Package 'BEAMR'

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```
Title Bootstrap Evaluation of Association Matrices
```

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Description A bootstrap-based approach to integrate multiple forms of high dimensional genomic data with multiple clinical endpoints. This method is used to find clinically meaningful groups of genomic features, such as genes or pathways. A manuscript describing this method is in preparation.

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Author Anna Eames Seffernick [aut, cre, cph]
      (<https://orcid.org/0000-0003-0848-4604>),
     Stanley Pounds [aut],
     Xueyuan Cao [aut]
Maintainer Anna Eames Seffernick <anna.seffernick@stjude.org>
```

beam_dat

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beam_dat

Pediatric T-ALL Clinical Data from COG trial AALL0434

Description

The beam.data object used in example beam analyses

Usage

beam_dat

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Format

beam_dat:

A beam.data object, which is a list with the following elements:

main.data A data.frame with clinical/endpoint data.

mtx.data A list of the omics data matrices.

mtx.anns A list of omic annotation data.frames.

anns.mtch A data.frame with information to link mtx.data and mtx.anns.

set.data A data.frame with set.id, mtx.id, and row.id to link omic features to sets.

set.anns Optional data.frame with set annotation data.

boot.index A matrix with bootstrap indices.

Source

NA

beam_dat_sm

Pediatric T-ALL Clinical Data from COG trial AALL0434

Description

The smaller beam.data object used in the example for compute_beam_stats function

Usage

beam_dat_sm

Format

beam_dat_sm:

A beam.data object, which is a list with the following elements:

main.data A data.frame with clinical/endpoint data.

mtx.data A list of the omics data matrices.

mtx.anns A list of omic annotation data.frames.

anns.mtch A data.frame with information to link mtx.data and mtx.anns.

set.data A data.frame with set.id, mtx.id, and row.id to link omic features to sets.

set.anns Optional data.frame with set annotation data.

boot.index A matrix with bootstrap indices.

Source

NA

beam_specs_sm

beam_specs

Pediatric T-ALL BEAM Analysis Specs Data from COG trial AALL0434

Description

The beam.specs object used in example beam analyses

Usage

beam_specs

Format

beam_specs:

A data frame with 6 rows and 3 columns:

name Analysis name with omic and endpoint

mtx Name of omics matrix used in the analysis

mdl Regression model

Source

NA

beam_specs_sm

Pediatric T-ALL BEAM Analysis Specs Data from COG trial AALL0434

Description

The small beam.specs object used in example compute_beam_stats function.

Usage

beam_specs_sm

Format

beam_specs_sm:

A data frame with 2 rows and 3 columns:

name Analysis name with omic and endpoint

mtx Name of omics matrix used in the analysis

mdl Regression model

Source

NA

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beam_stats

Pediatric T-ALL Clinical Data from COG trial AALL0434

Description

The beam.stats object used in example beam analyses

Usage

beam_stats

Format

beam_stats:

A beam.stats object, which contains the following objects

beam.stats A list of data.frames of association statistics for each omic-endpoint pair.

beam.specs A beam.specs object (data.frame with name, mtx, and mdl.)

beam.data The beam.data object.

Source

NA

beam_stats_sm

Pediatric T-ALL Clinical Data from COG trial AALL0434

Description

The small beam.stats object used in example for compute_beam_stats function.

Usage

```
beam_stats_sm
```

Format

beam_stats_sm:

A beam.stats object, which contains the following objects

beam.stats A list of data.frames of association statistics for each omic-endpoint pair.

beam.specs A beam.specs object (data.frame with name, mtx, and mdl.)

beam.data The beam.data object.

Source

NA

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check_beam_specs

Check that beam.specs satisfies all necessary conditions

Description

Check that beam.specs satisfies all necessary conditions

Usage

```
check_beam_specs(beam.specs, mtx.names)
```

Arguments

beam. specs A data.frame with column name, mtx, and mdl

mtx.names A vector with the names of the data matrices (beam.data\$mtx.data)

Value

A data.frame of beam.specs if all conditions satisfied, otherwise throws an error

Examples

```
data(beam_dat)
data(beam_specs)
test_specs <- check_beam_specs(beam_specs, names(beam_dat$mtx.data))</pre>
```

check_list_class

Check that each element of a list is of a required class

Description

Check that each element of a list is of a required class

Usage

```
check_list_class(list.object, required.class)
```

Arguments

```
list.object A list used in BEAMR analysis required.class Class for list elements, e.g. matrix
```

Value

Logical TRUE if list is of required class

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Examples

```
data(omicdat)
check_list_class(omicdat, "matrix")
```

clean_Bmtx

Clean up bootstrap coefficient matrix

Description

Clean up bootstrap coefficient matrix

Usage

```
clean_Bmtx(B)
```

Arguments

В

Matrix of bootstrap coefficients

Value

Matrix of cleaned bootstrap coefficients

Examples

```
data(beam_stats)
B.mtx <- beam_stats$beam.stats[[1]]
B.cln <- clean_Bmtx(B.mtx)</pre>
```

clinf

Pediatric T-ALL Clinical Data from COG trial AALL0434

Description

A subset of clinical data from pediatric and young adult t-lineage acute lymphoblastic leukmia patients in the Children's Oncology Group trial AALL0434, published in Liu et al., 2017 Nature Genetics

Usage

clinf

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Format

clinf:

A data frame with 265 rows and 8 columns:

ID Subject ID

MRD29 Minimal residual disease measured at day 29

RNA.clm Key to match to RNA matrix Lesion.clm Key to match Lesion matrix Lesion.id Key to match Lesion matrix

RNA.id Key to match RNA matrix

EFS Event-free survival Surv object

OS Overall survival Surv object

Source

https://www.nature.com/articles/ng.3909

compute_beam_stats

Compute bootstrap model coefficients for BEAM

Description

Compute bootstrap model coefficients for BEAM

Usage

```
compute_beam_stats(beam.data, beam.specs, stdize = TRUE)
```

Arguments

beam.data Result of prep.beam.data

beam. specs A data.frame of strings with columns name, mtx, mdl (string with R model with

mtx.row)

stdize Logical whether to standardize (center and scale) predictors or not. Default is

TRUE.

Value

A beam.stats object, which is a list with beam.stats (the association matrices), the beam.specs, and the beam.data

```
compute_feature_pvalues
```

Compute feature level p-values from BEAM statistics

Description

Compute feature level p-values from BEAM statistics

Usage

```
compute_feature_pvalues(beam.stats)
```

Arguments

beam.stats

A beam.stats object, which is a list with beam.stats (the association matrices), the beam.specs, and the beam.data

Value

A list of feature level p-values, with each entry a data frame for a different omics/endpoint association, with columns id, gene, beta, p, q

Examples

```
data(beam_stats)
test.feat.pvals <- compute_feature_pvalues(beam.stats=beam_stats)</pre>
```

compute_set_pvalues

Compute BEAMR p-values for sets

Description

Compute BEAMR p-values for sets

Usage

```
compute_set_pvalues(
  beam.stats,
  peel = FALSE,
  z = TRUE,
  alpha = 0.1,
  mess.freq = 25
)
```

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Arguments

beam.stats A beam.stats object from compute_beam_stats function

peel Logical indicating whether to peel in p-value calculation

z Logical indicating whether to z-scale each vector of one coefficient estimate

across bootstraps before analysis

alpha Maximum depth to peel (reduces computing time); default 0.1.

mess.freq Message frequency; default 25.

Value

A list with a data.frame of set p-values from BEAMR analysis, a data.frame of summary row p-values, and a data frame of set matching.

Examples

```
data(beam_stats_sm)
test.pvals <- compute_set_pvalues(beam.stats=beam_stats_sm)</pre>
```

extend_set_data Exte

Extend set definition data with genes on the same row separated by commas, semicolons, slashes, etc

Description

Extend set definition data with genes on the same row separated by commas, semicolons, slashes, etc

Usage

```
extend_set_data(set.data, sep)
```

Arguments

set.data A data frame with set definition data.

sep Punctuation to split on.

Value

A data frame.

```
data(setdat)
extend_set_data(setdat, sep=",")
```

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extract_beam_stats

Extract beam stats for a specific set

Description

Extract beam stats for a specific set

Usage

```
extract_beam_stats(beam.stats, set.id)
```

Arguments

beam.stats A beam.stats object, which is a list with beam.stats (the association matrices),

the beam.specs, and the beam.data

set.id A character of a set id name (an entry in in beam.data\$set.data\$set.id)

Value

A matrix with with estimated associations for each endpoint and each omic feature linked to the set

Examples

```
data(beam_stats)
test.stats <- extract_beam_stats(beam_stats, set.id="ENSG00000099810")</pre>
```

find_id_clm

Find the column of mtch.data with the most rows containing an element of ids

Description

Find the column of mtch.data with the most rows containing an element of ids

Usage

```
find_id_clm(mtch.data, ids)
```

Arguments

mtch.data A data.frame

ids A vector of row ids to match

Value

A vector of column names with the most matches.

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Examples

```
data(omicann)
data(omicdat)
lsn.data <- omicann[[1]]
mtx.rows <- rownames(omicdat[[1]])
test <- find_id_clm(lsn.data,mtx.rows)</pre>
```

gen_beam_plot_list

Generate BEAM Plot List

Description

Internal function: generate a list of clinical feature plots.

Usage

```
gen_beam_plot_list(
  beam.result,
  beam.specs,
  beam.feat.pvals,
  number.pairs = 1,
  set.id,
  feat.id = NULL,
  title.size = 10,
  pair.order = "both",
  endpt.order = NULL
)
```

Arguments

beam.result	Result of prep.beam.data				
beam.specs	A data.frame of strings with columns name, mtx, mdl, plot				
beam.feat.pvals					
	List of feature-level p-values from compute_feature_pvalues				
number.pairs	Numeric; number of features to display in clinical plots, ordered by significance				
set.id	A character with set name; must be in beam.result\$beam.data\$set.data\$set.id				
feat.id	Default NULL; a character with feature name; must be in beam.result\$beam.data\$set.data\$row.id				
title.size	A numeric. Specify the size of individual plot titles. Default is 10.				
pair.order	One of c("both", "omic", "endpoint"). Default is "both." Specify how to choose				
	feature-endpoint plots to include. If "both", find the best (based on q, p, effect				
	size) feature-omic pair for each type of omic and each endpoint separately. If				
	"omic", within each omic, find the best feature-endpoint pair and then plot this				
	feature with all endpoints. If "endpoint", need to specify endpt.order as the				
	name of chosen endpoint. Then, within each omic, find the feature with best				
	association with the selected endpoint, and plot this feature for all endpoints.				
endpt.order	Default NULL. If pair.order="endpoint", specify character with endpoint name				
	(from beam.specs\$name, after the period).				

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Value

A list of plots for the specified set and/or feature.

Examples

get_id_index

For each row of the data.frame main.data, find the index of the matching element in vector ids

Description

For each row of the data frame main.data, find the index of the matching element in vector ids

Usage

```
get_id_index(mtch.data, ids, warn = TRUE)
```

Arguments

mtch.data A data.frame to be linked with the ids ids A vector of ids to be linked in mtch.data

warn A logical value whether to include warnings with results

Value

A data frame with matching id index

```
data(clinf)
data(omicdat)
mtx.clms <- colnames(omicdat[[1]])
id_index <- get_id_index(clinf,mtx.clms)</pre>
```

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omicann

Pediatric T-ALL Omics Annotation Data from COG trial AALL0434

Description

A subset of genomic lesion and RNA expression data from pediatric and young adult t-lineage acute lymphoblastic leukmia patients in the Children's Oncology Group trial AALL0434, published in Liu et al., 2017 Nature Genetics. This is the annotation mapping feature id to gene name given by Ensembl ID.

Usage

omicann

Format

omicann:

A list with two data frames of omics annotation.

Lesion A dataframe with 20 rows and 2 columns with lesion ID and Ensembl ID.

RNA A dataframe with 20 rows and 2 columns with feature ID and Ensembl ID.

Source

https://www.nature.com/articles/ng.3909

omicdat

Pediatric T-ALL Omics Data from COG trial AALL0434

Description

A subset of genomic lesion and RNA expression data from pediatric and young adult t-lineage acute lymphoblastic leukmia patients in the Children's Oncology Group trial AALL0434, published in Liu et al., 2017 Nature Genetics

Usage

omicdat

Format

omicdat:

A list with two dataframes of omic data for each subject

Lesion A dataframe with 20 rows and 265 columns indicating presence of lesion.

RNA A dataframe with 20 rows and 265 columns with expression data.

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Source

https://www.nature.com/articles/ng.3909

plot_beam_boot

Plot bootstrap output for BEAM sets

Description

#' plot_beam_boot produces a pairs plot of the beam stats matrices. Default is maximum of 5 plots, ordered by most significant association direction.

Usage

```
plot_beam_boot(
   beam.result,
   beam.feat.pvals,
   beam.specs = NULL,
   set.id,
   max.plots = 4,
   z = TRUE
)
```

Arguments

beam.result A beam.stats object from compute_beam_stats

beam.feat.pvals

A list containing feature-level p-values from compute_feature_pvalues.

beam.specs A data.frame. Default NULL, in which case beam.result\$beam.specs is used.
Otherwise can input other beam.specs data.frame that must contain name, mtx, mdl, plot columns.

set.id A character specifying the name of a set. Must be in beam.result\$beam.data\$set.data
max.plots A number specifying the max number of rows in the pairs plot. Default is 4, ordered by feature-level p-value.

z Logical indicating whether to z-scale each vector of one coefficient estimate across bootstraps before plotting. Default is TRUE.

Value

A pairs plot figure.

plot_beam_clin

plot_beam_clin

Plot BEAM Sets

Description

plot_beam_clin produces a matrix of feature level clinical plots for a set. Users can specify which omic/endpoint pairs they want to see as well as the number of features from the set. Default is all omic/endpoint pairs and the top feature (smallest feature-level p-value).

Usage

```
plot_beam_clin(
   beam.result,
   beam.specs = NULL,
  beam.set.pvals,
  beam.feat.pvals,
  set.id,
  gene.name = NULL,
  pair.type = NULL,
  number.pairs = 1,
  pair.order = "both",
  endpt.order = NULL,
  n.col = NULL,
  n.row = NULL,
  title.size = 10
)
```

Arguments

beam.result	A beam.stats of	object from comput	te beam stats

beam.specs A data.frame. Default NULL, in which case beam.result\$beam.specs is used.

Otherwise can input other beam.specs data.frame that must contain name, mtx,

mdl, plot columns.

beam.set.pvals A list containing BEAMR set p-values from compute_set_pvalues.

beam.feat.pvals

A list containing feature-level p-values from compute_feature_pvalues.

set.id A character specifying the name of a set. Must be in beam.result\$beam.data\$set.data

gene.name A character specifying a Gene Name/Symbol for the set. Default is NULL

pair.type A character vector. Default NULL, in which case clinical plots for all omic/endpoint

pairs are produced. Otherwise specify pairs from beam.stats\$beam.specs\$name

number.pairs A numeric. Default 1, in which case only feature with best simple test for each

pair is plotted. If >1, show top n simple plots ordered by feature-level p-value

pair.order One of c("both", "omic", "endpoint"). Default is "both." Specify how to choose

feature-endpoint plots to include. If "both", find the best (based on q, p, effect

plot_feat_clin 17

size) feature-omic pair for each type of omic and each endpoint separately. If "omic", within each omic, find the best feature-endpoint pair and then plot this feature with all endpoints. If "endpoint", need to specify endpt.order as the name of chosen endpoint. Then, within each omic, find the feature with best association with the selected endpoint, and plot this feature for all endpoints.

Default NULL. If pair.order="endpoint", specify character with endpoint name (from beam.specs\$name, after the period).

A numeric. Specify the number of columns for the plot layout; default NULL will use the number of omics types.

A numeric. Specify the number of rows for the plot layout; default NULL will automatically define the number of rows after number of columns specified.

A numeric. Specify the size of individual plot titles. Default is 10.

Value

A figure (ggarrange object)

endpt.order

title.size

n.col

n.row

Examples

plot_feat_clin

Plot BEAM Feature

Description

plot_feat_clin produces a matrix of feature level clinical plots for a specific feature.

Usage

```
plot_feat_clin(
  feat.id,
  beam.result,
  beam.specs = NULL,
  beam.set.pvals,
  beam.feat.pvals,
```

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```
n.row = NULL,
n.col = NULL
)
```

Arguments

feat.id A character specifying the name of a feature. Must be in beam.result\$beam.data\$set.data

beam.result A beam.stats object from compute_beam_stats

beam. specs A data.frame. Default NULL, in which case beam.result\$beam.specs is used.

Otherwise can input other beam.specs data.frame that must contain name, mtx,

mdl, plot columns.

beam.set.pvals A list containing BEAMR set p-values from compute_set_pvalues.

beam.feat.pvals

A list containing feature-level p-values from compute_feature_pvalues.

n.row A numeric. Specify the number of rows for the plot layout; default NULL will

automatically define the number of rows after number of columns specified.

n.col A numeric. Specify the number of columns for the plot layout; default NULL

will use the number of omics types.

Value

A figure (ggarrange object)

Examples

prep_beam_data

Prepare data for BEAM analysis

Description

Prepare data for BEAM analysis

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Usage

```
prep_beam_data(
   main.data,
   mtx.data,
   mtx.anns = NULL,
   set.data = NULL,
   set.anns = NULL,
   n.boot = 1000,
   seed = NULL
)
```

Arguments

main.data	A data.frame
mtx.data	A list, each element is a matrix
mtx.anns	A list, each element is a data.frame
set.data	A data.frame with columns set.id, mtx.id, row.id
set.anns	A data frame with set.id and other columns
n.boot	Number of bootstraps
seed	Initial seed for random number generation

Value

A beam.data object, which is a list with main.data, mtx.data, mtx.anns, anns.mtch, set.data, set.anns, and boot.index

Examples

prep_beam_plot

Prepare for BEAM plotting

Description

Add a "plot" column to beam.specs, which includes string of plot commands.

Usage

```
prep_beam_plot(beam.data, beam.specs)
```

20 prep_beam_specs

Arguments

beam.data Result of prep.beam.data

beam. specs A data frame of strings with columns name, mtx, mdl (string with R model with

mtx.row)

Value

An updated beam.specs object that includes the column "plot"

Examples

prep_beam_specs

Prepare beam.specs

Description

Prepare the beam.specs data.frame for BEAM model fitting. Specifies the univariate models needed to compute the BEAMR set p-values.

Usage

```
prep_beam_specs(
  beam.data,
  endpts,
  firth = TRUE,
  adjvars = NULL,
  endptmdl = NULL)
```

Arguments

beam.data A beam.data object from prep_beam_data

endpts A vector of endpoint variable names in main.data

firth A logical value. If TRUE (defaul) fit Firth penalized Cox model to account for

monotone likelihood in the presence of rare events or predictors. If FALSE fit

usual Cox model.

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adjvars	Default NULL, optional vector of adjustment variable names in main.data
endptmdl	Optional model specification data.frame with endpoint name column called "endpt"

and model string column called "mdl"

Value

The beam.specs object, a data.frame specifying the omics-endpoint association models to be fit

Examples

print.beam.data

Print summary information about a beam.data object

Description

Print summary information about a beam.data object

Usage

```
## S3 method for class 'beam.data'
print(x, ...)
```

Arguments

x An object of class "beam.data"... Other arguments passed to or from other methods

Value

Messages about the beam.data object

```
data(beam_dat)
print(beam_dat)
```

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print.beam.stats

Print summary information about beam.stats object

Description

Print summary information about beam.stats object

Usage

```
## S3 method for class 'beam.stats' print(x, ...)
```

Arguments

x An object of class "beam.stats"

... Other arguments passed to or from other methods

Value

Messages about the beam.data object

Examples

```
data(beam_stats)
print(beam_stats)
```

setdat

Map of Pediatric Data from COG trial AALL0434

Description

Map between annotation and omic data for a subset of clinical data from pediatric and young adult t-lineage acute lymphoblastic leukmia patients in the Children's Oncology Group trial AALL0434, published in Liu et al., 2017 Nature Genetics

Usage

setdat

Format

```
setdat:
```

A data frame with 40 rows and 3 columns

set.id Ensembl ID that defines gene-feature set

mtx.id Name of omic matrix where corresponding feature data can be found

row.id Feature name in corresponding omic matrix

specs 23

Source

https://www.nature.com/articles/ng.3909

specs

Pediatric T-ALL BEAMR Analysis Specs Data from COG trial AALL0434

Description

The beam.specs object used in example beam analyses

Usage

specs

Format

specs:

A data frame with 6 rows and 3 columns:

name Analysis name with omic and endpointmtx Name of omics matrix used in the analysis

mdl Regression model

Source

NA

subset_beam_result

Subset beam.stats Result

Description

Filter the beam.stats object from compute_beam_stats with various filtering criteria. Default is to filter to top 50 sets with smallest q-value. At least one filtering criteria must be specified. Can also use intersection or union of multiple criteria.

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Usage

```
subset_beam_result(
  beam.result,
  beam.set.pvals = NULL,
  beam.feat.pvals = NULL,
  mtx.rows = NULL,
  set.ids = NULL,
  endpts = NULL,
  omics = NULL,
  p.limit = NULL,
  q.limit = NULL,
  q.feat.limit = NULL,
  intersect = TRUE,
  recalc = FALSE
)
```

Arguments

omics

beam.result	A beam.stats object from compute_beam_stats		
beam.set.pvals	A list containing BEAMR set p-values from compute_set_pvalues; required if p.limit or q.limit are specified.		
beam.feat.pvals			
	A list containing feature-level p-values from compute_feature_pvalues; required if p.feat.limit or q.feat.limit are specified.		
mtx.rows	A list of vectors of feature names corresponding to row.id in set.data. List names correspond to mtx.id in set.data. If specified, filter to all sets containing at least		

correspond to mtx.id in set.data. If specified, filter to all sets containing at leas one of these features.

Set.ids A character vector of set.ids. If specified, filter to these sets.

endpts A character vector of endpoint names. If specified, filter to sets that correspond to these endpoints.

A character vector of omics names. If specified, fitler to sets that correspond to

these omics.

p.limit A numeric value. If specified, determine mtx.rows that are below this threshold

if p<1 or top p sets if p>1.

q.limit A numeric value. If specified, determine mtx.rows that are below this threshold

if q < 1 or top q sets if q > 1.

 ${\tt p.feat.limit} \qquad \hbox{A numeric value. If specified, determine mtx.rows that are below this threshold}$

if p.feat<1 or top p.feat sets if p.feat>1 (feature p-values).

q.feat.limit A numeric value. If specified, determine mtx.rows that are below this threshold

if q.feat<1 or top q.feat sets if q.feat>1.

intersect A logical value. Default is TRUE. If TRUE, use intersection of all specified

criteria. If FALSE use union of all specified criteria.

recalc A logical value. Default is FALSE. If TRUE, recalculate p-values. If FALSE

use original set p-values..

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Value

A list with filtered beam.stats object, updated beam.set.pvals, and filtered beam.feat.pvals.

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