## Package 'graphicalMCP'

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Type Package

Title Graphical Multiple Comparison Procedures

Version 0.2.8

Description Multiple comparison procedures (MCPs) control the familywise error rate in clinical trials. Graphical MCPs include many commonly used procedures as special cases; see Bretz et al. (2011) <doi:10.1002/bimj.201000239>, Lu (2016) <doi:10.1002/sim.6985>, and Xi et al. (2017) <doi:10.1002/bimj.201600233>. This package is a low-dependency implementation of graphical MCPs which allow mixed types of tests. It also includes power simulations and visualization of graphical MCPs.

**License** Apache License (>= 2)

URL https://github.com/openpharma/graphicalMCP

BugReports https://github.com/openpharma/graphicalMCP/issues

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adjust\_p\_bonferroni Calculate adjusted p-values

## **Description**

For an intersection hypothesis, an adjusted p-value is the smallest significance level at which the intersection hypothesis can be rejected. The intersection hypothesis can be rejected if its adjusted p-value is less than or equal to  $\alpha$ . Currently, there are three test types supported:

- Bonferroni tests for adjust\_p\_bonferroni(),
- Parametric tests for adjust\_p\_parametric(),
  - Note that one-sided tests are required for parametric tests.
- Simes tests for adjust\_p\_simes(),
- Hochberg tests for adjust\_p\_hochberg().

## Usage

```
adjust_p_bonferroni(p, hypotheses)
adjust_p_parametric(
  р,
 hypotheses,
  test_corr = NULL,
 maxpts = 25000,
 abseps = 1e-06,
```

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```
releps = 0
adjust_p_simes(p, hypotheses)
adjust_p_hochberg(p, hypotheses)
```

#### **Arguments**

A numeric vector of p-values (unadjusted, raw), whose values should be bep tween 0 & 1. The length should match the length of hypotheses. hypotheses A numeric vector of hypothesis weights. Must be a vector of values between 0 & 1 (inclusive). The length should match the length of p. The sum of hypothesis weights should not exceed 1. (Optional) A numeric matrix of correlations between test statistics, which is test\_corr needed to perform parametric tests using adjust\_p\_parametric(). The number of rows and columns of this correlation matrix should match the length of (Optional) An integer scalar for the maximum number of function values, which maxpts is needed to perform parametric tests using the mytnorm::GenzBretz algorithm. The default is 25000. (Optional) A numeric scalar for the absolute error tolerance, which is needed to abseps perform parametric tests using the mytnorm::GenzBretz algorithm. The default is 1e-6. releps (Optional) A numeric scalar for the relative error tolerance as double, which is

needed to perform parametric tests using the mvtnorm::GenzBretz algorithm.

The default is 0.

## Value

A single adjusted p-value for the intersection hypothesis.

#### References

Bretz, F., Maurer, W., Brannath, W., and Posch, M. (2009). A graphical approach to sequentially rejective multiple test procedures. Statistics in Medicine, 28(4), 586-604.

Lu, K. (2016). Graphical approaches using a Bonferroni mixture of weighted Simes tests. Statistics in Medicine, 35(22), 4041-4055.

Xi, D., Glimm, E., Maurer, W., and Bretz, F. (2017). A unified framework for weighted parametric multiple test procedures. Biometrical Journal, 59(5), 918-931.

Xi, D., and Bretz, F. (2019). Symmetric graphs for equally weighted tests, with application to the Hochberg procedure. Statistics in Medicine, 38(27), 5268-5282.

#### See Also

adjust\_weights\_parametric() for adjusted hypothesis weights using parametric tests, adjust\_weights\_simes() for adjusted hypothesis weights using Simes tests, adjust\_weights\_hochberg() for adjusted hypothesis weights using Hochberg tests.

## **Examples**

```
hypotheses <- c(H1 = 0.5, H2 = 0.25, H3 = 0.25)
p <- c(0.019, 0.025, 0.05)
adjust_p_bonferroni(p, hypotheses)
set.seed(1234)
hypotheses <- c(H1 = 0.5, H2 = 0.25, H3 = 0.25)
p <- c(0.019, 0.025, 0.05)
# Using the `mvtnorm::GenzBretz` algorithm
corr \leftarrow matrix(0.5, nrow = 3, ncol = 3)
diag(corr) <- 1
adjust_p_parametric(p, hypotheses, corr)
hypotheses <- c(H1 = 0.5, H2 = 0.25, H3 = 0.25)
p \leftarrow c(0.019, 0.025, 0.05)
adjust_p_simes(p, hypotheses)
hypotheses <- c(H1 = .25, H2 = .25, H3 = 0.25, H4 = 0.25)
p \leftarrow c(0.019, 0.025, 0.05, .05)
adjust_p_hochberg(p, hypotheses)
```

adjust\_weights\_parametric

Calculate adjusted hypothesis weights

## **Description**

An intersection hypothesis can be rejected if its p-values are less than or equal to their adjusted significance levels, which are their adjusted hypothesis weights times  $\alpha$ . For Bonferroni tests, their adjusted hypothesis weights are their hypothesis weights of the intersection hypothesis. Additional adjustment is needed for parametric, Simes, and Hochberg tests:

- Parametric tests for adjust\_weights\_parametric(),
  - Note that one-sided tests are required for parametric tests.
- Simes tests for adjust\_weights\_simes(),
- Hochberg tests for adjust\_weights\_hochberg().

## Usage

```
adjust_weights_parametric(
   matrix_weights,
   matrix_intersections,
   test_corr,
   alpha,
   test_groups,
   ...
)
adjust_weights_simes(matrix_weights, p, test_groups)
adjust_weights_hochberg(matrix_weights, matrix_intersections, p, test_groups)
```

#### **Arguments**

matrix\_weights (Optional) A matrix of hypothesis weights of all intersection hypotheses. This can be obtained as the second half of columns from the output of graph\_generate\_weights(). matrix\_intersections (Optional) A matrix of hypothesis indicators of all intersection hypotheses. This can be obtained as the first half of columns from the output of graph\_generate\_weights(). (Optional) A numeric matrix of correlations between test statistics, which is test\_corr needed to perform parametric tests using adjust\_weights\_parametric(). The number of rows and columns of this correlation matrix should match the length alpha (Optional) A numeric value of the overall significance level, which should be between 0 & 1. The default is 0.025 for one-sided hypothesis testing problems; another common choice is 0.05 for two-sided hypothesis testing problems. Note when parametric tests are used, only one-sided tests are supported. test\_groups (Optional) A list of numeric vectors specifying hypotheses to test together. Grouping is needed to correctly perform Simes and parametric tests. Additional arguments to perform parametric tests using the mvtnorm::GenzBretz algorithm. maxpts is an integer scalar for the maximum number of function values, whose default value is 25000. abseps is a numeric scalar for the absolute error tolerance, whose default value is 1e-6. releps is a numeric scalar for the relative error tolerance as double, whose default value is 0. (Optional) A numeric vector of p-values (unadjusted, raw), whose values should р be between 0 & 1. The length should match the number of columns of matrix\_weights.

#### Value

- adjust\_weights\_parametric() returns a matrix with the same dimensions as matrix\_weights, whose hypothesis weights have been adjusted according to parametric tests.
- adjust\_weights\_simes() returns a matrix with the same dimensions as matrix\_weights, whose hypothesis weights have been adjusted according to Simes tests.
- adjust\_weights\_hochberg() returns a matrix with the same dimensions as matrix\_weights, whose hypothesis weights have been adjusted according to Hochberg tests.

#### References

Lu, K. (2016). Graphical approaches using a Bonferroni mixture of weighted Simes tests. *Statistics in Medicine*, 35(22), 4041-4055.

Xi, D., Glimm, E., Maurer, W., and Bretz, F. (2017). A unified framework for weighted parametric multiple test procedures. *Biometrical Journal*, 59(5), 918-931.

Xi, D., and Bretz, F. (2019). Symmetric graphs for equally weighted tests, with application to the Hochberg procedure. *Statistics in Medicine*, 38(27), 5268-5282.

#### See Also

adjust\_p\_parametric() for adjusted p-values using parametric tests, adjust\_p\_simes() for adjusted p-values using Simes tests, adjust\_p\_hochberg() for adjusted p-values using Hochberg tests.

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## **Examples**

```
alpha <- 0.025
num_hyps <- 4
g <- bonferroni_holm(num_hyps)</pre>
weighting_strategy <- graph_generate_weights(g)</pre>
matrix_intersections <- weighting_strategy[, seq_len(num_hyps)]</pre>
matrix_weights <- weighting_strategy[, -seq_len(num_hyps)]</pre>
set.seed(1234)
adjust_weights_parametric(
  matrix_weights = matrix_weights,
  matrix_intersections = matrix_intersections,
  test_corr = list(diag(2), diag(2)),
  alpha = alpha,
  test\_groups = list(1:2, 3:4)
)
alpha <- 0.025
p < -c(0.018, 0.01, 0.105, 0.006)
num_hyps <- length(p)</pre>
g <- bonferroni_holm(num_hyps)</pre>
weighting_strategy <- graph_generate_weights(g)</pre>
matrix_intersections <- weighting_strategy[, seq_len(num_hyps)]</pre>
matrix_weights <- weighting_strategy[, -seq_len(num_hyps)]</pre>
adjust_weights_simes(
  matrix_weights = matrix_weights,
  p = p,
  test\_groups = list(1:2, 3:4)
)
alpha <- 0.025
p \leftarrow c(0.018, 0.01, 0.105, 0.006)
num_hyps <- length(p)</pre>
g <- bonferroni_holm(num_hyps)</pre>
weighting_strategy <- graph_generate_weights(g)</pre>
matrix_intersections <- weighting_strategy[, seq_len(num_hyps)]</pre>
matrix_weights <- weighting_strategy[, -seq_len(num_hyps)]</pre>
adjust_weights_hochberg(
  matrix_weights = matrix_weights,
  matrix_intersections = matrix_intersections,
  p = p,
  test\_groups = list(1:2, 3:4)
)
```

as\_initial\_graph

Convert between graphicalMCP, gMCP, and igraph graph classes

#### Description

Graph objects have different structures and attributes in graphical MCP, gMCP, and igraph R packages. These functions convert between different classes to increase compatibility.

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Note that igraph and gMCP have additional attributes for vertices, edges, or a graph itself. These conversion functions only handle attributes related to hypothesis names, hypothesis weights and transition weights. Other attributes will be dropped when converting.

#### Usage

```
as_initial_graph(graph)

## S3 method for class 'graphMCP'
as_initial_graph(graph)

## S3 method for class 'igraph'
as_initial_graph(graph)

as_graphMCP(graph)

## S3 method for class 'initial_graph'
as_graphMCP(graph)

## S3 method for class 'initial_graph'
as_igraph(graph)

## S3 method for class 'initial_graph'
as_igraph(graph)
```

#### **Arguments**

graph

An initial\_graph object from the graphicalMCP package, a graphMCP object from the gMCP package, or an igraph object from the igraph package, depending on the conversion type.

#### Value

- as\_graphMCP() returns a graphMCP object for the gMCP package.
- as\_igraph() returns an igraph object for the igraph package.
- as\_initial\_graph() returns an initial\_graph object for the graphicalMCP package.

#### References

Csardi, G., Nepusz, T., Traag, V., Horvat, S., Zanini, F., Noom, D., and Mueller, K. (2024). *igraph*: Network analysis and visualization in R. R package version 2.0.3. https://CRAN.R-project.org/package=igraph.

Rohmeyer, K., and Klinglmueller, K. (2024). *gMCP*: Graph based multiple test procedures. R package version 0.8-17. https://cran.r-project.org/package=gMCP.

#### See Also

graph\_create() for the initial graph used in the graphicalMCP package.

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## **Examples**

```
g_graphicalMCP <- random_graph(5)

if (requireNamespace("gMCP", quietly = TRUE)) {
    g_gMCP <- as_graphMCP(g_graphicalMCP)

    all.equal(g_graphicalMCP, as_initial_graph(g_gMCP))
}

if (requireNamespace("igraph", quietly = TRUE)) {
    g_igraph <- as_igraph(g_graphicalMCP)

    all.equal(g_graphicalMCP, as_initial_graph(g_igraph))
}</pre>
```

bonferroni

Example graphs of commonly used multiple comparison procedures

#### **Description**

Built-in functions to quickly generate select graphical multiple comparison procedures.

#### Usage

```
bonferroni(num_hyps, hyp_names = NULL)
bonferroni_weighted(hypotheses, hyp_names = NULL)
bonferroni_holm(num_hyps, hyp_names = NULL)
bonferroni_holm_weighted(hypotheses, hyp_names = NULL)
dunnett_single_step(num_hyps, hyp_names = NULL)
dunnett_single_step_weighted(hypotheses, hyp_names = NULL)
dunnett_closure_weighted(hypotheses, hyp_names = NULL)
hochberg(num_hyps, hyp_names = NULL)
hommel(num_hyps, hyp_names = NULL)
huque_etal(hyp_names = NULL)
fallback(hypotheses, hyp_names = NULL)
fallback_improved_1(hypotheses, hyp_names = NULL)
```

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```
fallback_improved_2(hypotheses, epsilon = 1e-04, hyp_names = NULL)
fixed_sequence(num_hyps, hyp_names = NULL)
sidak(num_hyps, hyp_names = NULL)
simple_successive_1(hyp_names = NULL)
simple_successive_2(hyp_names = NULL)
two_doses_two_primary_two_secondary(hyp_names = NULL)
three_doses_two_primary_two_secondary(hyp_names = NULL)
random_graph(num_hyps, hyp_names = NULL)
```

#### **Arguments**

num_hyps hyp_names	(Optional) Number of hypotheses in a graphical multiple comparison procedure. (Optional) A character vector of hypothesis names. The length should match num_hyps and the length of hypotheses. If hyp_names are not specified, hypotheses will be named sequentially as H1, H2,
hypotheses	(Optional) A numeric vector of hypothesis weights in a graphical multiple comparison procedure. Must be a vector of values between 0 & 1 (inclusive). The length should match num_hyps and the length of hyp_names. The sum of hypothesis weights should not exceed 1.
epsilon	(Optional) A numeric scalar indicating the value of the $\epsilon$ edge. This should be a much smaller value than hypothesis and transition weights. The default is 1e-4.

## Value

An S3 object as returned by graph\_create().

#### References

Bretz, F., Maurer, W., Brannath, W., and Posch, M. (2009). A graphical approach to sequentially rejective multiple test procedures. *Statistics in Medicine*, 28(4), 586-604.

Bretz, F., Posch, M., Glimm, E., Klinglmueller, F., Maurer, W., and Rohmeyer, K. (2011). Graphical approaches for multiple comparison procedures using weighted Bonferroni, Simes, or parametric tests. *Biometrical Journal*, 53(6), 894-913.

Hochberg, Y. (1988). A sharper Bonferroni procedure for multiple tests of significance. *Biometrika*, 75(4), 800-802.

Hommel, G. (1988). A stagewise rejective multiple test procedure based on a modified Bonferroni test. *Biometrika*, 75(2), 383-386.

Huque, M. F., Alosh, M., and Bhore, R. (2011). Addressing multiplicity issues of a composite endpoint and its components in clinical trials. *Journal of Biopharmaceutical Statistics*, 21(4), 610-634.

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Maurer, W., Hothorn, L., and Lehmacher, W. (1995). Multiple comparisons in drug clinical trials and preclinical assays: a-priori ordered hypotheses. *Biometrie in der chemisch-pharmazeutischen Industrie*, 6, 3-18.

Šidák, Z. (1967). Rectangular confidence regions for the means of multivariate normal distributions. *Journal of the American Statistical Association*, 62(318), 626-633.

Westfall, P. H., and Krishen, A. (2001). Optimally weighted, fixed sequence and gatekeeper multiple testing procedures. *Journal of Statistical Planning and Inference*, 99(1), 25-40.

Wiens, B. L. (2003). A fixed sequence Bonferroni procedure for testing multiple endpoints. *Pharmaceutical Statistics*, 2(3), 211-215.

Wiens, B. L., and Dmitrienko, A. (2005). The fallback procedure for evaluating a single family of hypotheses. *Journal of Biopharmaceutical Statistics*, 15(6), 929-942.

Xi, D., and Bretz, F. (2019). Symmetric graphs for equally weighted tests, with application to the Hochberg procedure. *Statistics in Medicine*, 38(27), 5268-5282.

#### See Also

graph\_create() for a general way to create the initial graph.

```
# Bretz et al. (2009)
bonferroni(num_hyps = 3)
# Bretz et al. (2009)
hypotheses <- c(0.5, 0.3, 0.2)
bonferroni_weighted(hypotheses)
# Bretz et al. (2009)
bonferroni_holm(num_hyps = 3)
# Bretz et al. (2009)
hypotheses <- c(0.5, 0.3, 0.2)
bonferroni_holm_weighted(hypotheses)
# Xi et al. (2017)
dunnett_single_step(num_hyps = 3)
# Xi et al. (2017)
hypotheses <- c(0.5, 0.3, 0.2)
dunnett_single_step_weighted(hypotheses)
# Xi et al. (2009)
hypotheses <- c(0.5, 0.3, 0.2)
dunnett_closure_weighted(hypotheses)
# Hochberg (1988)
hochberg(num_hyps = 3)
# Hommel (1988)
hommel(num\_hyps = 3)
# Hugue et al. (2011)
huque_etal()
# Wiens (2003)
hypotheses <- c(0.5, 0.3, 0.2)
fallback(hypotheses)
# Wiens and Dmitrienko (2005)
hypotheses <- c(0.5, 0.3, 0.2)
fallback_improved_1(hypotheses)
```

graph\_calculate\_power

```
# Bretz et al. (2009)
hypotheses <- c(0.5, 0.3, 0.2)
fallback_improved_2(hypotheses)
# Maurer et al. (1995); Westfall and Krishen (2001)
fixed_sequence(num_hyps = 3)
# sidak (1967)
sidak(num_hyps = 3)
# Figure 1 in Bretz et al. (2011)
simple_successive_1()
# Figure 4 in Bretz et al. (2011)
simple_successive_2()
# Figure 6 in Xi and Bretz et al. (2019)
two_doses_two_primary_two_secondary()
# Add another dose to Figure 6 in Xi and Bretz et al. (2019)
three_doses_two_primary_two_secondary()
# Create a random graph with three hypotheses
random_graph(num_hyps = 3)
```

## **Description**

Under the alternative hypotheses, the distribution of test statistics is assumed to be a multivariate normal distribution. Given this distribution, this function calculates power values for a graphical multiple comparison procedure. By default, it calculate the local power, which is the probability to reject an individual hypothesis, the probability to reject at least one hypothesis, the probability to reject all hypotheses, the expected number of rejections, and the probability of user-defined success criteria. See vignette("shortcut-testing") and vignette("closed-testing") for more illustration of power calculation.

#### Usage

```
graph_calculate_power(
   graph,
   alpha = 0.025,
   power_marginal = rep(alpha, length(graph$hypotheses)),
   test_groups = list(seq_along(graph$hypotheses)),
   test_types = c("bonferroni"),
   test_corr = rep(list(NA), length(test_types)),
   sim_n = 1e+05,
   sim_corr = diag(length(graph$hypotheses)),
   sim_success = NULL,
   verbose = FALSE
)
```

#### **Arguments**

graph An initial graph as returned by graph\_create().

alpha A numeric value of the one-sided overall significance level, which should be

between 0 & 1. The default is 0.025 for one-sided hypothesis testing. Note that

only one-sided tests are supported.

power\_marginal A numeric vector of marginal power values to use when simulating p-values.

See Details for more on the simulation process.

test\_groups A list of numeric vectors specifying hypotheses to test together. Grouping is

needed to correctly perform Simes and parametric tests.

test\_types A character vector of test types to apply to each test group. This is needed

to correctly perform Simes and parametric tests. The length should match the

number of elements in test\_groups.

test\_corr (Optional) A list of numeric correlation matrices. Each entry in the list should

correspond to each test group. For a test group using Bonferroni or Simes tests, its corresponding entry in test\_corr should be NA. For a test group using parametric tests, its corresponding entry in test\_corr should be a numeric correlation matrix specifying the correlation between test statistics for hypotheses in this test group. The length should match the number of elements in

test\_groups.

sim\_n An integer scalar specifying the number of simulations. The default is 1e5.

sim\_corr A numeric matrix of correlations between test statistics for all hypotheses. The

dimensions should match the number of hypotheses in graph.

sim\_success A list of user-defined functions to specify the success criteria. Functions must

take one simulation's logical vector of results as an input, and return a lengthone logical vector. For instance, if "success" means rejecting hypotheses 1 and 2, use  $sim\_success = list("1 and 2" = function(x) x[1] && x[2])$ . If the list is not named, the function body will be used as the name. Lambda functions also work starting with R 4.1, e.g.  $sim\_success = list(\x) x[3] || x[4])$ .

verbose A logical scalar specifying whether the details of power simulations should be

included in results. The default is verbose = FALSE.

#### Value

A power\_report object with a list of 3 elements:

- inputs Input parameters, which is a list of:
  - graph Initial graph,
  - alpha Overall significance level,
  - test\_groups Groups of hypotheses for different types of tests,
  - test\_types Different types of tests,
  - test\_corr Correlation matrices for parametric tests,
  - sim\_n Number of simulations,
  - power\_marginal Marginal power of all hypotheses
  - sim\_corr Correlation matrices for simulations,

- sim\_success User-defined success criteria.
- power A list of power values
  - power\_local Local power of all hypotheses, which is the proportion of simulations in which each hypothesis is rejected,
  - rejection\_expected Expected (average) number of rejected hypotheses,
  - power\_at\_least\_1 Power to reject at least one hypothesis,
  - power\_all Power to reject all hypotheses,
  - power\_success Power of user-defined success, which is the proportion of simulations in which the user-defined success criterion
  - sim\_success is met.
- details An optional list of datasets showing simulated p-values and results for each simulation.

#### Simulation details

The power calculation is based on simulations. The distribution to simulate from is determined as a multivariate normal distribution by power\_marginal and sim\_corr. In particular, power\_marginal is a vector of marginal power values for all hypotheses. The marginal power is the power to reject the null hypothesis at the significance level alpha *without multiplicity adjustment*. This value could be readily available from standard software and other R packages. Then we can determine the mean of the multivariate normal distribution as

$$\Phi^{-1}(1-\alpha) - \Phi^{-1}(1-d_i)$$

, which is often called the non-centrality parameter or the drift parameter. Here  $d_i$  is the marginal power power\_marginal of hypothesis i. Given the correlation matrix sim\_corr, we can simulate from this multivariate normal distribution using the mvtnorm R package (Genz and Bretz, 2009).

Each set simulated values can be used to calculate the corresponding one-sided p-values. Then this set of p-values are plugged into the graphical multiple comparison procedure to determine which hypotheses are rejected. This process is repeated n\_sim times to produce the power values as the proportion of simulations in which a particular success criterion is met.

## References

Bretz, F., Posch, M., Glimm, E., Klinglmueller, F., Maurer, W., and Rohmeyer, K. (2011a). Graphical approaches for multiple comparison procedures using weighted Bonferroni, Simes, or parametric tests. *Biometrical Journal*, 53(6), 894-913.

Bretz, F., Maurer, W., and Hommel, G. (2011b). Test and power considerations for multiple endpoint analyses using sequentially rejective graphical procedures. *Statistics in Medicine*, 30(13), 1489-1501.

Genz, A., and Bretz, F. (2009). *Computation of Multivariate Normal and t Probabilities*, series Lecture Notes in Statistics. Springer-Verlag, Heidelberg.

Lu, K. (2016). Graphical approaches using a Bonferroni mixture of weighted Simes tests. *Statistics in Medicine*, 35(22), 4041-4055.

Xi, D., Glimm, E., Maurer, W., and Bretz, F. (2017). A unified framework for weighted parametric multiple test procedures. *Biometrical Journal*, 59(5), 918-931.

```
# A graphical multiple comparison procedure with two primary hypotheses (H1
# and H2) and two secondary hypotheses (H3 and H4)
# See Figure 4 in Bretz et al. (2011a).
alpha <- 0.025
hypotheses <- c(0.5, 0.5, 0, 0)
delta <- 0.5
transitions <- rbind(</pre>
  c(0, delta, 1 - delta, 0),
  c(delta, 0, 0, 1 - delta),
  c(0, 1, 0, 0),
  c(1, 0, 0, 0)
)
g <- graph_create(hypotheses, transitions)</pre>
marginal_power <- c(0.8, 0.8, 0.7, 0.9)
corr1 \leftarrow matrix(0.5, nrow = 2, ncol = 2)
diag(corr1) <- 1
corr <- rbind(</pre>
  cbind(corr1, 0.5 * corr1),
  cbind(0.5 * corr1, corr1)
success_fns <- list(</pre>
  # Probability to reject both H1 and H2
  `H1andH2` = function(x) x[1] \& x[2],
  # Probability to reject both (H1 and H3) or (H2 and H4)
  `(H1andH3)or(H2andH4)` = function(x) (x[1] & x[3]) | (x[2] & x[4])
)
set.seed(1234)
# Bonferroni tests
# Reduce the number of simulations to save time for package compilation
power_output <- graph_calculate_power(</pre>
  g,
  alpha,
  sim_corr = corr,
  sim_n = 1e2,
  power_marginal = marginal_power,
  sim_success = success_fns
)
# Parametric tests for H1 and H2; Simes tests for H3 and H4
# User-defined success: to reject H1 or H2; to reject H1 and H2
# Reduce the number of simulations to save time for package compilation
graph_calculate_power(
  g,
  alpha,
  test\_groups = list(1:2, 3:4),
  test_types = c("parametric", "simes"),
  test_corr = list(corr1, NA),
  sim_n = 1e2,
  sim_success = list(
    function(.) .[1] || .[2],
```

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```
function(.) .[1] && .[2]
)
)
```

graph\_create

Create the initial graph for a multiple comparison procedure

## **Description**

A graphical multiple comparison procedure is represented by 1) a vector of initial hypothesis weights hypotheses, and 2) a matrix of initial transition weights transitions. This function creates the initial graph object using hypothesis weights and transition weights.

#### Usage

```
graph_create(hypotheses, transitions, hyp_names = NULL)
```

#### **Arguments**

hypotheses A numeric vector of hypothesis weights in a graphical multiple comparison pro-

cedure. Must be a vector of values between 0 & 1 (inclusive). The length should match the row and column lengths of transitions. The sum of hypothesis

weights should not exceed 1.

transitions A numeric matrix of transition weights between hypotheses in a graphical multi-

ple comparison procedure. Must be a square matrix of values between 0 & 1 (inclusive). The row and column lengths should match the length of hypotheses. Each row (Transition weights leaving a hypothesis) can sum to no more than 1. The diagonal entries (Transition weights from a hypothesis to itself) must be all

0s.

hyp\_names (Optional) A character vector of hypothesis names. If not provided, names from

hypotheses and transitions will be used. If names are not specified, hy-

potheses will be named sequentially as H1, H2, ......

## Value

An S3 object of class initial\_graph with a list of 2 elements:

- Hypothesis weights hypotheses.
- Transition weights transitions.

#### Validation of inputs

Inputs are also validated to make sure of the validity of the graph:

- Hypothesis weights hypotheses are numeric.
- Transition weights transitions are numeric.

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- Length of hypotheses and dimensions of transitions match.
- Hypothesis weights hypotheses must be non-negative and sum to no more than 1.
- Transition weights transitions:
  - Values must be non-negative.
  - Rows must sum to no more than 1.
  - Diagonal entries must be all 0.
- Hypothesis names hyp\_names override names in hypotheses or transitions.

#### References

Bretz, F., Maurer, W., Brannath, W., and Posch, M. (2009). A graphical approach to sequentially rejective multiple test procedures. *Statistics in Medicine*, 28(4), 586-604.

Bretz, F., Posch, M., Glimm, E., Klinglmueller, F., Maurer, W., and Rohmeyer, K. (2011). Graphical approaches for multiple comparison procedures using weighted Bonferroni, Simes, or parametric tests. *Biometrical Journal*, 53(6), 894-913.

#### See Also

graph\_update() for the updated graph after hypotheses being deleted from the initial graph.

```
# A graphical multiple comparison procedure with two primary hypotheses (H1
# and H2) and two secondary hypotheses (H3 and H4)
# See Figure 1 in Bretz et al. (2011).
hypotheses <-c(0.5, 0.5, 0, 0)
transitions <- rbind(</pre>
  c(0, 0, 1, 0),
  c(0, 0, 0, 1),
  c(0, 1, 0, 0),
  c(1, 0, 0, 0)
hyp_names <- c("H11", "H12", "H21", "H22")
g <- graph_create(hypotheses, transitions, hyp_names)</pre>
# Explicit names override names in `hypotheses` (with a warning)
hypotheses <- c(h1 = 0.5, h2 = 0.5, h3 = 0, h4 = 0)
transitions <- rbind(</pre>
  c(0, 0, 1, 0),
  c(0, 0, 0, 1),
 c(0, 1, 0, 0),
  c(1, 0, 0, 0)
g <- graph_create(hypotheses, transitions, hyp_names)</pre>
g
# Use names in `transitions`
hypotheses <- c(0.5, 0.5, 0, 0)
transitions <- rbind(</pre>
```

```
H1 = c(0, 0, 1, 0),
  H2 = c(0, 0, 0, 1),
  H3 = c(0, 1, 0, 0),
  H4 = c(1, 0, 0, 0)
)
g <- graph_create(hypotheses, transitions)</pre>
g
# Unmatched names in `hypotheses` and `transitions` (with an error)
hypotheses <- c(h1 = 0.5, h2 = 0.5, h3 = 0, h4 = 0)
transitions <- rbind(</pre>
  H1 = c(0, 0, 1, 0),
  H2 = c(0, 0, 0, 1),
 H3 = c(0, 1, 0, 0),
 H4 = c(1, 0, 0, 0)
)
try(
  g <- graph_create(hypotheses, transitions)</pre>
# When names are not specified, hypotheses are numbered sequentially as
# H1, H2, ...
hypotheses <- c(0.5, 0.5, 0, 0)
transitions <- rbind(</pre>
  c(0, 0, 1, 0),
  c(0, 0, 0, 1),
  c(0, 1, 0, 0),
  c(1, 0, 0, 0)
)
g <- graph_create(hypotheses, transitions)</pre>
```

graph\_generate\_weights

Generate the weighting strategy based on a graphical multiple comparison procedure

## **Description**

A graphical multiple comparison procedure defines a closed test procedure, which tests each intersection hypothesis and reject an individual hypothesis if all intersection hypotheses involving it have been rejected. An intersection hypothesis represents the parameter space where individual null hypotheses involved are true simultaneously.

The closure based on a graph consists of all updated graphs (corresponding to intersection hypotheses) after all combinations of hypotheses are deleted. For a graphical multiple comparison procedure with m hypotheses, there are  $2^m-1$  updated graphs (intersection hypotheses), including the initial graph (the overall intersection hypothesis). The weighting strategy of this graph consists of hypothesis weights from all  $2^m-1$  updated graphs (intersection hypotheses). The algorithm to derive the weighting strategy is based on Algorithm 1 in Bretz et al. (2011).

#### Usage

```
graph_generate_weights(graph)
```

#### **Arguments**

graph

An initial graph as returned by graph\_create().

#### Value

A numeric matrix of all intersection hypotheses and their hypothesis weights. For a graphical multiple comparison procedure with m hypotheses, the number of rows is  $2^m-1$ , each of which corresponds to an intersection hypothesis. The number of columns is  $2 \cdot m$ . The first m columns indicate which individual hypotheses are included in a given intersection hypothesis and the second half of columns provide hypothesis weights for each individual hypothesis for a given intersection hypothesis.

#### Performance

Generation of intersection hypotheses is closely related to the power set of a given set of indices. As the number of hypotheses increases, the memory and time usage can grow quickly (e.g., at a rate of  $O(2^n)$ ). There are also multiple ways to implement Algorithm 1 in Bretz et al. (2011). See vignette("generate-closure") for more information about generating intersection hypotheses and comparisons of different approaches to calculate weighting strategies.

#### References

Bretz, F., Posch, M., Glimm, E., Klinglmueller, F., Maurer, W., and Rohmeyer, K. (2011). Graphical approaches for multiple comparison procedures using weighted Bonferroni, Simes, or parametric tests. *Biometrical Journal*, 53(6), 894-913.

#### See Also

graph\_test\_closure() for graphical multiple comparison procedures using the closed test.

```
# A graphical multiple comparison procedure with two primary hypotheses (H1 # and H2) and two secondary hypotheses (H3 and H4) # See Figure 1 in Bretz et al. (2011). hypotheses <- c(0.5, 0.5, 0.0) transitions <- rbind( c(0, 0, 1, 0), c(0, 0, 0, 1), c(0, 1, 0, 0), c(1, 0, 0, 0)) g <- graph_create(hypotheses, transitions) graph_generate_weights(g)
```

```
graph_rejection_orderings
```

Find alternate rejection orderings (sequences) for shortcut tests

#### **Description**

When multiple hypotheses are rejected by using graph\_test\_shortcut(), there may be multiple orderings or sequences in which hypotheses are rejected one by one. The default order in graph\_test\_shortcut() is based on the adjusted p-values, from the smallest to the largest. This function graph\_rejection\_orderings() provides all possible and valid orders (or sequences) of rejections. Although the order of rejection does not affect the final rejection decisions Bretz et al. (2009), different sequences could offer different ways to explain the step-by-step process of shortcut graphical multiple comparison procedures.

## Usage

```
graph_rejection_orderings(shortcut_test_result)
```

#### **Arguments**

```
shortcut_test_result

A graph_report object as returned by graph_test_shortcut().
```

#### Value

A modified graph\_report object containing all valid orderings of rejections of hypotheses

#### References

Bretz, F., Maurer, W., Brannath, W., and Posch, M. (2009). A graphical approach to sequentially rejective multiple test procedures. *Statistics in Medicine*, 28(4), 586-604.

Bretz, F., Posch, M., Glimm, E., Klinglmueller, F., Maurer, W., and Rohmeyer, K. (2011). Graphical approaches for multiple comparison procedures using weighted Bonferroni, Simes, or parametric tests. *Biometrical Journal*, 53(6), 894-913.

## See Also

graph\_test\_shortcut() for shortcut graphical multiple comparison procedures.

```
# A graphical multiple comparison procedure with two primary hypotheses (H1
# and H2) and two secondary hypotheses (H3 and H4)
# See Figure 4 in Bretz et al. (2011).
hypotheses <- c(0.5, 0.5, 0, 0)
delta <- 0.5
transitions <- rbind(
   c(0, delta, 1 - delta, 0),</pre>
```

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```
c(delta, 0, 0, 1 - delta),
 c(0, 1, 0, 0),
 c(1, 0, 0, 0)
)
g <- graph_create(hypotheses, transitions)</pre>
p \leftarrow c(0.018, 0.01, 0.105, 0.006)
alpha <- 0.025
shortcut_testing <- graph_test_shortcut(g, p, alpha, verbose = TRUE)</pre>
# Reject H1, H2, and H4
shortcut_testing$outputs$rejected
# Default order of rejections: H2, H1, H4
shortcut_testing$details$del_seq
# There is another valid sequence of rejection: H2, H4, H1
graph_rejection_orderings(shortcut_testing)$valid_orderings
# Finally, intermediate updated graphs can be obtained by providing the order
# of rejections into `[graph_update()]`
graph\_update(g, delete = c(2, 4, 1))
```

graph\_test\_closure

Perform closed graphical multiple comparison procedures

## **Description**

Closed graphical multiple comparison procedures, or graphical multiple comparison procedures based on the closure, generate the closure based on a graph consisting of all intersection hypotheses. It tests each intersection hypothesis and rejects an individual hypothesis if all intersection hypotheses involving it have been rejected. An intersection hypothesis represents the parameter space where individual null hypotheses involved are true simultaneously.

For a graphical multiple comparison procedure with \$m\$ hypotheses, there are  $2^m-1$  intersection hypotheses. For each intersection hypothesis, a test type could be chosen to determine how to reject the intersection hypothesis. Current choices of test types include Bonferroni, Simes and parametric. This implementation offers a more general framework covering Bretz et al. (2011), Lu (2016), and Xi et al. (2017). See vignette("closed-testing") for more illustration of closed test procedures and interpretation of their outputs.

#### Usage

```
graph_test_closure(
  graph,
  p,
  alpha = 0.025,
  test_groups = list(seq_along(graph$hypotheses)),
```

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```
test_types = c("bonferroni"),
test_corr = rep(list(NA), length(test_types)),
verbose = FALSE,
test_values = FALSE
)
```

## **Arguments**

graph An initial graph as returned by graph\_create().

p A numeric vector of p-values (unadjusted, raw), whose values should be be-

tween 0 & 1. The length should match the number of hypotheses in graph.

alpha A numeric value of the overall significance level, which should be between 0

& 1. The default is 0.025 for one-sided hypothesis testing problems; another common choice is 0.05 for two-sided hypothesis testing problems. Note when

parametric tests are used, only one-sided tests are supported.

test\_groups A list of numeric vectors specifying hypotheses to test together. Grouping is

needed to correctly perform Simes and parametric tests.

test\_types A character vector of test types to apply to each test group. This is needed

to correctly perform Simes and parametric tests. The length should match the

number of elements in test\_groups.

test\_corr (Optional) A list of numeric correlation matrices. Each entry in the list should

correspond to each test group. For a test group using Bonferroni or Simes tests, its corresponding entry in test\_corr should be NA. For a test group using parametric tests, its corresponding entry in test\_corr should be a numeric correlation matrix specifying the correlation between test statistics for hypotheses in this test group. The length should match the number of elements in

test\_groups.

verbose A logical scalar specifying whether the details of the adjusted p-value calcula-

tions should be included in results. When verbose = TRUE, adjusted p-values are provided for each intersection hypothesis. The default is verbose = FALSE.

test\_values A logical scalar specifying whether adjusted significance levels should be pro-

vided for each hypothesis. When test\_values = TRUE, it provides an equivalent way of performing graphical multiple comparison procedures by comparing each p-value with its significance level. If the p-value of a hypothesis is less than or equal to its significance level, the hypothesis is rejected. The default is

test values = FALSE.

#### Value

A graph\_report object with a list of 4 elements:

- inputs Input parameters, which is a list of:
  - graph Initial graph,
  - p (Unadjusted or raw) p-values,
  - alpha Overall significance level,
  - test\_groups Groups of hypotheses for different types of tests,

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- test\_types Different types of tests,
- test\_corr Correlation matrices for parametric tests.
- outputs Output parameters, which is a list of:
  - adjusted\_p Adjusted p-values,
  - rejected Rejected hypotheses,
  - graph Updated graph after deleting all rejected hypotheses.
- details Verbose outputs with adjusted p-values for intersection hypotheses, if verbose = TRUE
- test\_values Adjusted significance levels, if test\_values = TRUE.

#### **Details for test specification**

Test specification includes three components: test\_groups, test\_types, and test\_corr. Alignment among entries in these components is important for correct implementation. There are two ways to provide test specification. The first approach is the "unnamed" approach, which assumes that all 3 components are ordered the same way, i.e., the \$n\$-th element of test\_types and test\_corr should apply to the \$n\$-th group in test\_groups. The second "named" approach uses the name of each element of each component to connect the element of test\_types and test\_corr with the correct element of test\_groups. Consistency should be ensured for correct implementation.

#### References

Bretz, F., Posch, M., Glimm, E., Klinglmueller, F., Maurer, W., and Rohmeyer, K. (2011). Graphical approaches for multiple comparison procedures using weighted Bonferroni, Simes, or parametric tests. *Biometrical Journal*, 53(6), 894-913.

Lu, K. (2016). Graphical approaches using a Bonferroni mixture of weighted Simes tests. *Statistics in Medicine*, 35(22), 4041-4055.

Xi, D., Glimm, E., Maurer, W., and Bretz, F. (2017). A unified framework for weighted parametric multiple test procedures. *Biometrical Journal*, 59(5), 918-931.

## See Also

graph\_test\_shortcut() for shortcut graphical multiple comparison procedures.

```
# A graphical multiple comparison procedure with two primary hypotheses
# (H1 and H2) and two secondary hypotheses (H3 and H4)
# See Figure 4 in Bretz et al. (2011).
hypotheses <- c(0.5, 0.5, 0, 0)
delta <- 0.5
transitions <- rbind(
    c(0, delta, 1 - delta, 0),
    c(delta, 0, 0, 1 - delta),
    c(0, 1, 0, 0),
    c(1, 0, 0, 0)
)</pre>
```

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```
g <- graph_create(hypotheses, transitions)</pre>
p \leftarrow c(0.018, 0.01, 0.105, 0.006)
alpha <- 0.025
# Closed graphical multiple comparison procedure using Bonferroni tests
# Same results as `graph_test_shortcut(g, p, alpha)`
graph_test_closure(g, p, alpha)
# Closed graphical multiple comparison procedure using parametric tests for
# H1 and H2, and Bonferroni tests for H3 and H4
set.seed(1234)
corr_list \leftarrow list(matrix(c(1, 0.5, 0.5, 1), nrow = 2), NA)
graph_test_closure(
  graph = g,
  p = p,
  alpha = alpha,
  test\_groups = list(1:2, 3:4),
  test_types = c("parametric", "bonferroni"),
  test_corr = corr_list
)
# The "named" approach to obtain the same results
# Note that "group2" appears before "group1" in `test_groups`
set.seed(1234)
corr_list \leftarrow list(group1 = matrix(c(1, 0.5, 0.5, 1), nrow = 2), group2 = NA)
graph_test_closure(
  graph = g,
  p = p,
  alpha = alpha,
  test_groups = list(group1 = 1:2, group2 = 3:4),
  test_types = c(group2 = "bonferroni", group1 = "parametric"),
  test_corr = corr_list
)
# Closed graphical multiple comparison procedure using parametric tests for
# H1 and H2, and Simes tests for H3 and H4
set.seed(1234)
graph_test_closure(
  graph = g,
  p = p,
  alpha = alpha,
  test_groups = list(group1 = 1:2, group2 = 3:4),
  test_types = c(group1 = "parametric", group2 = "simes"),
  test_corr = corr_list
)
```

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## **Description**

Shortcut graphical multiple comparison procedures are sequentially rejective procedure based on Bretz et al. (2009). With \$m\$ hypotheses, there are at most \$m\$ steps to obtain all rejection decisions. These procedure are equivalent to closed graphical multiple comparison procedures using Bonferroni tests for intersection hypotheses, but shortcut procedures are faster to perform. See vignette("shortcut-testing") for more illustration of shortcut procedures and interpretation of their outputs.

#### Usage

```
graph_test_shortcut(
  graph,
  p,
  alpha = 0.025,
  verbose = FALSE,
  test_values = FALSE
)
```

## **Arguments**

graph An initial graph as returned by graph\_create().

p A numeric vector of p-values (unadjusted, raw), whose values should be be-

tween 0 & 1. The length should match the number of hypotheses in graph.

alpha A numeric scalar of the overall significance level, which should be between 0

& 1. The default is 0.025 for one-sided hypothesis testing problems; another

common choice is 0.05 for two-sided hypothesis testing problems.

verbose A logical scalar specifying whether the details of intermediate update graphs

should be included in results. When verbose = TRUE, intermediate update graphs are provided after deleting each hypothesis, which has been rejected. The de-

fault is verbose = FALSE.

test\_values A logical scalar specifying whether adjusted significance levels should be pro-

vided for each hypothesis. When test\_values = TRUE, it provides an equivalent way of performing graphical multiple comparison procedures by comparing each p-value with its significance level. If the p-value of a hypothesis is less than or equal to its significance level, the hypothesis is rejected. The order of rejection is based on the order of adjusted p-values from the smallest to the largest.

The default is test\_values = FALSE.

#### Value

An S3 object of class graph\_report with a list of 4 elements:

- inputs Input parameters, which is a list of:
  - graph Initial graph, \*p (Unadjusted or raw) p-values,
  - alpha Overall significance level,
  - test\_groups Groups of hypotheses for different types of tests, which are the list of all hypotheses for graph\_test\_shortcut(),

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- test\_types Different types of tests, which are "bonferroni" for graph\_test\_shortcut().
- Output parameters outputs, which is a list of:
  - adjusted\_p Adjusted p-values,
  - rejected Rejected hypotheses,
  - graph Updated graph after deleting all rejected hypotheses.
- details Verbose outputs with intermediate updated graphs, if verbose = TRUE.
- test\_values Adjusted significance levels, if test\_values = TRUE.

#### References

Bretz, F., Maurer, W., Brannath, W., and Posch, M. (2009). A graphical approach to sequentially rejective multiple test procedures. *Statistics in Medicine*, 28(4), 586-604.

Bretz, F., Posch, M., Glimm, E., Klinglmueller, F., Maurer, W., and Rohmeyer, K. (2011). Graphical approaches for multiple comparison procedures using weighted Bonferroni, Simes, or parametric tests. *Biometrical Journal*, 53(6), 894-913.

#### See Also

- graph\_test\_closure() for graphical multiple comparison procedures using the closed test,
- graph\_rejection\_orderings() for all possible rejection orderings.

## **Examples**

```
# A graphical multiple comparison procedure with two primary hypotheses (H1 # and H2) and two secondary hypotheses (H3 and H4) # See Figure 1 in Bretz et al. (2011). hypotheses <- c(0.5, 0.5, 0, 0) transitions <- rbind( c(0, 0, 1, 0), c(0, 0, 0, 1), c(0, 1, 0, 0), c(1, 0, 0, 0)) g <- graph_create(hypotheses, transitions) p <- c(0.018, 0.01, 0.105, 0.006) alpha <- 0.025 graph_test_shortcut(g, p, alpha)
```

graph\_update

Obtain an updated graph by updating an initial graphical after deleting hypotheses

#### **Description**

After a hypothesis is deleted, an initial graph will be updated. The deleted hypothesis will have the hypothesis weight of 0 and the transition weight of 0. Remaining hypotheses will have updated hypothesis weights and transition weights according to Algorithm 1 of Bretz et al. (2009).

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#### Usage

```
graph_update(graph, delete)
```

#### **Arguments**

graph

An initial graph as returned by graph\_create().

delete

A logical or integer vector, denoting which hypotheses to delete. A logical vector results in the "unordered mode", which means that hypotheses corresponding to TRUE in delete will be deleted. The sequence of deletion will follow the sequence of TRUE's in delete. In this case, the length of the logical vector must match the number of hypotheses in graph. An integer vector results in the "ordered mode", which means that delete specifies the sequence in which hypotheses should be deleted by indicating the location of deleted hypotheses, e.g., 1st, 2nd, etc. In this case, the integer vector can have any length, but must only contain valid hypothesis numbers (greater than 0, and less than or equal to he number of hypotheses in graph).

#### Value

An S3 object of class updated\_graph with a list of 4 elements:

- initial\_graph: The initial graph object.
- updated\_graph: The updated graph object with specified hypotheses deleted.
- deleted: A numeric vector indicating which hypotheses were deleted.
- intermediate\_graphs: When using the ordered mode, a list of intermediate updated graphs after each hypothesis is deleted according to the sequence specified by delete.

## Sequence of deletion

When there are multiple hypotheses to be deleted from a graph, there are many sequences of deletion in which an initial graph is updated to an updated graph. If the interest is in the updated graph after all hypotheses specified by delete are deleted, this updated graph is the same no matter which sequence of deletion is used. This property has been proved by Bretz et al. (2009). If the interest is in the intermediate updated graph after each hypothesis is deleted according to the sequence specified by delete, an integer vector of delete should be specified and these detailed outputs will be provided.

## References

Bretz, F., Maurer, W., Brannath, W., and Posch, M. (2009). A graphical approach to sequentially rejective multiple test procedures. *Statistics in Medicine*, 28(4), 586-604.

Bretz, F., Posch, M., Glimm, E., Klinglmueller, F., Maurer, W., and Rohmeyer, K. (2011). Graphical approaches for multiple comparison procedures using weighted Bonferroni, Simes, or parametric tests. *Biometrical Journal*, 53(6), 894-913.

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#### See Also

- graph\_create() for the initial graph.
- graph\_rejection\_orderings() for possible sequences of rejections for a graphical multiple comparison procedure using shortcut testing.

#### **Examples**

```
# A graphical multiple comparison procedure with two primary hypotheses (H1
# and H2) and two secondary hypotheses (H3 and H4)
# See Figure 1 in Bretz et al. (2011).
hypotheses <- c(0.5, 0.5, 0, 0)
transitions <- rbind(
  c(0, 0, 1, 0),
  c(0, 0, 0, 1),
  c(0, 1, 0, 0),
  c(1, 0, 0, 0)
g <- graph_create(hypotheses, transitions)</pre>
# Delete the second and third hypotheses in the "unordered mode"
graph_update(g, delete = c(FALSE, TRUE, TRUE, FALSE))
# Equivalent way in the "ordered mode" to obtain the updated graph after
# deleting the second and third hypotheses
# Additional intermediate updated graphs are also provided
graph_update(g, delete = 2:3)
```

plot.initial\_graph

S3 plot method for class initial\_graph

## **Description**

The plot of an initial\_graph translates the hypotheses into vertices and transitions into edges to create a network plot. Vertices are labeled with hypothesis names and hypothesis weights, and edges are labeled with transition weights. See vignette("graph-examples") for more illustration of commonly used multiple comparison procedure using graphs.

## Usage

```
## S3 method for class 'initial_graph'
plot(
    x,
    ...,
    v_palette = c("#6baed6", "#cccccc"),
    layout = "grid",
    nrow = NULL,
    ncol = NULL,
    edge_curves = NULL,
```

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```
precision = 4,
eps = NULL,
background_color = "white",
margins = c(1, 1, 1, 1)
)
```

#### **Arguments**

x An object of class initial\_graph to plot.

... Other arguments passed on to igraph::plot.igraph().

v\_palette A character vector of length two specifying the colors for retained and deleted

hypotheses. More extensive color customization must be done with vertex.color.

layout An igraph layout specification (See ?igraph.plotting), or "grid", which lays

out hypotheses left-to-right and top-to-bottom. nrow and ncol control the grid

shape.

nrow An integer scalar specifying the number of rows in the vertex grid. If row and

column counts are not specified, vertices will be laid out as close to a square as

possible.

ncol An integer scalar specifying the number of columns in the vertex grid. If row

and column counts are not specified, vertices will be laid out as close to a square

as possible.

edge\_curves A named numeric vector specifying the curvature of specific edges. Edge pairs

(Where two vertices share an edge in each possible direction) are detected automatically and get 0.25 curvature. Adjust edges by adding an entry with name "vertex1|vertex2, and adjust default edge pairs curvature by adding an entry with name "pairs" - edge\_curves = c("pairs" = 0.5, "H1|H3" = 0.25,

"H3|H4" = 0.75).

precision An integer scalar indicating the number of decimal places to display.

eps A numeric scalar. The transition weight of eps will be displayed as  $\epsilon$ , which

indicates edges with infinitesimally small weights. See Bretz et al. (2009) for

more details.

background\_color

A character scalar specifying a background color for the whole plotting area.

Passed directly to graphics::par() (bg).

margins A length 4 numeric vector specifying the margins for the plot. Defaults to

all 1, since igraph plots tend to have large margins. It is passed directly to

graphics::par() (mar).

#### Value

An object x of class initial\_graph, after plotting the initial graph.

#### **Customization of graphs**

There are a few values for <code>igraph::plot.igraph()</code> that get their defaults changed for graphicalMCP. These values can still be changed by passing them as arguments to <code>plot.initial\_graph()</code>. Here are the new defaults:

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```
vertex.color = "#6baed6",
vertex.label.color = "black",
vertex.size = 20,
edge.arrow.size = 1,
edge.arrow.width = 1,
edge.label.color = "black"
asp = 0.
```

Neither graphicalMCP nor igraph does anything about overlapping edge labels. If you run into this problem, and vertices can't practically be moved enough to avoid collisions of edge labels, using edge curves can help. igraph puts edge labels closer to the tail of an edge when an edge is straight, and closer to the head of an edge when it's curved. By setting an edge's curve to some very small value, an effectively straight edge can be shifted to a new position.

#### References

Bretz, F., Posch, M., Glimm, E., Klinglmueller, F., Maurer, W., and Rohmeyer, K. (2011). Graphical approaches for multiple comparison procedures using weighted Bonferroni, Simes, or parametric tests. *Biometrical Journal*, 53(6), 894-913.

Xi, D., and Bretz, F. (2019). Symmetric graphs for equally weighted tests, with application to the Hochberg procedure. *Statistics in Medicine*, 38(27), 5268-5282.

#### See Also

plot.updated\_graph() for the plot method for the updated graph after hypotheses being deleted from the initial graph.

```
# A graphical multiple comparison procedure with two primary hypotheses (H1
# and H2) and two secondary hypotheses (H3 and H4)
# See Figure 4 in Bretz et al. (2011).
hypotheses <- c(0.5, 0.5, 0, 0)
delta <- 0.5
transitions <- rbind(</pre>
 c(0, delta, 1 - delta, 0),
 c(delta, 0, 0, 1 - delta),
 c(0, 1, 0, 0),
 c(1, 0, 0, 0)
)
g <- graph_create(hypotheses, transitions)</pre>
# A graphical multiple comparison procedure with two primary hypotheses (H1
# and H2) and four secondary hypotheses (H31, H32, H41, and H42)
# See Figure 6 in Xi and Bretz (2019).
hypotheses <- c(0.5, 0.5, 0, 0, 0, 0)
epsilon <- 1e-5
transitions <- rbind(</pre>
```

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```
c(0, 0.5, 0.25, 0, 0.25, 0),
  c(0.5, 0, 0, 0.25, 0, 0.25),
  c(0, 0, 0, 0, 1, 0),
  c(epsilon, 0, 0, 0, 0, 1 - epsilon),
  c(0, epsilon, 1 - epsilon, 0, 0, 0),
  c(0, 0, 0, 1, 0, 0)
hyp_names <- c("H1", "H2", "H31", "H32", "H41", "H42")
g <- graph_create(hypotheses, transitions, hyp_names)</pre>
plot_layout <- rbind(</pre>
  c(0.15, 0.5),
  c(0.65, 0.5),
  c(0, 0),
  c(0.5, 0),
  c(0.3, 0),
  c(0.8, 0)
plot(g, layout = plot_layout, eps = epsilon, edge_curves = c(pairs = .5))
```

plot.updated\_graph

S3 plot method for the class updated\_graph

## **Description**

Plotting an updated graph is a *very* light wrapper around plot.initial\_graph(), only changing the default vertex color to use gray for deleted hypotheses.

## Usage

```
## S3 method for class 'updated_graph'
plot(x, ...)
```

#### **Arguments**

x An object of class updated\_graph to plot.

.. Arguments passed on to plot.initial\_graph

v\_palette A character vector of length two specifying the colors for retained and deleted hypotheses. More extensive color customization must be done with vertex.color.

layout An igraph layout specification (See ?igraph.plotting), or "grid", which lays out hypotheses left-to-right and top-to-bottom. nrow and ncol control the grid shape.

nrow An integer scalar specifying the number of rows in the vertex grid. If row and column counts are not specified, vertices will be laid out as close to a square as possible.

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ncol An integer scalar specifying the number of columns in the vertex grid. If row and column counts are not specified, vertices will be laid out as close to a square as possible.

- edge\_curves A named numeric vector specifying the curvature of specific edges. Edge pairs (Where two vertices share an edge in each possible direction) are detected automatically and get 0.25 curvature. Adjust edges by adding an entry with name "vertex1|vertex2, and adjust default edge pairs curvature by adding an entry with name "pairs" edge\_curves = c("pairs" = 0.5, "H1|H3" = 0.25, "H3|H4" = 0.75).
- precision An integer scalar indicating the number of decimal places to display.
- eps A numeric scalar. The transition weight of eps will be displayed as  $\epsilon$ , which indicates edges with infinitesimally small weights. See Bretz et al. (2009) for more details.
- background\_color A character scalar specifying a background color for the whole plotting area. Passed directly to graphics::par() (bg).
- margins A length 4 numeric vector specifying the margins for the plot. Defaults to all 1, since igraph plots tend to have large margins. It is passed directly to graphics::par() (mar).

#### Value

An object x of class updated\_graph, after plotting the updated graph.

#### References

Bretz, F., Posch, M., Glimm, E., Klinglmueller, F., Maurer, W., and Rohmeyer, K. (2011). Graphical approaches for multiple comparison procedures using weighted Bonferroni, Simes, or parametric tests. *Biometrical Journal*, 53(6), 894-913.

#### See Also

plot.initial\_graph() for the plot method for the initial graph.

```
# A graphical multiple comparison procedure with two primary hypotheses (H1
# and H2) and two secondary hypotheses (H3 and H4)
# See Figure 1 in Bretz et al. (2011).
hypotheses <- c(0.5, 0.5, 0, 0)
transitions <- rbind(
    c(0, 0, 1, 0),
    c(0, 0, 0, 1),
    c(0, 1, 0, 0),
    c(1, 0, 0, 0)
)
g <- graph_create(hypotheses, transitions)
# Delete the second and third hypotheses in the "unordered mode"
plot(</pre>
```

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```
graph_update(
    g,
    c(FALSE, TRUE, TRUE, FALSE)
),
    layout = "grid"
)
```

print.graph\_report

S3 print method for the class graph\_report

#### **Description**

A printed graph\_report displays the initial graph, p-values and significance levels, rejection decisions, and optional detailed test results.

## Usage

```
## S3 method for class 'graph_report'
print(x, ..., precision = 4, indent = 2, rows = 10)
```

#### **Arguments**

x An object of class graph\_report to print.

... Other values passed on to other methods (currently unused)

precision An integer scalar indicating the number of decimal places to to display.

indent An integer scalar indicating how many spaces to indent results.

rows An integer scalar indicating how many rows of detailed test results to print.

#### Value

An object x of class graph\_report, after printing the report of conducting a graphical multiple comparison procedure.

#### References

Bretz, F., Posch, M., Glimm, E., Klinglmueller, F., Maurer, W., and Rohmeyer, K. (2011). Graphical approaches for multiple comparison procedures using weighted Bonferroni, Simes, or parametric tests. *Biometrical Journal*, 53(6), 894-913.

```
# A graphical multiple comparison procedure with two primary hypotheses (H1 # and H2) and two secondary hypotheses (H3 and H4) # See Figure 1 in Bretz et al. (2011). hypotheses <- c(0.5, 0.5, 0, 0) transitions <- rbind( c(0, 0, 1, 0), c(0, 0, 0, 1),
```

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```
c(0, 1, 0, 0),
  c(1, 0, 0, 0)
)
g <- graph_create(hypotheses, transitions)

p <- c(0.018, 0.01, 0.105, 0.006)
alpha <- 0.025
graph_test_shortcut(g, p, alpha)</pre>
```

## Description

A printed initial\_graph displays a header stating "Initial graph", hypothesis weights, and transition weights.

#### **Usage**

```
## S3 method for class 'initial_graph'
print(x, ..., precision = 4, indent = 0)
```

## Arguments

х	An object of class initial_graph to print.
	Other values passed on to other methods (currently unused).
precision	An integer scalar indicating the number of decimal places to to display.
indent	An integer scalar indicating how many spaces to indent results.

## Value

An object x of class initial\_graph, after printing the initial graph.

#### References

Bretz, F., Posch, M., Glimm, E., Klinglmueller, F., Maurer, W., and Rohmeyer, K. (2011). Graphical approaches for multiple comparison procedures using weighted Bonferroni, Simes, or parametric tests. *Biometrical Journal*, 53(6), 894-913.

## See Also

print.updated\_graph() for the print method for the updated graph after hypotheses being deleted from the initial graph. 34 print.power\_report

#### **Examples**

```
# A graphical multiple comparison procedure with two primary hypotheses (H1
# and H2) and two secondary hypotheses (H3 and H4)
# See Figure 1 in Bretz et al. (2011).
hypotheses <- c(0.5, 0.5, 0, 0)
transitions <- rbind(
    c(0, 0, 1, 0),
    c(0, 0, 0, 1),
    c(0, 1, 0, 0),
    c(1, 0, 0, 0)
)
hyp_names <- c("H11", "H12", "H21", "H22")
g <- graph_create(hypotheses, transitions, hyp_names)
g</pre>
```

print.power\_report

S3 print method for the class power\_report

#### Description

A printed power\_report displays the initial graph, testing and simulation options, power outputs, and optional detailed simulations and test results.

#### Usage

```
## S3 method for class 'power_report'
print(x, ..., precision = 4, indent = 2, rows = 10)
```

## **Arguments**

An object of the class power\_report to print
 Other values passed on to other methods (currently unused)
 An integer scalar indicating the number of decimal places to to display.
 An integer scalar indicating how many spaces to indent results.

rows An integer scalar indicating how many rows of detailed test results to print.

#### Value

An object x of the class power\_report, after printing the report of conducting power simulations based on a graphical multiple comparison procedure.

#### References

Bretz, F., Posch, M., Glimm, E., Klinglmueller, F., Maurer, W., and Rohmeyer, K. (2011a). Graphical approaches for multiple comparison procedures using weighted Bonferroni, Simes, or parametric tests. *Biometrical Journal*, 53(6), 894-913.

Bretz, F., Maurer, W., and Hommel, G. (2011b). Test and power considerations for multiple endpoint analyses using sequentially rejective graphical procedures. *Statistics in Medicine*, 30(13), 1489-1501.

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## **Examples**

```
# A graphical multiple comparison procedure with two primary hypotheses (H1
# and H2) and two secondary hypotheses (H3 and H4)
# See Figure 4 in Bretz et al. (2011).
alpha <- 0.025
hypotheses <- c(0.5, 0.5, 0, 0)
delta <- 0.5
transitions <- rbind(</pre>
  c(0, delta, 1 - delta, 0),
  c(delta, 0, 0, 1 - delta),
  c(0, 1, 0, 0),
  c(1, 0, 0, 0)
)
g <- graph_create(hypotheses, transitions)</pre>
marginal_power <- c(0.8, 0.8, 0.7, 0.9)
corr1 \leftarrow matrix(0.5, nrow = 2, ncol = 2)
diag(corr1) <- 1
corr <- rbind(</pre>
  cbind(corr1, 0.5 * corr1),
  cbind(0.5 * corr1, corr1)
)
success_fns <- list(</pre>
  # Probability to reject both H1 and H2
  `H1andH2` = function(x) x[1] & x[2],
  # Probability to reject both (H1 and H3) or (H2 and H4)
  (H1andH3)or(H2andH4)^ = function(x) (x[1] & x[3]) | (x[2] & x[4])
)
set.seed(1234)
# Bonferroni tests
power_output <- graph_calculate_power(</pre>
  alpha,
  sim_corr = corr,
  sim_n = 1e5,
  power_marginal = marginal_power,
  sim_success = success_fns
)
```

## Description

A printed updated\_graph displays the initial graph, the (final) updated graph, and the sequence of intermediate updated graphs after hypotheses are deleted (if available).

#### Usage

```
## S3 method for class 'updated_graph'
print(x, ..., precision = 6, indent = 2)
```

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## Arguments

X	An object of the class updated_graph to print.
	Other values passed on to other methods (currently unused).
precision	An integer scalar indicating the number of decimal places to to display.
indent	An integer scalar indicating how many spaces to indent results.

#### Value

An object x of the class updated\_graph, after printing the updated graph.

#### References

Bretz, F., Posch, M., Glimm, E., Klinglmueller, F., Maurer, W., and Rohmeyer, K. (2011a). Graphical approaches for multiple comparison procedures using weighted Bonferroni, Simes, or parametric tests. *Biometrical Journal*, 53(6), 894-913.

#### See Also

print.initial\_graph() for the print method for the initial graph.

```
# A graphical multiple comparison procedure with two primary hypotheses (H1
# and H2) and two secondary hypotheses (H3 and H4)
# See Figure 1 in Bretz et al. (2011).
hypotheses <- c(0.5, 0.5, 0, 0)
transitions <- rbind(</pre>
  c(0, 0, 1, 0),
  c(0, 0, 0, 1),
 c(0, 1, 0, 0),
  c(1, 0, 0, 0)
g <- graph_create(hypotheses, transitions)</pre>
# Delete the second and third hypotheses in the "unordered mode"
graph_update(g, delete = c(FALSE, TRUE, TRUE, FALSE))
# Equivalent way in the "ordered mode" to obtain the updated graph after
# deleting the second and third hypotheses
# Additional intermediate updated graphs are also provided
graph_update(g, delete = 2:3)
```

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