Package ‘IHWpaper’

March 19, 2024

Title Reproduce figures in IHW paper
Version 1.30.0
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
License Artistic-2.0
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
NeedsCompilation yes
Author Nikos Ignatiadis [aut, cre]
Maintainer Nikos Ignatiadis <nikos.ignatiadis01@gmail.com>
git_url https://git.bioconductor.org/packages/IHWpaper
git_branch RELEASE_3_18
git_last_commit bba1a51
git_last_commit_date 2023-10-24
Repository Bioconductor 3.18
Date/Publication 2024-03-19
R topics documented:

analyze_dataset ............................... 2
bh .............................................. 3
bonf .......................................... 3
cfdr ........................................... 4
continuous_wrap ............................... 5
ddhf .......................................... 5
du_ttest_sim .................................. 6
gbh ............................................ 7
ihw_naive ...................................... 8
lsl_pio_est ................................... 10
null_sim ....................................... 10
pretty_legend ................................ 11
run_evals ..................................... 12
scott_fdrreg .................................. 13
storey_qvalue ................................ 14
stratified_bh ................................ 15
tst_pio_est ................................... 16
wasserman_normal_prds_sim ................ 16
wasserman_normal_sim ....................... 17

Index 19

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

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

**bh**  
*bh*: Wrapper for Benjamini Hochberg

**Description**

*bh*: Wrapper for Benjamini Hochberg

**Usage**

```r
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**

```r
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**

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

**Arguments**

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

Value

Bonferroni multiple testing object

Examples

```r
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

```r
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 local fdr, defaults to "fdrtool".

Value

Clfdr multiple testing object

References


Examples

```r
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**

```r
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**

```r
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**

```r
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**

```r
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**

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

```r
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

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 weighted average (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


Examples

```r
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))
```

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**

```r
lsl_pi0_est(pvalue)
```

**Arguments**

- `pvalue`  
  Numeric vector of unadjusted p-values.

**Value**

estimated proportion of null hypotheses (pi0)

**Examples**

```r
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**

```r
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)
null_sim_fun: Creates a closure function for a given seed

Examples

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

---

pretty_legend

### Description

Helper function to create nice legends

### Usage

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

### Arguments

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>gg</td>
<td>ggplot2 object</td>
</tr>
<tr>
<td>last_vals</td>
<td>data frame with columns label, colour, last_vals (i.e. place label with colour at y-coordinate last_vals)</td>
</tr>
<tr>
<td>xmin</td>
<td>Numeric, x axis position at which labels should be placed</td>
</tr>
<tr>
<td>fontsize</td>
<td>Integer, fontsize</td>
</tr>
</tbody>
</table>

### 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)

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,
   dhf)
fdr_methods <- lapply(continuous_methods_list, continuous_wrap)
eval_table <- run_evals(sim_funs, fdr_methods, nreps, 0.1, BiocParallel=FALSE)

scott_fdrreg

Description

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
storey_qvalue

Value

FDRreg multiple testing object

References


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

```r
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


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  

**Description**

TST (Two-Step) \( \pi_0 \) 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 \( (\pi_0) \)

**Examples**

```r
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**

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

```r
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

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

Description

Normal simulation: Covariate is effect size under alternative

Usage

```r
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
- `pi_0`  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

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

analyze_dataset, 2
bh, 3
bonf, 3
c1fdr, 4
continuous_wrap, 5
ddhf, 5
du_ttest_sim, 6
du_ttest_sim_fun (du_ttest_sim), 6
gbh, 7
ihw_5fold (ihw_naive), 8
ihw_5fold_reg (ihw_naive), 8
ihw_bonf_5fold_reg (ihw_naive), 8
ihw_ecdf_5fold (ihw_naive), 8
ihw_naive, 8
ihw_storey_5fold (ihw_naive), 8
lsl_gbh (gbh), 7
lsl_pi0_est, 10
null_sim, 10
null_sim_fun (null_sim), 10
pretty_legend, 11
run_evals, 12
scott_fdrreg, 13
storey_qvalue, 14
stratified_bh, 15
tst_gbh (gbh), 7
tst_pi0_est, 16
wasserman_normal_prds_sim, 16
wasserman_normal_prds_sim_fun
  (wasserman_normal_prds_sim), 16
wasserman_normal_sim, 17
wasserman_normal_sim_fun
  (wasserman_normal_sim), 17