Package ‘personalized’

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Type Package

Title Estimation and Validation Methods for Subgroup Identification and Personalized Medicine

Version 0.2.7

Description Provides functions for fitting and validation of models for subgroup identification and personalized medicine / precision medicine under the general subgroup identification framework of Chen et al. (2017) <doi:10.1111/biom.12676>. This package is intended for use for both randomized controlled trials and observational studies and is described in detail in Huling and Yu (2021) <doi:10.18637/jss.v098.i05>.


BugReports https://github.com/jaredhuling/personalized/issues

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Encoding UTF-8

LazyData true

Suggests knitr, rmarkdown, testthat, nnet

Imports survival, methods, kernlab, foreach, xgboost

Depends glmnet (>= 2.0-13), mgcv, ggplot2, plotly

RoxygenNote 7.2.0

VignetteBuilder knitr

NeedsCompilation no

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Description

Results in a plot to check whether the propensity score has adequate overlap between treatment groups

Usage

check.overlap(
  x,
  trt,
  propensity.func,
  type = c("histogram", "density", "both"),
  bins = 50L,
  alpha = ifelse(type == "both", 0.35, 0.5)
)

Arguments

x The design matrix (not including intercept term)

trt treatment vector with each element equal to a 0 or a 1, with 1 indicating treatment status is active.
propensity.func

function that inputs the design matrix x and the treatment vector trt and outputs the propensity score, i.e., Pr(trt = 1 | X = x). Function should take two arguments 1) x and 2) trt. See example below. For a randomized controlled trial this can simply be a function that returns a constant equal to the proportion of patients assigned to the treatment group, i.e.: 

```
propensity.func = function(x, trt)
0.5
```

type

Type of plot to create. Options are either a histogram (type = "histogram") for each treatment group, a density (type = "density") for each treatment group, or to plot both a density and histogram (type = "code")

bins

integer number of bins for histograms when type = "histogram"

alpha

value between 0 and 1 indicating transparency level (1 for solid, 0 for fully transparent)

Examples

```
library(personalized)

set.seed(123)
n.obs <- 250
n.vars <- 15
x <- matrix(rnorm(n.obs * n.vars, sd = 3), n.obs, n.vars)

# simulate non-randomized treatment
xbetat <- 0.25 + 0.5 * x[,11] - 0.5 * x[,12]
trt.prob <- exp(xbetat) / (1 + exp(xbetat))
trt01 <- rbinom(n.obs, 1, prob = trt.prob)

# create function for fitting propensity score model
prop.func <- function(x, trt)
{
  # fit propensity score model
  propens.model <- cv.glmnet(y = trt,
                             x = x, family = "binomial")
  pi.x <- predict(propens.model, s = "lambda.min",
                  newx = x, type = "response")[,1]
  pi.x
}

check.overlap(x = x,
               trt = trt01,
               propensity.func = prop.func)

# now add density plot with histogram
check.overlap(x = x,
               trt = trt01,
               type = "both",
               propensity.func = prop.func)
```
# simulated non-randomized treatment with multiple levels
xbetat_1 <- 0.15 + 0.5 * x[,9] - 0.25 * x[,12]
xbetat_2 <- 0.15 - 0.5 * x[,11] + 0.25 * x[,15]
trt.1.prob <- exp(xbetat_1) / (1 + exp(xbetat_1) + exp(xbetat_2))
trt.2.prob <- exp(xbetat_2) / (1 + exp(xbetat_1) + exp(xbetat_2))
trt.3.prob <- 1 - (trt.1.prob + trt.2.prob)
prob.mat <- cbind(trt.1.prob, trt.2.prob, trt.3.prob)
trt <- apply(prob.mat, 1, function(rr) rmultinom(1, 1, prob = rr))
trt <- apply(trt, 2, function(rr) which(rr == 1))

# use multinominal logistic regression model with lasso penalty for propensity
propensity.multinom.lasso <- function(x, trt)
{
  if (!is.factor(trt)) trt <- as.factor(trt)
gfit <- cv.glmnet(y = trt, x = x, family = "multinomial")

  # predict returns a matrix of probabilities:
  # one column for each treatment level
  propens <- drop(predict(gfit, newx = x, type = "response", s = "lambda.min",
                         nfolds = 5, alpha = 0))

  # return the probability corresponding to the
  # treatment that was observed
  probs <- propens[,match(levels(trt), colnames(propens))]

  probs
}

check.overlap(x = x,
              trt = trt,
              type = "histogram",
              propensity.func = propensity.multinom.lasso)

---

create.augmentation.function

Creation of augmentation functions

Description

Creates an augmentation function that optionally utilizes cross-fitting

Usage

create.augmentation.function(
  family,
  crossfit = TRUE,
  nfolds.crossfit = 10,
cv.glmnet.args = NULL
}

**Arguments**

- **family**: The response type (see options in `glmnet` help file)
- **crossfit**: A logical value indicating whether to use cross-fitting (`TRUE`) or not (`FALSE`). Cross-fitting is more computationally intensive, but helps to prevent overfitting, see Chernozhukov, et al. (2018)
- **nfolds.crossfit**: An integer specifying the number of folds to use for cross-fitting. Must be greater than 1
- **cv.glmnet.args**: A list of NAMED arguments to pass to the `cv.glmnet` function. For example, `cv.glmnet.args = list(type.measure = "mse", nfolds = 10)`. See `cv.glmnet` and `glmnet` for all possible options.

**Value**

A function which can be passed to the `augment.func` argument of the `fit.subgroup` function.

**References**


**See Also**

- `fit.subgroup` for estimating ITRs and `create.propensity.function` for creation of propensity functions

**Examples**

```r
library(personalized)

set.seed(123)
n.obs <- 500
n.vars <- 15
x <- matrix(rnorm(n.obs * n.vars, sd = 3), n.obs, n.vars)

# simulate non-randomized treatment
xbetat <- 0.5 + 0.5 * x[,7] - 0.5 * x[,9]
trt.prob <- exp(xbetat) / (1 + exp(xbetat))
trt01 <- rbinom(n.obs, 1, prob = trt.prob)
trt <- 2 * trt01 - 1

# simulate response
# delta below drives treatment effect heterogeneity
```
delta <- 2 * (0.5 + x[,2] - x[,3] - x[,11] + x[,1] * x[,12] )
xbeta <- x[,1] + x[,11] - 2 * x[,12]^2 + x[,13] + 0.5 * x[,15] ^ 2
xbeta <- xbeta + delta * trt

# continuous outcomes
y <- drop(xbeta) + rnorm(n.obs, sd = 2)

aug.func <- create.augmentation.function(family = "gaussian",
crossfit = TRUE,
nfolds.crossfit = 10,
cv.glmnet.args = list(type.measure = "mae",
                      nfolds = 5))

prop.func <- create.propensity.function(crossfit = TRUE,
nfolds.crossfit = 10,
cv.glmnet.args = list(type.measure = "auc",
nfolds = 5))

## Not run:
subgrp.model <- fit.subgroup(x = x, y = y,
                           trt = trt01,
                           propensity.func = prop.func,
                           augment.func = aug.func,
                           loss = "sq_loss_lasso",
                           nfolds = 10)  # option for cv.glmnet (for ITR estimation)

summary(subgrp.model)

## End(Not run)

---

create.propensity.function

Creation of propensity fitting function

Description

Creates an propensity function that optionally utilizes cross-fitting

Usage

create.propensity.function(
crossfit = TRUE,
nfolds.crossfit = 10,
cv.glmnet.args = NULL
)

Arguments

crossfit    A logical value indicating whether to use cross-fitting (TRUE) or not (FALSE). Cross-fitting is more computationally intensive, but helps to prevent overfitting, see Chernozhukov, et al. (2018)
create.propensity.function

nfolds.crossfit
An integer specifying the number of folds to use for cross-fitting. Must be
greater than 1

cv.glmnet.args A list of NAMED arguments to pass to the cv.glmnet function. For example,
cv.glmnet.args = list(type.measure = "mse", nfolds = 10). See cv.glmnet
and glmnet for all possible options.

Value
A function which can be passed to the augment.func argument of the fit.subgroup function.

References
Chernozhukov, V., Chetverikov, D., Demirer, M., Duflo, E., Hansen, C., Newey, W., & Robins,
J. (2018). Double/debiased machine learning for treatment and structural parameters
https://arxiv.org/abs/1608.00060

See Also
fit.subgroup for estimating ITRs and create.propensity.function for creation of propensity
functions

Examples
library(personalized)

set.seed(123)
n.obs <- 500
n.vars <- 15
x <- matrix(rnorm(n.obs * n.vars, sd = 3), n.obs, n.vars)

# simulate non-randomized treatment
xbetat <- 0.5 + 0.5 * x[,7] - 0.5 * x[,9]
trt.prob <- exp(xbetat) / (1 + exp(xbetat))
trt01 <- rbinom(n.obs, 1, prob = trt.prob)
trt <- 2 * trt01 - 1

# simulate response
# delta below drives treatment effect heterogeneity
delta <- 2 * (0.5 + x[,2] - x[,3] - x[,11] + x[,1] * x[,12])
xbeta <- x[,1] + x[,11] - 2 * x[,12]^2 + x[,13] + 0.5 * x[,15]^2
xbeta <- xbeta + delta * trt

# continuous outcomes
y <- drop(xbeta) + rnorm(n.obs, sd = 2)
aug.func <- create.augmentation.function(family = "gaussian",
crossfit = TRUE,
nfolds.crossfit = 10,
cv.glmnet.args = list(type.measure = "mae",


fit.subgroup

prop.func <- create.propensity.function(crossfit = TRUE,
                                         nfolds = 5))

subgrp.model <- fit.subgroup(x = x, y = y,
                             trt = trt01,
                             propensity.func = prop.func,
                             augment.func = aug.func,
                             loss = "sq_loss_lasso",
                             nfolds = 10)  # option for cv.glmnet (for ITR estimation)

summary(subgrp.model)

---

fit.subgroup

Fitting subgroup identification models

Description


Usage

fit.subgroup(
  x,
  y,
  trt,
  propensity.func = NULL,
  loss = c("sq_loss_lasso", "logistic_loss_lasso", "poisson_loss_lasso",
           "cox_loss_lasso", "owl_logistic_loss_lasso", "owl_logistic_flip_loss_lasso",
           "owl_hinge_loss", "owl_hinge_flip_loss", "sq_loss_lasso_gam",
           "poisson_loss_lasso_gam", "logistic_loss_lasso_gam", "sq_loss_gam",
           "poisson_loss_gam", "logistic_loss_gam", "owl_logistic_loss_gam",
           "owl_logistic_flip_loss_gam", "owl_logistic_loss_lasso_gam",
           "owl_logistic_flip_loss_lasso_gam", "sq_loss_xgboost", "custom"),
  method = c("weighting", "a_learning"),
  match.id = NULL,
  augment.func = NULL,
  fit.custom.loss = NULL,
  cutpoint = 0,
  larger.outcome.better = TRUE,
  reference.trt = NULL,
  retcall = TRUE,
  ...
)
Arguments

- **x** The design matrix (not including intercept term)
- **y** The response vector
- **trt** Treatment vector with each element equal to a 0 or a 1, with 1 indicating treatment status is active.
- **propensity.func** Function that inputs the design matrix x and the treatment vector trt and outputs the propensity score, i.e., Pr(trt = 1 | X = x). Function should take two arguments 1) x and 2) trt. See example below. For a randomized controlled trial this can simply be a function that returns a constant equal to the proportion of patients assigned to the treatment group, i.e.: propensity.func = function(x, trt) 0.5.
- **loss** Choice of both the M function from Chen, et al (2017) and potentially the penalty used for variable selection. All loss options starting with sq_loss use M(y, v) = (v - y)^2, all options starting with logistic_loss use the logistic loss: M(y, v) = y * log(1 + exp{-v}), and all options starting with cox_loss use the negative partial likelihood loss for the Cox PH model. All options ending with lasso have a lasso penalty added to the loss for variable selection. sq_loss_lasso_gam and logistic_loss_lasso_gam first use the lasso to select variables and then fit a generalized additive model with nonparametric additive terms for each selected variable. sq_loss_gam involves a squared error loss with a generalized additive model and no variable selection. sq_loss_xgboost involves a squared error loss with a gradient-boosted decision trees model using xgboost for the benefit score; this allows for flexible estimation using machine learning and can be useful when the underlying treatment-covariate interaction is complex. Must specify params, nrounds, nfold, and optionally, early_stopping_rounds; see xgb.train for details.

- **Continuous Outcomes**
  - "sq_loss_lasso" - M(y, v) = (v - y)^2 with linear model and lasso penalty
  - "owl_logistic_loss_lasso" - M(y, v) = ylog(1 + exp{-v}) (method of Regularized Outcome Weighted Subgroup Identification)
  - "owl_logistic_flip_loss_lasso" - M(y, v) = |y|log(1 + exp{-sign(y)v})
  - "owl_hinge_loss" - M(y, v) = ymax(0, 1 - v) (method of Estimating individualized treatment rules using outcome weighted learning)
  - "owl_hinge_flip_loss" - M(y, v) = |y|max(0, 1 - sign(y)v)
  - "sq_loss_lasso_gam" - M(y, v) = (v - y)^2 with variables selected by lasso penalty and generalized additive model fit on the selected variables
  - "sq_loss_gam" - M(y, v) = (v - y)^2 with generalized additive model fit on all variables
  - "owl_logistic_loss_gam" - M(y, v) = ylog(1 + exp{-v}) with generalized additive model fit on all variables
  - "owl_logistic_flip_loss_gam" - M(y, v) = |y|log(1 + exp{-sign(y)v}) with generalized additive model fit on all variables
- "owl_logistic_loss_lasso_gam" - $M(y, v) = y\log(1 + \exp{-v})$ with variables selected by lasso penalty and generalized additive model fit on the selected variables
- "owl_logistic_flip_loss_lasso_gam" - $M(y, v) = y\log(1 + \exp{-\text{sign}(y)v})$ with variables selected by lasso penalty and generalized additive model fit on the selected variables
- "sq_loss_xgboost" - $M(y, v) = (v - y)^2$ with gradient-boosted decision trees model

**Binary Outcomes**
- All losses for continuous outcomes can be used plus the following:
  - "logistic_loss_lasso" - $M(y, v) = -[yv - \log(1 + \exp{-v})]$ with linear model and lasso penalty
  - "logistic_loss_lasso_gam" - $M(y, v) = -[yv - \log(1 + \exp{-v})]$ with variables selected by lasso penalty and generalized additive model fit on the selected variables
  - "logistic_loss_gam" - $M(y, v) = -[yv - \log(1 + \exp{-v})]$ with generalized additive model fit on all variables

**Count Outcomes**
- All losses for continuous outcomes can be used plus the following:
  - "poisson_loss_lasso" - $M(y, v) = -[yv - \exp(v)]$ with linear model and lasso penalty
  - "poisson_loss_lasso_gam" - $M(y, v) = -[yv - \exp(v)]$ with variables selected by lasso penalty and generalized additive model fit on the selected variables
  - "poisson_loss_gam" - $M(y, v) = -[yv - \exp(v)]$ with generalized additive model fit on all variables

**Time-to-Event Outcomes**
- "cox_loss_lasso" - $M$ corresponds to the negative partial likelihood of the cox model with linear model and additionally a lasso penalty

**Method**

- **subgroup ID model type.** Either the weighting or A-learning method of Chen et al. (2017)

**match.id**

- **a (character, factor, or integer) vector with length equal to the number of observations in x** indicating using integers or levels of a factor vector which patients are in which matched groups. Defaults to NULL and assumes the samples are not from a matched cohort. Matched case-control groups can be created using any method (propensity score matching, optimal matching, etc). If each case is matched with a control or multiple controls, this would indicate which case-control pairs or groups go together. If match.id is supplied, then it is unnecessary to specify a function via the propensity.func argument. A quick usage example: if the first patient is a case and the second and third are controls matched to it, and the fourth patient is a case and the fifth through seventh patients are matched with it, then the user should specify match.id = c(1,1,1,2,2,2,2) or match.id = c(rep("Grp1", 3),rep("Grp2", 4))

**augment.func**

- **function which inputs the response y, the covariates x, and trt and outputs predicted values (on the link scale) for the response using a model constructed with x. augment.func() can also be simply a function of x and y. This function is**
used for efficiency augmentation. When the form of the augmentation function is correct, it can provide efficient estimation of the subgroups. Some examples of possible augmentation functions are:

Example 1: `augment.func <- function(x, y) {lmod <- lm(y ~ x); return(fitted(lmod))}

Example 2:

```r
augment.func <- function(x, y, trt) {
  data <- data.frame(x, y, trt)
  lmod <- lm(y ~ x * trt)
  ## get predictions when trt = 1
  data$trt <- 1
  preds_1 <- predict(lmod, data)

  ## get predictions when trt = -1
  data$trt <- -1
  preds_n1 <- predict(lmod, data)

  ## return predictions averaged over trt
  return(0.5 * (preds_1 + preds_n1))
}
```

For binary and time-to-event outcomes, make sure that predictions are returned on the scale of the predictors.

Example 3:

```r
augment.func <- function(x, y) {
  bmod <- glm(y ~ x, family = binomial())
  return(predict(bmod, type = "link"))
}
```

`fit.custom.loss`

A function which minimizes a user-specified custom loss function $M(y, v)$ to be used in model fitting. If provided, `fit.custom.loss` should take the modified design matrix (which includes an intercept term) as an argument and the responses and optimize a custom weighted loss function.

The loss function $M(y, v)$ to be minimized MUST meet the following two criteria:

1. $D_M(y, v) = \partial M(y, v)/\partial v$ must be increasing in $v$ for each fixed $y$. $D_M(y, v)$ is the partial derivative of the loss function $M(y, v)$ with respect to $v$
2. $D_M(y, 0)$ is monotone in $y$

An example of a valid loss function is $M(y, v) = (y - v)^2$. In this case $D_M(y, v) = -2(y - v)$. See Chen et al. (2017) for more details on the restrictions on the loss function $M(y, v)$.

The provided function MUST return a list with the following elements:

- `predict` a function that inputs a design matrix and a 'type' argument for the type of predictions and outputs a vector of predictions on the scale of the linear predictor. Note that the matrix provided to 'fit.custom.loss'
has a column appended to the first column of \( x \) corresponding to the treatment main effect. Thus, the prediction function should deal with this, e.g. 
\[
\text{predict(model, cbind(1, x))}
\]
- model a fitted model object returned by the underlying fitting function
- coefficients if the underlying fitting function yields a vector of coefficient estimates, they should be provided here

The provided function **MUST** be a function with the following arguments:
1. \( x \) design matrix
2. \( y \) vector of responses
3. weights vector for observations weights. The underlying loss function **MUST** have samples weighted according to this vector. See below example
4. ... additional arguments passed via `'...'. This can be used so that users can specify more arguments to the underlying fitting function if so desired.

The provided function can also optionally take the following arguments:

- match.id vector of case/control cluster IDs. This is useful if cross validation is used in the underlying fitting function in which case it is advisable to sample whole clusters randomly instead of individual observations.
- offset if efficiency augmentation is used, the predictions from the outcome model from `augment.func` will be provided via the offset argument, which can be used as an offset in the underlying fitting function as a means of incorporating the efficiency augmentation model’s predictions
- trt vector of treatment statuses
- family family of outcome
- n.trts number of treatment levels. Can be useful if there are more than 2 treatment levels

Example 1: Here we minimize \( M(y, v) = (y - v)^2 \)

```r
fit.custom.loss <- function(x, y, weights, ...) {
  df <- data.frame(y = y, x)
  # minimize squared error loss with NO lasso penalty
  lmf <- lm(y ~ x - 1, weights = weights,
           data = df, ...)
  # save coefficients
  cfs = coef(lmf)
  # create prediction function. Notice
  # how a column of 1's is appended
  # to ensure treatment main effects are included
  # in predictions
  prd = function(x, type = "response") {
    dfte <- cbind(1, x)
    colnames(dfte) <- names(cfs)
    predict(lmf, data.frame(dfte))
  }
}
```
Example 2: \( M(y, v) = y \exp(-v) \)

```r
fit.expo.loss <- function(x, y, weights, ...) {
  ## define loss function to be minimized
  expo.loss <- function(beta, x, y, weights) {
    sum(weights * y * exp(-drop(tcrossprod(x, t(beta)))))
  }

  # use optim() to minimize loss function
  opt <- optim(rep(0, NCOL(x)), fn = expo.loss, x = x, y = y, weights = weights)
  coefs <- opt$par

  pred <- function(x, type = "response") {
    tcrossprod(cbind(1, x), t(coefs))
  }

  # return list of required components
  list(predict = pred, model = opt, coefficients = coefs)
}
```

cutpoint numeric value for patients with benefit scores above which (or below which if larger.outcome.better = FALSE) will be recommended to be in the treatment group. Can also set cutpoint = "median", which will use the median value of the benefit scores as the cutpoint or can set specific quantile values via "quantx" where "x" is a number between 0 and 100 representing the quantile value; e.g. cutpoint = "quant75" will use the 75th percent upper quantile of the benefit scores as the quantile.

larger.outcome.better boolean value of whether a larger outcome is better/preferable. Set to TRUE if a larger outcome is better/preferable and set to FALSE if a smaller outcome is better/preferable. Defaults to TRUE.

reference.trt which treatment should be treated as the reference treatment. Defaults to the first level of trt if trt is a factor or the first alphabetical or numerically first treatment level. Not used for multiple treatment fitting with OWL-type losses.

retcall boolean value. if TRUE then the passed arguments will be saved. Do not set to FALSE if the validate.subgroup() function will later be used for your fitted subgroup model. Only set to FALSE if memory is limited as setting to TRUE saves the design matrix to the fitted object

... options to be passed to underlying fitting function. For all loss options with 'lasso', this will be passed to cv.glmnet. For all loss options with 'gam', this
will be passed to `gam()` from the `mgcv` package. Note that for all loss options that use `gam()` from the `mgcv` package, the user cannot supply the `gam` argument method because it is also an argument of `fit.subgroup`, so instead, to change the `gam` method argument, supply `method.gam`, i.e., `method.gam = "REML"`. For all loss options with 'hinge', this will be passed to both `weighted.ksvm` and `ipop` from the `kernlab` package.

Value

An object of class "subgroup_fitted".

- `predict` A function that returns predictions of the covariate-conditional treatment effects model
- `model` An object returned by the underlying fitting function used. For example, if the lasso use used to fit the underlying subgroup identification model, this will be an object returned by `cv.glmnet`.
- `coefficients` If the underlying subgroup identification model is parametric, `coefficients` will contain the estimated coefficients of the model.
- `call` The call that produced the returned object. If `retcall = TRUE`, this will contain all objects supplied to `fit.subgroup()`.
- `family` The family corresponding to the outcome provided
- `loss` The loss function used
- `method` The method used (either weighting or A-learning)
- `propensity.func` The propensity score function used
- `larger.outcome.better` If larger outcomes are preferred for this model
- `cutpoint` Benefit score cutoff value used for determining subgroups
- `var.names` The names of all variables used
- `n.trts` The number of treatment levels
- `comparison.trts` All treatment levels other than the reference level
- `reference.trt` The reference level for the treatment. This should usually be the control group/level
- `trts` All treatment levels
- `trt.received` The vector of treatment assignments
- `pi.x` A vector of propensity scores
- `y` A vector of outcomes
- `benefit.scores` A vector of conditional treatment effects, i.e., benefit scores
- `recommended.trts` A vector of treatment recommendations (i.e., for each patient, which treatment results in the best expected potential outcomes)
- `subgroup.trt.effects` (Biased) estimates of the conditional treatment effects and conditional outcomes. These are essentially just empirical averages within different combinations of treatment assignments and treatment recommendations
- `individual.trt.effects` estimates of the individual treatment effects as returned by `treat.effects`
References

Huling, J.D. and Yu, M. (2021), Subgroup Identification Using the personalized Package. Journal of Statistical Software 98(5), 1-60. doi:10.18637/jss.v098.i05


See Also

validate.subgroup for function which creates validation results for subgroup identification models, predict.subgroup_fitted for a prediction function for fitted models from fit.subgroup, plot.subgroup_fitted for a function which plots results from fitted models, and print.subgroup_fitted for arguments for printing options for fit.subgroup(). from fit.subgroup.

Examples

library(personalized)

set.seed(123)
n.obs <- 500
n.vars <- 15
x <- matrix(rnorm(n.obs * n.vars, sd = 3), n.obs, n.vars)

# simulate non-randomized treatment
xbetat <- 0.5 + 0.5 * x[,7] - 0.5 * x[,9]
trt.prob <- exp(xbetat) / (1 + exp(xbetat))
trt01 <- rbinom(n.obs, 1, prob = trt.prob)

trt <- 2 * trt01 - 1

# simulate response
# delta below drives treatment effect heterogeneity
delta <- 2 * (0.5 + x[,2] - x[,3] - x[,11] + x[,1] * x[,12])
xbeta <- x[,1] + x[,11] - 2 * x[,12]^2 + x[,13] + 0.5 * x[,15] ^ 2
xbeta <- xbeta + delta * trt

# continuous outcomes
y <- drop(xbeta) + rnorm(n.obs, sd = 2)

# binary outcomes
y.binary <- 1 * (xbeta + rnorm(n.obs, sd = 2) > 0)

# count outcomes
y.count <- round(abs(xbeta + rnorm(n.obs, sd = 2)))

# time-to-event outcomes
surv.time <- exp(-20 - xbeta + rnorm(n.obs, sd = 1))
cens.time <- exp(rnorm(n.obs, sd = 3))
y.time.to.event <- pmin(surv.time, cens.time)
status <- 1 * (surv.time <= cens.time)

# create function for fitting propensity score model
prop.func <- function(x, trt)
{
    # fit propensity score model
    propens.model <- cv.glmnet(y = trt,
                               x = x, family = "binomial")
    pi.x <- predict(propens.model, s = "lambda.min",
                    newx = x, type = "response")[,1]
    pi.x
}

######################################## Continuous outcomes ##################################

subgrp.model <- fit.subgroup(x = x, y = y,
                              trt = trt01,
                              propensity.func = prop.func,
                              loss = "sq_loss_lasso",
                              # option for cv.glmnet,
                              # better to use 'nfolds=10'
                              nfolds = 3)

summary(subgrp.model)

# estimates of the individual-specific
# treatment effect estimates:
subgrp.model$individual.trt.effects

# fit lasso + gam model with REML option for gam
subgrp.modelg <- fit.subgroup(x = x, y = y,
                               trt = trt01,
                               propensity.func = prop.func,
                               loss = "sq_loss_lasso_gam",
                               method.gam = "REML",  # option for gam
                               nfolds = 5)  # option for cv.glmnet

subgrp.modelg

######################################## Using an augmentation function ##################################
## augmentation functions involve modeling the conditional mean E[Y|T, X]
## and returning predictions that are averaged over the treatment values
## return <- 1/2 * (hat{E}[Y|T=1, X] + hat{E}[Y|T=-1, X])
##########################################################################
 augment.func <- function(x, y, trt) {
  data <- data.frame(x, y, trt)
  xm <- model.matrix(y-trt*x-1, data = data)

  lmod <- cv.glmnet(y = y, x = xm)
  ## get predictions when trt = 1
  data$trt <- 1
  xm <- model.matrix(y-trt*x-1, data = data)
  preds_1 <- predict(lmod, xm, s = "lambda.min")

  ## get predictions when trt = -1
  data$trt <- -1
  xm <- model.matrix(y-trt*x-1, data = data)
  preds_n1 <- predict(lmod, xm, s = "lambda.min")

  ## return predictions averaged over trt
  return(0.5 * (preds_1 + preds_n1))
}

subgrp.model.aug <- fit.subgroup(x = x, y = y,
  trt = trt01,
  propensity.func = prop.func,
  augment.func = augment.func,
  loss = "sq_loss_lasso",
  # option for cv.glmnet,
  # better to use 'nfolds=10'
  nfolds = 3)  # option for cv.glmnet
summary(subgrp.model.aug)

########################################################################## Binary outcomes ##########################################################################

# use logistic loss for binary outcomes
subgrp.model.bin <- fit.subgroup(x = x, y = y.binary,
  trt = trt01,
  propensity.func = prop.func,
  loss = "logistic_loss_lasso",
  type.measure = "auc",  # option for cv.glmnet
  nfolds = 3)  # option for cv.glmnet
subgrp.model.bin

########################################################################## Count outcomes ##########################################################################

# use poisson loss for count/poisson outcomes
subgrp.model.poisson <- fit.subgroup(x = x, y = y.count,
  trt = trt01,
propensity.func = prop.func,
loss = "poisson_loss_lasso",
type.measure = "mse",        # option for cv.glmnet
nfolds = 3)                   # option for cv.glmnet

subgrp.model.poisson

######################################### Time-to-event outcomes #########################################

library(survival)

subgrp.model.cox <- fit.subgroup(x = x, y = Surv(y.time.to.event, status),
trt = trt01,
propensity.func = prop.func,
loss = "cox_loss_lasso",
nfolds = 3)                   # option for cv.glmnet

subgrp.model.cox

######################################### Using custom loss functions #########################################

## Use custom loss function for binary outcomes

fit.custom.loss.bin <- function(x, y, weights, offset, ...) {
  df <- data.frame(y = y, x)

  # minimize logistic loss with NO lasso penalty
  # with allowance for efficiency augmentation
  glmf <- glm(y ~ x - 1, weights = weights,
              offset = offset, # offset term allows for efficiency augmentation
              family = binomial(), ...)

  # save coefficients
  cfs = coef(glmf)

  # create prediction function.
  prd = function(x, type = "response") {
    dfte <- cbind(1, x)
    colnames(dfte) <- names(cfs)
    ## predictions must be returned on the scale
    ## of the linear predictor
    predict(glmf, data.frame(dfte), type = "link")
  }

  # return lost of required components
  list(predict = prd, model = glmf, coefficients = cfs)
}

subgrp.model.bin.cust <- fit.subgroup(x = x, y = y.binary,
trt = trt01,
LaLonde

propensity.func = prop.func, 
fit.custom.loss = fit.custom.loss.bin)

subgrp.model.bin.cust

## try exponential loss for 
## positive outcomes
fit.expo.loss <- function(x, y, weights, ...)
{
  expo.loss <- function(beta, x, y, weights) {
    sum(weights * y * exp(-drop(x %*% beta)))
  }

  # use optim() to minimize loss function
  opt <- optim(rep(0, NCOL(x)), fn = expo.loss, x = x, y = y, weights = weights)

  coefs <- opt$par

  pred <- function(x, type = "response") {
    tcrossprod(cbind(1, x), t(coefs))
  }

  # return list of required components
  list(predict = pred, model = opt, coefficients = coefs)
}

# use exponential loss for positive outcomes
subgrp.model.expo <- fit.subgroup(x = x, y = y.count, 
    trt = trt01, 
    propensity.func = prop.func, 
    fit.custom.loss = fit.expo.loss)

subgrp.model.expo

LaLonde

National Supported Work Study Data

Description

The LaLonde dataset comes from the National Supported Work Study, which sought to evaluate the effectiveness of an employment training program on wage increases.
LaLonde

Usage

LaLonde

Format

A data frame with 722 observations and 12 variables:

- **outcome**: whether earnings in 1978 are larger than in 1975; 1 for yes, 0 for no
- **treat**: whether the individual received the treatment; "Yes" or "No"
- **age**: age in years
- **educ**: education in years
- **black**: black or not; factor with levels "Yes" or "No"
- **hisp**: hispanic or not; factor with levels "Yes" or "No"
- **white**: white or not; factor with levels "Yes" or "No"
- **marr**: married or not; factor with levels "Yes" or "No"
- **nodegr**: No high school degree; factor with levels "Yes" (for no HS degree) or "No"
- **log.re75**: log of earnings in 1975
- **u75**: unemployed in 1975; factor with levels "Yes" or "No"
- **wts.extrap**: extrapolation weights to the 1978 Panel Study for Income Dynamics dataset

Source

The National Supported Work Study.

References


Examples

data(LaLonde)
y <- LaLonde$outcome

trt <- LaLonde$treat

x.varnames <- c("age", "educ", "black", "hisp", "white", "marr", "nodegr", "log.re75", "u75")

# covariates
data.x <- LaLonde[, x.varnames]

# construct design matrix (with no intercept)
x <- model.matrix(~ -1 + ., data = data.x)
const.propens <- function(x, trt)
{
  mean.trt <- mean(trt == "Trt")
  rep(mean.trt, length(trt))
}

subgrp_fit_w <- fit.subgroup(x = x, y = y, trt = trt,
  loss = "logistic_loss_lasso",
  propensity.func = const.propens,
  cutpoint = 0,
  type.measure = "auc",
  nfolds = 10)

summary(subgrp_fit_w)

plot.subgroup_fitted

plot.subgroup_fitted  Plotting results for fitted subgroup identification models

Description

Plots results for estimated subgroup treatment effects

Plots validation results for estimated subgroup treatment effects

Usage

## S3 method for class 'subgroup_fitted'
plot(
  x,
  type = c("boxplot", "density", "interaction", "conditional"),
  avg.line = TRUE,
  ...
)

## S3 method for class 'subgroup_validated'
plot(
  x,
  type = c("boxplot", "density", "interaction", "conditional", "stability"),
  avg.line = TRUE,
  ...
)

Arguments

x  fitted object returned by validate.subgroup() or fit.subgroup() function

type  type of plot. "density" results in a density plot for the results across all observations (if x is from fit.subgroup()) or if x is from validate.subgroup() across iterations of either the bootstrap or training/test re-fitting. For the latter case the test results will be plotted. "boxplot" results in boxplots across all
observations/iterations of either the bootstrap or training/test re-fitting. For the latter case the test results will be plotted. “interaction” creates an interaction plot for the different subgroups (crossing lines here means a meaningful subgroup). For the interaction plot, the intervals around each point represent +1 one SE "conditional" For subgroup_fitted objects, plots smoothed (via a GAM smoother) means of the outcomes as a function of the estimated benefit score separately for the treated and untreated groups. For subgroup_validated objects, boxplots of summary statistics within subgroups will be plotted as subgroups are defined by different cutoffs of the benefit scores. These cutoffs can be specified via the benefit.score.quantiles argument of validate.subgroup.

avg.line boolean value of whether or not to plot a line for the average value in addition to the density (only valid for type = "density")

... not used

See Also

fit.subgroup for function which fits subgroup identification models.
validate.subgroup for function which creates validation results and fit.subgroup for function which fits subgroup identification models.

Examples

library(personalized)

set.seed(123)
n.obs <- 250
n.vars <- 15
x <- matrix(rnorm(n.obs * n.vars, sd = 3), n.obs, n.vars)
# simulate non-randomized treatment
xbetat <- 0.5 + 0.5 * x[,11] - 0.5 * x[,13]
trt.prob <- exp(xbetat) / (1 + exp(xbetat))
trt01 <- rbinom(n.obs, 1, prob = trt.prob)

trt <- 2 * trt01 - 1

# simulate response
delta <- 2 * (0.5 + x[,2] - x[,3] - x[,11] + x[,1] * x[,12])
xbeta <- x[,1] + x[,11] - 2 * x[,12]^2 + x[,13]
xbeta <- xbeta + delta * trt

# continuous outcomes
y <- drop(xbeta) + rnorm(n.obs, sd = 2)

# create function for fitting propensity score model
prop.func <- function(x, trt)
{
    # fit propensity score model
    propens.model <- cv.glmnet(y = trt,
x = x, family = "binomial")
pi.x <- predict(propens.model, s = "lambda.min",
newx = x, type = "response")[,1]
pi.x
}

subgrp.model <- fit.subgroup(x = x, y = y,
   trt = trt01,
   propensity.func = prop.func,
   loss = "sq_loss_lasso",
   # option for cv.glmnet,  
   # better to use 'nnews=10'
   nfolds = 3)  # option for cv.glmnet

subgrp.model$subgroup.trt.effects

plot(subgrp.model)
plot(subgrp.model, type = "boxplot")
plot(subgrp.model, type = "interaction")
plot(subgrp.model, type = "conditional")

valmod <- validate.subgroup(subgrp.model, B = 3,
   method = "training_test",
   benefit.score.quantiles = c(0.25, 0.5, 0.75),
   train.fraction = 0.75)

plot(valmod)

plot(valmod, type = "interaction")

# see how summary statistics of subgroups change when the subgroups are defined based on different cutoffs
# (25th quantile of bene score, 50th, and 75th)
plot(valmod, type = "conditional")

# visualize the frequency of particular variables of being selected across the resampling iterations with
# 'type = "stability"
# not run:
# plot(valmod, type = "stability")

plotCompare

Plot a comparison results for fitted or validated subgroup identification models
Description

Plots comparison of results for estimated subgroup treatment effects

Usage

plotCompare(
  ..., 
  type = c("boxplot", "density", "interaction", "conditional"), 
  avg.line = TRUE
)

Arguments

... the fitted (model or validation) objects to be plotted. Must be either objects returned from fit.subgroup() or validate.subgroup()
type type of plot. "density" results in a density plot for the results across all observations (if x is from fit.subgroup()) or if x is from validate.subgroup() across iterations of either the bootstrap or training/test re-fitting. For the latter case the test results will be plotted. "boxplot" results in boxplots across all observations/iterations of either the bootstrap or training/test re-fitting. For the latter case the test results will be plotted. "interaction" creates an interaction plot for the different subgroups (crossing lines here means a meaningful subgroup). "conditional" plots smoothed (via a GAM smoother) means of the outcomes as a function of the estimated benefit score separately for the treated and untreated groups.
avg.line boolean value of whether or not to plot a line for the average value in addition to the density (only valid for type = "density")

See Also

fit.subgroup for function which fits subgroup identification models and validate.subgroup for function which creates validation results.

Examples

library(personalized)
set.seed(123)
n.obs <- 100
n.vars <- 15
x <- matrix(rnorm(n.obs * n.vars, sd = 3), n.obs, n.vars)

# simulate non-randomized treatment
xbetat <- 0.5 + 0.5 * x[,1] - 0.5 * x[,4]
trt.prob <- exp(xbetat) / (1 + exp(xbetat))
trt01 <- rbinom(n.obs, 1, prob = trt.prob)
trt <- 2 * trt01 - 1
predict.subgroup_fitted

Function to predict either benefit scores or treatment recommendations

Description

Predicts benefit scores or treatment recommendations based on a fitted subgroup identification model

Function to obtain predictions for weighted ksvm objects
Usage

## S3 method for class 'subgroup_fitted'
predict(
  object,
  newx,
  type = c("benefit.score", "trt.group"),
  cutpoint = 0,
  ...
)

## S3 method for class 'wksvm'
predict(object, newx, type = c("class", "linear.predictor"), ...)

Arguments

object      fitted object returned by validate.subgrp() function.
            For predict.wksvm(), this should be a fitted wksvm object from the weighted.ksvm() function
newx        new design matrix for which predictions will be made

type        type of prediction. type = "benefit.score" results in predicted benefit scores
            and type = "trt.group" results in prediction of recommended treatment group.
            For predict.wksvm(), type = 'class' yields predicted class and type = 'linear.predictor'
            yields estimated function (the sign of which is the estimated class)
cutpoint    numeric value for patients with benefit scores above which (or below which if
            larger.outcome.better = FALSE) will be recommended to be in the treatment group. Can also set cutpoint = "median", which will use the median value of
            the benefit scores as the cutpoint or can set specific quantile values via "quantx" where "x" is a number between 0 and 100 representing the quantile value; e.g.
            cutpoint = "quant75" will use the 75th percent upper quantile of the benefit scores as the quantile.
            ...
            not used

See Also

fit.subgroup for function which fits subgroup identification models.
weighted.ksvm for fitting weighted.ksvm objects

Examples

library(personalized)

set.seed(123)
n.obs  <- 500
n.vars <- 15
x     <- matrix(rnorm(n.obs * n.vars, sd = 3), n.obs, n.vars)
# simulate non-randomized treatment
xbetat <- 0.5 + 0.5 * x[,11] - 0.5 * x[,3]
trt.prob <- exp(xbetat) / (1 + exp(xbetat))
trt01 <- rbinom(n.obs, 1, prob = trt.prob)
trt <- 2 * trt01 - 1

# simulate response
delta <- 2 * (0.5 + x[,2] - x[,3] - x[,11] + x[,1] * x[,12])
xbeta <- x[,1] + x[,11] - 2 * x[,12]^2 + x[,13]
xbeta <- xbeta + delta * trt

# continuous outcomes
y <- drop(xbeta) + rnorm(n.obs, sd = 2)

# create function for fitting propensity score model
prop.func <- function(x, trt)
{
  # fit propensity score model
  propens.model <- cv.glmnet(y = trt,
                             x = x, family = "binomial")
  pi.x <- predict(propens.model, s = "lambda.min",
                  newx = x, type = "response")[,1]
  pi.x
}

subgrp.model <- fit.subgroup(x = x, y = y, trt = trt01,
                              propensity.func = prop.func,
                              loss = "sq_loss_lasso",
                              nfolds = 3) # option for cv.glmnet

subgrp.model$subgroup.trt.effects
benefit.scores <- predict(subgrp.model, newx = x, type = "benefit.score")
rec.trt.grp <- predict(subgrp.model, newx = x, type = "trt.group")

print.individual_treatment_effects

---

**print.individual_treatment_effects**

*Printing individualized treatment effects*

---

**Description**

Prints results for estimated subgroup treatment effects

**Usage**

```
## S3 method for class 'individual_treatment_effects'
print(x, digits = max(getOption("digits") - 3, 3), ...)
```
print.subgroup_fitted

Printing results for fitted subgroup identification models

Arguments

- **x**
  - a fitted object from either `treat.effects` or `treatment.effects`
- **digits**
  - minimal number of significant digits to print.
- **...**
  - further arguments passed to or from `print.default`.

Description

Prints results for estimated subgroup treatment effects
Prints summary results for estimated subgroup treatment effects

Usage

```r
## S3 method for class 'subgroup_fitted'
print(x, digits = max(getOption("digits") - 3, 3), ...)

## S3 method for class 'subgroup_validated'
print(
x, 
digits = max(getOption("digits") - 3, 3),
  sample.pct = FALSE,
  which.quant = NULL,
  ...)

## S3 method for class 'subgroup_summary'
print(x, p.value = 0.001, digits = max(getOption("digits") - 3, 3), ...)
```

Arguments

- **x**
  - a fitted object from either `fit.subgroup`, `validate.subgroup`, or `summarize.subgroups()`
- **digits**
  - minimal number of significant digits to print.
- **...**
  - further arguments passed to or from `print.default`.
- **sample.pct**
  - boolean variable of whether to print the percent of the test sample within each subgroup. If false the sample size itself, not the percent is printed. This may not be informative if the test sample size is much different from the total sample size
- **which.quant**
  - when `validate.subgroup()` is called with a vector of quantile values specified for `benefit.score.quantiles`, i.e. `benefit.score.quantiles = c(0.25, 0.5, 0.75)`, the argument `which.quant` can be a vector of indexes specifying which quantile cutoff value validation results to display, i.e. `which.quant = c(1,3)` in the above example results in the display of validation results for subgroups defined by cutoff values of the benefit score defined by the 25th and 75th quantiles of the benefit score
subgroup.effects

p.value a p-value threshold for mean differences below which covariates will be displayed. P-values are adjusted for multiple comparisons by the Hommel approach. For example, setting p.value = 0.05 will display all covariates that have a significant difference between subgroups with p-value less than 0.05. Defaults to 0.001.

See Also
validate.subgroup for function which creates validation results and fit.subgroup for function which fits subgroup identification models.
summarize.subgroups for function which summarizes subgroup covariate values

---

subgroup.effects Computes treatment effects within various subgroups

Description
Computes treatment effects within various subgroups to estimate subgroup treatment effects

Usage
subgroup.effects(
  benefit.scores,
  y,
  trt,
  pi.x,
  cutpoint = 0,
  larger.outcome.better = TRUE,
  reference.trt = NULL
)

Arguments
benefit.scores vector of estimated benefit scores
y The response vector
trt treatment vector with each element equal to a 0 or a 1, with 1 indicating treatment status is active.
pi.x The propensity score for each observation
cutpoint numeric value for patients with benefit scores above which (or below which if larger.outcome.better = FALSE) will be recommended to be in the treatment group. Can also set cutpoint = "median", which will use the median value of the benefit scores as the cutpoint or can set specific quantile values via "quantx" where "x" is a number between 0 and 100 representing the quantile value; e.g. cutpoint = "quant75" will use the 75th percent upper quantile of the benefit scores as the cutpoint.
larger.outcome.better

boolean value of whether a larger outcome is better. Set to TRUE if a larger outcome is better and set to FALSE if a smaller outcome is better. Defaults to TRUE.

reference.trt

index of which treatment is the reference (in the case of multiple treatments). This should be known already, as for a trt with K-levels, there will be K-1 benefit scores (1 per column) of benefit.scores, where each column is a comparison of each K-1 treatments with the reference treatment. The default is the last level of trt if it is a factor.

See Also

fit.subgroup for function which fits subgroup identification models which generate benefit scores.

summarize.subgroups

Summarizing covariates within estimated subgroups

Description

Summarizes covariate values within the estimated subgroups

Usage

summarize.subgroups(x, ...)

## Default S3 method:
summarize.subgroups(x, subgroup, ...)

## S3 method for class 'subgroup_fitted'
summarize.subgroups(x, ...)

Arguments

x a fitted object from fit.subgroup() or a matrix of covariate values

... optional arguments to summarize.subgroups methods

subgroup vector of indicators of same length as the number of rows in x if x is a matrix. A value of 1 in the ith position of subgroup indicates patient i is in the subgroup of patients recommended the treatment and a value of 0 in the ith position of subgroup indicates patient i is in the subgroup of patients recommended the control. If x is a fitted object returned by fit.subgroup(), subgroup is not needed.

Details

The p-values shown are raw p-values and are not adjusted for multiple comparisons.
See Also

fit.subgroup for function which fits subgroup identification models and print.subgroup_summary for arguments for printing options for summarize.subgroups().

Examples

library(personalized)

set.seed(123)
n.obs <- 1000
n.vars <- 50
x <- matrix(rnorm(n.obs * n.vars, sd = 3), n.obs, n.vars)

# simulate non-randomized treatment
xbetat <- 0.5 + 0.5 * x[,21] - 0.5 * x[,41]
trt.prob <- exp(xbetat) / (1 + exp(xbetat))
trt01 <- rbinom(n.obs, 1, prob = trt.prob)

trt <- 2 * trt01 - 1

# simulate response
delta <- 2 * (0.5 + x[,2] - x[,3] - x[,11] + x[,1] * x[,12])
xbeta <- x[,1] + x[,11] - 2 * x[,12]^2 + x[,13]
xbeta <- xbeta + delta * trt

# continuous outcomes
y <- drop(xbeta) + rnorm(n.obs, sd = 2)

# create function for fitting propensity score model
prop.func <- function(x, trt)
{
  # fit propensity score model
  propens.model <- cv.glmnet(y = trt,
     x = x, family = "binomial"
  pi.x <- predict(propens.model, s = "lambda.min",
     newx = x, type = "response"[,1]

  pi.x
}

subgrp.model <- fit.subgroup(x = x, y = y,
   trt = trt01,
   propensity.func = prop.func,
   loss = "sq_loss_lasso",
   nfolds = 5)  # option for cv.glmnet

comp <- summarize.subgroups(subgrp.model)
print(comp, p.value = 0.01)

# or we can simply supply the matrix x and the subgroups
comp2 <- summarize.subgroups(x, subgroup = 1 * (subgrp.model$benefit.scores > 0))
treatment.effects

print(comp2, p.value = 0.01)

summary.subgroup_fitted

Summary of results for fitted subgroup identification models

Description

Prints summary of results for estimated subgroup treatment effects

Prints summary of results for estimated weighted ksvm

Usage

## S3 method for class 'subgroup_fitted'
summary(object, digits = max(getOption("digits") - 3, 3), ...)

## S3 method for class 'wksvm'
summary(object, digits = max(getOption("digits") - 3, 3), ...)

Arguments

object a fitted object from either fit.subgroup or validate.subgroup
digits minimal number of significant digits to print.
... further arguments passed to or from print.default.

See Also

validate.subgroup for function which creates validation results and fit.subgroup for function which fits subgroup identification models.

treatment.effects

Calculation of covariate-conditional treatment effects

Description

Calculates covariate conditional treatment effects using estimated benefit scores
treatment.effects

Usage

treatment.effects(x, ...)

## Default S3 method:
treatment.effects(x, ...)

treat.effects(
  benefit.scores,
  loss = c("sq_loss_lasso", "logistic_loss_lasso", "poisson_loss_lasso",
            "cox_loss_lasso", "owl_logistic_loss_lasso", "owl_logistic_flip_loss_lasso",
            "owl_hinge_loss", "owl_hinge_flip_loss", "sq_loss_lasso_gam",
            "poisson_loss_lasso_gam", "logistic_loss_lasso_gam", "sq_loss_gam",
            "poisson_loss_gam", "logistic_loss_gam", "owl_logistic_loss_gam",
            "owl_logistic_flip_loss_gam", "owl_logistic_loss_lasso_gam",
            "owl_logistic_flip_loss_lasso_gam", "sq_loss_xgboost", "custom"),
  method = c("weighting", "a_learning"),
  pi.x = NULL,
  ...
)

## S3 method for class 'subgroup_fitted'
treatment.effects(x, ...)

Arguments

x a fitted object from fit.subgroup()

... not used

benefit.scores vector of estimated benefit scores

loss loss choice USED TO CALCULATE benefit.scores of both the M function
      from Chen, et al (2017) and potentially the penalty used for variable selection.
      See fit.subgroup for more details.

method method choice USED TO CALCULATE benefit.scores. Either the "weighting"
         method or "a_learning" method. See fit.subgroup for more details

pi.x The propensity score for each observation

Value

A List with elements delta (if the treatment effects are a difference/contrast, i.e. \( E[Y|T = 1, X] - E[Y|T = -1, X] \)) and gamma (if the treatment effects are a ratio, i.e. \( E[Y|T = 1, X]/E[Y|T = -1, X] \))

See Also

fit.subgroup for function which fits subgroup identification models.

print.individual_treatment_effects for printing of objects returned by treat.effects or
treatment.effects
Examples

library(personalized)

set.seed(123)
n.obs <- 500
n.vars <- 25
x <- matrix(rnorm(n.obs * n.vars, sd = 3), n.obs, n.vars)

# simulate non-randomized treatment
xbetat <- 0.5 + 0.5 * x[,21] - 0.5 * x[,11]
trt.prob <- exp(xbetat) / (1 + exp(xbetat))
trt01 <- rbinom(n.obs, 1, prob = trt.prob)
trt <- 2 * trt01 - 1

# simulate response
delta <- 2 * (0.5 + x[,2] - x[,3] - x[,11] + x[,1] * x[,12])
xbeta <- x[,1] + x[,11] - 2 * x[,12]^2 + x[,13]
xbeta <- xbeta + delta * trt

# continuous outcomes
y <- drop(xbeta) + rnorm(n.obs, sd = 2)

# time-to-event outcomes
surv.time <- exp(-20 - xbeta + rnorm(n.obs, sd = 1))
cens.time <- exp(rnorm(n.obs, sd = 3))
y.time.to.event <- pmin(surv.time, cens.time)
status <- 1 * (surv.time <= cens.time)

# create function for fitting propensity score model
prop.func <- function(x, trt)
{
  # fit propensity score model
  propens.model <- cv.glmnet(y = trt,
                             x = x, family = "binomial")
  pi.x <- predict(propens.model, s = "lambda.min",
                  newx = x, type = "response")[,1]
  pi.x
}

subgrp.model <- fit.subgroup(x = x, y = y,
                             trt = trt01,
                             propensity.func = prop.func,
                             loss = "sq_loss_lasso",
                             nfolds = 3)  # option for cv.glmnet

trt_eff <- treatment.effects(subgrp.model)
str(trt_eff)

trt_eff
library(survival)
subgrp.model.cox <- fit.subgroup(x = x, y = Surv(y.time.to.event, status),
  trt = trt01,
  propensity.func = prop.func,
  loss = "cox_loss_lasso",
  nfolds = 3) # option for cv.glmnet

trt_eff_c <- treatment.effects(subgrp.model.cox)
str(trt_eff_c)

trt_eff_c

---

validate.subgroup

Validating fitted subgroup identification models

Description


Usage

validate.subgroup(
  model,
  B = 50L,
  method = c("training_test_replication", "boot_bias_correction"),
  train.fraction = 0.75,
  benefit.score.quantiles = c(0.1666667, 0.3333333, 0.5, 0.6666667, 0.8333333),
  parallel = FALSE
)

Arguments

model faked model object returned by fit.subgroup() function
B integer. number of bootstrap replications or refitting replications.
method validation method. "boot_bias_correction" for the bootstrap bias correction method of Harrell, et al (1996) or "training_test_replication" for repeated training and test splitting of the data (train.fraction should be specified for this option)
train.fraction fraction (between 0 and 1) of samples to be used for training in training/test replication. Only used for method = "training_test_replication"
benefit.score.quantiles a vector of quantiles (between 0 and 1) of the benefit score values for which to return bootstrapped information about the subgroups. ie if one of the quantile values is 0.5, the median value of the benefit scores will be used as a cutoff to
determine subgroups and summary statistics will be returned about these sub-
groups

parallel Should the loop over replications be parallelized? If FALSE, then no, if TRUE, then yes. If user sets parallel = TRUE and the fitted fit.subgroup() object uses the parallel version of an internal model, say for cv.glmnet(), then the internal parallelization will be overridden so as not to create a conflict of parallelism.

Details

Estimates of various quantities conditional on subgroups and treatment statuses are provided and displayed via the print.subgroup_validated function:

1. "Conditional expected outcomes" The first results shown when printing a subgroup_validated object are estimates of the expected outcomes conditional on the estimated subgroups (i.e. which subgroup is 'recommended' by the model) and conditional on treatment/intervention status. If there are two total treatment options, this results in a 2x2 table of expected conditional outcomes.

2. "Treatment effects conditional on subgroups" The second results shown when printing a subgroup_validated object are estimates of the expected outcomes conditional on the estimated subgroups. If the treatment takes levels \( j \in \{1, \ldots, K\} \), a total of \( K \) conditional treatment effects will be shown. For example, of the outcome is continuous, the \( j \)th conditional treatment effect is defined as \( E(Y|Trt = j, Subgroup = j) - E(Y|Trt = j, Subgroup = / = j) \), where \( Subgroup = j \) if treatment \( j \) is recommended, i.e. treatment \( j \) results in the largest/best expected potential outcomes given the fitted model.

3. "Overall treatment effect conditional on subgroups " The third quantity displayed shows the overall improvement in outcomes resulting from all treatment recommendations. This is essentially an average over all of the conditional treatment effects weighted by the proportion of the population recommended each respective treatment level.

Value

An object of class "subgroup_validated"

avg.results Estimates of average conditional treatment effects when subgroups are determined based on the provided cutoff value for the benefit score. For example, if cutoff = 0 and there is a treatment and control only, then the treatment is recommended if the benefit score is greater than 0.

se.results Standard errors of the estimates from avg.estimates

boot.results Contains the individual results for each replication. avg.results is comprised of averages of the values from boot.results

avg.quantile.results Estimates of average conditional treatment effects when subgroups are determined based on different quantile cutoff values for the benefit score. For example, if benefit.score.quantiles = 0.75 and there is a treatment and control only, then the treatment is recommended if the benefit score is greater than the 75th upper quantile of all benefit scores. If multiple quantile values are provided, e.g. benefit.score.quantiles = c(0.15, 0.5, 0.85), then results will be provided for all quantile levels.
validate.subgroup

se.quantile.results
   Standard errors corresponding to avg.quantile.results

boot.results.quantiles
   Contains the individual results for each replication. avg.quantile.results is comprised of averages of the values from boot.results.quantiles

family
   Family of the outcome. For example, "gaussian" for continuous outcomes

method
   Method used for subgroup identification model. Weighting or A-learning

n.trts
   The number of treatment levels

comparison.trts
   All treatment levels other than the reference level

reference.trt
   The reference level for the treatment. This should usually be the control group/level

larger.outcome.better
   If larger outcomes are preferred for this model

cutpoint
   Benefit score cutoff value used for determining subgroups

val.method
   Method used for validation

iterations
   Number of replications used in the validation process

n.obs
   Number of observations in x provided to fit.subgroup

n.vars
   Number of variables in x provided to fit.subgroup

References


Huling, J.D. and Yu, M. (2021), Subgroup Identification Using the personalized Package. Journal of Statistical Software 98(5), 1-60. doi:10.18637/jss.v098.i05

See Also

fit.subgroup for function which fits subgroup identification models, plot.subgroup_validated for plotting of validation results, and print.subgroup_validated for arguments for printing options for validate.subgroup().

Examples

library(personalized)

set.seed(123)
n.obs <- 500
n.vars <- 20
x <- matrix(rnorm(n.obs * n.vars, sd = 3), n.obs, n.vars)
# simulate non-randomized treatment
xbetat <- 0.5 + 0.5 * x[,11] - 0.5 * x[,13]
trt.prob <- exp(xbetat) / (1 + exp(xbetat))
trt01 <- rbinom(n.obs, 1, prob = trt.prob)

trt <- 2 * trt01 - 1

# simulate response
delta <- 2 * (0.5 + x[,2] - x[,3] - x[,11] + x[,1] * x[,12])
xbeta <- x[,1] + x[,11] - 2 * x[,12]^2 + x[,13]
xbeta <- xbeta + delta * trt

# continuous outcomes
y <- drop(xbeta) + rnorm(n.obs, sd = 2)

# create function for fitting propensity score model
prop.func <- function(x, trt)
{
  # fit propensity score model
  propens.model <- cv.glmnet(y = trt,
                              x = x, family = "binomial")
  pi.x <- predict(propens.model, s = "lambda.min",
                  newx = x, type = "response")[,1]
  pi.x
}

subgrp.model <- fit.subgroup(x = x, y = y,
                              trt = trt01,
                              propensity.func = prop.func,
                              loss = "sq_loss_lasso",
                              # option for cv.glmnet,
                              # better to use 'nfolds=10'
                              nfolds = 3)

x.test <- matrix(rnorm(10 * n.obs * n.vars, sd = 3), 10 * n.obs, n.vars)

# simulate non-randomized treatment
xbetat.test <- 0.5 + 0.5 * x.test[,11] - 0.5 * x.test[,13]
trt.prob.test <- exp(xbetat.test) / (1 + exp(xbetat.test))
trt01.test <- rbinom(10 * n.obs, 1, prob = trt.prob.test)

trt.test <- 2 * trt01.test - 1

# simulate response
delta.test <- 2 * (0.5 + x.test[,2] - x.test[,3] - x.test[,11] + x.test[,1] * x.test[,12])
xbeta.test <- xbeta.test + delta.test * trt.test

y.test <- drop(xbeta.test) + rnorm(10 * n.obs, sd = 2)

valmod <- validate.subgroup(subgrp.model, B = 2)
weighted.ksvm

```r
method = "training_test",
train.fraction = 0.75)

valmod

print(valmod, which.quant = c(4, 5))
```

---

**weighted.ksvm**

Fit weighted kernel svm model.

---

**Description**

Fits weighted kernel SVM. To be used for OWL with hinge loss (but can be used more generally)

**Usage**

```r
weighted.ksvm(
  y,
  x,
  weights,
  C = c(0.1, 0.5, 1, 2, 10),
  kernel = "rbfdot",
  kpar = "automatic",
  nfolds = 10,
  foldid = NULL,
  eps = 1e-08,
  ...
)
```

**Arguments**

- **y** The response vector (either a character vector, factor vector, or numeric vector with values in -1, 1)
- **x** The design matrix (not including intercept term)
- **weights** vector of sample weights for weighted SVM
- **C** cost of constraints violation, see `ksvm`
- **kernel** kernel function used for training and prediction. See `ksvm` and `kernels`
- **kpar** list of hyperparameters for the kernel function. See `ksvm`
- **nfolds** number of cross validation folds for selecting value of C
- **foldid** optional vector of values between 1 and nfolds specifying which fold each observation is in. If specified, it will override the nfolds argument.
- **eps** penalty nugget parameter. Defaults to 1e-8
- **...** extra arguments to be passed to `ipop` from the kernlab package
See Also

predict.wksvm for predicting from fitted weighted.ksvm objects

Examples

library(kernlab)

x <- matrix(rnorm(200 * 2), ncol = 2)

y <- 2 * (sin(x[,2]) ^ 2 * exp(-x[,2]) - 0.2 > rnorm(200, sd = 0.1)) - 1

weights <- runif(100, max = 1.5, min = 0.5)

wk <- weighted.ksvm(x = x[1:100,], y = y[1:100],
                     C = c(0.1, 0.5, 1, 2),
                     nfolds = 5,
                     weights = weights[1:100])

pr <- predict(wk, newx = x[101:200,])

mean(pr == y[101:200])
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