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Description Nonparametric estimation on survival analysis under order-restrictions.

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License GPL (>= 2)

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Author Yunro Chung [aut, cre] (<https://orcid.org/0000-0001-9125-9277>)

Maintainer Yunro Chung <yunro.chung@asu.edu>

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isoSurv-package *Isotonic Regression on Survival Analysis*

Description

Nonparametric estimation on survival analysis under order restrictions

Details

Package:	isoph
Type:	Package
Version:	0.3.0
Date:	2023-9-1
License:	GPL (>= 2)

Author(s)

Yunro Chung [aut,cre] Maintainer: Yunro Chung <yunro.chung@asu.edu>

References

Yunro Chung, Anastasia Ivanova, Michael G. Hudgens, Jason P. Fine (2018), Partial likelihood estimation of isotonic proportional hazards models, Biometrika, 105(1), 133-148. doi:10.1093/biomet/asx064

disoph *Fit Double Isotonic Proportional Hazards Model*

Description

Nonparametric estimation of monotone baseline hazard and monotone covariate effect functions in the proportional hazards model.

Usage

```
disoph(formula, bshape, data, maxiter, eps)
```

Arguments

formula	formula object: response ~ iso(z,shape="increasing")+$x_1 + x_2 + ... + x_p$. The response must be right-censored survival outcome using the Surv function in the survival package. The iso function attributes the covariate z' name, shape and anchor point.
bshape	direnction of the baseline hazard function ($bshape$="increasing" or "decreasing").
data	data.frame includes variables named in the formula argument.
maxiter	maximum number of iteration (default is 10^4).
eps	stopping convergence criteria (default is 10^-3).

Details

The disoph function computes $(\lambda 0, \psi, \beta)$ in the isotonic proportional hazards model, defined as

$$\lambda(t|z,x) = \lambda 0(t) exp(\psi(z) + \beta_1 x_1 + \beta_2 x_2 + ... + \beta_p x_p),$$

based on the full likelihood, where $\lambda 0$ is a monotone increasing (or decreasing) baseline hazard function, ψ is a monotone increasing (or decreasing) covariate effect function, z is a univariate variable, $(x_1, x_2, ..., x_p)$ is a set of covariates, and $\beta = (\beta_1, \beta_2, ..., \beta_p)$ is a set of corresponding regression parameters. It allows to estimate $(\lambda 0, \beta)$ only if iso(z,shape="increasing") is removed in the formula object. Likewise, It allows to estimate $(\lambda 0, \psi)$ only if x is removed in the formula object. Using the nonparametric maximum likelihood approaches, estimated $\lambda 0$ and ψ are right continuous increasing (or left continuos decreasing) step functions. Compared to the standard partial likelihood approach, the full likelihood approach in the disoph function additionally use shape-information on $\lambda 0$, resulting in more efficient estimators especially for a finate sampe size.

For the anchor constraint, one point has to be fixed with $\psi(K) = 0$ to solve the identifiability problem, e.g. $\lambda 0(t) exp(\psi(z)) = (\lambda 0(t) exp(-c))(exp(\psi(z) + c))$ for any constant c. K is called an anchor point. By default, we set K as a median of values of z's. The choice of anchor points are not important because, for example, different anchor points results in the same hazard ratios.

Value

A list of class fisoph:

iso.bh	data.frame with t and estimated $\lambda 0$(t).
iso.cov	data.frame with z and estimated ψ(z).
beta	estimated $\beta_1, \beta_2, ..., \beta_p$.
conv	algorithm convergence status.
iter	total number of iterations.
Zk	anchor satisfying estimated $\psi(Zk)$=0.
shape.bh	order restriction on $\lambda 0$.
shape.cov	order restriction on ψ.

Author(s)

Yunro Chung [auth, cre]

References

Yunro Chung, Double Isotonic Proportional Hazards Models with Applications to Dose-Finding Studies. In preparation.

Examples

```
#test1
test1=data.frame(
  time=  c(2, 5, 1, 7, 9, 5, 3, 6, 8, 9, 7, 4, 5, 2, 8),
  status=c(0, 1, 0, 1, 0, 1, 1, 1, 1, 1, 1, 1, 0, 1),
  z=     c(2, 1, 1, 3, 5, 6, 7, 9, 3, 0, 2, 7, 3, 9, 4)
)
disoph.fit1=disoph(Surv(time, status)~iso(z,shape="inc"),bshape="inc",data=test1)
print(disoph.fit1)
plot(disoph.fit1)

#test2
test2=data.frame(
  time=  c(2, 5, 1, 7, 9, 5, 3, 6, 8, 9, 7, 4, 5, 2, 8),
  status=c(0, 1, 0, 1, 0, 1, 1, 1, 1, 1, 1, 1, 0, 1),
  z=     c(2, 1, 1, 3, 5, 6, 7, 9, 3, 0, 2, 7, 3, 9, 4),
  trt=   c(1, 1, 1, 1, 1, 1, 1, 0, 0, 0, 0, 0, 0, 0, 0),
  x=     c(1, 2, 3, 4, 5, 6, 7, 8, 9, 1, 2, 3, 4, 5, 6)
)
disoph.fit2=disoph(Surv(time, status)~iso(z,shape="inc")+trt+x,bshape="inc",data=test2)
print(disoph.fit2)
plot(disoph.fit2)
```

`iso` *Attributions of isotonic covariate effect*

Description

attributes the covariate with respect to the name, direction, anchor point, and class.

Usage

```
iso(z, shape)
```

Arguments

z	a univariate covariate.
shape	a direction of z ($shape$="increasing" or "decreasing").

Details

Internal function. The iso function attributes the covariate z for its name, shape , anchor point and class, where the anchor point is set to a median of z's, and class is set to "iso covariate"

Value

The value z with attribution of its name, shape and median anchor point.

Author(s)

Yunro Chung [cre]

`isoph` *Fit Isotonic Proportional Hazards Model*

Description

Nonparametric estimation of a monotone covariate effect under the proportional hazards model.

Usage

```
isoph(formula, data, maxiter, eps)
```

Arguments

`formula`	a formula object: response ~ iso(z,shape="increasing")+$x_1 + x_2 + ... + x_p$. The response must be right-censored survival outcome using the Surv function in the survival package. The iso function attributes the covariate z' name, shape and anchor point.
`data`	data.frame includes variables named in the formula argument.
`maxiter`	maximum number of iteration (default is 10^4).
`eps`	stopping convergence criteria (default is 10^-3).

Details

The isoph function estimates (ψ, β) in the isotonic proportional hazards model, defined as

$$\lambda(t|z,x) = \lambda 0(t) exp(\psi(z) + \beta_1 x_1 + \beta_2 x_2 + ... + \beta_p x_p),$$

based on the partial likelihood with unspecified baseline hazard function $\lambda 0$, where ψ is a monotone increasing (or decreasing) covariate effect function, z is a univariate variable, $x = (x_1, x_2, ..., x_p)$ is a set of covariates, and $\beta = (\beta_1, \beta_2, ..., \beta_p)$ is a set of corresponding regression parameters. It allows to estimate ψ only if x is removed in the formula object. Using the nonparametric maximum likelihood approaches, estimated ψ is a right continuous increasing (or left continuos decreasing) step function.

For the anchor constraint, one point has to be fixed with $\psi(K) = 0$ to solve the identifiability problem, e.g. $\lambda 0(t) exp(\psi(z)) = (\lambda 0(t) exp(-c))(exp(\psi(z) + c))$ for any constant c. K is called an anchor point. By default, we set K as a median of values of z's. The choice of anchor points are not important because, for example, different anchor points results in the same hazard ratios.

Value

A list of class isoph:

iso.cov	data.frame with z and estimated ψ.
beta	estimated $\beta_1, \beta_2, ..., \beta_p$.
conv	algorithm convergence status.
iter	total number of iterations.
Zk	anchor point satisfying $\psi(Zk)$=0.
shape	Order-restriction imposed on ψ.

Author(s)

Yunro Chung [aut, cre]

References

Yunro Chung, Anastasia Ivanova, Michael G. Hudgens, Jason P. Fine, Partial likelihood estimation of isotonic proportional hazards models, Biometrika. 2018, 105 (1), 133-148. doi:10.1093/biomet/asx064

Examples

```
# test1
test1=data.frame(
  time=  c(2, 5, 1, 7, 9, 5, 3, 6, 8, 9, 7, 4, 5, 2, 8),
  status=c(0, 1, 0, 1, 0, 1, 1, 1, 1, 1, 1, 1, 0, 1),
  z=     c(2, 1, 1, 3, 5, 6, 7, 9, 3, 0, 2, 7, 3, 9, 4)
)
isoph.fit1=isoph(Surv(time, status)~iso(z,shape="inc"),data=test1)
print(isoph.fit1)
plot(isoph.fit1)

# test2
test2=data.frame(
  time=  c(2, 5, 1, 7, 9, 5, 3, 6, 8, 9, 7, 4, 5, 2, 8),
  status=c(0, 1, 0, 1, 1, 0, 1, 0, 1, 1, 1, 0, 1, 1, 1),
  z=     c(2, 1, 1, 3, 5, 6, 7, 9, 3, 0, 2, 7, 3, 9, 4),
  trt=   c(1, 1, 1, 0, 1, 0, 1, 0, 0, 1, 0, 1, 1, 0, 0)
)
isoph.fit2=isoph(Surv(time, status)~iso(z,shape="inc")+trt, data=test2)
print(isoph.fit2)
plot(isoph.fit2)
```

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