

Package ‘CSTE’

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Type Package

Title Covariate Specific Treatment Effect (CSTE) Curve

Description A uniform statistical inferential tool in making individualized treatment decisions, which implements the methods of Ma et al. (2017)<[DOI:10.1177/0962280214541724](https://doi.org/10.1177/0962280214541724)> and Guo et al. (2021)<[DOI:10.1080/01621459.2020.1865167](https://doi.org/10.1080/01621459.2020.1865167)>. It uses a flexible semiparametric modeling strategy for heterogeneous treatment effect estimation in high-dimensional settings and can give valid confidence bands. Based on it, one can find the subgroups of patients that benefit from each treatment, thereby making individualized treatment selection.

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Encoding UTF-8

Imports Rcpp (>= 1.0.4), fda, splines, survival, locpol, dfoptim

LinkingTo Rcpp

RoxygenNote 7.1.1

Suggests mvtnorm, sigmoid

NeedsCompilation yes

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Contents

cste_bin	2
cste_bin_SCB	5
cste_surv	6

cste_surv_SCB	7
penC	8
predict_cste_bin	8
select_cste_bin	9

Index	11
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cste_bin	<i>Estimate the CSTE curve for binary outcome.</i>
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Description

Estimate covariate-specific treatment effect (CSTE) curve. Input data contains covariates X , treatment assignment Z and binary outcome Y . The working model is

$$\text{logit}(\mu(X, Z)) = g_1(X\beta_1)Z + g_2(X\beta_2),$$

where $\mu(X, Z) = E(Y|X, Z)$. The model implies that $CSTE(x) = g_1(x\beta_1)$.

Usage

```
cste_bin(
  x,
  y,
  z,
  beta_ini = NULL,
  lam = 0,
  nknots = 1,
  max.iter = 200,
  eps = 0.001
)
```

Arguments

<code>x</code>	samples of covariates which is a $n * p$ matrix.
<code>y</code>	samples of binary outcome which is a $n * 1$ vector.
<code>z</code>	samples of treatment indicator which is a $n * 1$ vector.
<code>beta_ini</code>	initial values for $(\beta'_1, \beta'_2)'$, default value is NULL.
<code>lam</code>	value of the lasso penalty parameter λ for β_1 and β_2 , default value is 0.
<code>nknots</code>	number of knots for the B-spline for estimating g_1 and g_2 .
<code>max.iter</code>	maximum iteration for the algorithm.
<code>eps</code>	numeric scalar ≥ 0 , the tolerance for the estimation of β_1 and β_2 .

Value

A S3 class of cste, which includes:

- beta1: estimate of β_1 .
- beta2: estimate of β_2 .
- B1: the B-spline basis for estimating g_1 .
- B2: the B-spline basis for estimating g_2 .
- delta1: the coefficient of B-spline for estimating g_1 .
- delta2: the coefficient for B-spline for estimating g_2 .
- iter: number of iteration.
- g1: the estimate of $g_1(X\beta_1)$.
- g2: the estimate of $g_2(X\beta_2)$.

References

Guo W., Zhou X. and Ma S. (2021). Estimation of Optimal Individualized Treatment Rules Using a Covariate-Specific Treatment Effect Curve with High-dimensional Covariates, *Journal of the American Statistical Association*, 116(533), 309-321

See Also

[cste_bin_SCB](#), [predict_cste_bin](#), [select_cste_bin](#)

Examples

```
## Quick example for the cste

library(mvtnorm)
library(sigmoid)

# ----- Example 1: p = 20 ----- #
## generate data
n <- 2000
p <- 20
set.seed(100)

# generate X
sigma <- outer(1:p, 1:p, function(i, j){ 2^(-abs(i-j)) } )
X <- rmvnorm(n, mean = rep(0,p), sigma = sigma)
X <- relu(X + 2) - 2
X <- 2 - relu(2 - X)

# generate Z
Z <- rbinom(n, 1, 0.5)

# generate Y
beta1 <- rep(0, p)
beta1[1:3] <- rep(1/sqrt(3), 3)
```

```

beta2 <- rep(0, p)
beta2[1:2] <- c(1, -2)/sqrt(5)
mu1 <- X %>% beta1
mu2 <- X %>% beta2
g1 <- mu1*(1 - mu1)
g2 <- exp(mu2)
prob <- sigmoid(g1*Z + g2)
Y <- rbinom(n, 1, prob)

## estimate the CSTE curve
fit <- cste_bin(X, Y, Z)

## plot
plot(mu1, g1, cex = 0.5, xlim = c(-2,2), ylim = c(-8, 3),
      xlab = expression(X*beta), ylab = expression(g1(X*beta)))
ord <- order(mu1)
points(mu1[ord], fit$g1[ord], col = 'blue', cex = 0.5)

## compute 95% simultaneous confidence band (SCB)
res <- cste_bin_SCB(X, fit, alpha = 0.05)

## plot
plot(res$or_x, res$fit_x, col = 'red',
      type="l", lwd=2, lty = 3, ylim = c(-10,8),
      ylab=expression(g1(X*beta)), xlab = expression(X*beta),
      main="Confidence Band")
lines(res$or_x, res$lower_bound, lwd=2.5, col = 'purple', lty=2)
lines(res$or_x, res$upper_bound, lwd=2.5, col = 'purple', lty=2)
abline(h=0, cex = 0.2, lty = 2)
legend("topleft", legend=c("Estimates", "SCB"),
      lwd=c(2, 2.5), lty=c(3,2), col=c('red', 'purple'))

# ----- Example 2: p = 1 ----- #

## generate data
set.seed(15)
p <- 1
n <- 2000
X <- runif(n)
Z <- rbinom(n, 1, 0.5)
g1 <- 2 * sin(5*X)
g2 <- exp(X-3) * 2
prob <- sigmoid( Z*g1 + g2)
Y <- rbinom(n, 1, prob)

## estimate the CSTE curve
fit <- cste_bin(X, Y, Z)

## simultaneous confidence band (SCB)
X <- as.matrix(X)
res <- cste_bin_SCB(X, fit)

```

```
## plot
plot(res$or_x, res$fit_x, col = 'red', type="l", lwd=2,
      lty = 3, xlim = c(0, 1), ylim = c(-4, 4),
      ylab=expression(g1(X)), xlab = expression(X),
      main="Confidence Band")
lines(res$or_x, res$lower_bound, lwd=2.5, col = 'purple', lty=2)
lines(res$or_x, res$upper_bound, lwd=2.5, col = 'purple', lty=2)
abline(h=0, cex = 0.2)
lines(X[order(X)], g1[order(X)], col = 'blue', lwd = 1.5)
legend("topright", legend=c("Estimates", "SCB", "True CSTE Curve"),
      lwd=c(2, 2.5, 1.5), lty=c(3,2,1), col=c('red', 'purple', 'blue'))
```

cste_bin_SCB	<i>Calculate simultaneous confidence bands of CSTE curve for binary outcome.</i>
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Description

This function calculates simultaneous confidence bands of CSTE curve for binary outcome.

Usage

```
cste_bin_SCB(x, fit, h = NULL, alpha = 0.05)
```

Arguments

x	samples of predictor, which is a $m * p$ matrix.
fit	a S3 class of cste.
h	kernel bandwidth.
alpha	the simultaneous confidence bands are of $1 - \alpha$ confidence level.

Value

A list which includes:

- `or_x`: the ordered value of $X\beta_1$.
- `fit_x`: the fitted value of CSTE curve corresponding to `or_x`.
- `lower_bound`: the lower bound of CSTE's simultaneous confidence band.
- `upper_bound`: the upper bound of CSTE's simultaneous confidence band.

References

Guo W., Zhou X. and Ma S. (2021). Estimation of Optimal Individualized Treatment Rules Using a Covariate-Specific Treatment Effect Curve with High-dimensional Covariates, *Journal of the American Statistical Association*, 116(533), 309-321

See Also[cste_bin](#)

cste_surv	<i>Estimate the CSTE curve for time to event outcome with right censoring.</i>
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Description

Estimate the CSTE curve for time to event outcome with right censoring. The working model is

$$\lambda(t|X, Z) = \lambda_0(t) \exp(\beta^T(X)Z + g(X)),$$

which implies that $CSTE(x) = \beta(x)$.

Usage

```
cste_surv(x, y, z, s, h)
```

Arguments

x	samples of biomarker (or covariate) which is a $n * 1$ vector and should be scaled between 0 and 1.
y	samples of time to event which is a $n * 1$ vector.
z	samples of treatment indicator which is a $n * K$ matrix.
s	samples of censoring indicator which is a $n * 1$ vector.
h	kernel bandwidth.

Value

A $n * K$ matrix, estimation of $\beta(x)$.

References

Ma Y. and Zhou X. (2017). Treatment selection in a randomized clinical trial via covariate-specific treatment effect curves, *Statistical Methods in Medical Research*, 26(1), 124-141.

See Also[cste_surv_SCB](#)

cste_surv_SCB	<i>Calculate simultaneous confidence bands (SCB) of CSTE curve for time to event outcome with right censoring.</i>
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Description

This function calculates simultaneous confidence bands of CSTE curve for time to event outcome with right censoring.

Usage

```
cste_surv_SCB(l, x, y, z, s, h, m, alpha = 0.05)
```

Arguments

l	contraction vector with dimension K .
x	samples of biomarker (or covariate) which is a $n * 1$ vector and should be scaled between 0 and 1.
y	samples of time to event which is a $n * 1$ vector.
z	samples of treatment indicator which is a $n * K$ matrix.
s	samples of censoring indicator which is a $n * 1$ vector.
h	kernel bandwidth.
m	number of turns of resampling.
alpha	the $(1 - \alpha)$ -confidence level of SCB.

Value

A $n * 3$ matrix, estimation of $l^T \beta(x)$ and its simultaneous confidence bands.

References

Ma Y. and Zhou X. (2017). Treatment selection in a randomized clinical trial via covariate-specific treatment effect curves, *Statistical Methods in Medical Research*, 26(1), 124-141.

See Also

[cste_surv](#)

penC *Solve the penalized logistic regression.*

Description

Solve the penalized logistic regression.

Usage

```
penC(x, y, off, beta, lam, pen)
```

Arguments

x	samples of covariates which is a $n * p$ matrix.
y	samples of binary outcome which is a $n * 1$ vector.
off	offset in logistic regression.
beta	initial estimates.
lam	value of the lasso penalty parameter λ for β_1 and β_2 .
pen	1: MCP estimator; 2: SCAD estimator.

Value

A numeric vector, estimate of beta

predict_cste_bin *Predict the CSTE curve of new data for binary outcome.*

Description

Predict the CSTE curve of new data for binary outcome.

Usage

```
predict_cste_bin(obj, newx)
```

Arguments

obj	a S3 class of cste.
newx	samples of covariates which is a $m * p$ matrix.

Value

A S3 class of cste which includes

- g1: predicted $g_1(X\beta_1)$.
- g2: predicted $g_2(X\beta_2)$.
- B1: the B-spline basis for estimating g_1 .
- B2: the B-spline basis for estimating g_2 .

References

Guo W., Zhou X. and Ma S. (2021). Estimation of Optimal Individualized Treatment Rules Using a Covariate-Specific Treatment Effect Curve with High-dimensional Covariates, *Journal of the American Statistical Association*, 116(533), 309-321

See Also

[cste_bin](#)

select_cste_bin	<i>Select the optimal tuning parameters in CSTE estimation for binary outcome.</i>
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Description

select lasso penalty parameter λ for β_1 and β_2 in CSTE estimation.

Usage

```
select_cste_bin(
  x,
  y,
  z,
  lam_seq,
  beta_ini = NULL,
  nknots = 1,
  max.iter = 2000,
  eps = 0.001
)
```

Arguments

x	samples of covariates which is a $n * p$ matrix.
y	samples of binary outcome which is a $n * 1$ vector.
z	samples of treatment indicator which is a $n * 1$ vector.
lam_seq	a sequence for the choice of λ .

beta_ini	initial values for $(\beta'_1, \beta'_2)'$, default value is NULL.
nknots	number of knots for the B-spline for estimating g_1 and g_2 .
max.iter	maximum iteration for the algorithm.
eps	numeric scalar ≥ 0 , the tolerance for the estimation of β_1 and β_2 .

Value

A list which includes

- optimal: optimal cste within the given the sequence of λ .
- bic: BIC for the sequence of λ .
- lam_seq: the sequence of λ that is used.

References

Guo W., Zhou X. and Ma S. (2021). Estimation of Optimal Individualized Treatment Rules Using a Covariate-Specific Treatment Effect Curve with High-dimensional Covariates, *Journal of the American Statistical Association*, 116(533), 309-321

See Also

[cste_bin](#)

Index

cste_bin, [2](#), [6](#), [9](#), [10](#)

cste_bin_SCB, [3](#), [5](#)

cste_surv, [6](#), [7](#)

cste_surv_SCB, [6](#), [7](#)

penC, [8](#)

predict_cste_bin, [3](#), [8](#)

select_cste_bin, [3](#), [9](#)