Package ‘structSSI’

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Type Package

Title Multiple Testing for Hypotheses with Hierarchical or Group Structure

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Description Performs multiple testing corrections that take specific structure of hypotheses into account.

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structSSI-package  Structured Simultaneous and Selective Inference for Grouped or Hierarchically Structured Data

Description

Performs multiple corrections that take specific structure of hypotheses into account. The two procedures implemented are the Hierarchically FDR controlling procedure of Benjamini and Yekutieli and the Group Benjamini-Hochberg procedure of Hu, Zhou, and Zhao. The methods are applicable whenever information about hierarchical or group relationship between hypotheses can be ascertained before any data analysis.

Details

- Package: structSSI
- Type: Package
- Version: 1.0
- Date: 2012-03-14
- License: GPL-2

This package implements two recently developed techniques in the field of selective and simultaneous inference (SSI). The first method is the Adaptive Groups Benjamini-Hochberg procedure of Hu, Zhou, and Zhao 2011. The second is the Hierarchical FDR Controlling Procedure of Benjamini and Yekutieli. Both methods attempt to employ a priori known information about the relationships between hypotheses in testing them and correcting for the multiple testing problem. These methods have been employed in genetics, QTL analysis, and clinical trials; more details about these applications can be read in the references stated below.

The Group Benjamini-Hochberg procedure is implemented in its adaptive and oracle varieties through the functions Adaptive.GBH and Oracle.GBH, respectively. The Hierarchical Procedure is implemented in the function hfdr.adjust and uses the class hypothesesTree to organize the information required for the procedure. These functions describe the procedures in more detail. Further, the references listed below present the derivations and applications of these two procedures.

Author(s)

Kris Sankaran
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References

Examples

```r
set.seed(2249)
unadjp <- c(runif(40, 0, 0.001), runif(30, 0, 0.1), runif(130, 0, 1))
names(unadjp) <- paste("hyp", c(1:200))
groups <- c(sample(1:3, 200, replace = TRUE))
result <- Adaptive.GBH(unadjp, groups, method = "ls", alpha = 0.05)
```

```r
alternative.indices <- sample(1:49, 30)
unadj.p.values <- vector("numeric", length = 49)
unadj.p.values[alternative.indices] <- runif(30, 0, 0.01)
unadj.p.values[-alternative.indices] <- runif(19, 0, 1)
unadj.p.values[c(1:5)] <- runif(5, 0, 0.01)
names(unadj.p.values) <- paste("Hyp ", c(1:49))

tree <- as.igraph(rtree(25))
V(tree)$name <- names(unadj.p.values)
tree.el <- get.edgelist(tree)

hyp.tree <- hFDR.adjust(unadj.p.values, tree.el, 0.05)
plot(hyp.tree)
```

Description

Performs the Group Benjamini-Hochberg procedure using adaptive estimates of the proportions of null p-values in given groups. The method is applicable when we know some a-priori structure about whether certain hypotheses can be grouped. Once the hypotheses are grouped and tested individually, a Benjamini-Hochberg correction is performed within each of the groups. Finally, the fact that the Benjamini-Hochberg correction controls the FDR at level q*pi0_group within each group (q is the level used in the and p-value comparison and pi0 is the proportion of null hypotheses within the particular group) is used to increase the power of the procedure. The procedure is described in more detail in the paper "False Discovery Rate Control with Groups" by Hu, Zhao, and Zhou (see references below).
Usage
Adaptive.GBH(unadj.p, group.index, alpha = 0.05, method = 'lsl', lambda = 0.5)

Arguments
unadj.p A vector of the unadjusted p-values resulting from a multiple testing experiment.
group.index A vector of the same length as the vector of unadjusted p-values, where a "G" in
the jth coordinate indicates that the jth unadjusted p-values in unadj.p belongs
to group "G". This code can be either a factor giving group names, or a numeric
index.
alpha The level of that we are attempting to control the FDR at.
method The method for adaptively estimating the proportion of true null hypotheses
within a vector of unadjusted p-values. The possible options are "storey", "lsl",
and "tst". See the documentation for estimatePi0 for more details.
lambda The value of the tuning parameter for estimating the proportion of null hypothe-
ses, in the "storey" method.

Value
An object of class GBH, which provides the adjusted p-values.

Author(s)
Kris Sankaran

References
Hu, J.X., Zhao, H., and Zhou, H.H. False discovery rate control with groups. Journal of the Ameri-
Sankaran, K and Holmes, S. structSSI: Simultaneous and Selective Inference for Grouped or Hierar-

See Also
estimate.pi0 Oracle.GBH

Examples
## These are the unadjusted p-values corresponding to
## the outcome of some multiple testing experiment. The
## first 500 hypotheses are null and the last 1500 are
## true alternatives.
unadjp <- c(runif(500, 0, 0.01), runif(1500, 0, 1))
names(unadjp) <- paste("Hyp: ", 1:2000)

## Here there are two groups total we have randomly
## assigned hypotheses to these two groups.
group.index <- c(sample(1:2, 2000, replace = TRUE))
chlamydiae

# Perform the GBH adjustment.
result <- Adaptive.GBH(unadjp, group.index, method = "storey")

# A summary of the GBH adjustment
summary(result)

# The estimated proportions of null hypotheses, between groups
result@pi

# Visualizing the sorted p-values, before and after adjustment
plot(result, adjust = TRUE)
plot(result, adjust = FALSE)

chlamydiae  Chlamydiae Sub-Taxa of Global Patterns Data

Description

A phyloseq class object containing data on 16s rRNA diversity within the Chlamydiae bacteria taxon, originally appearing in PNAS.

Usage

data(chlamydiae)

Format

The format is: phyloseq-class experiment-level object.

References


This can be viewed/downloaded at: http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0061217


Examples

data(chlamydiae)
**Description**

This function makes three routines available for estimating the true proportion of null hypotheses from a vector of unadjusted p-values arising from a multiple testing experiment. The specific methods are the Least Slope method (lsl), the Two Step Test method (tst), and the Storey tail proportion of p-values method (storey). These methods are derived and explained in the references given below.

**Usage**

```r
estimate.pi0(pvalues, method, alpha = 0.05, lambda = 0.5)
```

**Arguments**

- `pvalues`: A vector of the unadjusted p-values resulting from a multiple testing experiment.
- `method`: The technique used to estimate the proportion of true null hypotheses. Valid arguments are `lsl`, `tst`, or `storey`, which correspond to the Least Slope, Two Step Test, and Storey tail proportion of p-values methods, respectively.
- `alpha`: In the Two Step Test method, the level of the Benjamini-Hochberg procedure used to estimate the proportion of true null hypotheses.
- `lambda`: In the Storey tail proportion of p-values method, the cutoff used to differentiate p-values.

**Details**

The Least Slope method uses the insight that, if we plot the sorted unadjusted p-values, then the p-values corresponding to null hypotheses will have steep slopes, as they are uniformly distributed between 0 and 1. If we find the position where the slope of the sorted p-values increases the most, we can fix that slope and extrapolate to the x-axis, and the position where the line intersects the x-axis is the proportion of p-values estimated to be null. The formal derivation is presented in the reference below.

Storey’s method uses the idea that most of the p-values above some parameter lambda (usually set to 0.5) correspond to null hypotheses. The number of hypotheses in this interval can then be used to estimate the number of hypotheses overall which are null hypotheses. See the paper

The Two Step Test method uses the idea that the result of a multiple comparisons procedure gives an estimate for how many hypotheses are null. That is, if we perform the BH procedure on 100 hypotheses, and 10 of them are rejected, then a reasonable estimate of the proportion of null hypotheses among those 100 is \( \pi_0 = 0.9 \).

**Value**

An estimate of the proportion of true null hypotheses from the result of the multiple testing experiment that the unadjusted p-values were extracted from.
EstimatedHFDRControl

Author(s)
Kris Sankaran

References


Examples

```r
true.p.1 <- runif(20, 0, 0.01)
null.p.1 <- runif(980, 0, 1)
p.val.1 <- c(true.p.1, null.p.1)

estimate.pi0(p.val.1, "isl")
estimate.pi0(p.val.1, "storey", lambda = 0.2)
estimate.pi0(p.val.1, "tst")
```

---

**EstimatedHFDRControl**

*Estimate FDR control variations for HFDR procedure*

**Description**

This function estimates two types of HFDR control appropriate for trees of hypotheses. If the BH procedure is applied at level alpha within each of the tree families, this is defined as

\[
FDR_{\text{est}} := \alpha \times \frac{\text{#discoveries} + \text{#families tested}}{\text{#discoveries} + 1}
\]

where a discovery is defined as an adjusted p value below alpha within the entire tree or at the tips FDR, respectively.

**Usage**

```
EstimatedHFDRControl(hyp.tree)
```
Arguments

hyp.tree An object of class HypothesesTree, such as the result to a call of hFDR.adjust.

Value

tree The estimated full-tree FDR.
tip The estimated outer-nodes FDR.
n.families.tested The number of families of hypotheses tested by the HFDR procedure.
n.tree.discoveries The number of discoveries over the whole tree.
n.tip.discoveries The number of discoveries among the tree tips.

Author(s)

Kris Sankaran

References


Benjamini, Y, and Yekutieli, D. Hierarchical fdr testing of trees of hypotheses. 2002.


See Also

hypothesesTree-class hFDR.adjust

Examples

library('igraph')
library('ape')

alternative.indices <- sample(1:49, 30)
unadj.p.values <- vector("numeric", length = 49)
unadj.p.values[alternative.indices] <- runif(30, 0, 0.01)
unadj.p.values[-alternative.indices] <- runif(19, 0, 1)
unadj.p.values[c(1:5)] <- runif(5, 0, 0.01)
names(unadj.p.values) <- paste("Hyp ", c(1:49))

tree <- as.igraph(rtree(25))
V(tree)$name <- names(unadj.p.values)
tree.el <- get.edgelist(tree)

hyp.tree <- hFDR.adjust(unadj.p.values, tree.el, 0.05)

EstimatedHFDRControl(hyp.tree)
Description

Class to facilitate performing the Group Benjamini-Hochberg procedure and interpreting its output.

Slots

p.vals: Object of class "data.frame". Each row corresponds to an individual hypothesis. The first column stores the p-values before GBH adjustment, while the second gives the GBH adjusted p-values. The hypotheses are sorted in order of significance according to these GBH adjusted p-values. The group column gives the group membership of each hypothesis, and adj.significance codes the significance of each hypothesis, according to the GBH adjusted p-values.

pi0: Object of class "numeric". The proportion of null hypotheses within each group. This is either known a priori or estimated adaptively from the unadjusted p-values.

adaptive: Object of class "logical". An indicator of whether the proportion pi0 was estimated adaptively from the data or known a priori.

alpha: Object of class "numeric". The level at which the FDR is controlled, during the GBH procedure.

Methods

plot signature(x = "GBH", y = "ANY"): ... Plots the p-values of the hypothesis, sorted according to GBH adjusted significance, shape coded according to group membership, and color coded according to pre and post GBH p-value adjustment.

show signature(object = "GBH"): ... Prints the entire table of adjusted p-values and their associated FDR adjusted significance levels, together with the estimated proportions of null hypotheses, within each group.

summary signature(object = "GBH"): ... Prints the most significant hypothesis, after adjusting for multiple testing via GBH. Also supplies the estimated proportion of null hypothesis within each group and a table of counts of adjusted significance across groups.

Author(s)

Kris Sankaran

References


See Also

Adaptive.GBH Oracle.GBH

Examples

## These are the unadjusted p-values corresponding to
## the outcome of some multiple testing experiment. The
## first 500 hypotheses are null and the last 1500 are
## true alternatives.

unadjp <- c(runif(500, 0, 0.01), runif(1500, 0, 1))
names(unadjp) <- paste("Hyp: ", 1:2000)

## These are the unadjusted p-values corresponding to
## the outcome of some multiple testing experiment. The
## first 500 hypotheses are null and the last 1500 are
## true alternatives.
unadjp <- c(runif(500, 0, 0.01), runif(1500, 0, 1))
names(unadjp) <- paste("Hyp: ", 1:2000)

## Here there are two groups total we have randomly
## assigned hypotheses to these two groups.
group.index <- c(sample(1:2, 2000, replace = TRUE))

# Perform the GBH adjustment.
result <- Adaptive.GBH(unadjp, group.index, method = "storey")

# A summary of the GBH adjustment
summary(result)

---

gtemp  

*Global mean land-ocean temperature deviations*

Description

Global mean land-ocean temperature deviations, measured by the Goddard Institute for Space Studies and supplied in package astsa, used in teaching Shumway and Stoffer's Time Series Analysis textbook.

Usage

data(gtemp)

Format

A data frame with 130 observations on the following 2 variables.

- year  a numeric vector
- temp  a numeric vector
**hFDR.adjust**

**Source**

http://data.giss.nasa.gov/gistemp/

**References**

http://www.stat.pitt.edu/stoffer/tsa3/


**Examples**

```r
data(gtemp)
plot(gtemp, type = 'l')
```

---

**hFDR.adjust**  
*FDR Controlling Procedure for Hierarchically Structured Hypotheses*

**Description**

This function implements the Hierarchical FDR controlling procedure developed Benjamini and Yekutieli. The procedure incorporates structural information about the hierarchical relationships between hypotheses in order to increase power and interpretability of a testing procedure while controlling the False Discovery Rate at a prespecified level. It is applicable whenever there is a natural hierarchical structure between the hypotheses being tested before the data analysis begins. For example, the method has been used before in Clinical Studies, where nodes deeper in the tree correspond to secondary or tertiary endpoints. It has also been used in QTL analysis, where we first make statements about regions of chromosomes being associated with specific brain activity and then focus on more and more detailed subsets of chromosomes.

**Usage**

```r
hFDR.adjust(unadjp, tree.el, alpha = 0.05)
```

**Arguments**

- `unadjp`: A vector of raw p-values resulting from an experiment. The names of this vector should be contained in the edgelist parameterizing the hierarchical structure between hypothesis, inputted as `tree.el`.
- `tree.el`: The edgelist parameterizing the hierarchical structure between hypotheses. The edges must be stored so that each edge is a row of a two column matrix, where the first column gives the parent and the second gives the child.
- `alpha`: The level of FDR control within families of the tree. Note that this is NOT necessarily the level of FDR control within the entire tree. Refer to the paper by Yekutieli and Benjamini for bounds on various FDR criterion.
Details

The FDR controlling procedure is described in more detail in the paper by Yekutieli and Benjamini 2009. The idea is to control for multiple testing error within families of hypotheses, and only test a descendant family of hypotheses if the associated parent hypotheses was deemed significant in the higher level. The families of hypotheses are taken to be the children of any particular node, and error is controlled within these families using the Benjamini-Hochberg procedure. Different bounds can be proven for the FDR when considered along whole tree, within a single level, and tips. In particular, the whole tree FDR is typically controlled at three times the FDR control within individual families, and this result holds for arbitrary hypotheses tests and configurations of trees.

Value

An object of class hypothesesTree.

Author(s)

Kris Sankaran

References


Benjamini, Y, and Yekutieli, D. Hierarchical fdr testing of trees of hypotheses. 2002.


See Also

hypothesesTree-class

Examples

library('igraph')
library('ape')

alternative.indices <- sample(1:49, 30)
unadj.p.values <- vector("numeric", length = 49)
unadj.p.values[alternative.indices] <- runif(30, 0, 0.01)
unadj.p.values[!alternative.indices] <- runif(19, 0, 1)
unadj.p.values[c(1:5)] <- runif(5, 0, 0.01)
names(unadj.p.values) <- paste("Hyp ", c(1:49))

tree <- as.igraph(rtree(25))
V(tree)$name <- names(unadj.p.values)
tree.el <- get.edgelist(tree)

hyp.tree <- hFDR.adjust(unadj.p.values, tree.el, 0.05)

## We can visualize the difference between the unadjusted and the
## adjusted trees.
hypothesesTree-class  

```r
plot(hyp.tree, adjust = FALSE)
plot(hyp.tree, adjust = TRUE)
```

---

**hypothesesTree-class**  
**Class** "hypothesesTree"

---

**Description**

Class for performing hierarchical multiple testing corrections.

**Slots**

- **tree**: Object of class "matrix". The edgelist for the hypotheses tree.
- **p.vals**: Object of class "data.frame". Each row corresponds to an individual hypothesis. The first column stores the p-values before GBH adjustment, while the second gives the hFDR adjusted p-values. The hypotheses are sorted in order of significance according to these GBH adjusted p-values. The group column gives the group membership of each hypothesis, and adj.significance codes the significance of each hypothesis, according to the GBH adjusted p-values.
- **alpha**: Object of class "numeric". The level at which the FDR is controlled among children of each parent node.

**Methods**

- **initialize** signature(.Object = "hypothesesTree"): ... Check that the hypotheses tree is correctly initialized. It ensures that the number of unadjusted p-values, hypotheses names, and nodes in the hypotheses tree all agree. It also checks that the hypotheses tree is in fact a tree.
- **plot** signature(x = "hypothesesTree", y = "ANY"): ... Plots the tree of hypotheses and their p-values either before or after adjustment. If a particular node hypothesis was not tested, it is colored grey. If it was tested and rejected, it is green; if it was tested and not rejected, it is shaded blue. The deeper the shade, the lower (more significant) the p-value was.
- **show** signature(object = "hypothesesTree"): ... This prints the unadjusted and adjusted p-values of the hypotheses tree associated with the HFDR procedure.
- **summary** signature(object = "hypothesesTree"): This prints the most significant adjusted p-values, along with estimates of the FDR across the tree and at tips.

**Author(s)**

Kris Sankaran

**See Also**

hFDR.adjust EstimatedHFDRControl
Oracle Group Benjamini-Hochberg Correction

Description

Performs the Group Benjamini-Hochberg procedure when the true proportion of null hypotheses is known within each group. The procedure is applicable whenever group structure about the relationship between different hypotheses is known before testing begins. The idea is to control the FDR within each group and to use the proportion of null hypotheses present within each group to make the testing procedure within that group either more or less conservative – this is in fact the idea behind all adaptive multiple testing procedures.

The Oracle GBH method can also be used when we would like to use the Adaptive GBH procedure but with estimates of proportions of true null hypotheses within groups that are not made directly available through the Adaptive.GBH function – in this case those estimates can be inputted as the argument pi.groups in the this function Oracle.GBH.

Usage

Oracle.GBH(unadj.p, group.index, pi.groups, alpha = 0.05)

Arguments

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>unadj.p</td>
<td>A vector of the unadjusted p-values resulting from a multiple testing experiment.</td>
</tr>
<tr>
<td>group.index</td>
<td>A vector of the same length as the vector of unadjusted p-values, where a &quot;G&quot; in the jth coordinate indicates that the jth unadjusted p-values in unadj.p belongs to group &quot;G&quot;. This code can be either a factor giving group names, or a numeric index.</td>
</tr>
<tr>
<td>pi.groups</td>
<td>A vector of the known proportions of true null hypotheses within each of the groups. This vector should be named so that each element of the group.index vector correspond to one of the names of the pi.groups vector.</td>
</tr>
</tbody>
</table>
alpha

The level that we are attempting to control the FDR at.

Value

An object of class GBH, which provides the adjusted p-values.

Author(s)

Kris Sankaran

References


See Also

GBH-class estimate.pi0 Adaptive.GBH

Examples

# A very simple example, with only 5 hypotheses.
unadjp <- c(0.002, 0.1, 0.001, 0.01, 0.4)
names(unadjp) <- paste("hyp", 1:5)
groups <- c(1, 2, 1, 2, 2)

# Say we know goup 1 has pi.1 = 0.3 and pi.0,2 = 0.9
pi.groups <- c("1" = 0.3, "2" = 0.9)
result <- Oracle.GBH(unadjp, groups, pi.groups)

# An example where we use an external pi0 estimation routine
unadjp.2 <- c(runif(500, 0, 0.01), runif(1500, 0, 1))
names(unadjp.2) <- paste("hyp", 1:2000)
groups.2 <- c(sample(1:2, 2000, replace = TRUE))
pi.groups <- c("1" = NA, "2" = NA)
for(i in 1:2){
  pi.groups[i] <- estimate.pi0(unadjp.2[which(groups.2 == i)], method = "storey")
}
result <- Oracle.GBH(unadjp.2, groups.2, pi.groups, 0.05)
result@pi0
result@p.vals
Create tree of p-values for phyloseq data

Description

This helper function is used to aggregate abundances of individual microbes to higher levels in the tree and test whether those aggregated abundances are significantly different between environments, using the data structures from the phyloseq package framework.

Usage

treePValues(tree, abundances, environments)

Arguments

- **tree**: An edgelist for a tree containing the phylogenetic relationships between different microbes.
- **abundances**: A phyloseq class OTU table specifying the abundances of different microbes across environments.
- **environments**: A phyloseq class Sample Data object associating the different environments with variables of interest.

Value

A vector containing the p-values of the linear model predicting the abundances of microbes aggregated to different levels in the taxonomy from environmental variables.

Author(s)

Kris Sankaran

Examples

```r
library('igraph')

# Example with random data
if(require('ape')) {
  rand.tree <- as.igraph(rtree(50))
  V(rand.tree)$name <- paste("hyp", 1:50)
  rand.tree <- get.edgelist(rand.tree)
  X <- matrix(rnorm(50 * 4), 50, 4)
  rownames(X) <- paste("hyp", 1:50)
  colnames(X) <- 1:4
  X[, 1:2] <- X[, 1:2] + 1
  groups <- factor(c("A", "A", "B", "B"))
  treePValues(rand.tree, X, groups)
}
```
# Example using phyloseq
if(require('ape') & require('phyloseq')) {
  data(chlamydiae)
  abundances <- otu_table(chlamydiae)
  environments <- sample_data(chlamydiae)$SampleType
  ch.tree <- get.edgelist(as.igraph(phy_tree(chlamydiae)))
  ch.pval <- treePValues(ch.tree, abundances, environments)
}
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