Package 'IHWpaper'

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Title Reproduce figures in IHW paper

Version 1.36.0

Description This package conveniently wraps all functions needed to reproduce the figures in the IHW paper (https://www.nature.com/articles/nmeth.3885) and the data analysis in https://rss.onlinelibrary.wiley.com/doi/10.1111/rssb.12411, cf. the arXiv preprint (http://arxiv.org/abs/1701.05179). Thus it is a companion package to the Bioconductor IHW package.

Depends R (>= 3.3), IHW

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LazyData true

LinkingTo Rcpp

Imports Rcpp, stats, splines, methods, utils, DESeq2, SummarizedExperiment, fdrtool, genefilter, qvalue, Biobase, BiocGenerics, BiocParallel, dplyr, grid, ggplot2, cowplot

VignetteBuilder knitr

biocViews ReproducibleResearch, ExperimentData, RNASeqData, ExpressionData

RoxygenNote 7.1.2

Suggests testthat, RColorBrewer, wesanderson, scales, gridExtra, BiocStyle, knitr, rmarkdown, airway, locfdr, tidyr, latex2exp

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`analyze_dataset` *analyze_dataset: Basically performs preprocessing and then returns analyzed RNASeq dataset (diff. expression) , i.e. the DESeq2 result whose p-values and baseMean statistics can then be used with IHW*

Description

analyze_dataset: Basically performs preprocessing and then returns analyzed RNASeq dataset (diff. expression) , i.e. the DESeq2 result whose p-values and baseMean statistics can then be used with IHW

Usage

```
analyze_dataset(dataset = c("airway", "bottomly", "hammer"), res = TRUE)
```

Arguments

`dataset`	Character, name of dataset to be preprocessed, only 3 choices currently available ("airway","bottomly","hammer")
`res`	(default TRUE): return result table, rather than DESeq2 object

Value

Preprocessed dataset

Examples

```
bottomly <- analyze_dataset("bottomly")
```

---

bh *bh: Wrapper for Benjamini Hochberg*

Description

bh: Wrapper for Benjamini Hochberg

Usage

```
bh(unadj_p, alpha)
```

Arguments

unadj_p	Numeric vector of unadjusted p-values.
alpha	Significance level at which to apply method

Value

BH multiple testing object

Examples

```
sim_df <- du_ttest_sim(20000,0.95, 1.5)
obj <- bh(sim_df$pvalue, .1)
sum(rejected_hypotheses(obj))
```

---

bonf *bonf: Wrapper for Bonferroni*

Description

bonf: Wrapper for Bonferroni

Usage

```
bonf(unadj_p, alpha)
```

Arguments

unadj_p	Numeric vector of unadjusted p-values.
alpha	Significance level at which to apply method

Value

Bonferroni multiple testing object

Examples

```
sim_df <- du_ttest_sim(20000,0.95, 1.5)
obj <- bonf(sim_df$pvalue, .1)
sum(rejected_hypotheses(obj))
```

---

clfdr *clfdr: Cai's local fdr based method*

Description

clfdr: Cai's local fdr based method

Usage

```
clfdr(unadj_p, groups, alpha, lfdr_estimation = "fdrtool")
```

Arguments

unadj_p	Numeric vector of unadjusted p-values.
groups	Factor to which different hypotheses belong
alpha	Significance level at which to apply method
lfdr_estimation	Method used to estimate the loca fdr, defaults to "fdrtool"

Value

Clfdr multiple testing object

References

Cai, T. Tony, and Wenguang Sun. "Simultaneous testing of grouped hypotheses: Finding needles in multiple haystacks." Journal of the American Statistical Association 104.488 (2009).

Examples

```
sim_df <- du_ttest_sim(20000,0.95, 1.5)
sim_df$group <- groups_by_filter(sim_df$filterstat, 20)
obj <- clfdr(sim_df$pvalue, sim_df$group, .1)
sum(rejected_hypotheses(obj))
```

`continuous_wrap` *Benchmarking wrapper: Given a multiple testing method, convert it so that it takes a simulation object (see simulation function) and a nominal level alpha as inputs*

Description

Benchmarking wrapper: Given a multiple testing method, convert it so that it takes a simulation object (see simulation function) and a nominal level alpha as inputs

Usage

```
continuous_wrap(mt_method, nbins = 20)
```

Arguments

`mt_method`	Multiple testing method (e.g. a function such as gbh or ddhf)
`nbins`	Integer, number of equally sized bins into which to stratify hypotheses

Value

A new multiple testing function which has an interface of the form f(sim_data_frame, alpha)

Examples

```
sim_df <- du_ttest_sim(20000,0.95, 1.5)
sim_df$group <- groups_by_filter(sim_df$filterstat, 20)
obj <- tst_gbh(sim_df$pvalue, sim_df$group, .1)
sum(rejected_hypotheses(obj))

tst_gbh_continuous <- continuous_wrap(tst_gbh)
obj2 <- tst_gbh_continuous(sim_df, .1)
sum(rejected_hypotheses(obj2))
```

`ddhf` *ddhf: Greedy independent filtering*

Description

ddhf: Greedy independent filtering

Usage

```
ddhf(unadj_p, filterstat, alpha)
```

Arguments

unadj_p	Numeric vector of unadjusted p-values.
filterstat	Factor to which different hypotheses belong
alpha	Significance level at which to apply method

Value

DDHF multiple testing object

Examples

```
sim_df <- du_ttest_sim(20000,0.95, 1.5)
obj <- ddhf(sim_df$pvalue, sim_df$filterstat, .1)
sum(rejected_hypotheses(obj))
```

---

du_ttest_sim *t-test simulation: Simulate rowwise t-tests*

Description

t-test simulation: Simulate rowwise t-tests

Usage

```
du_ttest_sim(
  m,
  pi0,
  effect_size,
  n_samples = 10,
  uninformative_filter = FALSE,
  seed = NULL
)

du_ttest_sim_fun(
  m,
  pi0,
  effect_size,
  n_samples = 10,
  uninformative_filter = FALSE
)
```

Arguments

m	Integer, total number of hypotheses
pi0	Numeric, proportion of null hypotheses
effect_size	Numeric, the alternative hypotheses will be
n_samples	Integer, number of samples for t-test, i.e. the comparison will be n_samples/2 vs n_samples/2
uninformative_filter	Boolean, if TRUE will generate uniformly distributed filter statistic Otherwise will use the pooled standard deviations
seed	Integer, Random seed to be used for simulation (default: NULL, i.e. RNG state will be used as is)

Value

A data frame containing all information about the simulation experiment

Functions

- du_ttest_sim_fun: Creates a closure function for a given seed

Examples

```
sim_df <- du_ttest_sim(20000,0.95, 1.5)
```

---

gbh *gbh: Grouped Benjamini Hochberg*

Description

gbh: Grouped Benjamini Hochberg

tst_gbh: wrapper for gbh with method="TST" lsl_gbh: wrapper for gbh with method="LSL"

Usage

```
gbh(unadj_p, groups, alpha, method = "TST", pi0_global = "weighted_average")

tst_gbh(unadj_p, groups, alpha, ...)

lsl_gbh(unadj_p, groups, alpha, ...)
```

Arguments

unadj_p	Numeric vector of unadjusted p-values.
groups	Factor to which different hypotheses belong
alpha	Significance level at which to apply method
method	What pi0 estimator should be used (available "TST","LSL")
pi0_global	GBH requires also a pi0 estimate for the marginal p-value distribution. Can either apply pi0 estimation method to all p-values (pi0_global="global") or use a weigted averarage (pi0_global="weighted_average") of the pi0 estimates within each stratum. This is not explicitly stated in the paper, but based on a reproduction of their paper figures it seems to be the weighted_average.
...	Additional arguments passed from tst_gbh/lsl_gbh to gbh

Value

GBH multiple testing object

Functions

- tst_gbh: Wrapper of GBH with TST pi0 estimator
- lsl_gbh: Wrapper of GBH with LSL pi0 estimator

References

Hu, James X., Hongyu Zhao, and Harrison H. Zhou. "False discovery rate control with groups." Journal of the American Statistical Association 105.491 (2010).

Examples

```
sim_df <- du_ttest_sim(20000,0.95, 1.5)
sim_df$group <- groups_by_filter(sim_df$filterstat, 20)
obj <- tst_gbh(sim_df$pvalue, sim_df$group, .1)
sum(rejected_hypotheses(obj))
```

---

ihw_naive *IHW wrappers*

Description

IHW wrappers

Usage

```
ihw_naive(unadj_p, filterstat, alpha)

ihw_ecdf_5fold(unadj_p, filterstat, alpha)

ihw_5fold(unadj_p, filterstat, alpha)

ihw_5fold_reg(unadj_p, filterstat, alpha)

ihw_bonf_5fold_reg(unadj_p, filterstat, alpha)

ihw_storey_5fold(unadj_p, filterstat, alpha)
```

Arguments

unadj_p	Numeric vector of unadjusted p-values.
filterstat	Factor to which different hypotheses belong
alpha	Significance level at which to apply method

Details

These are closures, which apply IHW with custom prespecified parameters. These correspond to interesting settings, for which it is convenient to be able to immediately call the corresponding functions, rather than having to specify parameters each time. Thus they make it easier to benchmark. All of these wrappers are defined in 2 lines of code, so the settings pertaining to each one can be inspected by typing the functions name into the console.

Value

ihwResult multiple testing object

Functions

- ihw_naive: IHW naive
- ihw_ecdf_5fold: IHW (E2) with 5 folds
- ihw_5fold: IHW (E1-E2) with 5 folds
- ihw_5fold_reg: IHW (E1-E2-E3) with 5 folds
- ihw_bonf_5fold_reg: IHW-Bonferroni (E1-E2-E3) with 5 folds
- ihw_storey_5fold: IHW (E1-E2) with 5 folds and Storey's pi0 estimator

Examples

```
sim_df <- du_ttest_sim(20000,0.95, 1.5)
obj <- ihw_5fold(sim_df$pvalue, sim_df$filterstat, .1)
sum(rejected_hypotheses(obj))
```

lsl_pi0_est *LSL (Least-Slope) pi0 estimator*

Description

LSL (Least-Slope) pi0 estimator

Usage

```
lsl_pi0_est(pvalue)
```

Arguments

pvalue	Numeric vector of unadjusted p-values.

Value

estimated proportion of null hypotheses (pi0)

Examples

```
sim_df <- du_ttest_sim(20000,0.95, 1.5)
lsl_pi0_est(sim_df$pvalue)
```

null_sim *Null simulation: Generate uniformly distributed p-values and covariates*

Description

Null simulation: Generate uniformly distributed p-values and covariates

Usage

```
null_sim(m, seed = NULL)

null_sim_fun(m)
```

Arguments

m	Integer, total number of hypotheses
seed	Integer, Random seed to be used for simulation (default: NULL, i.e. RNG state will be used as is)

Value

A data frame containing all information about the simulation experiment

Functions

- `null_sim_fun`: Creates a closure function for a given seed

Examples

```
sim_df <- null_sim(20000)
```

`pretty_legend` *helper function to create nice legends*

Description

helper function to create nice legends

Usage

```
pretty_legend(gg, last_vals, xmin, fontsize = 13)
```

Arguments

`gg`	ggplot2 object
`last_vals`	data frame with columns label, colour, last_vals (i.e. place label with colour at y-coordinate last_vals)
`xmin`	Numeric, x axis position at which labels should be placed
`fontsize`	Integer, fontsize

Value

Another ggplot2 object

This replaces the default legend of a ggplot2 object. In particular, given a ggplot2 object ,it removes the existing legend and then places new labels based on the annotation data frame ‘last_vals‘ (see parameter description) at a given x-coordinate of the original plot.

This function can be attributed to and is described in more detail in the following blog post: http://www.r-bloggers.com/coloring-and-drawing-outside-the-lines-in-ggplot/

Examples

```
library("ggplot2")
labels  <- c("A","B","C")
mypoints <- rbind(data.frame(y=1:3, x=1, label=as.factor(labels)),
                  data.frame(y=2:4, x=2, label=as.factor(labels)))
mycolours <- c("#F8766D","#00BA38","#619CFF")
gg <- ggplot(mypoints,aes(x=x,y=y,color=label)) +
             geom_line(size=2) +
             scale_color_manual(values=mycolours) +
             xlim(c(0,2.2))
gg
annotation_df <- data.frame(colour=mycolours, last_vals=2:4, label=labels)
pretty_legend(gg, annotation_df, 2.1)
```

`run_evals` *run_evals: Main function to benchmark FDR methods on given simulations.*

Description

run_evals: Main function to benchmark FDR methods on given simulations.

Usage

```
run_evals(sim_funs, fdr_methods, nreps, alphas, ...)
```

Arguments

`sim_funs`	List of simulation settings
`fdr_methods`	List of FDR controlling methods to be benchmarked
`nreps`	Integer, number of Monte Carlo replicates for the simulations
`alphas`	Numeric, vector of nominal significance levels at which to apply FDR controlling methods
`...`	Additional arguments passed to sim_fun_eval

Details

This is the main workhorse function which runs all simulation benchmarks for IHWpaper. It receives input as described above, and the output is a data.frame with the following columns:

- fdr_method: Multiple testing method which was used
- fdr_pars: Custom parameters of the multiple testing method
- alpha: Nominal significance level at which the benchmark was run
- FDR: False Discovery Rate of benchmarked method on simulated dataset
- power: Power of benchmarked method on simulated dataset

- rj_ratio: Average rejections divided by total number of hypotheses
- FPR: False positive rate of benchmarked method on simulated dataset
- FWER: Familywise Error Rate of benchmarked method on simulated dataset
- nsuccessful: Number of successful evaluations of the method
- sim_method: Simulation scenario under which benchmark was run
- m: Total number of hypotheses
- sim_pars: Custom parameters of the simulation scenario

Value

data.frame which summarizes results of numerical experiment

Examples

```
nreps <- 3 # monte carlo replicates
ms <- 5000 # number of hypothesis tests
eff_sizes <- c(2,3)
sim_funs <- lapply(eff_sizes,
function(x) du_ttest_sim_fun(ms,0.95,x, uninformative_filter=FALSE))
continuous_methods_list <- list(bh,
                                lsl_gbh,
                               clfdr,
                                   ddhf)
 fdr_methods <- lapply(continuous_methods_list, continuous_wrap)
eval_table <- run_evals(sim_funs, fdr_methods, nreps, 0.1, BiocParallel=FALSE)
```

`scott_fdrreg` *scott_fdrreg: Wrapper for FDR regression (https://github.com/jgscott/FDRreg)*

Description

scott_fdrreg: Wrapper for FDR regression (https://github.com/jgscott/FDRreg)

Usage

```
scott_fdrreg(unadj_p, filterstat, alpha, df = 3, lambda = 0.01)
```

Arguments

`unadj_p`	Numeric vector of unadjusted p-values.
`filterstat`	Factor to which different hypotheses belong
`alpha`	Significance level at which to apply method
`df`	Degrees of freedom for B-slines
`lambda`	Ridge regularization parameter

Value

FDRreg multiple testing object

References

James G. Scott, Ryan C. Kelly, Matthew A. Smith, Pengcheng Zhou, and Robert E. Kass. "False discovery rate regression: application to neural synchrony detection in primary visual cortex." Journal of the American Statistical Association (2015).

`storey_qvalue` *storey_qvalue: Wrapper for Storey's qvalue package*

Description

storey_qvalue: Wrapper for Storey's qvalue package

Usage

```
storey_qvalue(unadj_p, alpha)
```

Arguments

`unadj_p`	Numeric vector of unadjusted p-values.
`alpha`	Significance level at which to apply method

Value

StoreyQValue multiple testing object

Examples

```
sim_df <- du_ttest_sim(20000,0.95, 1.5)
obj <- storey_qvalue(sim_df$pvalue, .1)
sum(rejected_hypotheses(obj))
```

stratified_bh *stratified_bh: Stratified Benjamini Hochberg*

Description

stratified_bh: Stratified Benjamini Hochberg

Usage

```
stratified_bh(unadj_p, groups, alpha)
```

Arguments

unadj_p	Numeric vector of unadjusted p-values.
groups	Factor to which different hypotheses belong
alpha	Significance level at which to apply method

Value

SBH multiple testing object

References

Sun, Lei, et al. "Stratified false discovery control for large-scale hypothesis testing with application to genome-wide association studies." Genetic epidemiology 30.6 (2006): 519-530.

Yoo, Yun J., et al. "Were genome-wide linkage studies a waste of time? Exploiting candidate regions within genome-wide association studies." Genetic epidemiology 34.2 (2010): 107-118.

Examples

```
sim_df <- du_ttest_sim(20000,0.95, 1.5)
sim_df$group <- groups_by_filter(sim_df$filterstat, 20)
obj <- stratified_bh(sim_df$pvalue, sim_df$group, .1)
sum(rejected_hypotheses(obj))
```

tst_pi0_est *TST (Two-Step) pi0 estimator*

Description

TST (Two-Step) pi0 estimator

Usage

```
tst_pi0_est(pvalue, alpha)
```

Arguments

pvalue	Numeric vector of unadjusted p-values.
alpha	Nominal level for applying the TST procedure

Value

estimated proportion of null hypotheses (pi0)

Examples

```
sim_df <- du_ttest_sim(20000,0.95, 1.5)
tst_pi0_est(sim_df$pvalue, .1)
```

wasserman_normal_prds_sim *Normal PRDS simulation: Covariate is effect size under alternative, there are latent factors driving PRDS correlations among hypotheses*

Description

Normal PRDS simulation: Covariate is effect size under alternative, there are latent factors driving PRDS correlations among hypotheses

Usage

```
wasserman_normal_prds_sim(
  m,
  pi0,
  rho = 0,
  latent_factors = 1,
  xi_min = 0,
  xi_max = 2.5,
  seed = NULL
```

```
)

wasserman_normal_prds_sim_fun(
  m,
  pi0,
  rho = 0,
  latent_factors = 1,
  xi_min = 0,
  xi_max = 2.5
)
```

Arguments

m	Integer, total number of hypotheses
pi0	Numeric, proportion of null hypotheses
rho	Numeric, correlation between z-scores of hypotheses driven by same latent factor
latent_factors	Integer, number of latent factors driving the correlations
xi_min, xi_max	Numeric, covariates are drawn as uniform on xi_min, xi_max
seed	Integer, Random seed to be used for simulation (default: NULL, i.e. RNG state will be used as is)

Value

A data frame containing all information about the simulation experiment

Functions

- wasserman_normal_prds_sim_fun: Creates a closure function for a given seed

Examples

```
sim_df <- wasserman_normal_prds_sim(20000,0.9, rho=0.1)
```

---

wasserman_normal_sim *Normal simulation: Covariate is effect size under alternative*

Description

Normal simulation: Covariate is effect size under alternative

Usage

```
wasserman_normal_sim(m, pi0, xi_min, xi_max, seed = NULL)

wasserman_normal_sim_fun(m, pi0, xi_min, xi_max)
```

Arguments

m	Integer, total number of hypotheses
pi0	Numeric, proportion of null hypotheses
xi_min, xi_max	Numeric, covariates are drawn as uniform on xi_min, xi_max
seed	Integer, Random seed to be used for simulation (default: NULL, i.e. RNG state will be used as is)

Value

A data frame containing all information about the simulation experiment

Functions

- wasserman_normal_sim_fun: Creates a closure function for a given seed

Examples

```
sim_df <- wasserman_normal_sim(20000,0.9, 1, 5)
```

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