# Package: TSDT (via r-universe)

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Type Package Title Treatment-Specific Subgroup Detection Tool Version 1.0.8 Date 2025-01-07 **Description** Implements a method for identifying subgroups with superior response relative to the overall sample. Imports methods, mlbench, hash, party, rpart, survival, survRM2, stats, modeltools, utils, parallel LazyLoad no License GPL (>= 2) URL https://github.com/EliLillyCo/CRAN\_TSDT BugReports https://github.com/EliLillyCo/CRAN\_TSDT/issues **Encoding** UTF-8 RoxygenNote 7.2.3 Repository https://elilillyco.r-universe.dev RemoteUrl https://github.com/elilillyco/cran\_tsdt RemoteRef HEAD RemoteSha 1736c44cedf5f07e20ab21aab12e56acabfaf8a2 RemoteSubdir TSDT

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binary\_transform binary transform

#### Description

Converts any variable with two possible values to a  $\{0,1\}$  binary variable.

## Usage

```
binary_transform(x)
```

#### Arguments

х

A variable with two possible values.

## Value

A vector with values in  $\{0,1\}$ .

## Examples

```
## Convert a variable that takes values 'A' and 'B' to 0 and 1
x <- sample( c('A', 'B'), size = 10, prob = c(0.5,0.5), replace = TRUE )
print(x);flush.console()
binary_transform( x )</pre>
```

bootstrap

bootstrap

#### Description

Generate a vector of bootstrap samples.

## Usage

```
bootstrap(
    x,
    trt = NULL,
    trt_control = "Control",
    FUN = NULL,
    varname = NULL,
    varcol = NULL,
    arglist = NULL,
    n_samples = 1
)
```

#### Arguments

х	Source data to bootstrap.
trt	Treatment variable. (optional)
trt_control	Value for treatment control arm. Default value is 'Control'.
FUN	Function to compute statistic for each bootstrap sample. (optional)
varname	Name of variable in x on which to compute FUN. If x has only one column varname is not needed. If x has more than one column then either varname or varcol must be specified.
varcol	Column index of x on which to compute FUN. If x has only one column varcol is not needed. If x has more than one column then either varname or varcol must be specified.
arglist	List of additional arguments to pass to FUN.
n_samples	Number of bootstrap samples to generate.

#### Details

Each bootstrap sample will retain the in-bag and out-of-bag data. Optionally, the user may specify a function to compute a statistic for each in-bag and out-of-bag sample. This function may be a builtin R function (e.g. mean, median, etc.) or a user-defined function (see Examples). If no statistic function is provided bootstrap returns a vector of objects of class Bootstrap. If a statistic function is provided bootstrap returns a vector of objects of class BootstrapStatistic, which in addition to the in-bag and out-of-bag samples contains the name of the statistic, variable on which the statistic is computed, and the numerical result of the statistic for each in-bag and out-of-bag sample.

## Value

If FUN is NULL returns a vector of objects of class Bootstrap. If FUN is non-NULL returns a vector of objects of class BootstrapStatistic

#### See Also

Bootstrap, BootstrapStatistic

## Bootstrap-class

```
## For each bootstrap sample compute a statistic on the in-bag and out-of-bag data
ex3 <- bootstrap( x, FUN = mean, varname = "response", n_samples = 2 )
## Specify a user-defined function that takes a numeric vector input and
## returns a numeric result
sort_and_rank <- function( z, rank ){
    z <- sort( z )
    return( z[rank] )
}
ex4 <- bootstrap( x, FUN = sort_and_rank, arglist = list( rank = 1 ),
    varname = "response", n_samples = 2 )</pre>
```

Bootstrap-class Bootstrap

#### Description

Bootstrap is a container class for bootstrap samples.

#### Value

Object of class Bootstrap

## Slots

inbag In-bag bootstrap sample.

oob Out-of-bag bootstrap sample.

## See Also

BootstrapStatistic, bootstrap

BootstrapStatistic-class

**BootstrapStatistic** 

## Description

BootstrapStatistic is a container class for bootstrap samples augmented with a computed statistic.

#### Value

Object of class BootstrapStatistic

## Slots

statname The name of a (possibly user-defined) statistic to compute on the bootstrap sample.

arglist A list of arguments passed to the function referenced by statname.

variable The name of the variable on which to compute statname.

inbag\_stat The value of statname for the in-bag bootstrapped sample.

oob\_stat The value of statname for the out-of-bag bootstrapped sample.

## See Also

Bootstrap, bootstrap

CTree-class

#### Description

CTree is a container class for trees created by ctree.

CTree

## Value

An object of class CTree

## Slots

tree An object of class BinaryTree-class produced by ctree.

data Training data.

parameters Control parameters

## See Also

ctree, BinaryTree-class

ctree\_wrapper ctree\_wrapper

#### Description

A wrapper function to ctree

## Usage

```
ctree_wrapper(response, covariates = NULL, tree_builder_parameters = list())
```

## Arguments

response	Response variable to use in ctree model.		
covariates	Covariates to use in ctree model.		
<pre>tree_builder_parameters</pre>			
	A named list of parameters to pass to ctree.		

## Value

An object of class CTree

#### See Also

ctree

cutpoints

## Description

Get distribution of cutpoints for subgroups.

## Usage

cutpoints(object, subgroup = NULL, subsub = NULL)

## Arguments

object	An object of class TSDT
subgroup	A string decscription of a subgroup (optional)
subsub	A string description of a sub-subgroup (optional)

## Value

A vector containing the subgroup cutpoints.

## See Also

**TSDT** 

diff\_mean\_deviance\_residuals

 $diff\_mean\_deviance\_residuals$ 

## Description

Computes the difference in the mean of deviance residuals function across treatment groups.

#### Usage

diff\_mean\_deviance\_residuals(data, scoring\_function\_parameters = NULL)

#### Arguments

data data.frame containing response data scoring\_function\_parameters named list of scoring function control parameters

#### Details

The deviance residual is the observed number of events at time t minus the expected number of events at time t. See documentation for mean\_deviance\_residuals (linked below) for more details. A smaller value for the deviance residual is preferred when the event under study is an undesirable event – i.e. it is preferred to observe fewer events than predicted by the survival model. A two-arm TSDT model computes the mean deviance residual in the treatment arm minus the mean deviance residual in the control arm. The treatment arm is superior to the control arm when the mean deviance residual in the treatment arm for desirable\_response = 'decreasing'. If the event under study is a desirable event the appropriate value for desirable\_response is desirable\_response is desirable event, so the default value for desirable\_response when the scoring\_function is diff\_mean\_deviance\_residuals is desirable\_response = 'decreasing'. Note this differs from all other TSDT configurations, for which the default value for desirable\_response is desirable\_response = 'increasing'.

## Value

Difference in mean deviance residuals across treatment arms.

## See Also

mean\_deviance\_residuals, Surv, coxph, survreg, residuals.coxph, residuals.survreg, TSDT

diff\_quantile\_response

diff\_quantile\_response

#### Description

Return the difference across treatment arms of a specified response quantile

#### Usage

```
diff_quantile_response(data, scoring_function_parameters = NULL)
```

#### Arguments

data data.frame containing response data scoring\_function\_parameters named list of scoring function control parameters

#### Details

This function returns the difference across treatment arms of the response quantile associated with a specified percentile. The default behavior is to return the difference in medians.

A difference of response quantiles across treatment arms

## See Also

TSDT, quantile\_response, quantile

#### Examples

```
## Generate example data containing response and treatment
N <- 100
y = runif(min = 0, max = 20, n = N)
df <- as.data.frame( y )</pre>
names( df ) <- "y"</pre>
df$trt <- sample( c('Control', 'Experimental'), size = N, prob = c(0.4,0.6),</pre>
                  replace = TRUE )
## Default behavior is to return the median
diff_quantile_response( df )
# should match previous result from quantile_response
median( df$y[df$trt!='Control'] ) - median( df$y[df$trt=='Control'] )
## Get Q1 response
diff_quantile_response( df, scoring_function_parameters = list( percentile = 0.25 ) )
# should match previous result from quantile_response
quantile( df$y[df$trt!='Control'], 0.25 ) - quantile( df$y[df$trt=='Control'], 0.25 )
## Get max response
diff_quantile_response( df, scoring_function_parameters = list( percentile = 1 ) )
# should match previous result from quantile_response
max( df$y[df$trt!='Control'] ) - max( df$y[df$trt=='Control'] )
```

#### Description

Computes the difference in restricted mean survival time across treatment arms.

#### Usage

```
diff_restricted_mean_survival_time(data, scoring_function_parameters = NULL)
```

#### Arguments

data data.frame containing response data scoring\_function\_parameters named list of scoring function control parameters

## Details

Computes the restricted mean survival time for the treatment and control arms and returns the difference.

## Value

Difference in restricted mean survival time across treatment arms.

## See Also

TSDT, Surv, rmst2

diff\_survival\_time\_quantile

*diff\_survival\_time\_quantile* 

## Description

Computes the difference in the quantile of a survival function across treatment groups.

#### Usage

```
diff_survival_time_quantile(data, scoring_function_parameters = NULL)
```

### Arguments

data data.frame containing response data scoring\_function\_parameters named list of scoring function control parameters

## Details

Computes the survival function quantile for the treatment and control arms and returns the difference.

## Value

A difference in a survival time quantile across treatment arms.

## See Also

TSDT, survival\_time\_quantile, Surv, coxph, survfit, survreg, predict.coxph, predict.survreg

#### Examples

```
requireNamespace( "survival", quiet = TRUE )
N <- 200
df <- data.frame( y = survival::Surv( runif( min = 0, max = 20, n = N ),
                         sample( c(0,1), size = N, prob = c(0.2,0.8), replace = TRUE ) ),
                  trt = sample( c('Control', 'Experimental'), size = N,
                                prob = c(0.4, 0.6), replace = TRUE ) )
## Compute difference in median survival time between Experimental arm and
## Control arm. It is not actually necessary to provide the value for the
## time_var, trt_var, trt_control, and percentile parameters because these
## values are all equal to their default values. The value are explicitly
## provided here simply for clarity.
ex1 <- diff_survival_time_quantile( data = df,</pre>
                                    scoring_function_parameters = list( trt_var = "trt",
                                     trt_control = "Control",
                                    percentile = 0.50 ) )
## Compute difference in Q1 survival time. In this example the default value
## for all scoring function parameters are used except percentile, which here
## takes the value 0.25.
ex2 <- diff_survival_time_quantile( data = df,</pre>
                                scoring_function_parameters = list( percentile = 0.25 ) )
```

distribution distribution

#### Description

Returns the distribution of values used to compute TSDT summary statistics.

## Usage

```
distribution(object, statistic, subgroup = NULL, subsub = NULL)
```

## Arguments

object	An object of class TSDT
statistic	The desired statistic distribution
subgroup	The desired subgroup
subsub	A subset of the subgroup

#### Details

This function returns the distribution of all values used to compute summary statistics for superior subgroups identified by the TSDT algorithm. The summary statistics returned for a TSDT object include the mean subgroup size, mean response value, and median value of the scoring function. These statistics reported seperately for in-bag and out-of-bag data sets, and also stratified by treatment arm. This function can also provide the distribution of all cutpoints for a numeric splitting variable in a subgroup definition.

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#### distribution

## Value

A vector containing the observed values for the specified subgroup

## See Also

TSDT, summary-methods

```
set.seed(0)
N <- 200
continuous_response = runif( min = 0, max = 20, n = N )
trt <- sample( c('Control', 'Experimental'), size = N, prob = c(0.4,0.6),</pre>
               replace = TRUE )
X1 \leq runif(N, min = 0, max = 1)
X2 <- runif(N, min = 0, max = 1)
X3 <- sample( c(0,1), size = N, prob = c(0.2,0.8), replace = TRUE )
X4 <- sample( c('A', 'B', 'C'), size = N, prob = c(0.6,0.3,0.1), replace = TRUE )
covariates <- data.frame( X1 )</pre>
covariates$X2 <- X2</pre>
covariates$X3 <- factor( X3 )</pre>
covariates$X4 <- factor( X4 )</pre>
## Create a TSDT object
ex1 <- TSDT( response = continuous_response,</pre>
            trt = trt, trt_control = 'Control',
            covariates = covariates[,1:4],
            inbag_score_margin = 0,
            desirable_response = "increasing",
            oob_score_margin = 0,
            min_subgroup_n_control = 5,
            min_subgroup_n_trt = 5,
            n_sample = 5 )
## Show summary statistics
summary( ex1 )
## Get the number of subjects in each superior in-bag subgroup
distribution( ex1, statistic = 'Inbag_Subgroup_Size' )
## Get the vector of subgroup sample sizes for a particular subgroup
distribution( ex1, statistic = 'Inbag_Subgroup_Size',
              subgroup = 'X1<xxxx & X1>=xxxxx' )
## Get the observed cutpoints for the numeric splitting variables in a subgroup
distribution( ex1, statistic = 'Cutpoints', subgroup = 'X1<xxxxx & X1>=xxxxx' )
## If the subgroup definition has more than one numeric splitting variable you
## can retrieve the numeric cutpoints for the splitting variables individually
distribution( ex1, statistic = 'Cutpoints', subgroup = 'X1<xxxxx & X1>=xxxxx',
              subsub = 'X1<xxxx' )</pre>
distribution( ex1, statistic = 'Cutpoints', subgroup = 'X1<xxxxx & X1>=xxxxx',
```

```
subsub = 'X1>=xxxxx' )
## Valid statistic names come from the column names in the summary output. If
## you are uncertain what the possible statistic values could be, you can pass
## any arbitrary string as the statistic and an error message is returned
## listing valid statistic values.
## Not run:
distribution( ex1, statistic = 'Invalid_Statistic' )
## End(Not run)
```

folds

folds

#### Description

Partition data into k folds for k-fold cross-validation. Adds a variable fold\_id to the data.frame.

## Usage

folds(x, k)

#### Arguments

х	data.frame to partition into k folds for k-fold cross-validation.
k	Number of folds to use in cross-validation

#### Value

A list of partitions of the vector x.

```
# Generate random example data
N <- 200
ID <- 1:N
continuous_response = runif( min = 0, max = 20, n = N )
X1 <- runif( N, min = 0, max = 1 )
X2 <- runif( N, min = 0, max = 1 )
X3 <- sample( c(0,1), size = N, prob = c(0.2,0.8), replace = TRUE )
X4 <- sample( c('A','B','C'), size = N, prob = c(0.6,0.3,0.1), replace = TRUE )
df <- data.frame( ID )
names( df ) <- "ID"
df$response <- continuous_response
df$X1 <- X1
df$X2 <- X2
df$X3 <- factor( X3 )
df$X4 <- factor( X4 )</pre>
```

```
## Partition data into 5 folds
ex1 <- folds( df, k = 5 )
## Partition data into 10 folds</pre>
```

```
ex2 <- folds(df, k = 10)
```

function\_parameter\_names

function\_parameter\_names

#### Description

Returns a character vector of the specified function's parameters

#### Usage

function\_parameter\_names(FUN)

## Arguments

FUN The name of a function

#### Value

A character vector of function parameter names

## Examples

```
## Define a function
example_function <- function( parm1, arg2, x, bool = FALSE ){
   cat( "This is an example function.\n" )
}
## Return the function parameter names</pre>
```

function\_parameter\_names( example\_function )

get\_covariates get\_covariates

## Description

Returns the covariate variables in the in-bag or out-of-bag data.

## Usage

get\_covariates(data, scoring\_function\_parameters)

## Arguments

data A data.frame containing in-bag or out-of-bag data

scoring\_function\_parameters

A list of named elements containing control parameters and other data required by the scoring function

## Details

If the user provides a covariate\_vars parameter in the list of scoring\_function\_parameters this function will return the variables specified by that parameter. If the user specifies a covariate\_cols parameter in the list of scoring\_function\_parameters the function returns the columns in data indexed by that parameter. Otherwise, NULL is returned.

## Value

A data.frame of covariates.

## See Also

get\_y, get\_trt

#### Examples

```
## Create an example data.frame
df <- data.frame( y <- 1:5 )
names( df ) <- "y"
df$time <- 10:14
df$time2 <- 20:24
df$time2 <- 20:24
df$event <- sample( c(0:1), size = 5, replace = TRUE )
df$trt <- sample( c("Control", "Treatment"), size = 5, replace = TRUE )
df$x1 <- runif( n = 5 )
df$x2 <- LETTERS[1:5]</pre>
```

## Select the covariate variables by name
get\_covariates( df, scoring\_function\_parameters = list( covariate\_vars = c("x1","x2") ) )

```
## Select the covariate variables by column index
get_covariates( df, scoring_function_parameters = list( covariate_cols = c(6:7) ) )
```

get\_cutpoints get\_cutpoints

#### Description

Accessor method for cutpoints slot in TSDT objects.

## Usage

```
get_cutpoints(.Object, subgroup, subsub = NULL)
## S4 method for signature 'TSDT_CutpointDistribution'
get_cutpoints(.Object, subgroup = character, subsub = NULL)
## S4 method for signature 'TSDT'
get_cutpoints(.Object, subgroup = character, subsub = NULL)
```

## Arguments

.Object	A TSDT object.
subgroup	The anonymized subgroup.
subsub	A particular component of the subgroup to retrieve.

## Details

The summary results from TSDT provide a set of 'anonymized' subgroups in a form similar to 'X1<xxxx'. The variable X1 may have been selected as a splitting variable in several boot-strapped samples. The exact numerical cutpoint for X1 could vary from one sample to the next. The get\_cutpoints method returns all the numerical cutpoints associated with this subgroup. If the subgroup is a compound subgroup defined on more than one spliting variable the user can specify the 'subsub' parameter to get the cutpoints associated with a particular component of the subgroup.

#### Examples

```
## Not run:
example( TSDT )
## You can access the cutpoints slot of a TSDT object directly
ex2@cutpoints
## You can also use the accessor method
get_cutpoints( ex2@cutpoints, subgroup = 'X1<xxxxx' )
## Retrieving a compound subgroup defined on multiple splits
get_cutpoints( ex2, subgroup = 'X1<xxxxx & X1>=xxxxx' )
## Retrieving a single component from the compound subgroup
get_cutpoints( ex2, subgroup = 'X1<xxxxx & X1>=xxxxx', subsub = 'X1>=xxxxx' )
## End(Not run)
```

get\_suggested\_subgroup

get\_suggested\_subgroup

#### Description

Get a string definition of the suggested subgroup definition.

## Usage

```
get_suggested_subgroup(anonymized_subgroup, suggested_cutoff, anon = "xxxxx")
```

## Arguments

anonymized_sub	group
	A string containing the the anonymized subgroup.
suggested_cuto	ff
	A string containing the suggested cutoff.
anon	The anonymization string. By default this is 'xxxxx'.

#### Details

Subgroups are reported in an anonymized fashion – e.g. a subgroup defined on a variable X1 could be reported as X1<xxxx, 'xxxxx' is a string used to represent an exact numeric cutoff. For each anonymized subgroup, the distribution of exact numeric cutpoints is retained across all bootrstrapped samples. TSDT then provides a suggested cutoff got each anonymized subgroup. By default, this suggested cutoff is the median of the observed cutpoints. Note that this anonymization applies only to numeric splitting variables. Categorical splitting variables are not anonymized.

```
set.seed(0)
N <- 200
continuous_response = runif( min = 0, max = 20, n = N )
trt <- sample( c('Control', 'Experimental'), size = N, prob = c(0.4,0.6), replace = TRUE )</pre>
X1 <- runif(N, min = 0, max = 1)
X2 <- runif(N, min = 0, max = 1)
X3 <- sample( c(0,1), size = N, prob = c(0.2,0.8), replace = TRUE )
X4 <- sample( c('A','B','C'), size = N, prob = c(0.6,0.3,0.1), replace = TRUE )
covariates <- data.frame( X1 )</pre>
covariates$X2 <- X2</pre>
covariates$X3 <- factor( X3 )</pre>
covariates$X4 <- factor( X4 )</pre>
## Create a TSDT object
ex1 <- TSDT( response = continuous_response,</pre>
             trt = trt, trt_control = 'Control',
             covariates = covariates[,1:4],
             inbag_score_margin = 0,
             desirable_response = "increasing",
             oob_score_margin = 0,
             min_subgroup_n_control = 10,
             min_subgroup_n_trt = 20,
             maxdepth = 2,
             rootcompete = 2 )
```

get\_trt get\_trt

#### Description

Returns the treatment variable in the in-bag or out-of-bag data.

## Usage

```
get_trt(data, scoring_function_parameters = NULL)
```

#### Arguments

data

A data.frame containing in-bag or out-of-bag data

scoring\_function\_parameters

A list of named elements containing control parameters and other data required by the scoring function

## Details

If the user provides a trt\_var parameter in the list of scoring\_function\_parameters this function will return the variable specified by that parameter. If the user specifies a trt\_col parameter in the list of scoring\_function\_parameters the function returns the column in data indexed by that parameter. Lastly, if data contains a variable called 'trt' that variable is returned. Otherwise, NULL is returned.

#### Value

Treatment variable (if available) or NULL.

#### See Also

get\_y, get\_covariates

## Examples

```
## Create an example data.frame
df <- data.frame( y <- 1:5 )
names( df ) <- "y"</pre>
df$time <- 10:14
df$time2 <- 20:24
df$event <- sample( c(0:1), size = 5, replace = TRUE )
df$trt <- sample( c("Control", "Treatment"), size = 5, replace = TRUE )</pre>
df <- runif( n = 5 )
df$x2 <- LETTERS[1:5]
## Select the trt variable by name
get_trt( df, scoring_function_parameters = list( trt_var = 'trt' ) )
## Select the trt variable by column index
get_trt( df, scoring_function_parameters = list( trt_col = 5 ) )
## The default behavior works for this example because the trt variable in df
## is actually called trt.
get_trt( df )
## If the user's data does not contain a variable called
## 'y' the default behavior will fail. In this case the user must explicitly
## identify the 'y' variable via one of the two previous methods.
names( df )[which(names(df) == "trt")] <- "treatment" # rename the 'trt' variable to 'treatment'</pre>
get_trt( df ) # now default behavior fails (i.e. returns NULL)
get_trt( df, scoring_function_parameters = list( trt_var = 'treatment' ) ) # this works
```

get\_y get\_y

#### Description

Returns the response variable in the in-bag or out-of-bag data.

#### Usage

```
get_y(data, scoring_function_parameters = NULL)
```

#### Arguments

data	A data.frame	containing	in-bag	or out-of-ba	g data

scoring\_function\_parameters

A list of named elements containing control parameters and other data required by the scoring function

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#### get\_y

## Details

If the user provides a y\_var parameter in the list of scoring\_function\_parameters this function will return the variable specified by that parameter. If the user specifies a y\_col parameter in the list of scoring\_function\_parameters the function returns the column in data indexed by that parameter. Lastly, if data contains a variable called 'y' that variable is returned. Otherwise, NULL is returned.

## Value

Response variable (if present) or NULL.

## See Also

get\_trt, get\_covariates

```
## Create an example data.frame
df <- data.frame( y <- 1:5 )</pre>
names( df ) <- "y"</pre>
df$time <- 10:14
df$time2 <- 20:24
df$event <- sample( c(0:1), size = 5, replace = TRUE )</pre>
df$trt <- sample( c("Control", "Treatment"), size = 5, replace = TRUE )</pre>
dfx1 <- runif( n = 5 )
df$x2 <- LETTERS[1:5]
## Select the y variable by name
get_y( df, scoring_function_parameters = list( y_var = 'y' ) )
## Select the y variable by column index
get_y( df, scoring_function_parameters = list( y_col = 1 ) )
## The default behavior works for this example because the y variable in df
## is actually called y.
get_y( df )
## If the user's data does not contain a variable called
## 'y' the default behavior will fail. In this case the user must explicitly
## identify the 'y' variable via one of the two previous methods.
names( df )[which(names(df) == "y")] <- "response" # rename the 'y' variable to 'response'</pre>
get_y( df ) # now default behavior fails (i.e. returns NULL)
get_y( df, scoring_function_parameters = list( y_var = 'response' ) ) # this works
```

hazard\_ratio hazard\_ratio

#### Description

Computes the hazard ratio across treatment arms using a CoxPH model.

## Usage

```
hazard_ratio(data, scoring_function_parameters = NULL)
```

## Arguments

data data.frame containing response data scoring\_function\_parameters named list of scoring function control parameters

#### Value

Hazard ratio across treatment arms.

### See Also

TSDT, Surv, coxph,

mean\_deviance\_residuals

mean\_deviance\_residuals

## Description

Computes the mean of the deviance residuals from a survival model

#### Usage

```
mean_deviance_residuals(data, scoring_function_parameters = NULL)
```

## Arguments

data data.frame containing response data scoring\_function\_parameters named list of scoring function control parameters

#### Details

Computes the mean of the deviance residuals from a survival model. The deviance residual at time t is computed as the observed number of events at time t minus the expected number of events at time t (see Therneau, et. al. linked below). The expected number of events is the number of events predicted by the survival model. If the event under study is an undesirable event (as would likely be the case in a clinical context), then a smaller value for the deviance residual is desirable – i.e. it is desirable to observe fewer events than expected from the survival model. In this case the appropriate value for desirable\_response = 'decreasing'. If the event under study is desirable then the appropriate value for desirable\_response is desirable\_response = 'increasing'. It is assumed that most survival models are modeling an undesirable event. Therefore, when the user specifies mean\_deviance\_residual or diff\_mean\_deviance\_residual, the default value for desirable\_response = 'increasing'. Note this differs from all other TSDT configurations, for which the default value for desirable\_response = 'increasing'.

#### Value

Mean of deviance residuals

#### References

Therneau, T.M., Grambsch, P.M., and Fleming, T.R. (1990). Martingale-based residuals for survival models. Biometrika, 77(1), 147-160. doi:10.1093/biomet/77.1.147

#### See Also

TSDT, Surv, coxph, survfit

mean\_response mean\_response

#### Description

Compute the mean response.

#### Usage

mean\_response(data, scoring\_function\_parameters = NULL)

#### Arguments

data data.frame containing response data

scoring\_function\_parameters

named list of scoring function control parameters

#### Details

This function will compute the mean of the response variable. If a value for trt\_arm is provided the mean in that treatment arm only will be computed (and the trt variable must also be provided), otherwise the mean for all data passed to the function will be computed.

#### Value

The mean of the provided response variable.

#### See Also

TSDT, treatment\_effect

#### Examples

```
mean( data$continuous_response[ data$trt == 'Experimental' ] )
```

MOB-class MOB

#### Description

MOB is a container class for trees created by mob.

#### Value

An object of class MOB

#### Slots

tree An object of class BinaryTree-class produced by mob. data Training data. parameters Control parameters mob\_wrapper

## See Also

mob, BinaryTree-class

mob\_wrapper mob\_wrapper

## Description

Wrapper function for mob.

## Usage

```
mob_wrapper(
  response,
  x = NULL,
  z = NULL,
  covariates = NULL,
  tree_builder_parameters = list()
)
```

## Arguments

response	Response variable to use in mob model.	
X	Covariates passed to model in mob. mob uses fits the formula $y \sim x1 + + xk   z1 + + zl$ where the variables before the   are passed to the model and the variables after the   are used for partitioning. x represents the x variables. See mob help page for more information.	
z	Covariates used to parition the mob model. mob uses fits the formula $y \sim x1 + + xk   z1 + + zl$ where the variables before the   are passed to the model and the variables after the   are used for partitioning. z represents the z variables. See mob help page for more information.	
covariates	An alias for z.	
tree_builder_parameters		
	A named list of parameters to pass to mob	

A named list of parameters to pass to mob.

## Value

An object of class MOB

#### See Also

mob

na2empty

## Description

Replace all instances of NA in character variable with empty string.

## Usage

na2empty(x)

## Arguments

х

A character vector.

## Value

A character vector with NA values replaced with empty string.

## See Also

unfactor

## Examples

```
## Create character variable with missing values
ex1 <- c( 'A', NA, 'B', NA, 'C', NA )
ex1
## Replace NAs with empty string
ex1 <- na2empty( ex1 )
ex1</pre>
```

parse\_party parse\_party

## Description

Parse output from ctree() and mob() functions in party package.

## Usage

```
parse_party(tree, data = NULL, include_subgroups = FALSE, digits = NULL)
```

#### parse\_party

### Arguments

tree	An object of class BinaryTree or mob resulting from a call to the ctree() or mob() function.	
data	data.frame containing covariates used to create tree.	
include_subgroups		
	A logical value indicating whether or not to include a string representation of the subgroups in the results. Defaults to FALSE.	
digits	Number of digits for rounding.	

#### Details

Collects text output from party::ctree() or party::mob(), parses the splits, and populates a data.frame with the relevant data.

#### Value

A data.frame containing a parsed tree.

#### See Also

ctree, mob

```
requireNamespace( "party", quietly = TRUE )
requireNamespace( "modeltools", quietly = TRUE )
## From party::ctree() examples:
set.seed(290875)
## regression
airq <- subset(airquality, !is.na(Ozone))</pre>
airct <- party::ctree(Ozone ~ ., data = airq,</pre>
               controls = party::ctree_control(maxsurrogate = 3))
## Parse the results into a new data.frame
ex1 <- parse_party( airct )</pre>
ex1
## From party::mob() examples:
data("BostonHousing", package = "mlbench")
## and transform variables appropriately (for a linear regression)
BostonHousing$lstat <- log(BostonHousing$lstat)</pre>
BostonHousing$rm <- BostonHousing$rm^2</pre>
## as well as partitioning variables (for fluctuation testing)
BostonHousing$chas <- factor( BostonHousing$chas, levels = 0:1,</pre>
                               labels = c("no", "yes") )
BostonHousing$rad <- factor(BostonHousing$rad, ordered = TRUE)</pre>
## partition the linear regression model medv ~ lstat + rm
## with respect to all remaining variables:
fmBH <- party::mob( medv ~ lstat + rm | zn + indus + chas + nox + age +</pre>
```

```
dis + rad + tax + crim + b + ptratio,
    control = party::mob_control(minsplit = 40), data = BostonHousing,
    model = modeltools::linearModel )
## Parse the results into a new data.frame
ex2 <- parse_party( fmBH )
ex2
```

parse\_rpart

parse\_rpart

## Description

Extract splits from an rpart.object returned from a call to rpart().

#### Usage

```
parse_rpart(tree, include_subgroups = FALSE)
```

#### Arguments

tree

An rpart.object returned from call to rpart().

include\_subgroups

A logical value indicating whether or not to include a string representation of the subgroups in the results. Defaults to FALSE.

## Details

This function takes as its input an rpart.object returned from a call to rpart. It parses this rpart.object using rpart\_nodes() and returns the splits in the tree. The data returned include the NodeID of the node to split, the NodeID of that node's parent, the NodeID of that nodes left child and right child, the number of observations in that node, the variable used in the split, the data type for the splitting variable, the logic indicating which observations will go to the node's left child, the value of the splitting variable at which the split ocurrs, the mean response value of the node, and (optionally) the string representation of the node's subgroup. A node's subgroup is defined by the sequence of splits from the root to that node.

#### Value

A data.frame containing a parsed tree.

#### See Also

rpart\_nodes, rpart, rpart.object

## partition

## Examples

```
requireNamespace( "rpart", quietly = TRUE )
## Generate example data containing response, treatment, and covariates
N <- 50
continuous_response = runif( min = 0, max = 20, n = N )
trt <- sample( c('Control', 'Experimental'), size = N, prob = c(0.4,0.6),</pre>
              replace = TRUE )
X1 <- runif(N, min = 0, max = 1)
X2 <- runif(N, min = 0, max = 1)
X3 <- sample( c(0,1), size = N, prob = c(0.2,0.8), replace = TRUE )
X4 <- sample( c('A', 'B', 'C'), size = N, prob = c(0.6, 0.3, 0.1), replace = TRUE )
## Fit an rpart model
fit <- rpart::rpart( continuous_response ~ trt + X1 + X2 + X3 + X4,</pre>
                      control = rpart::rpart.control( maxdepth = 3L ) )
fit
## Parse the results into a new data.frame
ex1 <- parse_rpart( fit, include_subgroups = TRUE )</pre>
ex1
```

partition

## Description

Partitions a vector x into n groups of roughly equal size.

partition

## Usage

```
partition(x, n)
```

## Arguments

х	Vector to partition.
n	Number of (roughly) equally-sized groups

## Value

A list of partitions of the vector x.

## Examples

x <- 1:10
partition( x, 3 )</pre>

permutation

#### Description

Permute response, treatment, or response for one treatment arm only.

#### Usage

```
permutation(response = NULL, trt = NULL, permute_arm = NULL)
```

#### Arguments

response	Response (or other) variable(s) to be permuted. This can be a data.frame of
	multiple variables (e.g. a data.frame of covariates or a multivariate response).
trt	Treatment variable.
permute_arm	reatment arm to permute.

#### Details

If a response variable is provided and treatment is not provided the response variable is permuted.

If a treatment variable is provided and response is not provided the treatment variable is permuted.

If a response variable and treatment variable and permute are provided the response variable is permuted only for the treatment arm indicated by permute\_arm.

If a response variable and treatment variable are provided, but permute\_arm

#### Value

If permuting response or treatment, returns vector of permuted response or treatment. If permuting response and treatment, returns a list of permuted response and treatment.

```
N <- 20
x <- data.frame( 1:N )
names( x ) <- "response"
x$trt <- factor( c( rep( "Experimental", 9 ), rep( "Control", N - 9 ) ) )
x$time <- x$response
x$event <- 0:1
## Permute treatment variable
ex1 <- x[,c("response","trt")]
ex1$permuted_trt <- permutation( trt = ex1$trt )
## Permute response variable
ex2 <- x[,c("response","trt")]
ex2$permuted_response <- permutation( response = ex2$response )</pre>
```

```
## Permute the response for treatment arm only
ex3 <- x[,c("response","trt")]</pre>
permuted3 <- permutation( response = ex3$response, trt = ex3$trt, permute_arm = "Experimental" )</pre>
names( permuted3 ) <- paste( "permuted_", names(permuted3), sep = "" )</pre>
ex3 <- cbind( ex3, permuted3 )</pre>
## Permute response and treatment together
ex4 <- x[,c("response","trt")]</pre>
permutation_list4 <- permutation( response = ex4$response, trt = ex4$trt )</pre>
ex4$permuted_response <- permutation_list4$response</pre>
ex4$permuted_trt <- permutation_list4$trt
## Permute a survival response for treatment arm only
ex5 <- x[,c("time","event","trt")]</pre>
permuted5 <- permutation( response = ex5[,c("time","event")], trt = ex5$trt,</pre>
                            permute_arm = "Experimental" )
names( permuted5 ) <- paste( "permuted_", names(permuted5), sep = "" )</pre>
ex5 <- cbind( ex5, permuted5 )</pre>
## Permute a survival outcome and treatment together
ex6 <- x[,c("time","event","trt")]</pre>
permutation_list6 <- permutation( response = ex6[,c("time","event")], trt = ex6$trt )</pre>
ex6$permuted_time <- permutation_list6$response$time</pre>
ex6$permuted_event <- permutation_list6$response$event</pre>
```

quantile\_response quantile\_response

## Description

Return the specified quantile of the response distribution.

#### Usage

```
quantile_response(data, scoring_function_parameters = NULL)
```

#### Arguments

data data.frame containing response data scoring\_function\_parameters

named list of scoring function control parameters

#### Details

This function returns the response quantiles associated with a specified percentile. The default behavior is to return the median -i.e. 50th-percentile.

A quantile of the response variable.

## See Also

TSDT, diff\_quantile\_response, quantile

## Examples

```
## Generate example data containing response and treatment
N <- 100
y = runif(min = 0, max = 20, n = N)
df <- as.data.frame( y )</pre>
names( df ) <- "y"</pre>
df$trt <- sample( c('Control', 'Experimental'), size = N, prob = c(0.4,0.6),
                  replace = TRUE )
## Default behavior is to return the median
quantile_response( df )
median( df$y ) # should match previous result from quantile_response
## Get Q1 response
quantile_response( df, scoring_function_parameters = list( percentile = 0.25 ) )
quantile( df$y, 0.25 ) # should match previous result from quantile_response
## Get max response
quantile_response( df, scoring_function_parameters = list( percentile = 1 ) )
max( df$y ) # should match previous result from quantile_response
```

reset\_factor\_levels reset\_factor\_levels

#### Description

Reset the list of levels associated with a factor variable.

#### Usage

```
reset_factor_levels(data)
```

#### Arguments

data A data.frame containing factor variables.

## Details

After subsetting a factor variable some factor levels that were previously present may be lost. This is particularly true for relatively rare factor levels. This function resets the list of factor levels to include only the levels currently present.

rpart\_nodes

#### Value

A data.frame with factor variable that now have reset levels.

#### Examples

```
ex1 = as.factor( c( rep('A', 3), rep('B',3), rep('C',3) ) )
```

```
## The levels associated with the factor variable include the letters A, B, C ex1 \, # Levels are A, B, C
```

## If the last three observations are dropped the value C no longer occurs
## in the data, but the list of associated factor levels still contains C.
## This mismatch between the data and the list of factor levels may cause
## problems, particularly for algorithms that iterate over the factor levels.

```
ex1 <- ex1[1:6]
ex1 # Levels are still A, B, C, but the data contains only A and B
## If the factor levels are reset the data and list of levels will once again
## be consistent
ex1 <- reset_factor_levels( ex1 )
ex1 # Levels now contain only A and B, which is consistent with data
```

rpart\_nodes rpart\_nodes

#### Description

Extract node information from an rpart.object.

## Usage

```
rpart_nodes(tree)
```

#### Arguments

tree

An rpart.object returned from call to rpart().

#### Details

Information about nodes and splits returned in an rpart.object is contained in strings printed to the console. This function parses those strings and populates a data.frame.

## Value

A data.frame containing the nodes of a parsed tree.

#### See Also

rpart, rpart.object

#### Examples

```
requireNamespace( "rpart", quietly = TRUE )
## Generate example data containing response, treatment, and covariates
N <- 50
continuous_response = runif( min = 0, max = 20, n = N )
binary_response <- sample( c('A', 'B'), size = N, prob = c(0.5, 0.5),</pre>
                            replace = TRUE )
trt <- sample( c('Control', 'Experimental'), size = N, prob = c(0.4,0.6),</pre>
               replace = TRUE )
X1 <- runif(N, min = 0, max = 1)
X2 <- runif(N, min = 0, max = 1)
X3 <- sample( c(0,1), size = N, prob = c(0.2,0.8), replace = TRUE )
X4 <- sample( c('A', 'B', 'C'), size = N, prob = c(0.6, 0.3, 0.1), replace = TRUE )
## Fit an rpart model with continuous response (i.e. regression)
fit1 <- rpart::rpart( continuous_response ~ trt + X1 + X2 + X3 + X4 )</pre>
fit1
## Parse the results into a new data.frame
ex1 <- rpart_nodes( fit1 )</pre>
ex1
## Fit an rpart model with binary response (i.e. classification)
fit2 <- rpart::rpart( binary_response ~ trt + X1 + X2 + X3 + X4 )</pre>
fit2
```

rpart\_wrapper rpart\_wrapper

## Description

A wrapper function to rpart.

#### Usage

```
rpart_wrapper(
  response,
  response_type = NULL,
  covariates = NULL,
  tree_builder_parameters = NULL,
  prune = FALSE
)
```

## Arguments

response	Response variable to use in rpart model.
response_type	Class of response variable.
covariates	Covariates to use in rpart model.

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#### subgroup

tree_builder_pa	arameters
	A named list of parameters to pass to rpart. This includes all input parameters that rpart can take.
prune	Logical variable indicating whether the tree shold be pruned to the subtree with the smallest cross-validation error. Defaults to FALSE.

#### Details

This function provides a wrapper to rpart that provides a convenient interface for specifying the response variable and covariates for the rpart model. The user may indicate whether the tree should be pruned to the size that yields the smallest cross-validation error. An rpart.object is returned.

#### Value

An object of class rpart.

#### See Also

rpart, rpart.object, Surv

#### Examples

```
## Generate example data containing response, treatment, and covariates
N <- 100
continuous_response = runif( min = 0, max = 20, n = N )
trt <- sample( c('Control', 'Experimental'), size = N, prob = c(0.4,0.6), replace = TRUE )</pre>
X1 <- runif( N, min = 0, max = 1 )
X2 <- runif(N, min = 0, max = 1)
X3 <- sample( c(0,1), size = N, prob = c(0.2,0.8), replace = TRUE )
X4 <- sample( c('A', 'B', 'C'), size = N, prob = c(0.6,0.3,0.1), replace = TRUE )
covariates <- data.frame( trt )</pre>
names( covariates ) <- "trt"</pre>
covariates$X1 <- X1
covariates$X2 <- X2
covariates$X3 <- X3
covariates$X4 <- X4
## Fit an rpart model
ex1 <- rpart_wrapper( response = continuous_response, covariates = covariates )</pre>
ex1
```

subgroup

subgroup

#### Description

Subset a user-provided data.frame according to the subgroup specified by a node in a tree.

#### Usage

```
subgroup(splits, node, xdata, ydata = xdata)
```

#### Arguments

splits	A data.frame of splits returned from a call to parse_rpart().
node	The NodeID of the node defining the desired split.
xdata	The data.frame of covariates to subset according to the subgroup definition.
ydata	The associated vector of response values to subset according to the subgroup definition. (optional)

#### Details

After the splits from an rpart.object are extracted by a call to parse\_rpart(), the extracted splits define a subgroup for each node. This subgroup can be used to subset a user-provided data.frame. This function takes as its input a data.frame of splits obtained from a call to parse\_rpart(), a NodeID indicating which node specifies the desired subgroup, a data.frame of covariates to subset, and (optionally) the associated response data to subset. If only xdata is specified by the user, the subset of xdata implied by the subgroup will be returned. If xdata and ydata are provided by the user, the subset of ydata will be returned (xdata is still required from the user because the subsetting is computed on the covariate values even when the data returned to the user are from ydata).

#### Value

A data.frame containing the data consistent with the specified subgroup.

#### See Also

parse\_rpart, rpart, rpart.object

#### Examples

requireNamespace( "rpart", quietly = TRUE )

```
## Generate example data containing response, treatment, and covariates
N <- 20
continuous_response = runif( \min = 0, \max = 20, n = N )
trt <- sample( c('Control', 'Experimental'), size = N, prob = c(0.4,0.6), replace = TRUE )</pre>
X1 <- runif( N, min = 0, max = 1 )
X2 <- runif(N, min = 0, max = 1)
X3 <- sample( c(0,1), size = N, prob = c(0.2,0.8), replace = TRUE )
X4 <- sample( c('A', 'B', 'C'), size = N, prob = c(0.6, 0.3, 0.1), replace = TRUE )
covariates <- data.frame( trt )</pre>
names( covariates ) <- "trt"</pre>
covariates$X1 <- X1
covariates$X2 <- X2
covariates$X3 <- X3
covariates$X4 <- X4
## Fit an rpart model
fit <- rpart::rpart( continuous_response ~ trt + X1 + X2 + X3 + X4 )</pre>
```

## Return parsed splits with subgroups

# subsample

```
splits1 <- parse_rpart( fit, include_subgroups = TRUE )
splits1
## Subset covariate data according to split for NodeID 3
ex1 <- subgroup( splits = splits1, node = 3, xdata = covariates )
ex1
## Subset response data according to split for NodeID 3
ex2 <- subgroup( splits = splits1, node = 3, xdata = covariates, ydata = continuous_response )
ex2</pre>
```

subsample

#### Description

Generate a vector of subsamples.

subsample

# Usage

```
subsample(
    x,
    trt = NULL,
    trt_control = "Control",
    training_fraction = NULL,
    validation_fraction = NULL,
    test_fraction = NULL,
    n_samples = 1
)
```

#### Arguments

х	<source data="" subsample.<="" th="" to=""/>	
trt	Treatment variable. (optional)	
trt_control	Value for treatment control arm. Defaulte value is 'Control'.	
training_fraction		
	Fraction of source data to include in training subsample.	
validation_fraction		
	Fraction of source data to include in validation subsample.	
test_fraction	Fraction of source data to include in test subsample.	
n_samples	Number of subsamples to generate.	

#### Details

Each subsample will contain training, validation, and test data in proportions specified by the user. If a treatment variable is supplied the ratio of treatments will be preserved as closely as possible.

## Value

Vector of objects of class Subsample.

# See Also

Subsample

# Examples

```
## Generate example data frame containing response and treatment
N <- 50
x <- data.frame( runif( N ) )</pre>
names( x ) <- "response"</pre>
x$treatment <- factor( sample( c("Control", "Experimental"), size = N,</pre>
                        prob = c(0.8, 0.2), replace = TRUE ) )
## Generate two subsamples
ex1 <- subsample( x,</pre>
                   training_fraction = 0.9,
                   test_fraction = 0.1,
                   n_{samples} = 2 )
## Generate two subsamples preserving treatment ratio
ex2 <- subsample( x,</pre>
                   trt = x$treatment,
                   trt_control = "Control",
                   training_fraction = 0.7,
                   validation_fraction = 0.2,
                   test_fraction = 0.1,
                   n_{samples} = 2 )
```

Subsample-class Subsample

#### Description

Subsmaple is a container class for subsamples.

## Value

Object of class

## Slots

training Training data. validation Validation data. test Test data.

# summary, TSDT-method

#### See Also

subsample

summary, TSDT-method Summary function for class TSDT.

## Description

Summary function for class TSDT.

## Usage

## S4 method for signature 'TSDT'
summary(object)

## Arguments

object An object of class TSDT.

## Value

A data.frame containing the superior subgroups identified by TSDT.

#### See Also

**TSDT** 

survival\_time\_quantile

survival\_time\_quantile

# Description

Computes the quantile of a survival function.

#### Usage

survival\_time\_quantile(data, scoring\_function\_parameters = NULL)

#### Arguments

data data.frame containing response data scoring\_function\_parameters named list of scoring function control parameters

#### Details

Computes the quantile of a survival function. The user specifies the percentile associated with the desired quantile in scoring\_function\_parameters. The default is percentile = 0.50, which returns the median survival. A user may also specify a value for the trt\_arm parameter in scoring\_function\_parameters to compute the survival quantile for only one arm.

#### Value

A quantile of the response survival time.

#### See Also

TSDT, diff\_survival\_time\_quantile, Surv, coxph, survfit, survreg, quantile.survfit, predict.coxph, predict.survreg

#### Examples

```
N <- 200
time <- runif( min = 0, max = 20, n = N )</pre>
event <- sample( c(0,1), size = N, prob = c(0.2,0.8), replace = TRUE )
trt <- sample( c('Control', 'Experimental'), size = N, prob = c(0.4,0.6), replace = TRUE )</pre>
df <- data.frame( y = survival::Surv( time, event ), trt = trt )</pre>
## Compute median survival time in Experimental treatment arm.
ex1 <- survival_time_quantile( data = df,</pre>
                                scoring_function_parameters = list( trt_var = "trt",
                                trt_arm = "Experimental",
                                percentile = 0.50 ) )
## Compute Q1 survival time for all data. It is necessary here to explicitly
## specify trt = NULL because a variable called trt exists in df. The default
## behavior is to use this variable as the treatment variable. To override
## the default behavior trt = NULL is included in scoring_function_parameters.
ex2 <- survival_time_quantile( data = df,</pre>
                       scoring_function_parameters = list( trt = NULL, percentile = 0.25 ) )
```

treatment\_effect treatment\_effect

#### Description

Compute treatment effect as mean( treatment response ) - mean( control response )

#### Usage

```
treatment_effect(data, scoring_function_parameters = NULL)
```

# TSDT

## Arguments

data	data.frame containing response data	
scoring_function_parameters		
named list of scoring function control parameters		

# Details

This function will compute the treatment for the response. The treatment effect is computed as the difference in means between the non-control treatment arm and the control treatment arm. The user must provide the treatment variable as well as the control value.

## Value

The difference in mean response across treatment arms.

# See Also

TSDT, mean\_response

#### Examples

TSDT

Treatment-Specific Subgroup Detection Tool

#### Description

Implements a method for identifying subgroups with superior response relative to the overall sample.

# Usage

```
TSDT(
  response = NULL,
  response_type = NULL,
  survival_model = "kaplan-meier",
  percentile = 0.5,
  tree_builder = "rpart",
  tree_builder_parameters = list(),
  covariates,
  trt = NULL,
  trt_control = 0,
  permute_method = NULL,
  permute_arm = NULL,
  n_samples = 1,
  desirable_response = NULL,
  sampling_method = "bootstrap",
  inbag_proportion = 0.5,
  scoring_function = NULL,
  scoring_function_parameters = list(),
  inbag_score_margin = 0,
  oob_score_margin = 0,
  eps = 1e-05,
 min_subgroup_n_control = NULL,
 min_subgroup_n_trt = NULL,
 min_subgroup_n_oob_control = NULL,
 min_subgroup_n_oob_trt = NULL,
 maxdepth = 30,
  rootcompete = 0,
  competedepth = 1,
  strength_cutpoints = c(0.1, 0.2, 0.3),
  n_permutations = 0,
  n_{cpu} = 1,
  trace = FALSE
)
```

# Arguments

response	Response variable.
response_type	Data type of response. Must be one of binary, continuous, survival. If none provided it will be inferred from the data type of response. (optional)
survival_model	The model to use for a survival response. Defaults to kaplan-meier. Other pos- sible values are: coxph, fleming-harrington, fh2, weibull, exponential, gaussian, logistic, lognormal, and loglogistic. (optional)
percentile	For a two-arm study this parameter specifies a test for the difference in response percentile across the two treatment arms. For a continuous response the de- fault value for percentile is NULL. Instead, the difference in mean response is computed by default for a continuous response. If the user provides a values of

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	percentile = 0.50 then the difference in median response would be computed. For a survival outcome, the default value for percentile is 0.50, which computes the difference in median survival.	
tree_builder	The algorithm to use for building the trees. Defaults to rpart. Other possible values include ctree and mob (both from the party package). (optional)	
tree_builder_p		
	A named list of parameters to pass to the tree-builder. The default tree-builder is rpart. In this case, the parameters passed here would be rpart parameters. Examples might include parameters such as control, cost, weights, na.action, etc. Consult the rpart documentation (or the documentation of your selected tree-builder) for a complete list. (optional)	
covariates	A data.frame containing the covariates.	
trt	Treatment variable. Only needed if there are two treatment arms. (optional)	
trt_control	Value for treatment control arm. This parameter is relevant only for two-arm data. (defaults to 0)	
permute_method	Indicates whether only the response variable should be permuted in the com- putation of the p-value, or the response and treatment variable should be per- muted together (preserving the treatment-response correlation, but eliminating the correlation with the covariates), or the response variable should be permuted within one treatment arm only. The parameter values for these permutation schemes are (respectively) simple, permute_response_and_treatment, and per- mute_response_one_arm. See permute_arm to specify which treatment arm is to be permuted. The default permutation scheme is response_one_arm. As noted in the documentation for the permute_arm parameter is to permute the non-control arm. Taken together, this implies the default permutation method for p-value computation is to permute the response in the non-control arm only. For one-arm data only the response is permuted. (optional)	
permute_arm	Which treatment arm should be permuted? Defaults to the experimental treatment arm – i.e. the treatment arm not matching the value provided in trt_control. For one-arm data only the response is permuted. (optional)	
n_samples	Number of TSDT_Samples to draw.	
desirable_resp		
	Direction of desirable response. Valid values are 'increasing' or 'decreasing'. The default value is 'increasing'. It is important to note that although the parameter is called desirable_response, it actually refers to the desirable direction of scoring function values. In most cases there is a positive correlation between the response and scoring function values – i.e. as the response increases the scoring function also increases. One instance for which this relationship between response and scoring function may not hold is when mean_deviance_residuals or diff_mean_deviance_residuals is used as the scoring function. See the help for these scorings function for further details.	
sampling_metho	-	
	Sampling method used to populate samples for TSDT in-bag and out-of-bag data. Must be either bootstrap or subsample. Default is bootstrap.	
inbag_proportion		
	The proportion of the data to use as the in-bag subset when sampling_method is subsample.	

#### scoring\_function

Scoring function to compute treatment effect. Links to several possible scoring functions are provided in the See Also section below.

# scoring\_function\_parameters

Parameters passed to the scoring function. As an example, the scoring function quantile\_response takes a parameter "percentile" which indicates the desired percentile of the response distribution. Thus, if the median response is desired, this parameter could be set as follows: scoring\_function\_parameters = list( percentile = 0.50 ). Most of the built-in scoring functions have sensible defaults for the scoring function parameters so it is not necessary to specify them explicitly in the call to TSDT. But this parameter could be very useful for user-defined custom scoring functions. (optional)

inbag\_score\_margin

Required margin above overall mean for a subgroup to be considered superior. If a subgroup mean must be 10% larger than the overall subgroup mean to be superior then inbag\_score\_margin = 0.10. If desirable\_response = "decreasing" then inbag\_score\_margin should be negative or zero.

oob\_score\_margin

Similar to inbag\_score\_margin but for classifying out-of-bag subgroups as superior.

- eps Tolerance value for floating-point precision. The default is 1E-5. (optional)
- min\_subgroup\_n\_control

Minimum number of Control arm observations in an in-bag subgroup. A value greater than or equal to one will be interpreted as the required minimum number of observations. A value between zero and one will be interpreted as a proportion of the in-bag Control observations. For a bootstrapped in-bag sample the default for this parameter is 10 of Control observations in the overall sample. For an in-bag sample obtained via subsampling the default value is the inbag\_proportion times 10 number of Control observations in the overall sample.

min\_subgroup\_n\_trt

Minimum number of Experimental arm observations in an in-bag subgroup. A value greater than or equal to one will be interpreted as the required minimum number of observations. A value between zero and one will be interpreted as a proportion of the in-bag Experimental observations. For a bootstrapped in-bag sample the default for this parameter is 10 number of Experimental observations in the overall sample. For an in-bag sample obtained via subsampling the default value is the inbag\_proportion times 10% of the number of Experimental observations in the overall sample.

min\_subgroup\_n\_oob\_control

Minimum number of Control arm observations in an out-of-bag subgroup. A value greater than or equal to one will be interpreted as the required minimum number of observations. A value between zero and one will be interpreted as a proportion of the out-of-bag Control observations. For a bootstrapped out-of-bag sample the default for this parameter is  $\exp(-1)*10\%$  of the number of Control observations in the overall sample. For an out-of-bag sample obtained via subsampling the default value is the inbag\_proportion times (1-inbag\_proportion)\*10 Control observations in the overall sample.

min\_subgroup\_n\_oob\_trt

	Minimum number of Experimental arm observations in an out-of-bag subgroup. A value greater than or equal to one will be interpreted as the required minimum number of observations. A value between zero and one will be interpreted as a proportion of the out-of-bag Experimental observations. For a bootstrapped out-of-bag sample the default for this parameter is exp(-1)*10% of the number of Experimental observations in the overall sample. For an out-of-bag sample obtained via subsampling the default value is the inbag_proportion times (1-inbag_proportion)*10% of the number of Experimental observations in the overall sample.
maxdepth	Maximum depth of trees.
rootcompete	Number of competitor splits to retain for root node split.
competedepth	Depth of competitor split trees (defaults to 1)
strength_cutpoi	ints
	Cutpoints for permuted p-values to classify a subgroup as Strong, Moderate, Weak, or Not Confirmed. The default cutpoints are 0.10, 0.20, and 0.30 for Strong, Moderate, and Weak subgroups, respectively. (optional)
n_permutations	Number of permutations to compute for adjusted p-value. Defaults to zero (no p-value computation). If p-values are desired, it is recommended to use at least 500 permutations.
n_cpu	Number of CPUs to use. Defaults to 1.
trace	Report number of permutations computed as algorithm proceeds.

# Details

The Treatment-Specific Subgroup Detection Tool (TSDT) creates several bootstrapped samples from the input data. For each of these bootstrapped samples the in-bag and out-of-bag data are retained. A tree is grown on the in-bag data of each bootstrapped sample using the response variable and supplied covariates. Each split in the tree defines a subgroup. The overall mean response for the in-bag data is computed as well as the mean response within each subgroup. Additionally, a scoring function is provided. Example scoring functions might be mean response, difference in mean response between treatment arms (i.e. treatment effect), or a quantile of the response (e.g. median), or a difference in quantiles across treatment arms. Sensible defaults are provided given the data type of the response and treatment variables. The user can also specify a custom scoring function. The value of the scoring function is computed for the overall in-bag data and each subgroup. Subgroups with mean response larger than the overall in-bag mean response and a mean scoring function value larger than the overall in-bag scoring function value are identified as superior subgroups. This definition of a superior subgroup assumes a larger value of the response variable is desirable. If a smaller value of the response is desirable then subgroups with mean response and mean scoring function smaller than the overall in-bag mean are superior. The same computation of overall and subgroup mean response and mean scoring function are done for the out-of-bag data. This is repeated for all bootstrapped samples. Measures of internal and external consistency are then computed. Internal consistency is computed for each subgroup that is identified as superior in one of the in-bag samples. Internal consistency for each of these subgroups is the fraction of bootstrapped samples where that subgroup is identified as superior in the in-bag data. External consistency is also defined only for subgroups that are identified as superior in at least one of the in-bag samples. For each of these subgroups, external consistency is the number of bootstrapped

samples where the subgroup is defined as superior in the in-bag and out-of-bag data divided by the number of bootstrapped samples where the subgroup is identified as superior in the in-bag data. The internal and external consistency results are returned for each subgroup that identified as superior in the in-bag data of at least one bootstrapped sample. A score for the overall strength of each subgroup is computed as the product of the internal and external consistency. Optionally, a permutation-adjusted p-value for the strength of each subgroup can be computed. Based on this p-value subgroups are classified as strong, moderate, weak, or not confirmed. A suggested cutoff for each subgroup is also provided. This is helpful because two subgroups defined on the same continuous splitting variable but with different cutpoints are considered equivalent. That is, one subgroup X1<0.6 and another X1<0.7 would be considered equivalent and listed in the results as X1<xxxxx. (Note that X1<0.6 and X1>=0.7 would be considered distinct subgroups and listed in the output as X1<xxxx and X1>=xxxxx, respectively.) So if a subgroup listed in the output as X1<xxxxx could actually represent many different numeric values for xxxxx it is helpful to provide a final suggestion for the cutpoint. The algorithm retains all the numeric values and uses the median as the suggested cutoff. The user can also request the vector of numeric cutpoints and use any function of their choosing to compute a suggested cutoff.

#### Value

An object of class TSDT

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#### References

Battioui, C., Shen, L., Ruberg, S., (2014). A Resampling-based Ensemble Tree Method to Identify Patient Subgroups with Enhanced Treatment Effect. JSM proceedings, 2014

Shen, L., Battioui, C., Ding, Y., (2013). Chapter "A Framework of Statistical methods for Identification of Subgroups with Differential Treatment Effects in Randomized Trials" in the book "Applied Statistics in Biomedicine and Clinical Trials Design"

#### See Also

mean\_response, quantile\_response, diff\_quantile\_response, treatment\_effect, survival\_time\_quantile, diff\_survival\_time\_quantile, mean\_deviance\_residuals, diff\_mean\_deviance\_residuals, diff\_restricted\_mean\_survival\_time, TSDT, rpart, ctree, mob

#### Examples

```
## Create example data for constructing TSDT object
N <- 200
continuous_response = runif( min = 0, max = 20, n = N )
trt <- sample( c('Control', 'Experimental'), size = N, prob = c(0.4,0.6), replace = TRUE )
X1 <- runif( N, min = 0, max = 1 )
X2 <- runif( N, min = 0, max = 1 )
X3 <- sample( c(0,1), size = N, prob = c(0.2,0.8), replace = TRUE )
X4 <- sample( c('A', 'B', 'C'), size = N, prob = c(0.6,0.3,0.1), replace = TRUE )</pre>
```

```
covariates <- data.frame( X1 )</pre>
covariates$X2 <- X2
covariates$X3 <- factor( X3 )</pre>
covariates$X4 <- factor( X4 )</pre>
## In the following examples n_samples and n_permutations are set to small
## values so the examples complete quickly. The intent here is to provide
## a small functional example to demonstrate the structure of the output. In
## a real-world use of TSDT these values should be at least 100 and 500,
## respectively.
## Single-arm TSDT
ex1 <- TSDT( response = continuous_response,</pre>
            covariates = covariates[,1:4],
            inbag_score_margin = 0,
            desirable_response = "increasing",
            n_samples = 5,
                                ## use value >= 100 in real world application
            n_permutations = 5, ## use value >= 500 in real world application
            rootcompete = 1,
            maxdepth = 2 )
## Two-arm TSDT
ex2 <- TSDT( response = continuous_response,</pre>
            trt = trt, trt_control = 'Control',
            covariates = covariates[,1:4],
            inbag_score_margin = 0,
            desirable_response = "increasing",
            oob_score_margin = 0,
            min_subgroup_n_control = 10,
            min_subgroup_n_trt = 20,
            maxdepth = 2,
            rootcompete = 1,
            n_{samples} = 5,
                                 ## use value >= 100 in real world application
            n_{permutations} = 5) ## use value >= 500 in real world application
```

TSDT-class TSDT

#### Description

TSDT is a container class for TSDT samples and metadata.

#### Value

Object of class TSDT

#### Slots

parameters List of parameters used in construction of TSDT samples.

samples Vector of TSDT\_Sample objects.

superior\_subgroups data.frame containing summary statistics for superior subgroups

cutpoints An object of class TSDT\_CutpointDistribution.

distributions A list of distributions of TSDT statistics.

#### See Also

TSDT, TSDT\_Sample, TSDT\_CutpointDistribution

TSDT\_CutpointDistribution-class

TSDT\_CutpointDistribution

## Description

Implementation of TSDT\_CutpointDistribution class. This class continuous split variable. If the subgroup contains more than one split variable a distribution of numeric cutpoints is collected for each continuous split variable in the subgroup definition.

# Value

Object of class TSDT\_CutpointDistribution

# Slots

Cutpoints An object of class hash-class

## See Also

TSDT, hash

TSDT\_Sample-class TSDT\_Sample

#### Description

TSDT\_Sample is a container class containing the in-bag and out-of-bag data from a subsampled or bootstrapped dataset. This container class also contains a data.frame containing the parsed tree that is fit on the in-bag data.

#### Value

Object of class TSDT\_Sample

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## unfactor

# Slots

inbag A data.frame containing in-bag dataoob A data.frame containing out-of-bag datasubgroups A data.frame containing a parsed tree

#### See Also

TSDT

unfactor

unfactor

# Description

Convert the factor columns of a data.frame to character or numeric.

#### Usage

unfactor(data)

#### Arguments

data A factor variable or a data.frame containing factor variables.

# Details

If the levels of a factor variable in data represent numeric values the variable will be converted to a numeric data type, otherwise it is converted to a character data type.

# Value

A vector or data.frame no longer containing any factor variables.

## See Also

na2empty

#### Examples

```
replace = TRUE ) )
## Initially the data type of all variables in ex1 is factor
ex1
class( ex1$num ) #factor
class( ex1$char ) #factor
class( ex1$mixed ) #factor
## Now convert all factor variables to numeric or character
ex2 <- unfactor( ex1 )</pre>
ex2
## The data types are now numeric or character
class( ex2$num ) # numeric
class( ex2$char ) # character
class( ex2$mixed ) # character
## The <NA> notation for missing factor values that have been converted to
## character can be changed to an empty string for easier reading by use of
## the function na2empty().
ex2$char <- na2empty( ex2$char )</pre>
ex2$mixed <- na2empty( ex2$mixed )</pre>
ex2
```

unpack\_args unpack\_args

#### Description

Assign the elements of a named list in current environment.

#### Usage

```
unpack_args(args)
```

#### Arguments

args List of entities to be assigned.

#### Details

This function takes a list of named entities and assigns each element of the list to its name in the calling environment.

#### See Also

assign, parent.frame

#### %nin%

# Examples

```
## Create a list of named elements
arglist <- list( one = 1, two = 2, color = "blue" )
## The variables one, two, and color do not exist in the current environment
ls()
## Unpack the elements in arglist
unpack_args( arglist )
## Now the variables one, two, and color do exist in the current environment
ls()
one
```

|--|

# Description

Negation of the built-in %in% operator. %nin% is a short-hand for !( a %in% b ).

# Usage

a %nin% b

## Arguments

а	Any R object for which the binary operator %in% is defined. This would include many built-in R primitives.
b	Any R object for which the binary operator %in% is defined. This would include many built-in R primitives.

# See Also

%in%

# Examples

# 4 is not an element in {5,6,7}.
4 %nin% 5:7 # Evaluates to TRUE
# 4 is an element in {4,5,6,7}.

4 %nin% 4:7 # Evaluates to FALSE

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