Package 'RareComb'

October 12, 2022

Title Combinatorial and Statistical Analyses of Rare Events

Version 1.1

Description A custom implementation of the apriori algorithm and binomial tests to identify combinations of features (genes, variants etc) significantly enriched for simultaneous mutations/events from sparse Boolean input, see Vijay Kumar Pounraja, Santhosh Girirajan (2021). Version 1.1 includes a minor adjustment to the number of combinations to be considered for multiple testing correction. This updated version is more conservative in its approach and hence more selective. <doi:10.1101/2021.10.01.462832>.

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LazyData true

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Imports magrittr, arules, dplyr, methods, pwr, stringr, tidyr, reshape2, sqldf

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NeedsCompilation no

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R topics documented:

analyze_in_out_simultaneity 2
boolean_input_df 3
boolean_input_mult_df 17
compare_enrichment 31
compare_enrichment_depletion 32
compare_enrichment_modifiers 34
compare_expected_vs_observed 35

custom_left_join 36
input_list 37
run_apriori_freqitems 37
run_apriori_rules 38
run_apriori_rules_inout_simult 39
run_apriori_rules_modifiers 40
run_apriori_w_sample_names 41

Index **43**

`analyze_in_out_simultaneity`
Analyze relationships between rare events among multiple input and output variables

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Description

This function takes a Boolean dataframe as input and analyzes the relationship between input and output variables for the combinations that that include at least a single output variable andmeet all the input criteria specified by the user.

Usage

```
analyze_in_out_simultaneity(boolean_input_mult_df, combo_length, min_output_count,
                      max_output_count, min_indv_threshold, max_freq_threshold,
                           input_format, output_format, pval_filter_threshold,
                           adj_pval_type)
```

Arguments

`boolean_input_mult_df`	An input Boolean dataframe with multiple input and outcome variables
`combo_length`	The length of the combinations specified by the user
`min_output_count`	Minimum number of output variables present in the combination
`max_output_count`	Maximum number of output variables present in the combination
`min_indv_threshold`	Minimum number of instances that support the combination
`max_freq_threshold`	Maximum fraction of the cohort size that could support a combination (i.e., filter out highly frequent events)
`input_format`	Optional | Naming convention used for input variables (Default = 'Input_')
`output_format`	Optional | Naming convention used for output variables (Default = 'Output_')
`pval_filter_threshold`	Optional | p-value cut-off to use to identify significant combinations (Default = 0.05)

`adj_pval_type` Optional | Type of multiple testing corrections to use (Default = 'BH'; Alternative option = 'bonferroni')

Value

A dataframe with the list of multiple-testing adjusted statistically significant combinations along with quantitative measures (frequencies, p-values etc) that support the findings.

Author(s)

Vijay Kumar Pounraja

Examples

```
analyze_in_out_simultaneity(boolean_input_mult_df, 3, 1, 2, 5, 0.25,
                            input_format = 'Input_', output_format = 'Output_',
                            pval_filter_threshold = 0.05, adj_pval_type = 'BH')
```

---

boolean_input_df *Sparse Boolean dataframe with rare variant information and a single outcome variable*

Description

A synthetic dataset containing information about 5000 individuals (rows) and 1000 rare variants (columns).

Usage

```
boolean_input_df
```

Format

A data frame with 5000 rows and 1002 variables:

Sample_Name Unique identifier of the samples

Input_1 Presence and absense of rare variant 1

Input_2 Presence and absense of rare variant 2

Input_3 Presence and absense of rare variant 3

Input_4 Presence and absense of rare variant 4

Input_5 Presence and absense of rare variant 5

Input_6 Presence and absense of rare variant 6

Input_7 Presence and absense of rare variant 7

Input_8 Presence and absense of rare variant 8

Input_9 Presence and absense of rare variant 9
Input_10 Presence and absense of rare variant 10
Input_11 Presence and absense of rare variant 11
Input_12 Presence and absense of rare variant 12
Input_13 Presence and absense of rare variant 13
Input_14 Presence and absense of rare variant 14
Input_15 Presence and absense of rare variant 15
Input_16 Presence and absense of rare variant 16
Input_17 Presence and absense of rare variant 17
Input_18 Presence and absense of rare variant 18
Input_19 Presence and absense of rare variant 19
Input_20 Presence and absense of rare variant 20
Input_21 Presence and absense of rare variant 21
Input_22 Presence and absense of rare variant 22
Input_23 Presence and absense of rare variant 23
Input_24 Presence and absense of rare variant 24
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Input_26 Presence and absense of rare variant 26
Input_27 Presence and absense of rare variant 27
Input_28 Presence and absense of rare variant 28
Input_29 Presence and absense of rare variant 29
Input_30 Presence and absense of rare variant 30
Input_31 Presence and absense of rare variant 31
Input_32 Presence and absense of rare variant 32
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Output_1 Disease outcome or phenotype

`boolean_input_mult_df` *Sparse Boolean dataframe with rare variant information and multiple outcome variables*

Description

A synthetic dataset containing information about 5000 individuals (rows) and 1000 rare variants (columns) and 3 outcome variables.

Usage

```
boolean_input_mult_df
```

Format

A data frame with 5000 rows and 1004 variables:

Sample_Name Unique identifier of the samples

Input_1 Presence and absense of rare variant 1

Input_2 Presence and absense of rare variant 2

Input_3 Presence and absense of rare variant 3

Input_4 Presence and absense of rare variant 4

Input_5 Presence and absense of rare variant 5

Input_6 Presence and absense of rare variant 6

Input_7 Presence and absense of rare variant 7

Input_8 Presence and absense of rare variant 8

Input_9 Presence and absense of rare variant 9

Input_10 Presence and absense of rare variant 10

Input_11 Presence and absense of rare variant 11
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Output_1 Disease outcome or phenotype 1

Output_2 Disease outcome or phenotype 2

Output_3 Disease outcome or phenotype 3

`compare_enrichment` *Compare the enrichment in combinations of input variables between the binary outcomes (case/control)*

Description

This function takes a Boolean dataframe as input and quantifies the enrichment in the observed frequency of combinations that meet the criteria specified by the users compared to their corresponding expectation derived under the assumption of independence between the constituent elements of each combination. The function then reports the multiple-testing adjusted significant combinations in which enrichment is observed in cases but not in controls.

Usage

```
compare_enrichment(boolean_input_df, combo_length, min_indv_threshold,
                   max_freq_threshold, input_format, output_format,
                   pval_filter_threshold, adj_pval_type, min_power_threshold,
                   sample_names_ind)
```

Arguments

`boolean_input_df`
: An input Boolean dataframe with multiple input and a single binary outcome variable

`combo_length`
: The length of the combinations specified by the user

`min_indv_threshold`
: Minimum number of instances that support the combination

`max_freq_threshold`
: Maximum fraction of the cohort size that could support a combination (i.e., filter out highly frequent events)

`input_format` Optional | Naming convention used for input variables (Default = 'Input_')

`output_format` Optional | Naming convention used for output variables (Default = 'Output_')

`pval_filter_threshold`
Optional | p-value cut-off to use to identify significant combinations in cases (Default = 0.05)

`adj_pval_type` Optional | Type of multiple testing corrections to use (Default = 'BH'; Alternative option = 'bonferroni')

`min_power_threshold`
Optional | Minimum statistical power (at 5% sig.threshold) required for significant combinations to be returned in the results (Default = 0.7)

`sample_names_ind`
Optional | Indicator to specify if the output should includes row names that support each significant combination (Default = 'N'; Alternative option = 'Y')

Value

A dataframe with the list of multiple-testing adjusted statistically significant combinations along with quantitative measures (frequencies, p-values etc) that support the findings.

Author(s)

Vijay Kumar Pounraja

Examples

```
compare_enrichment(boolean_input_df, 3, 5, 0.25, input_format = 'Input_',
                   output_format = 'Output_', adj_pval_type = 'bonferroni',
                   sample_names_ind = 'N')
```

---

compare_enrichment_depletion

Compare the enrichment in combinations of input variables between the binary outcomes (case/control)

Description

This function takes a Boolean dataframe as input and quantifies the enrichment in the observed frequency of combinations that meet the criteria specified by the users compared to their corresponding expectation derived under the assumption of independence between the constituent elements of each combination. The function then reports the multiple-testing adjusted significant combinations in which enrichment is observed in cases and depletion is observed in controls.

Usage

```
compare_enrichment_depletion(boolean_input_df, combo_length, min_indv_threshold,
                             max_freq_threshold, input_format, output_format,
                          pval_filter_threshold, adj_pval_type, min_power_threshold,
                             sample_names_ind)
```

Arguments

boolean_input_df	An input Boolean dataframe with multiple input and a single binary outcome variable
combo_length	The length of the combinations specified by the user
min_indv_threshold	Minimum number of instances that support the combination
max_freq_threshold	Maximum fraction of the cohort size that could support a combination (i.e., filter out highly frequent events)
input_format	Optional | Naming convention used for input variables (Default = 'Input_')
output_format	Optional | Naming convention used for output variables (Default = 'Output_')
pval_filter_threshold	Optional | p-value cut-off to use to identify significant combinations in cases (Default = 0.05)
adj_pval_type	Optional | Type of multiple testing corrections to use (Default = 'BH'; Alternative option = 'bonferroni')
min_power_threshold	Optional | Minimum statistical power (at 5% sig.threshold) required for significant combinations to be returned in the results (Default = 0.7)
sample_names_ind	Optional | Indicator to specify if the output should includes row names that support each significant combination (Default = 'N'; Alternative option = 'Y')

Value

A dataframe with the list of multiple-testing adjusted statistically significant combinations along with quantitative measures (frequencies, p-values etc) that support the findings.

Author(s)

Vijay Kumar Pounraja

Examples

```
compare_enrichment_depletion(boolean_input_df, 3, 5, 0.25, input_format = 'Input_',
                             output_format = 'Output_', adj_pval_type = 'bonferroni',
                             sample_names_ind = 'N')
```

`compare_enrichment_modifiers` *Compare the enrichment in combinations of input variables between the binary outcomes (case/control)*

Description

This function takes a Boolean dataframe as input and quantifies the enrichment in the observed frequency of combinations that include at least one of the input variables supplied by the user as well as meet other user-specified criteria compared to their corresponding expectation derived under the assumption of independence between the constituent elements of each combination. The function then reports the combinations in which enrichment is observed in cases but not in controls.

Usage

```
compare_enrichment_modifiers(boolean_input_df, combo_length, min_indv_threshold,
                      max_freq_threshold, primary_input_entities, input_format,
                           output_format, pval_filter_threshold, adj_pval_type,
                             min_power_threshold, sample_names_ind)
```

Arguments

`boolean_input_df`
: An input Boolean dataframe with multiple input and a single binary outcome variable

`combo_length`
: The length of the combinations specified by the user

`min_indv_threshold`
: Minimum number of instances that support the combination

`max_freq_threshold`
: Maximum fraction of the cohort size that could support a combination (i.e., filter out highly frequent events)

`primary_input_entities`
: List of variables that MUST be part of the combinations identified by the method

`input_format`
: Optional | Naming convention used for input variables (Default = 'Input_')

`output_format`
: Optional | Naming convention used for output variables (Default = 'Output_')

`pval_filter_threshold`
: Optional | p-value cut-off to use to identify significant combinations in cases (Default = 0.05)

`adj_pval_type`
: Optional | Type of multiple testing corrections to use (Default = 'BH'; Alternative option = 'bonferroni')

`min_power_threshold`
: Optional | Minimum statistical power (at 5% sig.threshold) required for significant combinations to be returned in the results (Default = 0.7)

`sample_names_ind`
: Optional | Indicator to specify if the output should includes row names that support each significant combination (Default = 'N'; Alternative option = 'Y')

Value

A dataframe with the list of multiple-testing adjusted statistically significant combinations along with quantitative measures (frequencies, p-values etc) that support the findings.

Author(s)

Vijay Kumar Pounraja

Examples

```
compare_enrichment_modifiers(boolean_input_df, 2, 4, 0.25, input_format = 'Input_',
                        output_format = 'Output_', primary_input_entities = input_list,
                              adj_pval_type = 'bonferroni', sample_names_ind = 'N')
```

---

compare_expected_vs_observed

Compare the observed frequencies of combinations with their expected frequencies under the assumption of independence within a single group

---

Description

This function takes a Boolean dataframe as input and compares the observed frequency of combinations that meet the criteria specified by the users with their corresponding expectation derived under the assumption of independence between the constituent elements of each combination

Usage

```
compare_expected_vs_observed(boolean_input_df, combo_length, min_indv_threshold,
                             max_freq_threshold, input_format,
                             pval_filter_threshold, adj_pval_type)
```

Arguments

boolean_input_df	An input Boolean dataframe with multiple input variables
combo_length	The length of the combinations specified by the user
min_indv_threshold	Minimum number of instances that support the combination
max_freq_threshold	Maximum fraction of the cohort size that could support a combination (i.e., filter out highly frequent events)
input_format	Optional | Naming convention used for input variables (Default = 'Input_')

pval_filter_threshold
: Optional | p-value cut-off to use for multiple testing adjustment (Default = 0.05)

adj_pval_type
: Optional | Type of multiple testing corrections to use (Default = 'BH'; Alternative option = 'bonferroni')

Value

A dataframe with the list of multiple-testing adjusted statistically significant combinations along with quantitative measures (frequencies, p-values etc) that support the findings.

Author(s)

Vijay Kumar Pounraja

Examples

```
compare_expected_vs_observed(boolean_input_df, 2, 10, 0.25, 0.05,
                             input_format = 'Input_', adj_pval_type = 'BH')
```

---

custom_left_join *Perform successive left joins to fetch information about the constituent elements of the combinations*

Description

Fetching the frequency of multiple individual elements that make up the combinations of varying length and hence varying variable names or to join two similar data frames using identical variable names necessitates this function that supplements and joins data based on the length of the combinations.

Usage

```
custom_left_join(
  left_df,
  right_df,
  combo_length = combo_length,
  diff_colnames = diff_colnames
)
```

Arguments

left_df
: The data frame with information about the combinations

right_df
: The data frame with information either about the combinations or their constituent elements

combo_length	The length of the combinations specified by the user used to determine the number of successive joins to attempt
diff_colnames	Indicator that specifies if the joins are to be made based on same or different column names

Value

An output dataframe with the results of the join operation

Author(s)

Vijay Kumar Pounraja

---

input_list *A list of 50 random input variables*

Description

A list of 50 random input variables

Usage

```
input_list
```

Format

A list of 50 random input variables:

---

run_apriori_freqitems *Generate frequent items using the apriori algorithm*

Description

This function takes in a factorized Boolean matrix and generate frequent itemsets that meet all the user provided criteria provided by the calling function.

Usage

```
run_apriori_freqitems(
  apriori_input_df,
  combo_length,
  support_threshold,
  input_colname_list,
  confidence_threshold = confidence_threshold,
  include_output_ind = include_output_ind,
  output_colname_list = output_colname_list
)
```

Arguments

`apriori_input_df`
: An input factorized Boolean dataframe with multiple input and outcome variables

`combo_length`
: The length of the combinations specified by the user

`support_threshold`
: Minimum support value calculated based on the minimum absolute observed frequency threshold specified by the user

`input_colname_list`
: A list of column names that identify the input variables

`confidence_threshold`
: Minimum confidence threshold specified by the user

`include_output_ind`
: Specifies if the outcome variables must also be made part of the analysis using the algorithm

`output_colname_list`
: A list of column names that identify the outcome variables

Details

This is a function leveraged by few of the four main methods available to the users.

Value

A list of frequent item sets that meet all the constraints supplied to the apriori algorithm

Author(s)

Vijay Kumar Pounraja

`run_apriori_rules` *Generate rules using the apriori algorithm*

Description

This function takes in a factorized Boolean matrix and generate rules that meet all the user provided criteria while restricting the RHS of the rule based on the list of variables allowed in RHS provided by the calling function.

Usage

```
run_apriori_rules(
  apriori_input_df,
  combo_length,
  support_threshold,
  input_colname_list,
  confidence_threshold = confidence_threshold,
  output_colname_list = output_colname_list
)
```

Arguments

apriori_input_df	An input factorized Boolean dataframe with multiple input and outcome variables
combo_length	The length of the combinations specified by the user
support_threshold	Minimum support value calculated based on the minimum absolute observed frequency threshold specified by the user
input_colname_list	A list of column names that identify the input variables
confidence_threshold	Minimum confidence threshold specified by the user
output_colname_list	Optional | A list of column names that identify the outcome variables

Details

This is a function leveraged by few of the four main methods available to the users.

Value

A list of rules that meet all the constraints supplied to the apriori algorithm

Author(s)

Vijay Kumar Pounraja

---

run_apriori_rules_inout_simult

Generate rules using the apriori algorithm

Description

This function takes in a factorized Boolean matrix and generate rules that meet all the user provided criteria while allowing the outcome variables to be part of either LHS or RHS of the rules but restricting the input variables to the LHS of the rules.

Usage

```
run_apriori_rules_inout_simult(
  apriori_input_df,
  combo_length,
  support_threshold,
  input_colname_list,
  output_colname_list = output_colname_list
)
```

Arguments

apriori_input_df	An input factorized Boolean dataframe with multiple input and outcome variables
combo_length	The length of the combinations specified by the user
support_threshold	Minimum support value calculated based on the minimum absolute observed frequency threshold specified by the user
input_colname_list	A list of column names that identify the input variables
output_colname_list	Optional | A list of column names that identify the outcome variables

Details

This is a function leveraged by few of the four main methods available to the users.

Value

A list of rules that meet all the constraints supplied to the apriori algorithm

Author(s)

Vijay Kumar Pounraja

---

run_apriori_rules_modifiers

Generate rules using the apriori algorithm

Description

This function takes in a factorized Boolean matrix and generate rules that meet all the user provided criteria while restricting the RHS of the rule based on the list of variables allowed in RHS provided by the calling function.

Usage

```
run_apriori_rules_modifiers(
  apriori_input_df,
  combo_length,
  support_threshold,
  input_colname_list,
  output_colname_list = output_colname_list
)
```

Arguments

apriori_input_df	An input factorized Boolean dataframe with multiple input and outcome variables
combo_length	The length of the combinations specified by the user
support_threshold	Minimum support value calculated based on the minimum absolute observed frequency threshold specified by the user
input_colname_list	A list of column names that identify the input variables
output_colname_list	Optional | A list of column names that identify the outcome variables

Details

This is a function leveraged by few of the four main methods available to the users.

Value

A list of rules that meet all the constraints supplied to the apriori algorithm

Author(s)

Vijay Kumar Pounraja

---

run_apriori_w_sample_names

Generate frequent items along with the names of supporting observations using the apriori algorithm

---

Description

This function takes in a factorized Boolean matrix and generate frequent item sets that meet all the user provided criteria provided by the calling function. This function includes in it's output the identifiers of observations that support each significant combination.

Usage

```
run_apriori_w_sample_names(
  apriori_input_df,
  combo_length,
  support_threshold,
  input_colname_list,
  input_sample_list,
  confidence_threshold = confidence_threshold,
  include_output_ind = include_output_ind,
  output_colname_list = output_colname_list
)
```

Arguments

apriori_input_df	An input factorized Boolean dataframe with multiple input and outcome variables
combo_length	The length of the combinations specified by the user
support_threshold	Minimum support value calculated based on the minimum absolute observed frequency threshold specified by the user
input_colname_list	A list of column names that identify the input variables
input_sample_list	A list of row names that identify the samples/observations
confidence_threshold	Minimum confidence threshold specified by the user
include_output_ind	Specifies if the outcome variables must also be made part of the analysis using the algorithm
output_colname_list	A list of column names that identify the outcome variables

Details

This is a function leveraged by few of the four main methods available to the users.

Value

A list of frequent item sets that meet all the constraints supplied to the apriori algorithm

Author(s)

Vijay Kumar Pounraja

Index

∗ **datasets**
boolean_input_df, 3
boolean_input_mult_df, 17
input_list, 37

analyze_in_out_simultaneity, 2

boolean_input_df, 3
boolean_input_mult_df, 17

compare_enrichment, 31
compare_enrichment_depletion, 32
compare_enrichment_modifiers, 34
compare_expected_vs_observed, 35
custom_left_join, 36

input_list, 37

run_apriori_freqitems, 37
run_apriori_rules, 38
run_apriori_rules_inout_simult, 39
run_apriori_rules_modifiers, 40
run_apriori_w_sample_names, 41