a phenotype while being connected in an underlying network.

Usage

```
sigmod(
  gwas,
  net,
  eta,
  lambda,
  covars = data.frame(),
  score = c("chi2", "glm", "r2"),
  family = c("binomial", "poisson", "gaussian", "gamma"),
  link = c("logit", "log", "identity", "inverse")
)
```

Arguments

`gwas`	A SnpMatrix object with the GWAS information.
`net`	An igraph network that connects the SNPs.
`eta`	Value of the eta parameter.
`lambda`	Value of the lambda parameter.
`covars`	A data frame with the covariates. It must contain a column 'sample' containing the sample IDs, and an additional columns for each covariate.
`score`	Association score to measure association between genotype and phenotype. Possible values: chi2 (default), glm.
`family`	A string defining the generalized linear model family. This should match one of "binomial", "poisson", "gaussian" or "gamma". See snp.rhs.tests for details.
`link`	A string defining the link function for the GLM. This should match one of "logit", "log", "identity" or "inverse". See snp.rhs.tests for details.

Value

A copy of the `SnpMatrix$map` `data.frame`, with the following additions:

- c: contains the univariate association score for every single SNP.
- selected: logical vector indicating if the SNP was selected by SConES or not.
- module: integer with the number of the module the SNP belongs to.

References

Liu, Y., Brossard, M., Roqueiro, D., Margaritte-Jeannin, P., Sarnowski, C., Bouzigon, E., Demenais, F. (2017). SigMod: an exact and efficient method to identify a strongly interconnected disease-associated module in a gene network. Bioinformatics, 33(10), 1536–1544. `https://doi.org/10.1093/bioinformatics/btx004`

Examples

```
gi <- get_GI_network(minigwas, snpMapping = minisnpMapping, ppi = minippi)
sigmod(minigwas, gi, 10, 1)
```

`sigmod.cv` *Find connected explanatory SNPs.*

Description

Finds the SNPs maximally associated with a phenotype while being connected in an underlying network. Select the hyperparameters by cross-validation.

Usage

```
sigmod.cv(
  gwas,
  net,
  covars = data.frame(),
  score = c("chi2", "glm", "r2"),
  criterion = c("stability", "bic", "aic", "aicc", "global_clustering",
    "local_clustering"),
  etas = numeric(),
  lambdas = numeric(),
  family = c("binomial", "poisson", "gaussian", "gamma"),
  link = c("logit", "log", "identity", "inverse"),
  max_prop_snp = 0.5
)
```

Arguments

`gwas`	A SnpMatrix object with the GWAS information.
`net`	An igraph network that connects the SNPs.
`covars`	A data frame with the covariates. It must contain a column 'sample' containing the sample IDs, and an additional columns for each covariate.
`score`	Association score to measure association between genotype and phenotype. Possible values: chi2 (default), glm.
`criterion`	String with the function to measure the quality of a split.
`etas`	Numeric vector with the etas to explore in the grid search. If ommited, it's automatically created based on the association scores.
`lambdas`	Numeric vector with the lambdas to explore in the grid search. If ommited, it's automatically created based on the association scores.
`family`	A string defining the generalized linear model family. This should match one of "binomial", "poisson", "gaussian" or "gamma". See snp.rhs.tests for details.
`link`	A string defining the link function for the GLM. This should match one of "logit", "log", "identity" or "inverse". See snp.rhs.tests for details.
`max_prop_snp`	Maximum proportion of SNPs accepted in the model (between 0 and 1). Larger solutions will be discarded.

Value

A copy of the `SnpMatrix$map` `data.frame`, with the following additions:

- c: contains the univariate association score for every single SNP.
- selected: logical vector indicating if the SNP was selected by SConES or not.
- module: integer with the number of the module the SNP belongs to.

References

Liu, Y., Brossard, M., Roqueiro, D., Margaritte-Jeannin, P., Sarnowski, C., Bouzigon, E., Demenais, F. (2017). SigMod: an exact and efficient method to identify a strongly interconnected disease-associated module in a gene network. Bioinformatics, 33(10), 1536–1544. `https://doi.org/10.1093/bioinformatics/btx004`

Examples

```
gi <- get_GI_network(minigwas, snpMapping = minisnpMapping, ppi = minippi)
sigmod.cv(minigwas, gi)
sigmod.cv(minigwas, gi, score = "glm")
```

`sigmod.cv_` *Find connected explanatory features*

Description

Finds the features maximally associated with a phenotype while being connected in an underlying network. Select the hyperparameters by cross-validation.

Usage

```
sigmod.cv_(X, y, featnames, net)
```

Arguments

`X`	n x d design matrix
`y`	Vector of length n with the outcomes
`featnames`	Vector of length d with the feature names
`net`	An igraph network that connects the SNPs.

Value

A copy of the `SnpMatrix$map` `data.frame`, with the following additions:

- c: contains the univariate association score for every single SNP.
- selected: logical vector indicating if the SNP was selected by SConES or not.
- module: integer with the number of the module the SNP belongs to.

Examples

```
X <- as(minigwas[['genotypes']], 'numeric')
X <- X + matrix(rnorm(2500, sd = 0.1), nrow(X), ncol(X))
gi <- get_GI_network(minigwas, snpMapping = minisnpMapping, ppi = minippi)
sigmod.cv_(X, minigwas[['fam']]$affected, minigwas[['map']]$snp, gi)
```

`sigmod_` *Find connected explanatory features*

Description

Finds the features maximally associated with a phenotype while being connected in an underlying network.

Usage

```
sigmod_(X, y, featnames, net, eta, lambda)
```

Arguments

`X`	n x d design matrix
`y`	Vector of length n with the outcomes
`featnames`	Vector of length d with the feature names
`net`	An igraph network that connects the SNPs.
`eta`	Value of the eta parameter.
`lambda`	Value of the lambda parameter.

Value

A copy of the `SnpMatrix$map` `data.frame`, with the following additions:

- c: contains the univariate association score for every single SNP.
- selected: logical vector indicating if the SNP was selected by SConES or not.
- module: integer with the number of the module the SNP belongs to.

Examples

```
X <- as(minigwas[['genotypes']], 'numeric')
X <- X + matrix(rnorm(2500, sd = 0.1), nrow(X), ncol(X))
gi <- get_GI_network(minigwas, snpMapping = minisnpMapping, ppi = minippi)
sigmod_(X, minigwas[['fam']]$affected, minigwas[['map']]$snp, gi, 10, 1)
```

`simulate_causal_snps` *Simulate causal SNPs*

Description

Selects randomly interconnected genes as causal, then selects a proportion of them as causal.

Usage

```
simulate_causal_snps(net, ngenes = 20, pcausal = 1)
```

Arguments

`net`	An igraph gene-interaction (GI) network that connects the SNPs.
`ngenes`	Number of causal genes.
`pcausal`	Number between 0 and 1, proportion of the SNPs in causal genes that are causal themselves.

Value

A vector with the ids of the simulated causal SNPs.

Examples

```
gi <- get_GI_network(minigwas, snpMapping = minisnpMapping, ppi = minippi)
simulate_causal_snps(gi, ngenes=2)
```

`simulate_phenotype` *Simulate phenotype*

Description

Simulates a phenotype from a GWAS experiment and a specified set of causal SNPs. If the data is qualitative, only controls are used.

Usage

```
simulate_phenotype(
  gwas,
  snps,
  h2,
  model = "additive",
  effectSize = rnorm(length(snps)),
  qualitative = FALSE,
  ncases,
  ncontrols,
  prevalence
)
```

Arguments

`gwas`	A SnpMatrix object with the GWAS information.
`snps`	Character vector with the SNP ids of the causal SNPs. Must match SNPs in gwas[["map"]][["snp.name"]].
`h2`	Heritability of the phenotype (between 0 and 1).
`model`	String specifying the genetic model under the phenotype. Accepted values: "additive".
`effectSize`	Numeric vector with the same lenght as the number of causal SNPs. It indicates the effect size of each of the SNPs; if absent, they are sampled fron a normal distribution.
`qualitative`	Bool indicating if the phenotype is qualitative or not (quantitative).

`ncases`	Integer specifying the number of cases to simulate in a qualitative phenotype. Required if qualitative = TRUE.
`ncontrols`	Integer specifying the number of controls to simulate in a qualitative phenotype. Required if qualitative = TRUE.
`prevalence`	Value between 0 and 1 specifying the population prevalence of the disease. Note that ncases cannot be greater than prevalence * number of samples. Required if qualitative = TRUE.

Value

A copy of the GWAS experiment with the new phenotypes in `gwas[["fam"]][["affected"]]`.

References

Inspired from GCTA simulation tool: http://cnsgenomics.com/software/gcta/Simu.html.

Examples

```
gi <- get_GI_network(minigwas, snpMapping = minisnpMapping, ppi = minippi)
causal <- simulate_causal_snps(gi, ngenes = 2)
simulate_phenotype(minigwas, causal, h2 = 1)
```

`snp2ensembl` *Map SNPs to Ensembl genes.*

Description

Maps SNPs from a GWAS experiment to genes.

Usage

```
snp2ensembl(gwas, organism = 9606, flank = 0)
```

Arguments

`gwas`	A SnpMatrix object with the GWAS information.
`organism`	Tax ID of the studied organism. The default is 9606 (human).
`flank`	A number with the flanking regions around genes to be considered part of the gene i.e. SNPs mapped to them will be considered mapped to the gene.

Value

A data.frame with two columns: one for the SNP and another for the gene it has been mapped to.

`snp_test` *Calculate genotype-phhenotype associations*

Description

Calculate the association between genotypes and a phenotype, adjusting by covariates.

Usage

```
snp_test(gwas, covars, score, family, link)
```

Arguments

`gwas`	A SnpMatrix object with the GWAS information.
`covars`	A data frame with the covariates. It must contain a column 'sample' containing the sample IDs, and an additional columns for each covariate.
`score`	Association score to measure association between genotype and phenotype. Possible values: chi2 (default), glm.
`family`	A string defining the generalized linear model family. This should match one of "binomial", "poisson", "gaussian" or "gamma". See snp.rhs.tests for details.
`link`	A string defining the link function for the GLM. This should match one of "logit", "log", "identity" or "inverse". See snp.rhs.tests for details.

Value

A named vector with the association scores.

`subnet` *Subgraph of vertices with an attribute*

Description

Returns a subgraph matching some condition.

Usage

```
subnet(net, attr, values, affirmative = TRUE)
```

Arguments

`net`	An igraph network.
`attr`	An attribute of the vertices.
`values`	Possible values of `attr`.
`affirmative`	Logical. States if a condition must be its affirmation (e.g. all nodes with gene name "X"), or its negation (all nodes not with gene name "X").

Value

A subgraph containing only the vertices with attribute equal to any of the values in `values`.

Examples

```
gi <- get_GI_network(minigwas, snpMapping = minisnpMapping, ppi = minippi)
martini:::subnet(gi, "gene", "A")
martini:::subnet(gi, "name", c("1A1", "1A3"))
```

`subset_snpMatrix` *Subsample snpMatrix*

Description

Compute a permutation of the samples of a snpMatrix object. Useful to make sure that the folds are not stratified by phenotype.

Usage

```
subset_snpMatrix(gwas, samples)
```

Arguments

`gwas`	A SnpMatrix object with the GWAS information.
`samples`	Vector (logical or numeric) containing the samples to select.

`subvert` *Vertices with an attribute*

Description

Returns the nodes matching some condition.

Usage

```
subvert(net, attr, values, affirmative = TRUE)
```

Arguments

`net`	An igraph network.
`attr`	An attribute of the vertices.
`values`	Possible values of `attr`
`affirmative`	Logical. States if a condition must be its affirmation (e.g. all nodes with gene name "X"), or its negation (all nodes not with gene name "X").

Value

The vertices with attribute equal to any of the values in `values`.

Examples

```
gi <- get_GI_network(minigwas, snpMapping = minisnpMapping, ppi = minippi)
martini:::subvert(gi, "gene", "A")
martini:::subvert(gi, "name", c("1A1", "1A3"))
```

`wrap_Xy` *Make pseudo SnpMatrix object*

Description

Wrap design matrix and outcome vector into a pseudo SnpMatrix object.

Usage

```
wrap_Xy(X, y, featnames, net)
```

Arguments

`X`	n x d design matrix
`y`	Vector of length n with the outcomes
`featnames`	Vector of length d with the feature names
`net`	An igraph network that connects the SNPs.

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