Package ‘LongDat’

February 26, 2022

Type Package

Title A Tool for ‘Confounder’-Sensitive Longitudinal Analysis on ‘Multi-omics’ Data

Version 1.0.3

Description This tool takes longitudinal dataset as input and analyzes if there is significant change of the features over time (a proxy for treatments), while detects and controls for ‘confounders’ simultaneously. ‘LongDat’ is able to take in several data types as input, including count, proportion, binary, ordinal and continuous data. The output table contains p values, effect sizes and ‘confounders’ of each feature, making the downstream analysis easy.

License GPL-2

Encoding UTF-8

Language en-US

LazyData true

URL https://github.com/CCY-dev/LongDat

BugReports https://github.com/CCY-dev/LongDat/issues

RoxygenNote 7.1.2

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Suggests rmarkdown, knitr, tidyverse, kableExtra

VignetteBuilder knitr

NeedsCompilation no

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c\texttt{\_cal} \hspace{1cm} \textit{Effect size (Cliff’s delta) calculation in longdat_disc() pipeline}

\vspace{0.5cm}

\textbf{Description}

Effect size (Cliff’s delta) calculation in longdat_disc() pipeline

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\textbf{Arguments}

- \texttt{melt_data} Internal function argument.
- \texttt{Ps_poho_fdr} Internal function argument.
- \texttt{variables} Internal function argument.
- \texttt{test_var} Internal function argument.
- \texttt{data} Internal function argument.
**ConModelTest_cont**

Confounding model test in longdat_cont() pipeline

**Description**

Confounding model test in longdat_cont() pipeline

**Arguments**

<table>
<thead>
<tr>
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<th>Description</th>
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<tbody>
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<td>test_var</td>
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<td>verbose</td>
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**ConModelTest_disc**

Confounding model test in longdat_disc() pipeline

**Description**

Confounding model test in longdat_disc() pipeline

**Arguments**

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<td>Internal function argument.</td>
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<tr>
<td>verbose</td>
<td>Internal function argument.</td>
</tr>
</tbody>
</table>
correlation_posthoc  Post-hoc test based on correlation test for longdat_cont().

Description
Post-hoc test based on correlation test for longdat_cont().

Usage
correlation_posthoc(variables, verbose, melt_data, test_var, N)

Arguments
- variables: Internal function argument.
- verbose: Internal function argument.
- melt_data: Internal function argument.
- test_var: Internal function argument.
- N: Internal function argument.

cuneiform_plot  Create cuneiform plots of result table from longdat_disc() or longdat_cont()

Description
Create cuneiform plots of result table from longdat_disc() or longdat_cont().

Arguments
- result_table: The result table from longdat_disc() or longdat_cont() output, or any data frame that has the same format.
- x_axis_order: The plotting order of the x axis. It should be a character vector (e.g. c("Effect_1_2", "Effect_2_3", "Effect_1_3")).
- confound_panel: A boolean vector indicating whether to plot confounding status alongside the effect panel. The default is TRUE.
- pos_color: The color for a positive effect size. It should be a hex color code (e.g. "#b3e6ff") or the colors recognized by R. The default is "red".
- neg_color: The color for a negative effect size. It should be a hex color code (e.g. "#b3e6ff") or the colors recognized by R. The default is "blue".
- panel_width: The width of the effect size panel on the left relative to the confounding status panel on the right (width set to 1). It should be a numerical vector. The default is 4.
Details

This function creates a cuneiform plot which displays the result of longdat_disc() or longdat_cont(). It plots the effect sizes within each time interval for each feature, and also shows the confounding status. Only the features with non-NS signals will be included in the plot. The output is a ggplot object in patchwork structure. For further customization of the plot, please refer to the vignette.

Value

a 'ggplot' object

Examples

test_disc <- longdat_disc(input = LongDat_disc_master_table,
data_type = "count", test_var = "Time_point",
variable_col = 7, fac_var = c(1:3))
test_plot <- cuneiform_plot(result_table = test_disc[1],
x_axis_order = c("Effect_1_2", "Effect_2_3", "Effect_1_3"))

Description

Data preprocessing

Usage

data_preprocess(input, test_var, variable_col, fac_var, not_used)

Arguments

input Internal function argument.
test_var Internal function argument.
variable_col Internal function argument.
fac_var Internal function argument.
not_used Internal function argument.
### factor_p_cal

*Calculate the p values for every factor (used for selecting factors later)*

#### Description

Calculate the p values for every factor (used for selecting factors later)

#### Usage

```r
factor_p_cal(melt_data, variables, factor_columns, factors, data, N, verbose)
```

#### Arguments

- `melt_data`: Internal function argument.
- `variables`: Internal function argument.
- `factor_columns`: Internal function argument.
- `factors`: Internal function argument.
- `data`: Internal function argument.
- `N`: Internal function argument.
- `verbose`: Internal function argument.

### final_result_summarize_cont

*Generate result table as output in longdat_cont()*

#### Description

Generate result table as output in longdat_cont()

#### Usage

```r
final_result_summarize_cont(
    variable_col,
    N,
    Ps_conf_inv_model_unlist,
    variables,
    sel_fac,
    Ps_conf_model_unlist,
    model_q,
    posthoc_q,
    Ps_null_model_fdr,
    Ps_null_model,
    assoc,
```
final_result_summarize_disc

prevalence,
mean_abundance,
p_poho,
not_used,
Ps_effectsize,
data_type,
false_pos_count
)

 Arguments

 variable_col     Internal function argument.
 N                Internal function argument.
 Ps_conf_inv_model_unlist 
 variables        Internal function argument.
 sel_fac          Internal function argument.
 Ps_conf_model_unlist 
 model_q          Internal function argument.
 posthoc_q        Internal function argument.
 Ps_null_model_fdr 
 Ps_null_model    Internal function argument.
 assoc            Internal function argument.
 prevalence       Internal function argument.
 mean_abundance   Internal function argument.
 p_poho           Internal function argument.
 not_used         Internal function argument.
 Ps_effectsize    Internal function argument.
 data_type        Internal function argument.
 false_pos_count  Internal function argument.

 final_result_summarize_disc

 Generate result table as output in longdat_disc()

Description

Generate result table as output in longdat_disc()
Usage

final_result_summarize_disc(
  variable_col,
  N,
  Ps_conf_inv_model_unlist,
  variables,
  sel_fac,
  Ps_conf_model_unlist,
  model_q,
  posthoc_q,
  Ps_null_model_fdr,
  Ps_null_model,
  delta,
  case_pairs,
  prevalence,
  mean_abundance,
  Ps_poho_fdr,
  not_used,
  Ps_effectsize,
  case_pairs_name,
  data_type,
  false_pos_count,
  p_wilcox_final
)

Arguments

variable_col     Internal function argument.
N                 Internal function argument.
Ps_conf_inv_model_unlist
  Internal function argument.
variables        Internal function argument.
sel_fac          Internal function argument.
Ps_conf_model_unlist
  Internal function argument.
model_q          Internal function argument.
posthoc_q         Internal function argument.
Ps_null_model_fdr
  Internal function argument.
Ps_null_model
  Internal function argument.
delta            Internal function argument.
file_pairs       Internal function argument.
prevalence       Internal function argument.
mean_abundance   Internal function argument.
**fix_name_fun**

Replace the symbols in variable and confounder names in raw input

**Description**

Replace the symbols in variable and confounder names in raw input

**Usage**

```r
fix_name_fun(z)
```

**Arguments**

- `z` A character vector. This is the character vector that needs to be changed.

**longdat_cont**

Longitudinal analysis with time as continuous variable

**Description**

longdat_cont calculates the p values, effect sizes and discover confounding effects of time variables from longitudinal data.

**Usage**

```r
longdat_cont(
  input,  # a character vector. This is the character vector that needs to be changed.
  data_type = "Continuous",  # a character vector. This is the character vector that needs to be changed.
  test_var,  # a character vector. This is the character vector that needs to be changed.
  variable_col = NULL,  # a character vector. This is the character vector that needs to be changed.
  fac_var,  # a character vector. This is the character vector that needs to be changed.
  adjustMethod = "fdr",  # a character vector. This is the character vector that needs to be changed.
  model_q = 0.1,  # a character vector. This is the character vector that needs to be changed.
)```
posthoc_q = 0.05,
theta_cutoff = 2^20,
nonzero_count_cutoff1 = 9,
nonzero_count_cutoff2 = 5,
verbose = TRUE
)

Arguments

input  A data frame with the first column as "Individual" and all the columns of dependent variables (features, e.g. bacteria) at the end of the table. The time variable here should be continuous, if time is discrete, please apply longdat_disc() instead. Please avoid using characters that don’t belong to ASCII printable characters for potential confounders names (confounders are any column apart from individual, test_var and dependent variables).
data_type The data type of the dependent variables (features). Can either be "proportion", "measurement", "count", "binary", "ordinal" or "others". Proportion (or ratio) data range from 0 to 1. Measurement data are continuous and can be measured at finer and finer scale (e.g. weight). Count data consist of discrete non-negative integers resulted from counting. Binary data are the data of sorting things into one of two mutually exclusive categories. Ordinal data consist of ranks. Any data that doesn’t belong to the previous categories should be classified as "others".
test_var The name of the independent variable you are testing for, should be a string (e.g. "Time") identical to its column name and make sure there is no space in it.
variable_col The column number of the position where the dependent variable columns (features, e.g. bacteria) start in the table.
fac_var The column numbers of the position where the columns that aren’t numerical (e.g. characters, categorical numbers, ordinal numbers). This should be a numerical vector (e.g. c(1, 2, 5:7)).
not_used The column position of the columns not are irrelevant and can be ignored when in the analysis. This should be a numerical vector, and the default is NULL.
adjustMethod Multiple testing p value correction. Choices are the ones in p.adjust(), including 'holm', 'hochberg', 'hommel', 'bonferroni', 'BH', 'BY' and 'fdr.' The default is 'fdr'.
model_q The threshold for significance of model test after multiple testing correction. The default is 0.1.
posthoc_q The threshold for significance of post-hoc test after multiple testing correction. The default is 0.05.
theta_cutoff Required when the data type is set as "count". Variable with theta value from negative binomial regression larger than or equal to the cutoff will be filtered out if it also doesn’t meet the non-zero count threshold. Users can use the function "theta_plot()" to help with specifying the value for theta_cutoff. The default is 2^20.
nonzero_count_cutoff1 Required when the data type is set as "count". Variable with non-zero counts lower than or equal to this value will be filtered out if it doesn’t meet the theta
threshold either. Users can use the function "theta_plot()" to help with specifying the value for nonzero_count_cutoff1. The default is 9.

nonzero_count_cutoff2
Required when the data type is set as "count". Variable with non-zero counts lower than or equal to this value will be filtered out. Users can use the function "theta_plot()" to help with specifying the value for nonzero_count_cutoff2. The default is 5.

verbose
A boolean vector indicating whether to print detailed message. The default is TRUE.

Details
The brief workflow of longdat_cont() is as below:
When there’s no potential confounder in the input data (confounders are anything apart from individual, test_var and dependent variables): First, the model test tests the significance of test_var on dependent variables. Different generalized linear mixed effect models are implemented for different types of dependent variable. Negative binomial mixed model for "count", linear mixed model (dependent variables normalized first) for "measurement", beta mixed model for "proportion", binary logistic mixed model for "binary", and proportional odds logistic mixed model for "ordinal". Then, post-hoc test (Spearman’s correlation test) on the model is done. When the data type is "count" mode, a control model test will be run on randomized data (the rows are shuffled). If there are false positive signals in this control model test, users will get a warning at the end of the run.
When there are potential confounders in the input data: After the model test and post-hoc test described above, a confounding model test will be added to the workflow. The potential confounders will be added to the model one by one and test for its significance on each dependent variable. The rest are the same as the description above.
Also, when your data type is count data, please use set.seed() before running longdat_cont() so that you can get reproducible randomized negative check.

Value
longdat_cont() returns a list which contains a "Result_table", and if there are confounders in the input data frame, there will be another table called "Confounder_table". For count mode, if there is any false positive in the randomized control result, then another table named "Randomized_control_table" will also be generated. The detailed description is as below.

Result_table
1. The first column: The dependent variables in the input data. This can be used as row name when being imported into R.
2. Prevalence_percentage: The percentage of each dependent variable present across individuals and time points
3. Mean_abundance: The mean value of each dependent variable across individuals and time points
4. Signal: The final decision of the significance of the test_var (independent variable) on each dependent variable. NS: This represents "Non-significant", which means that there’s no effect of time.

OK_nc: This represents "OK and no confounder". There’s an effect of time and there’s no potential confounder.
OK_d: This represents "OK but doubtful". There’s an effect of time and there’s no potential confounder, however the confidence interval of the test_var estimate in the model test covers zero, and thus it is doubtful of this signal.

OK_sd: This represents "OK and strictly deconfounded". There are potential confounders, however there’s an effect of time and it is independent of those of confounders.

AD: This represents "Ambiguously deconfounded". There are potential confounders, and it isn’t possible to conclude whether the effect is resulted from time or confounders.

C: This represents "Confounded". There’s an effect of time, but it can be reduced to the confounder effects.

5. Effect: This column contains the value of each dependent variable decreases/increases/NS(non-significant) along the time. A positive correlation between with time dependent variable value yields "increase", while a negative correlation yields "decrease". NS means no significant correlation.

6. 'EffectSize': This column reports the correlation coefficient (Spearman’s rho) between each dependent variable value and time.

7. Null_time_model_q: This column shows the multiple-comparison-adjusted p values (Wald test) of the significance of test_var in the models.

8. Post-hoc_q: These are the multiple-comparison-adjusted p values from the post-hoc test (Spearman’s correlation test) of the model.

Confounder_table
The first column contains the dependent variables in the input data. This can be used as row name when being imported into R. Then every 3 columns are a group. Confounder column shows the confounder’s name; Confounding_type column shows how test_var is confounded with this confounder; Effect_size column shows the effect size of dependent variable value between different values of confounders. Due to the different number of confounders for each dependent variable, there may be NAs in the table and they can simply be ignored. If the confounder table is totally empty, this means that there are no confounders detected.

Randomized_control_table (for user’s reference)
We assume that there shouldn’t be positive results in the randomized control test, because all the rows in the original dataset are shuffled randomly. Therefore, any signal that showed significance here will be regarded as false positive. And if there’s false positive in this randomized control result, longdat_disc will warn the user at the end of the run. This Randomized_control table is only generated when there is false positive in the randomized control test. It is intended to be a reference for users to see the effect size of false positive features.

1. The first column "Model_q" shows the multiple-comparison-adjusted p values (Wald test) of the significance of test_var in the negative- binomial models in the randomized dataset. Only the features with Model_q lower than the defined model_q (default = 0.1) will be listed in this table.

2. Signal: This column describes if test_var is significant on each dependent variable based on the post-hoc test p values (Spearman’s correlation test). "False positive" indicates that test_var is significant, while "Negative" indicates non-significance.

3. 'Posthoc_q': This column describes the multiple-comparison-adjusted p values from the post-hoc test (Spearman’s correlation test) of the model in the randomized control dataset.

4. Effect_size: This column describes the correlation coefficient (Spearman’s rho) of each dependent variable between each dependent variable value and time.
Examples

```
test_cont <- suppressWarnings(longdat_cont(input = LongDat_cont_master_table,
data_type = "count", test_var = "Day",
variable_col = 7, fac_var = c(1, 3)))
```

Description

Example feature data frame for longdat_cont(). This is a dummy data which contains features (dependent variables).

Usage

```
data(LongDat_cont_feature_table)
```

Format

An object of class `data.frame` with 20 rows and 4 columns.

Examples

```
## Not run:
data(LongDat_cont_feature_table)
## End(Not run)
```

Description

Example master data frame for longdat_cont(). This is a dummy data which contains metadata and features.

Usage

```
data(LongDat_cont_master_table)
```

Format

An object of class `data.frame` with 20 rows and 9 columns.
Examples

```r
## Not run:
data(LongDat_cont_master_table)

## End(Not run)
```

LongDat_cont_metadata_table
data/LongDat_cont_metadata_table.RData documentation

Description

Example metadata data frame for longdat_cont(). This is a dummy data which contains metadata.

Usage

data(LongDat_cont_metadata_table)

Format

An object of class `data.frame` with 20 rows and 7 columns.

Examples

```r
## Not run:
data(LongDat_cont_metadata_table)

## End(Not run)
```

longdat_disc

*Longitudinal analysis with time as discrete variable*

Description

longdat_disc calculates the p values, effect sizes and discover confounding effects of time variables from longitudinal data.

Usage

```r
longdat_disc(
  input,
  data_type,
  test_var,
  variable_col,
  fac_var,
  not_used = NULL,
```
adjustMethod = "fdr",
model_q = 0.1,
posthoc_q = 0.05,
theta_cutoff = 2^20,
nonzero_count_cutoff1 = 9,
nonzero_count_cutoff2 = 5,
verbose = TRUE
)

Arguments

input A data frame with the first column as "Individual" and all the columns of dependent variables (features, e.g. bacteria) at the end of the table. The time variable here should be discrete, if time is continuous, please apply longdat_cont() instead. Please avoid using characters that don’t belong to ASCII printable characters for potential confounders names (confounders are any column apart from individual, test_var and dependent variables).

data_type The data type of the dependent variables (features). Can either be "proportion", "measurement", "count", "binary", "ordinal" or "others". Proportion (or ratio) data range from 0 to 1. Measurement data are continuous and can be measured at finer and finer scale (e.g. weight). Count data consist of discrete non-negative integers resulted from counting. Binary data are the data of sorting things into one of two mutually exclusive categories. Ordinal data consist of ranks. Any data that doesn’t belong to the previous categories should be classified as "others".

test_var The name of the independent variable you are testing for, should be a string (e.g. "Time") identical to its column name and make sure there is no space in it.

variable_col The column number of the position where the dependent variable columns (features, e.g. bacteria) start in the table.

fac_var The column numbers of the position where the columns that aren’t numerical (e.g. characters, categorical numbers, ordinal numbers). This should be a numerical vector (e.g. c(1, 2, 5:7)).

not_used The column position of the columns not are irrelevant and can be ignored when in the analysis. This should be a numerical vector, and the default is NULL.

adjustMethod Multiple testing p value correction. Choices are the ones in p.adjust(), including 'holm', 'hochberg', 'hommel', 'bonferroni', 'BH', 'BY' and 'fdr'. The default is 'fdr'.

model_q The threshold for significance of model test after multiple testing correction. The default is 0.1.

posthoc_q The threshold for significance of post-hoc test of the model after multiple testing correction. The default is 0.05.

theta_cutoff Required when the data type is set as "count". Variable with theta value from negative binomial regression larger than or equal to the cutoff will be filtered out if it also doesn’t meet the non-zero count threshold. Users can use the function "theta_plot()" to help with specifying the value for theta_cutoff. The default is 2^20.
nonzero_count_cutoff1
Required when the data type is set as "count". Variable with non-zero counts lower than or equal to this value will be filtered out if it doesn’t meet the theta threshold either. Users can use the function "theta_plot()" to help with specifying the value for nonzero_count_cutoff1. The default is 9.

nonzero_count_cutoff2
Required when the data type is set as "count". Variable with non-zero counts lower than or equal to this value will be filtered out. Users can use the function "theta_plot()" to help with specifying the value for nonzero_count_cutoff2. The default is 5.

verbose
A boolean vector indicating whether to print detailed message. The default is TRUE.

Details
The brief workflow of longdat_disc() is as below:
When there’s no potential confounder in the input data (confounders are anything apart from individual, test_var and dependent variables): First, the model test tests the significance of test_var on dependent variables. Different generalized linear mixed effect models are implemented for different types of dependent variable. Negative binomial mixed model for "count", linear mixed model (dependent variables normalized first) for "measurement", beta mixed model for "proportion", binary logistic mixed model for "binary", and proportional odds logistic mixed model for "ordinal". Then, post-hoc test ('emmeans') on the model is done. When the data type is "count" mode, a control model test will be run on randomized data (the rows are shuffled). If there are false positive signals in this control model test, then additional Wilcoxon post-hoc test will be done because it is more conservative.

When there are potential confounders in the input data: After the model test and post-hoc test described above, a confounding model test will be added to the work flow. The potential confounders will be added to the model one by one and test for its significance on each dependent variable. The rest are the same as the description above.
Also, when your data type is count data, please use set.seed() before running longdat_disc() so that you can get reproducible randomized negative check.

Value

longdat_disc() returns a list which contains a "Result_table", and if there are confounders in the input data frame, there will be another table called "Confounder_table". For count mode, if there is any false positive in the randomized control result, then another table named "Randomized_control_table" will also be generated. The detailed description is as below.

Result_table
1. The first column: The dependent variables in the input data. This can be used as row name when being imported into R.
2. Prevalence_percentage: The percentage of each dependent variable present across individuals and time points.
3. Mean_abundance: The mean value of each dependent variable across individuals and time points.
4. **Signal**: The final decision of the significance of the test_var (independent variable) on each dependent variable. **NS**: This represents "Non-significant", which means that there's no effect of time.

**OK_nc**: This represents "OK and no confounder". There's an effect of time and there's no potential confounder.

**OK_d**: This represents "OK but doubtful". There's an effect of time and there's no potential confounder, however the confidence interval of the test_var estimate in the model test covers zero, and thus it is doubtful of this signal.

**OK_sd**: This represents "OK and strictly deconfounded". There are potential confounders, however there's an effect of time and it is independent of those of confounders.

**AD**: This represents "Ambiguously deconfounded". There are potential confounders, and it isn't possible to conclude whether the effect is resulted from time or confounders.

**C**: This represents "Confounded". There's an effect of time, but it can be reduced to the confounder effects.

5. **Effect_a_b**: The "a" and "b" here are the names of the time points. These columns describe the value of each dependent variable decreases/increases/NS(non-significant) at time point b comparing with time point a. The number of Effect columns depends on how many combinations of time points in the input data.

6. **EffectSize_a_b**: The "a" and "b" here are the names of the time points. These columns describe the effect size (Cliff's delta) of each dependent variable between time point b and a. The number of 'EffectSize' columns depends on how many combinations of time points in the input data.

7. **Null_time_model_q**: This column shows the multiple-comparison-adjusted p values (Wald test) of the significance of test_var in the models.

8. **Post-hoc_q_a_b**: The "a" and "b" here are the names of the time points. These are the multiple-comparison-adjusted p values from the post-hoc test of the model. The number of Post-hoc_q columns depends on how many combinations of time points in the input data.

9. **Wilcox_p_a_b**: The "a" and "b" here are the names of the time points. These columns only appear when data type is "count" and there exist false positives in the model test on randomized data. Wilcoxon test are more conservative than the default post-hoc test ('emmeans'), and thus it is a good reference for getting a more conservative result of the significant outcomes.

**Confounder_table**

The first column contains the dependent variables in the input data. This can be used as row name when being imported into R. Then every 3 columns are a group. Confounder column shows the confounder's name; Confounding_type column shows how test_var is confounded with this confounder; Effect_size column shows the effect size of dependent variable value between different values of confounders. Due to the different number of confounders for each dependent variable, there may be NAs in the table and they can simply be ignored. If the confounder table is totally empty, this means that there are no confounders detected.

**Randomized_control_table (for user's reference)**

We assume that there shouldn't be positive results in the randomized control test, because all the rows in the original dataset are shuffled randomly. Therefore, any signal that showed significance here will be regarded as false positive. And if there's false positive in this randomized control result, longdat_disc() will warn the user at the end of the run. This Randomized_control table is
only generated when there is false positive in the randomized control test. It is intended to be a reference for users to see the effect size of false positive features.

1. "Model_q": It shows the multiple-comparison-adjusted p values (Wald test) of the significance of test_var in the negative-binomial models in the randomized dataset. Only the features with Model_q lower than the defined model_q (default = 0.1) will be listed in this table.

2. Final_signal: It show the overall signal being either false positive or negative. "False positive" indicates that test_var is significant, while "Negative" indicates non-significance.

3. 'Signal_a_b': The "a" and "b" here are the names of the time points. These columns describe if test_var is significant on each dependent variable between each time point based on the post-hoc test p values (listed right to Signal_a_b). "False positive" indicates that test_var is significant, while "Negative" indicates non-significance. The number of Signal_a_b columns depends on how many combinations of time points in the input data.

4. 'Posthoc_q_a_b': The "a" and "b" here are the names of the time points. These columns describe the multiple-comparison-adjusted p values from the post-hoc test of the model between time point b and a in the randomized control dataset. The number of 'Posthoc_q_a_b' columns depends on how many combinations of time points in the input data.

5. 'Effect_size_a_b': The "a" and "b" here are the names of the time points. These columns describe the effect size (Cliff’s delta) of each dependent variable between time point b and a in the randomized control dataset. The number of Effect_size_a_b columns depends on how many combinations of time points in the input data.

Examples

test_disc <- longdat_disc(input = LongDat_disc_master_table,  
data_type = "count", test_var = "Time_point",  
variable_col = 7, fac_var = c(1:3))
**LongDat_disc_master_table**

Examples

```r
## Not run:
data(LongDat_disc_feature_table)
## End(Not run)
```

**LongDat_disc_master_table**

data/LongDat_disc_master_table.RData documentation

Description

Example master data frame for longdat_disc(). This is a dummy data which contains metadata and features.

Usage

data(LongDat_disc_master_table)

Format

An object of class `data.frame` with 30 rows and 9 columns.

Examples

```r
## Not run:
data(LongDat_disc_master_table)
## End(Not run)
```

**LongDat_disc_metadata_table**

data/LongDat_disc_metadata_table.RData documentation

Description

Example metadata data frame for longdat_disc(). This is a dummy data which contains metadata.

Usage

data(LongDat_disc_metadata_table)

Format

An object of class `data.frame` with 30 rows and 7 columns.
make_master_table

Create input master table from metadata and feature tables for longdat_disc() and longdat_cont()

Description

Create input master table from metadata and feature tables for longdat_disc() and longdat_cont()

Usage

make_master_table(
  metadata_table,
  feature_table,
  sample_ID,
  individual,
  keep_id = FALSE
)

Arguments

metadata_table  A data frame whose columns consist of sample identifiers (sample_ID), individual, time point and other meta data. Each row corresponds to one sample_ID. Metadata table should have the same number of rows as feature table does. Please avoid using characters that don’t belong to ASCII printable characters for the column names.

feature_table    A data frame whose columns only consist of sample identifiers (sample_ID) and features (dependent variables, e.g. microbiome). Each row corresponds to one sample_ID. Please do not include any columns other than sample_ID and features. Please avoid using characters that don’t belong to ASCII printable characters for the column names. Also, feature table should have the same number of rows as metadata table does.

sample_ID        The name of the column which stores sample identifiers. Please make sure that sample_IDs are unique for each sample, and that metadata and feature tables have the same sample_IDs. If sample_IDs don’t match between the two tables, it will fail to join them together. This should be a string, e.g. "Sample_ID"

individual       The name of the column which stores individual information in the metadata table. This should be a string, e.g. "Individual"

keep_id          A boolean vector indicating whether keep sample_ID column in the output master table. The default is FALSE.

Examples

## Not run:
data(LongDat_disc_metadata_table)

## End(Not run)
Details

This function joins metadata and feature tables by the sample_ID column. Users can create master tables compatible with the format of longdat_disc() and longdat_cont() input easily. This function outputs a master table with individual as the first column, followed by time point and other metadata, and then by feature columns.

Value

a data frame which complies with the required format of an input data frame for longdat_disc() and longdat_cont().

Examples

test_master <- make_master_table(
  metadata_table = LongDat_disc_metadata_table,
  feature_table = LongDat_disc_feature_table,
  sample_ID = "Sample_ID",
  individual = "Individual")

Description

Null Model Test and post-hoc Test in longdat_cont() pipeline

Arguments

N Internal function argument.
data_type Internal function argument.
test_var Internal function argument.
melt_data Internal function argument.
variables Internal function argument.
verbose Internal function argument.
### NuModelTest_disc

**Null Model Test and post-hoc Test in longdat_disc() pipeline**

**Description**
Null Model Test and post-hoc Test in longdat_disc() pipeline

**Arguments**

- `N` Internal function argument.
- `data_type` Internal function argument.
- `test_var` Internal function argument.
- `melt_data` Internal function argument.
- `variables` Internal function argument.
- `verbose` Internal function argument.

### random_neg_ctrl_cont

**Randomized negative control for count data in longdat_cont()**

**Description**
Randomized negative control for count data in longdat_cont()

**Arguments**

- `test_var` Internal function argument.
- `variable_col` Internal function argument.
- `fac_var` Internal function argument.
- `not_used` Internal function argument.
- `factors` Internal function argument.
- `data` Internal function argument.
- `N` Internal function argument.
- `data_type` Internal function argument.
- `variables` Internal function argument.
- `adjustMethod` Internal function argument.
- `model_q` Internal function argument.
- `posthoc_q` Internal function argument.
- `theta_cutoff` Internal function argument.
- `nonzero_count_cutoff1` Internal function argument.
- `nonzero_count_cutoff2` Internal function argument.
- `verbose` Internal function argument.
random_neg_ctrl_disc  
*Randomized negative control for count data in longdat_disc()*

---

**Description**

Randomized negative control for count data in longdat_disc()

**Arguments**

- **test_var**: Internal function argument.
- **variable_col**: Internal function argument.
- **fac_var**: Internal function argument.
- **not_used**: Internal function argument.
- **factors**: Internal function argument.
- **data**: Internal function argument.
- **N**: Internal function argument.
- **data_type**: Internal function argument.
- **variables**: Internal function argument.
- **case_pairs**: Internal function argument.
- **adjustMethod**: Internal function argument.
- **model_q**: Internal function argument.
- **posthoc_q**: Internal function argument.
- **theta_cutoff**: Internal function argument.
- **nonzero_count_cutoff1**: Internal function argument.
- **nonzero_count_cutoff2**: Internal function argument.
- **verbose**: Internal function argument.

---

rm_sparse_cont  
*Remove the dependent variables that are below the threshold of sparsity when the data type is count data in longdat_cont()*

---

**Description**

Remove the dependent variables that are below the threshold of sparsity when the data type is count data in longdat_cont()
Arguments

values  Internal function argument.
data  Internal function argument.
nonzero_count_cutoff1  Internal function argument.
nonzero_count_cutoff2  Internal function argument.
theta_cutoff  Internal function argument.
Ps_null_model  Internal function argument.
prevalence  Internal function argument.
absolute_sparsity  Internal function argument.
mean_abundance  Internal function argument.
p_poho  Internal function argument.
assoc  Internal function argument.

---

**rm_sparse_disc**  Remove the dependent variables that are below the threshold of sparsity when the data type is count data in longdat_disc()

---

Description

Remove the dependent variables that are below the threshold of sparsity when the data type is count data in longdat_disc()

Arguments

values  Internal function argument.
data  Internal function argument.
nonzero_count_cutoff1  Internal function argument.
nonzero_count_cutoff2  Internal function argument.
theta_cutoff  Internal function argument.
Ps_null_model  Internal function argument.
prevalence  Internal function argument.
absolute_sparsity  Internal function argument.
mean_abundance  Internal function argument.
P_s_poho_fdr  Internal function argument.
delta  Internal function argument.
theta_plot

Plot theta values of negative binomial models versus non-zero count for count data

Description

Plot theta values of negative binomial models versus non-zero count for count data

Arguments

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>input</td>
<td>A data frame with the first column as &quot;Individual&quot; and all the columns of dependent variables (features, e.g. bacteria) at the end of the table.</td>
</tr>
<tr>
<td>test_var</td>
<td>The name of the independent variable you are testing for, should be a character vector (e.g. c(&quot;Time&quot;)) identical to its column name and make sure there is no space in it.</td>
</tr>
<tr>
<td>variable_col</td>
<td>The column number of the position where the dependent variable columns (e.g. bacteria) start in the table</td>
</tr>
<tr>
<td>fac_var</td>
<td>The column numbers of the position where the columns that aren't numerical (e.g. characters, categorical numbers, ordinal numbers), should be a numerical vector (e.g. c(1, 2, 5:7))</td>
</tr>
<tr>
<td>not_used</td>
<td>The column position of the columns not are irrelevant and can be ignored when in the analysis. This should be a number vector, and the default is NULL.</td>
</tr>
<tr>
<td>point_size</td>
<td>The point size for plotting in 'ggplot2'. The default is 1.</td>
</tr>
<tr>
<td>x_interval_val</td>
<td>The interval value for tick marks on x-axis. The default is 5.</td>
</tr>
<tr>
<td>y_interval_val</td>
<td>The interval value for tick marks on y-axis. The default is 5.</td>
</tr>
<tr>
<td>verbose</td>
<td>A boolean vector indicating whether to print detailed message. The default is TRUE.</td>
</tr>
</tbody>
</table>

Details

This function outputs a plot that facilitates the setting of theta_cutoff in longdat_disc() and longdat_cont(). This only applies when the dependent variables are count data. longdat_disc() and longdat_cont() implements negative binomial (NB) model for count data, and if the theta (dispersion parameter) of NB model gets too high, then the p value of it will be extremely low regardless of whether there is real significance or not. Therefore, the highest threshold of theta value is set and any variable beyond the threshold will be excluded from the test. The default value of theta_cutoff is set to $2^{20}$ from the observation that $2^{20}$ is a clear cutoff line for several datasets. Users can change theta_cutoff value to fit their own data.

Value

a 'ggplot' object
Examples

test_theta_plot <- theta_plot(input = LongDat_disc_master_table,
       test_var = "Time_point", variable_col = 7, fac_var = c(1:3))

unlist_table

Unlist confound and inverse confound tables, turn them into tables

Description

Unlist confound and inverse confound tables, turn them into tables

Usage

unlist_table(x, N, variables)

Arguments

x The list to be unlisted and turned into table
N Internal function argument.
variables Internal function argument.

wilcox_posthoc

Wilcoxon post-hoc test

Description

Wilcoxon post-hoc test

Usage

wilcox_posthoc(
result_neg_ctrl,
model_q,
melt_data,
test_var,
variables,
data,
N,
verbose
)

Arguments

- `result_neg_ctrl` Internal function argument.
- `model_q` Internal function argument.
- `melt_data` Internal function argument.
- `test_var` Internal function argument.
- `variables` Internal function argument.
- `data` Internal function argument.
- `N` Internal function argument.
- `verbose` Internal function argument.
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