

# Package ‘RareComb’

February 24, 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](https://doi.org/10.1101/2021.10.01.462832)>.

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reshape2, sqldf

**RoxygenNote** 7.1.1

**NeedsCompilation** no

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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 include at least a single output variable and meet 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')
```

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boolean_input_df	<i>Sparse Boolean dataframe with rare variant information and a single outcome variable</i>
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### 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 absence of rare variant 1

**Input\_2** Presence and absence of rare variant 2

**Input\_3** Presence and absence of rare variant 3

**Input\_4** Presence and absence of rare variant 4

**Input\_5** Presence and absence of rare variant 5

**Input\_6** Presence and absence of rare variant 6

**Input\_7** Presence and absence of rare variant 7

**Input\_8** Presence and absence 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  
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**Input\_497** Presence and absense of rare variant 497  
**Input\_498** Presence and absense of rare variant 498  
**Input\_499** Presence and absense of rare variant 499  
**Input\_500** Presence and absense of rare variant 500  
**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  
**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  
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**Input\_45** Presence and absense of rare variant 45  
**Input\_46** Presence and absense of rare variant 46  
**Input\_47** Presence and absense of rare variant 47

<b>Input_48</b>	Presence and absense of rare variant	48
<b>Input_49</b>	Presence and absense of rare variant	49
<b>Input_50</b>	Presence and absense of rare variant	50
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<b>Input_82</b>	Presence and absense of rare variant	82
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<b>Input_84</b>	Presence and absense of rare variant	84

**Input\_85** Presence and absense of rare variant 85  
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**Input\_121** Presence and absense of rare variant 121

<b>Input_122</b>	Presence and absense of rare variant	122
<b>Input_123</b>	Presence and absense of rare variant	123
<b>Input_124</b>	Presence and absense of rare variant	124
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**Input\_233** Presence and absense of rare variant 233  
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**Input\_270** Presence and absense of rare variant 270  
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**Input\_292** Presence and absense of rare variant 292  
**Input\_293** Presence and absense of rare variant 293  
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**Input\_307** Presence and absense of rare variant 307  
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**Input\_492** Presence and absense of rare variant 492  
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**Input\_497** Presence and absense of rare variant 497  
**Input\_498** Presence and absense of rare variant 498  
**Input\_499** Presence and absense of rare variant 499  
**Input\_500** Presence and absense of rare variant 500  
**Output\_1** Disease outcome or phenotype 1  
**Output\_2** Disease outcome or phenotype 2  
**Output\_3** Disease outcome or phenotype 3

---

compare_enrichment	<i>Compare the enrichment in combinations of input variables between the binary outcomes (case/control)</i>
--------------------	---

---

### 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 include 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	<i>Perform successive left joins to fetch information about the constituent elements of the combinations</i>
------------------	--

---

**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	<i>A list of 50 random input variables</i>
------------	--

---

**Description**

A list of 50 random input variables

**Usage**

```
input_list
```

**Format**

A list of 50 random input variables:

---

run_apriori_freqitems	<i>Generate frequent items using the apriori algorithm</i>
-----------------------	--

---

**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)**

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