

Package ‘intccr’

April 25, 2018

Type Package

Title Semiparametric Competing Risks Regression under Interval
Censoring

Version 1.0.1

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Description Semiparametric regression models for the cumulative incidence function with interval-censored competing risks data as described in Bakoyannis, Yu, & Yiannoutsos (2017) <doi:10.1002/sim.7350>. The main function fits the proportional subdistribution hazards model (Fine-Gray model), the proportional odds model, and other models that belong to the class of semiparametric generalized odds rate transformation models.

Date 2018-02-27

Imports alabama (>= 2015.3.1), doParallel, foreach, parallel,
numDeriv, stats, utils

Depends R (>= 2.14.0)

License GPL (>= 2)

Encoding UTF-8

LazyData true

RoxygenNote 6.0.1

NeedsCompilation no

Repository CRAN

Date/Publication 2018-04-25 19:51:27 UTC

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bssmle	<i>B-spline Sieve Maximum Likelihood Estimation</i>
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Description

Routine that performs B-spline sieve maximum likelihood estimation with linear and nonlinear inequality constraints

Usage

```
bssmle(formula, data, alpha)
```

Arguments

formula	a formula object relating survival object <code>Surv2(v, u, event)</code> to a set of co-variates
data	a data frame that includes the variables named in the formula argument
alpha	$\alpha = (\alpha_1, \alpha_2)$ contains parameters that define the link functions from class of generalized odds-rate transformation models. The components α_1 and α_2 should both be ≥ 0 . If $\alpha_1 = 0$, the user assumes a proportional subdistribution hazards model or Fine-Gray model for the cause of failure 1. If $\alpha_2 = 1$, the user assumes a proportional odds model for the cause of failure 2.

Details

The function `bssmle` performs B-spline sieve maximum likelihood estimation.

Value

The function `bssmle` returns a list of components:

beta	a vector of the estimated coefficients for the B-splines
varnames	a vector containing variable names
alpha	a vector of the link function parameters
loglikelihood	a loglikelihood of the fitted model
convergence	an indicator of convergence
tms	a vector of the minimum and maximum observation times
Bv	a list containing the B-splines basis functions evaluated at v

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Examples

```
est.simdata <- intccr::bssmle(Surv2(v, u, c) ~ z1 + z2, data = simdata, alpha = c(1, 1))
newdata <- intccr::dataprep(data = longdata, ID = "id", time = "t",
  event = "c", Z = c("z1", "z2"))
est.longdata <- intccr::bssmle(Surv2(v, u, c) ~ z1 + z2, data = newdata, alpha = c(1, 1))
```

bssmle_se

Bootstrap varince-covariance estimation

Description

Bootstrap varince estimation for the estimated regression coefficients

Usage

```
bssmle_se(formula, data, alpha, do.par, nboot)
```

Arguments

formula	a formula object relating survival object <code>Surv2(v, u, event)</code> to a set of co-variates
data	a data frame that includes the variables named in the formula argument
alpha	$\alpha = (\alpha_1, \alpha_2)$ contains parameters that define the link functions from class of generalized odds-rate transformation models. The components α_1 and α_2 should both be ≥ 0 . If $\alpha_1 = 0$, the user assumes a proportional subdistribution hazards model or Fine-Gray model for the cause of failure 1. If $\alpha_2 = 1$, the user assumes a proportional odds model for the cause of failure 2.
do.par	using parallel computing for bootstrap calculation. If <code>do.par = TRUE</code> , parallel computing will be used during the bootstrap estimation of the variance-covariance matrix for the regression parameter estimates.
nboot	a number of bootstrap samples for estimating variances and covariances of the estimated regression coefficients. If <code>nboot = 0</code> , the function <code>ciregic</code> does not perform bootstrap estimation of the variance matrix of the regression parameter estimates and returns NA in the place of the estimated variance matrix of the regression parameter estimates.

Details

The function `bssmle_se` estimates bootstrap standard errors for the estimated regression coefficients from the function `bssmle`.

Value

The function `bssmle_se` returns a list of components:

<code>numboot</code>	a number of bootstrap converged
<code>Sigma</code>	an estimated bootstrap variance-covariance matrix of the estimated regression coefficients

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Examples

```
est.vcov <- intccr:::bssmle_se(Surv2(v, u, c) ~ z1 + z2, data = simdata,
                             alpha = c(1, 1), do.par = FALSE, nboot = 1)
```

ciregic

Competing Risks Regression with Interval-Censored Data

Description

The function `ciregic` performs semiparametric regression on cumulative incidence function with interval-censored competing risks data. It fits the proportional subdistribution hazards model (Fine-Gray model), the proportional odds model, and other models that belong to the class of semiparametric generalized odds rate transformation models.

Usage

```
ciregic(formula, data, alpha, do.par, nboot)
```

Arguments

<code>formula</code>	a formula object relating the survival object <code>Surv2(v, u, event)</code> to a set of covariates
<code>data</code>	a data frame that includes the variables named in the formula argument
<code>alpha</code>	$\alpha = (\alpha_1, \alpha_2)$ contains parameters that define the link functions from class of generalized odds-rate transformation models. The components α_1 and α_2 should both be ≥ 0 . If $\alpha_1 = 0$, the user assumes a proportional subdistribution hazards model or Fine-Gray model for the cause of failure 1. If $\alpha_2 = 1$, the user assumes a proportional odds model for the cause of failure 2.
<code>do.par</code>	an option to use parallel computing for bootstrap. If <code>do.par = TRUE</code> , parallel computing will be used during the bootstrap estimation of the variance-covariance matrix for the regression parameter estimates.

`nboot` a number of bootstrap samples for estimating variances and covariances of the estimated regression coefficients. If `nboot = 0`, the function `ciregic` does not perform bootstrap estimation of the variance-covariance matrix of the regression parameter estimates and returns NA in the place of the estimated variance-covariance matrix of the regression parameter estimates.

Details

The formula for the model has the form of `response ~ predictors`. The response in the formula is a `Surv2(v, u, event)` object where `v` is the last observation time prior to the failure, `u` is the first observation time after the failure, and `event` is the event or censoring indicator. `event` should include 0, 1 or 2, denoting right-censoring, failure from cause 1 and failure from cause 2, respectively. If `event=0` (i.e. right-censored observation) then `u` is not included in any calculation as it corresponds to ∞ . The user can provide any value in `u` for the right-censored cases, even NA. The function `ciregic` fits models that belong to the class of generalized odds rate transformation models which includes the proportional subdistribution hazards or the Fine-Gray model and the proportional odds model. The parameter $\alpha = (\alpha_1, \alpha_2)$ defines the link function/model to be fitted for cause of failure 1 and 2, respectively. A value of 0 corresponds to the Fine-Gray model and a value of 1 corresponds to the proportional odds model. For example, if $\alpha = (0, 1)$ then the function `ciregic` fits the Fine-Gray model for cause 1 and the proportional odds model for cause 2.

Value

The function `ciregic` provides an object of class `ciregic` with components:

<code>varnames</code>	a vector containing variable names
<code>coefficients</code>	a vector of the regression coefficient estimates
<code>gamma</code>	a vector of the estimated coefficients for the B-splines
<code>vcov</code>	a variance-covariance matrix of the estimated regression coefficients
<code>alpha</code>	a vector of the link function parameters
<code>loglikelihood</code>	a loglikelihood of the fitted model
<code>convergence</code>	an indicator of convergence
<code>tms</code>	a vector of the minimum and maximum observation times
<code>Bv</code>	a list containing the B-splines basis functions evaluated at <code>v</code>
<code>numboot</code>	a number of converged bootstrap
<code>call</code>	a matched call

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References

Bakoyannis, G., Yu, M., and Yiannoutsos C. T. (2017). Semiparametric regression on cumulative incidence function with interval-censored competing risks data. *Statistics in Medicine*, **36**:3683-3707.

Fine, J. P. and Gray, R. J. (1999). A proportional hazards model for the subdistribution of a competing risk. *Journal of the American Statistical Association*, **94**:496-509.

See Also

[summary.ciregic](#) for the summarized results and [predict.ciregic](#) for value of the predicted cumulative incidence functions. [coef](#) and [vcov](#) are the generic functions. [dataprep](#) for reshaping data from a long format to a suitable format to be used in the function [ciregic](#).

Examples

```
## Set seed in order to have reproducibility of the bootstrap standard error estimate
set.seed(1234)

## Reshaping data from a long format to a suitable format
newdata <- dataprep(data = longdata, ID = "id", time = "t",
                    event = "c", Z = c("z1", "z2"))
## Estimation of regression parameters only. No bootstrap variance estimation.
## with 'newdata'
fit <- ciregic(Surv2(v, u, c) ~ z1 + z2, data = newdata,
              alpha = c(1, 1), nboot = 0, do.par = FALSE)
fit

## Estimation of regression parameters only. No bootstrap variance estimation.
## with 'simdata'
fit.simdata <- ciregic(Surv2(v, u, c) ~ z1 + z2, data = simdata,
                      alpha = c(1, 1), nboot = 0, do.par = FALSE)
fit.simdata

## Not run:
## Bootstrap variance estimation based on 50 replications
fit <- ciregic(Surv2(v, u, c) ~ z1 + z2, data = newdata,
              alpha = c(1, 1), nboot = 50, do.par = FALSE)

## End(Not run)
## Note that the user can use parallel computing to decrease
## the computation time of the bootstrap variance-covariance
## estimation (e.g. nboot = 50)

## Summarize semiparametric regression model
summary(fit)

## Predict and draw plot the cumulative incidence function evaluated at z1=1 and z2=0.5
t <- seq(from = 0, to = 2.8, by = 2.8/99)
pred <- predict(object = fit, covp = c(1, 0.5), times = t)
pred
plot(pred$t, pred$scif1, type = "l", ylim=c(0, 1))
```

```
points(pred$t, pred$cif2, type = "1", col = 2)
```

dataprep

Data manipulation

Description

The function `dataprep` reshapes data from a long format to a ready-to-use format to be used directly in the function `ciregic`.

Usage

```
dataprep(data, ID, time, event, Z)
```

Arguments

<code>data</code>	a data frame that includes the variables named in the <code>ID</code> , <code>time</code> , <code>event</code> , and <code>z</code> arguments
<code>ID</code>	a variable indicating individuals' ID
<code>time</code>	a variable indicating observed time points
<code>event</code>	a vector of event indicator. If an observation is right-censored, <code>event = 0</code> ; otherwise, <code>event = 1</code> or <code>event = 2</code> , where 1 represents the first cause of failure, and 2 represents the second cause of failure. The current version of package only allows two causes of failure.
<code>Z</code>	a vector of variables indicating name of covariates

Details

The function `dataprep` provides a ready-to-use data format that can be directly used in the function `ciregic`. The returned data frame consists of `id`, `v`, `u`, `c`, and `covariates` as columns. The `v` and `u` indicate time window with the last observation time before the event and the first observation after the event. The `c` represents a type of event, for example, `c = 1` for the first cause of failure, `c = 2` for the second cause of failure, and `c = 0` for the right-censored. Individuals who have only one time record with right-censored event will be omitted because its time interval is $(0, \text{Inf})$, and the lower bound `v` will be replaced by zero, for example $(0, v]$, if individuals are not right-censored and have only one time record.

Value

a data frame

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Examples

```
library(intccr)
dataprep(data = longdata, ID = "id", time = "t", event = "c", Z = c("z1", "z2"))
```

longdata	<i>Simulated data consisting of 200 individuals with 2 covariates.</i>
----------	--

Description

Data containing subject id, a series of time points, cause of failure, and covariates.

Usage

```
longdata
```

Format

A data frame with 868 rows and 5 variables.

Examples

```
longdata
```

naive_b	<i>Initial values for the sieve maximum likelihood estimation</i>
---------	---

Description

The function `naive_b` provides a vector of initial values for the B-spline sieve maximum likelihood estimation.

Usage

```
naive_b(data, v, u, c, q)
```

Arguments

<code>data</code>	a data frame that includes the variables named in each argument
<code>v</code>	the last observation time prior to the failure.
<code>u</code>	the first observation time after the failure.
<code>c</code>	an indicator of cause of failure. If an observation is right-censored, <code>event = 0</code> ; otherwise, <code>event = 1</code> or <code>event = 2</code> , where 1 represents the first cause of failure, and 2 represents the second cause of failure. The current version of package only allows for two causes of failure.
<code>q</code>	a dimension of design matrix.

Details

The function naive_b provides initial values for the optimization procedure.

Value

Initial values of B-spline estimation

b a vector of the initial values to be used in the optimization process

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Examples

```
attach(simdata)
intccr::naive_b(data = simdata, v = v, u = u, c = c, q = 2)
```

predict.ciregic

Covariate-Specific Cumulative Incidence Prediction

Description

predict method for class ciregic. It provides the predicted cumulative incidence function for a given covariate pattern and timepoint(s).

Usage

```
## S3 method for class 'ciregic'
predict(object, covp, times, ...)
```

Arguments

object	an object of class ciregic, which is a result of a call to ciregic
covp	a desired values for covariates
times	time points that user wants to predict value of cumulative incidence function
...	further arguments

Details

predict.ciregic returns the predicted cumulative incidence function for a given covariate pattern and timepoint(s).

Value

The function `predict.ciregic` returns a list of predicted values of the model from object.

<code>t</code>	time points
<code>cif1</code>	the predicted value of cumulative incidence function for cause 1
<code>cif2</code>	the predicted value of cumulative incidence function for cause 2

See Also

The fitted semiparametric regression on cumulative incidence function with interval-censored competing risks data [ciregic](#) and summary of the fitted semiparametric regression model [summary.ciregic](#)

Examples

```
## Continuing the ciregic(...) example

pfit <- predict(object = fit, covp = c(1, 0.5), times = c(0.1, 0.15, 0.5, 0.7))
pfit
mint <- fit$tms[1]
maxt <- fit$tms[2]
pfit1 <- predict(object = fit, covp = c(1, 0.5),
                times = seq(mint, maxt, by = (maxt-mint)/99))
plot(pfit1$t, pfit1$cif1, ylim = c(0, 1), type = "l")
lines(pfit1$t, pfit1$cif2, ylim = c(0, 1), lty = 2, col = 2)
```

<code>simdata</code>	<i>Simulated data consisting of 200 interval-censored observations with 2 covariates.</i>
----------------------	---

Description

Data containing the last time point prior to the event, the first time point after the event, cause of failure, and covariates.

Usage

```
simdata
```

Format

A data frame with 200 rows and 5 variables.

Examples

```
simdata
```

summary.ciregic	<i>Summary of ciregic</i>
-----------------	---------------------------

Description

summary method for class ciregic

Usage

```
## S3 method for class 'ciregic'  
summary(object, ...)
```

Arguments

object	an object of class ciregic, which is a result of a call to ciregic
...	further arguments

Details

The function `summary.ciregic` returns the coefficients, bootstrap standard errors, and etc. Additionally, 'significance star' is included.

Value

The function `summary.ciregic` returns a list of summary statistics of the model from object.

varnames	a vector containing variable names
coefficients	a vector of the regression coefficient estimates
se	a bootstrap standard error of the coefficients
z	z value of the estimated coefficients
p	p value of the estimated coefficients
call	a matched call

See Also

The fitted semiparametric regression on cumulative incidence function with interval-censored competing risks data `ciregic` and values of the predicted cumulative incidence functions `predict.ciregic`

Examples

```
## Continuing the ciregic(...) example  
  
sfit <- summary(fit)  
sfit
```

`Surv2`*Creating data frame*

Description

The function `Surv2` generates the survival object to be treated as the response from `ciregic`.

Usage

```
Surv2(v, u, event)
```

Arguments

<code>v</code>	the last observation time prior to the failure; $0 \leq v \leq u$.
<code>u</code>	the first observation time after the failure; $u \geq 0$.
<code>event</code>	an indicator of cause of failure. If an observation is right-censored, <code>event = 0</code> ; otherwise, <code>event = 1</code> or <code>event = 2</code> , where 1 represents the first cause of failure, and 2 represents the second cause of failure. The current version of package only allows for two causes of failure.

Details

The function `Surv2` provides a response data frame which is used in the function `ciregic`.

Value

data frame

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Examples

```
attach(simdata)
Surv2(v, u, c)
```

vcov.ciregic	<i>Variance-covariance matrix of ciregic</i>
--------------	--

Description

vcov method for class ciregic

Usage

```
## S3 method for class 'ciregic'  
vcov(object, ...)
```

Arguments

object	an object of class ciregic, which is a result of a call to ciregic
...	further arguments

Details

The function vcov returns the variance-covariance matrix of the fitted semiparametric regression model.

Value

The estimated bootstrap variance-covariance matrix

See Also

The fitted semiparametric regression on cumulative incidence function with interval-censored competing risks data [ciregic](#), summary of the fitted semiparametric regression model [summary.ciregic](#), and values of predicted cumulative incidence functions [predict.ciregic](#)

Examples

```
## Continuing the ciregic(...) example  
  
vcov(fit)
```

vcov.summary.ciregic *Variance-covariance matrix of* summary.ciregic

Description

vcov method for class `summary.ciregic`

Usage

```
## S3 method for class 'summary.ciregic'  
vcov(object, ...)
```

Arguments

`object` an object of class `summary.ciregic`, which is a result of a call to `ciregic`
`...` further arguments

Details

The `vcov` returns the variance-covariance matrix of the fitted semiparametric regression model.

Value

The estimated bootstrap variance-covariance matrix

See Also

The fitted semiparametric regression on cumulative incidence function with interval-censored competing risks data [ciregic](#), summary of the fitted semiparametric regression model [summary.ciregic](#), and values of the predicted cumulative incidence functions [predict.ciregic](#)

Examples

```
## Continuing the ciregic(...) example  
  
vcov(summary(fit))
```

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