

Package ‘rolypoly’

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Type Package

Title Identifying Trait-Relevant Functional Annotations

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Description Using enrichment of genome-wide association summary statistics to identify trait-relevant cellular functional annotations.

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Imports data.table (>= 1.9.6), dplyr (>= 0.4.3), foreach (>= 1.4.3),
ggplot2 (>= 1.0.1), glmnet (>= 2.0-5), MASS (>= 7.3-45), Matrix
(>= 1.2-6), matrixcalc (>= 1.0-3),

LinkingTo

Suggests CompQuadForm (>= 1.4.1), knitr, testthat, rmarkdown

License GPL-3

VignetteBuilder knitr

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URL <https://github.com/dcalderon/rolypoly>

BugReports <https://github.com/dcalderon/rolypoly/issues>

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bootstrap_estimator *Bootstrap parameter estimates for confidence intervals.*

Description

Bootstrap parameter estimates for confidence intervals.

Usage

```
bootstrap_estimator(rolypoly, bootstrap_iters, run_light, run_parallel)
```

Arguments

<code>rolypoly</code>	rolypoly object
<code>bootstrap_iters</code>	number of bootstrap iterations to run
<code>run_light</code>	if we throw away bootstrap data
<code>run_parallel</code>	if we want to collect bootstrap data in parallel

Examples

```
## Not run: bootstrap_estimator(rolypoly)
```

```
calculate_annotation_block_heritability
```

Caclulate the contribution of block annotations to the heritability of a trait.

Description

A vector of indenpendent heritability contributions of block annotations is returned. Sum the vector to get total explained heritability and divide by sum to get proportion.

Usage

```
calculate_annotation_block_heritability(block_data, params)
```

Arguments

<code>block_data</code>	functional information of blocks
<code>params</code>	parameter fit

Examples

```
## Not run: calculate_annotation_block_heritability(block_data, params)
```

```
calculate_block_values
```

Caclulate predicted block values based on block information and model fit.

Description

From a model fit we can predict expected variance of a block based on information we have about the block. In the example of gene expression this would equate to predicting the importance of a gene based on its signature of expression.

Usage

```
calculate_block_values(block_data, params)
```

Arguments

block_data	block_data
params	parameter fit

Value

returns block values

Examples

```
## Not run: calculate_gene_values(block_data, params)
```

```
calculate_expected_block_values_given_ld
```

Caclulate predicted block values based on block information and model fit.

Description

From a model fit we can predict expected variance of a block based on information we have about the block. In the example of gene expression this would equate to predicting the importance of a gene based on its signature of expression.

Usage

```
calculate_expected_block_values_given_ld(rolypoly, block_values)
```

Arguments

rolypoly rolypoly object
 block_values estimated block values.

Examples

```
## Not run: calculate_expected_block_values_given_ld(rolypoly, block_values)
```

```
cv_regularized_parameter_estimator
      Perform regularization inference.
```

Description

Use CV to find appropriate values of lambda for either feature selection or for prediction.

Usage

```
cv_regularized_parameter_estimator(vectorized_rolypoly_data, n_folds = 10,
  ...)
```

Arguments

vectorized_rolypoly_data
 rolypoly data used for inference
 n_folds number of folds for cross validation
 ... other arguments to pass to cv.glmnet

Value

results from cross validation

Examples

```
## Not run: cv_regularized_parameter_estimator(vectorized_rolypoly_data)
```

```
data_io                         Functions for opening and organizing data.
```

Description

We must open block annotation data, gwas data, snp annotations, gene annotations. Here, you'll find functions that to this and organize these data into a rolypoly object.

inference	<i>Inference functions.</i>
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Description

Functions for inferring relevant annotations using the polyTest model.

main_wrapper	<i>Main wrapper functions.</i>
--------------	--------------------------------

Description

The main endpoint user functions.

make_ld_matrix	<i>Helper function to pull LD data from NCBI.</i>
----------------	---

Description

Given the path of a gwas file open it into a data.table object

Usage

```
make_ld_matrix(all_snps, ld_data)
```

Arguments

all_snps	The snps that were queried
ld_data	A returned LD matrix with SNP, Proxy, and RSquared columns

Value

an LD matrix where query snps will be the first columns in the correct order

Examples

```
## Not run: make_ld_matrix(all_snps, ld_data)
```

make_results_df	<i>Helper function to make a summary table of results from bootstrap data.</i>
-----------------	--

Description

Helper function to make a summary table of results from bootstrap data.

Usage

```
make_results_df(value_collection, annotations, model_estimates)
```

Arguments

value_collection	collection of bootstrapped value estimates
annotations	vector of annotation names
model_estimates	estimates for bias parameter estimates

Value

data frame with results summary

Examples

```
## Not run: make_results_df(value_collection)
```

parameter_estimator	<i>Find parameter estimates for the data.</i>
---------------------	---

Description

Find parameter estimates for the data.

Usage

```
parameter_estimator(vectorized_rolpoly_data)
```

Arguments

vectorized_rolpoly_data	rolpoly data that has been vectorized
-------------------------	---------------------------------------

Value

results of inference

Examples

```
## Not run: parameter_estimator(rolypoly)
```

```
plot_rolypoly_annotation_estimates
```

Visualize parameter estimates after running inference

Description

Visualize parameter estimates after running inference

Usage

```
plot_rolypoly_annotation_estimates(rolypoly)
```

Arguments

rolypoly a rolypoly object

Value

ggplot2 object

Examples

```
## Not run: plot_rolypoly_annotation_estimates(rolypoly)
```

```
plot_rolypoly_annotation_ranking
```

Rank annotations by p-value after running inference

Description

Rank annotations by p-value after running inference

Usage

```
plot_rolypoly_annotation_ranking(rolypoly)
```

Arguments

rolypoly a rolypoly object

Value

ggplot2 object

Examples

```
## Not run: plot_rolypoly_annotation_ranking(rolypoly)
```

regularized_inference *Inference functions that include regularization*

Description

Functions for inferring relevant annotations using the polyTest model.

robust_parameter_estimator
Find robust parameter estimates for the data.

Description

Find robust parameter estimates for the data.

Usage

```
robust_parameter_estimator(vectorized_rolypoly_data, outlier_threshold = 10)
```

Arguments

vectorized_rolypoly_data
vectorized rolypoly data

outlier_threshold
outlier threshold for robust inference

Examples

```
## Not run: parameter_estimator(rolypoly)
```

rolypoly *The rolypoly package for identifying annotations associated with complex traits.*

Description

The rolypoly package for identifying annotations associated with complex traits.

```
rolypoly_add_ld_corrected_gwas_block_scores
    Add LD corrected block scores to rolypoly.
```

Description

Add LD corrected block scores to rolypoly.

Usage

```
rolypoly_add_ld_corrected_gwas_block_scores(rolypoly, fast_calculation = T)
```

Arguments

```
rolypoly      rolypoly data
fast_calculation
                if F then LD deconvolution else quadratic form.
```

Value

rolypoly object with LD corrected gwas scores attached

Examples

```
## Not run: rolypoly_add_ld_corrected_gwas_block_scores(rolypoly)
```

```
rolypoly_link_blocks_and_gwas
    Link blocks and gwas
```

Description

Takes block information, potentially independent LD blocks or gene blocks, and gwas data and organizes the data for interenal processing

Usage

```
rolypoly_link_blocks_and_gwas(rolypoly, ld_folder, r2_threshold = 0.2,
    run_parallel = F)
```

Arguments

```
rolypoly      a rolypoly object
ld_folder     path to a folder with ld data
r2_threshold  LD threshold to look at data
run_parallel  check if user wants to run in parallel
```

Value

rolypoly object with data attached

Examples

```
## Not run: rolypoly_link_blocks_and_gwas(rolypoly, ld_folder, r2_threshold)
```

rolypoly_load_block_annotation

Load annotations for blocks of LD, in some cases this is a gene annotation with a window around a gene.

Description

Load annotations for blocks of LD, in some cases this is a gene annotation with a window around a gene.

Usage

```
rolypoly_load_block_annotation(rolypoly, block_annotation, genes = T)
```

Arguments

rolypoly	rolypoly data object
block_annotation	annotation information for block
genes	if these are genes

Value

rolypoly data with block annotations attached

Examples

```
## Not run: rolypoly_load_block_annotation(rolypoly, block_annotation)
```

rolypoly_load_block_data

Block annotations, usually gene model.

Description

Block annotations, usually gene model.

Usage

```
rolypoly_load_block_data(rolypoly, block_data)
```

Arguments

rolypoly	a rolypoly object
block_data	a data frame of block information, usually gene expression. Requires rownames that are identical to block labels loaded previously.

Value

a rolypoly object with block information loaded

Examples

```
## Not run: rolypoly_load_block_data(rolypoly, block_data)
```

rolypoly_load_gwas *Load gwas data*

Description

Load gwas data

Usage

```
rolypoly_load_gwas(rolypoly, gwas_data, snp_annotatons = NULL,  
  gwas_z_filter = -1, add_spline = F, n_knots = 1, add_poly = F,  
  n_degree = 2)
```

Arguments

rolypoly	rolypoly data
gwas_data	gwas data
snp_annotations	if there are additional snp annotations included
gwas_z_filter	if we want to remove large effect SNPs
add_spline	for fitting a spline to maf
n_knots	number of knots for spline
add_poly	for fitting a polynomial to maf
n_degree	degree of polynomial to fit

Value

rolypoly object with gwas data loaded

Examples

```
## Not run: rolypoly_load_gwas(rolypoly, gwas_data)
```

```
rolypoly_perform_inference
```

Run inference.

Description

Coordinates running inference.

Usage

```
rolypoly_perform_inference(rolypoly, bootstrap_iters = 50,
  outlier_threshold = -1, run_light = F, run_parallel = F)
```

Arguments

rolypoly	rolypoly object
bootstrap_iters	number of bootstrap iterations to perform
outlier_threshold	threshold for performing robust regression, still experimental.
run_light	if we throw out bootstrap data
run_parallel	if we collect bootstraps in parallel

Value

rolypoly object with inference information attached

Examples

```
## Not run: run_inference(rolypoly)
```

```
rolypoly_perform_regularized_inference  
    Run inference with added regularization.
```

Description

If p-values are desired use the other inference function. This for prediction purposes.

Usage

```
rolypoly_perform_regularized_inference(rolypoly, ...)
```

Arguments

rolypoly	a rolypoly object
...	other arguments to pass to cv.glmnet

Value

rolypoly object with regularization results

Examples

```
## Not run: rolypoly_perform_regularized_inference(rolypoly)
```

```
rolypoly_plots    Plot functions.
```

Description

Functions for rolypoly results.

rolypoly_roll	<i>Main rolypoly wrapper function.</i>
---------------	--

Description

The entry point for rolypoly analysis. If no expression data, we assume that we are running just the vegas score processing.

Usage

```
rolypoly_roll(rolypoly = NULL, gwas_data = NULL, block_annotation = NULL,
  block_data = NULL, ld_folder = NULL, bootstrap_iters = 50,
  outlier_threshold = -1, perform_cv = F, n_folds = 10,
  gwas_z_filter = -1, add_spline = F, n_knots = 1, add_poly = F,
  n_degree = 2, run_light = T, gwas_link_parallel = F,
  bootstrap_parallel = F, keep_model = F, keep_gwas = F, ...)
```

Arguments

rolypoly	Previous rolypoly run to parts of pipeline.
gwas_data	Gwas data for a trait, including snp annotations.
block_annotation	Start and end points for blocks
block_data	Information about blocks.
ld_folder	Folder with LD information.
bootstrap_iters	Number bootstrap iterations to perform for inference.
outlier_threshold	Set to positive if we want to run robusted regression.
perform_cv	If we want to interpret annotation effects do not set this to T. However, if our goal is prediction accuracy then set this to T.
n_folds	number of folds for cross validation
gwas_z_filter	Z-score filter for SNPs, helps prevent large effects biasing inference.
add_spline	If we want to fit a spline to maf.
n_knots	number of knots to add to the spline.
add_poly	If we want to fit a polynomial to maf.
n_degree	the degree of the polynomial.
run_light	if we want to throw away bootstrap data, and save memory
gwas_link_parallel	if user wants to run in gwas linking in parallel, registerDoParallel must have been run in advance.

bootstrap_parallel if user wants to run in bootstraps in parallel, registerDoParallel must have been run in advance.

keep_model if we should keep the regression model, can be large.

keep_gwas set to T if we want to include gwas in returned rolypoly object.

... other arguments to pass to cv.glmnet

Value

rolypoly object

Examples

```
## Not run: rolypoly_roll(rolypoly)
```

sim_block_annotation *Simulated block data annotation.*

Description

A dataset containing simulated block data annotation for use in the rolypoly vignette.

Usage

```
sim_block_annotation
```

Format

A data frame with 1000 rows and 4 variables:

chrom chromosome, we only use autosomes

start base pair position of variant

end rsid identifier of variant

label effect size, univariate regression coefficient

Source

I generated these fields to link with SNP positions

sim_expression_data_normalized
Simulated expression data.

Description

A dataset containing simulated expression data for use in the rolypoly vignette.

Usage

sim_expression_data_normalized

Format

A data frame with 1000 rows and 5 variables:

Liver simulated expression data for tissue. This tissue has a significant effect on the simulated gwas.

Adrenal.Gland simulated expression data for tissue

Blood simulated expression data for tissue. This tissue has a significant effect on the simulated gwas.

Heart simulated expression data for tissue

Lung simulated expression data for tissue

Source

I generated this dataset

sim_gwas_data *Simulated GWAS summary statistics*

Description

A dataset containing simulated genome-wide association summary statistics for use in the rolypoly vignette.

Usage

sim_gwas_data

Format

A data frame with 14934 rows and 6 variables:

chrom chromosome, we only use autosomes
pos base pair position of variant
rsid rsid identifier of variant
beta effect size, univariate regression coefficient
se standard error of effect size
maf minor allele frequency

Source

rsids were from 1000g and I generated the other fields

vectorize_rolypoly *Take a list of rolypoly data and vectorize it for inference.*

Description

Take a list of rolypoly data and vectorize it for inference.

Usage

```
vectorize_rolypoly(data)
```

Arguments

data the list of block information from rolypoly object

Value

list of necessary information for inference

Examples

```
## Not run: vectorize_rolypoly(data)
```

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