

Package ‘CopulaCenR’

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Type Package

Title Copula-Based Regression Models for Bivariate Censored Data

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Description Copula-based regression models for bivariate censored data, including bivariate right-censored data and bivariate interval-censored data. Currently supports Clayton, Gumbel, Frank, Joe, AMH and Copula2 copula models. For marginal models, it supports parametric (Weibull, Loglogistic, Gompertz) and semiparametric (Cox and transformation) models. Includes methods for convenient prediction and plotting. Also provides a bivariate time-to-event simulation function. Method details can be found in Sun et.al (2019) Lifetime Data Analysis and Sun et.al (In Press) Biostatistics.

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 ACTG181

 ACTG181

Description

An example real dataset of bivariate interval-censored data with 204 subjects and one covariate. The data come from the AIDS Clinical Trials Group protocol ACTG 181. Two events are the shedding time (in months) of cytomegalovirus (CMV) in urine/blood and the colonization time (in months) of mycobacterium avium complex (MAC) in sputum/stool (Betensky and Finkelstein, 1999).

Usage

```
data("ACTG181")
```

Format

A data frame with 408 observations on the following 6 variables.

`id` subject id

`ind` margin indicator, 1=shedding time, 2=colonization time

`Left` left bound of observed interval

`Right` right bound of observed interval

`status` censoring indicator; 1=interval-censor, 0=right censor. All observations are interval-censored in this dataset

`x` covariate

Source

Betensky and Finkelstein (1999). A non-parametric maximum likelihood estimator for bivariate interval censored data. *Statistics in Medicine* **18** 3089-3100.

Examples

```
data(ACTG181)
clayton_sp <- ic_spTran_copula(data = ACTG181,
                             copula = "Clayton",
                             l = 0, u = 25,
                             r = 3, m = 3,
                             var_list = "x")
summary(clayton_sp)
```

AIC.CopulaCenR	<i>the AIC of a CopulaCenR object</i>
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Description

the AIC of a CopulaCenR object

Usage

```
## S3 method for class 'CopulaCenR'
AIC(object, ..., k = 2)
```

Arguments

object	a CopulaCenR object
...	further arguments
k	numeric, with k = 2 for AIC

AREDS	<i>AREDS</i>
-------	--------------

Description

A real dataset of bivariate interval-censored data with 629 subjects and 4 non-genetic covariates and 1 genetic covariate. The dataset is selected from the Age-related Eye Disease Study (AREDS) (AREDS Group, 1999). Two events are the progression times (in years) to late-AMD in the left and right eyes.

Usage

```
data("AREDS")
```

Format

A data frame with 1258 observations (629 subjects with 2 eyes) on the following 8 variables.

id subject id

ind margin indicator, 1=shedding time, 2=colonization time

Left left bound of observed interval

Right right bound of observed interval

status censoring indicator; 1=interval-censor, 0=right censor.

SevScaleBL baseline AMD severity score, margin-specific

ENROLLAGE age at baseline

rs2284665 a SNP covariate highly associated with late-AMD progression, coded as 0,1,2

Source

AREDS Group (1999). The Age-Related Eye Disease Study (AREDS): design implications. AREDS report no. 1. *Control Clinical Trials* **20**, 573-600.

Examples

```
data(AREDS)
copula2_sp <- ic_spTran_copula(data = AREDS,
  copula = "Copula2",
  var_list = c("ENROLLAGE",
    "rs2284665",
    "SevScaleBL"),
  l = 0, u = 15, m = 3, r = 3)
summary(copula2_sp)
```

BIC.CopulaCenR

the BIC of a CopulaCenR object

Description

the BIC of a CopulaCenR object

Usage

```
## S3 method for class 'CopulaCenR'
BIC(object, ...)
```

Arguments

object a CopulaCenR object
 ... further arguments

coef.CopulaCenR	<i>the coefficient estimates of a CopulaCenR object</i>
-----------------	---

Description

the coefficient estimates of a CopulaCenR object

Usage

```
## S3 method for class 'CopulaCenR'
coef(object, ...)
```

Arguments

object	a CopulaCenR object
...	further arguments

CopulaCenR	<i>Copula-based regression models for bivariate censored data</i>
------------	---

Description

Bivariate time-to-event data frequently arise in research areas such as clinical trials and epidemiological studies, where the occurrence of two events are correlated. In many cases, the exact event times are unknown due to censoring. Specifically, bivariate right-censored data occur when the study ends prior to the occurrence of one or both events. In another situation, bivariate interval-censored data occur when the status of both events are periodically examined at intermittent assessment times. In this case, the right censoring could also happen if the event still does not occur at the last assessment time. A special case of interval-censored data is the current status data if there is only one assessment time and the event is only known to occur or not by its assessment time.

The copula model is a popular approach for modeling correlated bivariate censored data. One unique feature of copula is that it models the two marginal distributions and the between-margin dependence separately, allowing flexibility in marginal models and straightforward interpretation for covariate effects. Moreover, the challenge from censoring can be naturally handled through the marginal distributions within the copula function. Besides, the joint, marginal and conditional distributions can be obtained based on the copula model. However, there is a lack of R package implementing copula-based regression models for bivariate data under both right- and interval-censoring.

The CopulaCenR package can build copula-based regression models for both bivariate right-censored data and bivariate interval-censored data (including the special case of bivariate current status data). The package is flexible in terms of various built-in Archimedean copulas (such as Clayton, Gumbel, Frank, Joe, AMH), together with a two-parameter copula (Copula2) that incorporates the popular Clayton and Gumbel copulas as special cases. It also allows a broad class of marginal distributions,

including parametric (i.e., Weibull, Gompertz, Loglogistic) and semiparametric (i.e., unspecified functions, such as Cox, transformation) margins.

The main features of CopulaCenR are:

- (1) Copula models with parametric margins: `rc_par_copula` and `ic_par_copula`) for bivariate right-censored data and bivariate interval-censored data, respectively.
- (2) Copula models with semiparametric margins: `rc_spCox_copula` and `ic_spTran_copula`) for bivariate right-censored data and bivariate interval-censored data, respectively.
- (3) Wald (performed during model fitting), score (`score_copula`) and likelihood-ratio (`lrt_copula`) tests for covariate effects.
- (4) Calculate Kendall's tau from a fitted model: `tau_copula`.
- (5) Calculate other model parameters using S3 methods: `print`, `summary`, `coef`, `logLik`, `AIC`, `BIC`.
- (6) Extract fitted values (such as linear predictors and survival probabilities) from a fitted model: `fitted`.
- (7) Predict in new observations (such as linear predictors and survival probabilities) from a fitted model: `predict`.
- (8) Plot joint, conditional and marginal survival probability profiles for given subjects based on a fitted model: `plot`, `lines`.
- (9) A user-friendly function to simulate bivariate event times: `data_sim_copula`.

Source

Tao Sun, Yi Liu, Richard J. Cook, Wei Chen and Ying Ding (2018). Copula-based Score Test for Bivariate Time-to-event Data, with Application to a Genetic Study of AMD Progression. *#' Lifetime Data Analysis* 25(3), 546-568.

Tao Sun and Ying Ding (In Press). Copula-based Semiparametric Regression Method for Bivariate Data under General Interval Censoring. <http://arxiv.org/abs/1901.01918>.

Examples

```
### bivariate right-censored data
data(DRS)
# fit a Clayton-Weibull model
clayton_wb <- rc_par_copula(data = DRS,
                           var_list = "treat",
```

```

                                copula = "Clayton",
                                m.dist = "Weibull")
summary(clayton_wb)

### bivariate interval-censored data
data(AREDS)
copula2_sp <- ic_spTran_copula(data = AREDS,
                              copula = "Copula2", l = 0, u = 15,
                              m = 3, r = 3, var_list =
                                c("ENROLLAGE", "rs2284665",
                                  "SevScaleBL"))
summary(copula2_sp)

```

data_sim_copula	<i>Simulate bivariate time-to-event times based on specific copula and marginal distributions</i>
-----------------	---

Description

To generate a sample of subjects with two correlated event times based on specific copula and marginal models

Usage

```
data_sim_copula(n, copula, eta, dist, baseline, var_list, COV_beta, x1, x2)
```

Arguments

n	sample size
copula	types of copula, including "Clayton", "Gumbel", "Frank", "AMH", "Joe"
eta	copula parameter η
dist	marginal distributions, including "Weibull", "Gompertz", "Loglogistic"
baseline	marginal distribution parameters. For Weibull and Loglogistic, it shall be λ (scale) and k (shape); for Gompertz, it shall be a (shape) and b (rate)
var_list	a vector of covariate names; assume the same covariates for two margins
COV_beta	a vector of regression coefficients corresponding to var_list; assume the same coefficients between two margins
x1	a data frame of covariates for margin 1; it shall have n rows, with columns corresponding to the var_list
x2	a data frame of covariates for margin 2

Details

The parametric generator functions of copula functions are list below:

The Clayton copula has a generator

$$\phi_{\eta}(t) = (1 + t)^{-1/\eta},$$

with $\eta > 0$ and Kendall's $\tau = \eta/(2 + \eta)$.

The Gumbel copula has a generator

$$\phi_{\eta}(t) = \exp(-t^{1/\eta}),$$

with $\eta \geq 1$ and Kendall's $\tau = 1 - 1/\eta$.

The Frank copula has a generator

$$\phi_{\eta}(t) = -\eta^{-1} \log\{1 + e^{-t}(e^{-\eta} - 1)\},$$

with $\eta \geq 0$ and Kendall's $\tau = 1 + 4\{D_1(\eta) - 1\}/\eta$, in which $D_1(\eta) = \frac{1}{\eta} \int_0^{\eta} \frac{t}{e^t - 1} dt$.

The AMH copula has a generator

$$\phi_{\eta}(t) = (1 - \eta)/(e^t - \eta),$$

with $\eta \in [0, 1)$ and Kendall's $\tau = 1 - 2\{(1 - \eta)^2 \log(1 - \eta) + \eta\}/(3\eta^2)$.

The Joe copula has a generator

$$\phi_{\eta}(t) = 1 - (1 - e^{-t})^{1/\eta},$$

with $\eta \geq 1$ and Kendall's $\tau = 1 - 4 \sum_{k=1}^{\infty} \frac{1}{k(\eta k + 2)\{\eta(k-1) + 2\}}$.

The marginal survival distributions are listed below:

The Weibull (PH) survival distribution is

$$\exp\{-(t/\lambda)^k e^{Z^T \beta}\},$$

with $\lambda > 0$ as scale and $k > 0$ as shape.

The Gompertz (PH) survival distribution is

$$\exp\{-\frac{b}{a}(e^{at} - 1)e^{Z^T \beta}\},$$

with $a > 0$ as shape and $b > 0$ as rate

The Loglogistic (PO) survival distribution is

$$\{1 + (t/\lambda)^k e^{Z^T \beta}\}^{-1},$$

with $\lambda > 0$ as scale and $k > 0$ as shape.

Value

a data frame of bivariate time-to-event data with covariates

Examples

```

library(CopulaCenR)
set.seed(1)
dat <- data_sim_copula(n = 500, copula = "Clayton", eta = 3,
  dist = "Weibull", baseline = c(0.1,2),
  var_list = c("var1", "var2"),
  COV_beta = c(0.1, 0.1),
  x1 = cbind(rnorm(500, 6, 2),
    rbinom(500, 1, 0.5)),
  x2 = cbind(rnorm(500, 6, 2),
    rbinom(500, 1, 0.5)))
plot(x = dat$time[dat$ind == 1], y = dat$time[dat$ind == 2],
  xlab = expression(t[1]), ylab = expression(t[2]),
  cex.axis = 1, cex.lab = 1.3)

```

DRS

DRS

Description

A real dataset of bivariate right-censored data with 197 subjects and 3 covariates. The patients were a 50% random sample of the patients with "high-risk" diabetic retinopathy as defined by the Diabetic Retinopathy Study (DRS) (Huster, 1989).

Usage

```
data("DRS")
```

Format

A data frame with 394 observations on the following 7 variables.

`id` subject id

`ind` margin indicator, 1 for right eye, 2 for left eye

`obs_time` time of blindness (in months) from treatment

`status` censoring indicator, 1 = blindness, 0 = right censoring

`treat` laser treatment type, 0 = no treatment, 1 = xenon, 2 = argon

`age` age at diagnosis of diabetes

`type` type of diabetes, 1 = juvenile (age at treatment < 20), 2 = adult

Details

Each patient had one eye randomized to laser treatment and the other eye received no treatment. For each eye, the event of interest was the time from initiation of treatment to the time when visual acuity dropped below 5/200 (call it "blindness"). Survival times in this dataset are the actual time to blindness in months. Censoring was caused by death, dropout, or end of the study.

Source

<https://www.mayo.edu/research/documents/DRShtml/DOC-10027460>

References

Huster WJ, Brookmeyer R, Self SG (1989). Modeling paired survival data with covariates. *Biometrics* **45**, 145-156.

Examples

```
data(DRS)
clayton_wb <- rc_par_copula(data = DRS,
  var_list = "treat",
  copula = "Clayton",
  m.dist = "Weibull")
summary(clayton_wb)
```

fitted.CopulaCenR *Fitted values from CopulaCenR regression models*

Description

Fitted values based on models from `ic_spTran_copula`, `rc_spCox_copula`, `ic_par_copula` and `rc_par_copula`.

Usage

```
## S3 method for class 'CopulaCenR'
fitted(object, type = "lp", ...)
```

Arguments

<code>object</code>	a CopulaCenR object from <code>ic_spTran_copula</code> , <code>rc_spCox_copula</code> , <code>ic_par_copula</code> and <code>rc_par_copula</code>
<code>type</code>	"lp" for linear predictors or "survival" for marginal and joint survival probabilities
<code>...</code>	further arguments

Details

When the argument `type = "lp"`, it gives a linear predictor for each margin (i.e., log hazards ratio in the proportional hazards model, log proportional odds in the proportional odds model).

When the argument `type = "survival"` and the fitted data is bivariate right-censored, the marginal and joint survival values will be evaluated at the observed times. For bivariate interval-censored, evaluation times are the interval middle points or left bound (if right bound is infinity).

Value

If type = "lp", it returns a data frame with id, lp1 (linear predictor for margin 1), lp2. If type = "survival", it returns a data frame with id, t1 (evaluated times for the margin 1), t2, S1 (predicted marginal survival probabilities for margin 1), S2 and S12 (the predicted joint survival probabilities)

Examples

```
data(AREDS)
# fit a Copula2-Sieve model
copula2_sp <- ic_spTran_copula(data = AREDS, copula = "Copula2",
                             l = 0, u = 15, m = 3, r = 3,
                             var_list = c("ENROLLAGE", "rs2284665", "SevScaleBL"))
output <- fitted(object = copula2_sp)
```

ic_par_copula	<i>Copula regression models with parametric margins for bivariate interval-censored data</i>
---------------	--

Description

Fits a copula model with parametric margins for bivariate interval-censored data.

Usage

```
ic_par_copula(data, var_list, copula, m.dist = "Weibull",
              method = "BFGS", iter = 300, stepsize = 1e-05, hes = TRUE,
              control = list())
```

Arguments

data	a data frame; must have id (subject id), ind (1,2 for two units in each subject), Left (0 if left-censoring), Right (Inf if right-censoring), status (0 for right-censoring, 1 for interval-censoring or left-censoring), and covariates by column.
var_list	the list of covariates to be fitted into the copula model.
copula	Types of copula model.
m.dist	baseline marginal distribution.
method	optimization method (see ?optim); default is "BFGS"; also can be "Newton" (see ?nlm).
iter	number of iterations when method is "Newton"; default is 300.
stepsize	size of optimization step when method is "Newton"; default is 1e-5.
hes	default is TRUE for hessian calculation.
control	a list of control parameters for methods other than "Newton"; see ?optim.

Details

The input data must be a data frame. with columns `id` (sample id), `ind` (1,2 for the two units from the same id), `Left` (0 if left-censoring), `Right` (Inf if right-censoring), `status` (0 for right-censoring, 1 for interval-censoring or left-censoring), and `covariates`. The function does not allow `Left == Right`.

The supported copula models are "Clayton", "Gumbel", "Frank", "AMH", "Joe" and "Copula2". The "Copula2" model is a two-parameter copula model that incorporates Clayton and Gumbel as special cases. The parametric generator functions of copula functions are list below:

The Clayton copula has a generator

$$\phi_{\eta}(t) = (1 + t)^{-1/\eta},$$

with $\eta > 0$ and Kendall's $\tau = \eta/(2 + \eta)$.

The Gumbel copula has a generator

$$\phi_{\eta}(t) = \exp(-t^{1/\eta}),$$

with $\eta \geq 1$ and Kendall's $\tau = 1 - 1/\eta$.

The Frank copula has a generator

$$\phi_{\eta}(t) = -\eta^{-1} \log\{1 + e^{-t}(e^{-\eta} - 1)\},$$

with $\eta \geq 0$ and Kendall's $\tau = 1 + 4\{D_1(\eta) - 1\}/\eta$, in which $D_1(\eta) = \frac{1}{\eta} \int_0^{\eta} \frac{t}{e^t - 1} dt$.

The AMH copula has a generator

$$\phi_{\eta}(t) = (1 - \eta)/(e^t - \eta),$$

with $\eta \in [0, 1)$ and Kendall's $\tau = 1 - 2\{(1 - \eta)^2 \log(1 - \eta) + \eta\}/(3\eta^2)$.

The Joe copula has a generator

$$\phi_{\eta}(t) = 1 - (1 - e^{-t})^{1/\eta},$$

with $\eta \geq 1$ and Kendall's $\tau = 1 - 4 \sum_{k=1}^{\infty} \frac{1}{k(\eta k + 2)\{\eta(k-1) + 2\}}$.

The Two-parameter copula (Copula2) has a generator

$$\phi_{\eta}(t) = \{1/(1 + t^{\alpha})\}^{\kappa},$$

with $\alpha \in (0, 1]$, $\kappa > 0$ and Kendall's $\tau = 1 - 2\alpha\kappa/(2\kappa + 1)$.

The supported marginal distributions are "Weibull" (proportional hazards), "Gompertz" (proportional hazards) and "Loglogistic" (proportional odds). These marginal distributions are listed below and we assume the same baseline parameters between two margins.

The Weibull (PH) survival distribution is

$$\exp\{-(t/\lambda)^k e^{Z^T \beta}\},$$

with $\lambda > 0$ as scale and $k > 0$ as shape.

The Gompertz (PH) survival distribution is

$$\exp\left\{-\frac{b}{a}(e^{at} - 1)e^{Z^T\beta}\right\},$$

with $a > 0$ as shape and $b > 0$ as rate.

The Loglogistic (PO) survival distribution is

$$\{1 + (t/\lambda)^k e^{Z^T\beta}\}^{-1},$$

with $\lambda > 0$ as scale and $k > 0$ as shape.

Optimization methods can be all methods (except "Brent") from `optim`, such as "Nelder-Mead", "BFGS", "CG", "L-BFGS-B", "SANN". Users can also use "Newton" (from `nlm`).

Value

a `CopulaCenR` object summarizing the model. Can be used as an input to general S3 methods including `summary`, `print`, `plot`, `lines`, `coef`, `logLik`, `AIC`, `BIC`, `fitted`, `predict`.

Source

Tao Sun, Yi Liu, Richard J. Cook, Wei Chen and Ying Ding (2019). Copula-based Score Test for Bivariate Time-to-event Data, with Application to a Genetic Study of AMD Progression. *Lifetime Data Analysis* 25(3), 546-568.

Tao Sun and Ying Ding (In Press). Copula-based Semiparametric Regression Model for Bivariate Data under General Interval Censoring. *Biostatistics*. DOI: 10.1093/biostatistics/kxz032.

Examples

```
# fit a Copula2-Weibull model
data(AREDS)
copula2_wb <- ic_par_copula(data = AREDS, copula = "Copula2",
                           m.dist = "Weibull",
                           var_list = c("ENROLLAGE", "rs2284665"))
summary(copula2_wb)
```

ic_spTran_copula	<i>Copula regression models with semiparametric margins for bivariate interval-censored data</i>
------------------	--

Description

Fits a copula model with semiparametric margins for bivariate interval-censored data.

Usage

```
ic_spTran_copula(data, var_list, l = 0, u, copula = "Copula2", m = 3,
                 r = 3, method = "BFGS", iter = 300, stepsize = 1e-06,
                 hes = TRUE, control = list())
```

Arguments

<code>data</code>	a data frame; must have <code>id</code> (subject id), <code>ind</code> (1,2 for two units in each subject), <code>Left</code> (0 if left-censoring), <code>Right</code> (Inf if right-censoring), <code>status</code> (0 for right-censoring, 1 for interval-censoring or left-censoring), and <code>covariates</code> by column.
<code>var_list</code>	the list of covariates to be fitted into the copula model.
<code>l</code>	the left bound for all <code>Left</code> and <code>Right</code> endpoints of observed finite intervals; default is 0.
<code>u</code>	the right bound for all <code>Left</code> and <code>Right</code> endpoints of observed finite intervals; has to be a finite value
<code>copula</code>	Types of copula model.
<code>m</code>	integer, degree of Bernstein polynomials for both margins; default is 3
<code>r</code>	postive transformation parameter for the semiparametric transformation marginal model.
<code>method</code>	optimization method (see <code>?optim</code>); default is "BFGS"; also can be "Newton" (see <code>?nlm</code>).
<code>iter</code>	number of iterations when <code>method = "Newton"</code> ; default is 300.
<code>stepsize</code>	size of optimization step when <code>method = "Newton"</code> ; default is 1e-6.
<code>hes</code>	default is TRUE for hessian calculation; if LRT is desired, can set <code>hes = FALSE</code> to save time.
<code>control</code>	a list of control parameters for methods other than "Newton"; see <code>?optim</code> .

Details

The input data must be a data frame. with columns `id` (sample id), `ind` (1,2 for the two units from the same id), `Left` (0 if left-censoring), `Right` (Inf if right-censoring), `status` (0 for right-censoring, 1 for interval-censoring or left-censoring), and `covariates`. The function does not allow `Left == Right`.

The supported copula models are "Clayton", "Gumbel", "Frank", "AMH", "Joe" and "Copula2". The "Copula2" model is a two-parameter copula model that incorporates Clayton and Gumbel as special cases. The parametric generator functions of copula functions are list below:

The Clayton copula has a generator

$$\phi_{\eta}(t) = (1 + t)^{-1/\eta},$$

with $\eta > 0$ and Kendall's $\tau = \eta/(2 + \eta)$.

The Gumbel copula has a generator

$$\phi_{\eta}(t) = \exp(-t^{1/\eta}),$$

with $\eta \geq 1$ and Kendall's $\tau = 1 - 1/\eta$.

The Frank copula has a generator

$$\phi_{\eta}(t) = -\eta^{-1} \log\{1 + e^{-t}(e^{-\eta} - 1)\},$$

with $\eta \geq 0$ and Kendall's $\tau = 1 + 4\{D_1(\eta) - 1\}/\eta$, in which $D_1(\eta) = \frac{1}{\eta} \int_0^{\eta} \frac{t}{e^t - 1} dt$.

The AMH copula has a generator

$$\phi_{\eta}(t) = (1 - \eta)/(e^t - \eta),$$

with $\eta \in [0, 1)$ and Kendall's $\tau = 1 - 2\{(1 - \eta)^2 \log(1 - \eta) + \eta\}/(3\eta^2)$.

The Joe copula has a generator

$$\phi_{\eta}(t) = 1 - (1 - e^{-t})^{1/\eta},$$

with $\eta \geq 1$ and Kendall's $\tau = 1 - 4 \sum_{k=1}^{\infty} \frac{1}{k(\eta k + 2)\{\eta(k-1) + 2\}}$.

The Two-parameter copula (Copula2) has a generator

$$\phi_{\eta}(t) = \{1/(1 + t^{\alpha})\}^{\kappa},$$

with $\alpha \in (0, 1]$, $\kappa > 0$ and Kendall's $\tau = 1 - 2\alpha\kappa/(2\kappa + 1)$.

The marginal semiparametric transformation models are built based on Bernstein polynomials, which is formulated below:

$$S(t|Z) = \exp[-G\{\Lambda(t)e^{Z^T \beta}\}],$$

where t is time, Z is covariate, β is coefficient and $\Lambda(t)$ is an unspecified function with infinite dimensions. We approximate $\Lambda(t)$ in a sieve space constructed by Bernstein polynomials with degree m . By default, $m = 3$. In the end, all model parameters are estimated by the sieve estimators (Sun and Ding, In Press).

The $G(\cdot)$ function is the transformation function with a parameter $r > 0$, which has a form of $G(x) = \frac{(1+x)^r - 1}{r}$, when $0 < r \leq 2$ and $G(x) = \frac{\log\{1+(r-2)x\}}{r-2}$ when $r > 2$. When $r = 1$, the marginal model becomes a proportional hazards model; when $r = 3$, the marginal model becomes a proportional odds model. In practice, m and r can be selected based on the AIC value.

Optimization methods can be all methods (except "Brent") from `optim`, such as "Nelder-Mead", "BFGS", "CG", "L-BFGS-B", "SANN". Users can also use "Newton" (from `nlm`).

Value

a `CopulaCenR` object summarizing the model. Can be used as an input to general S3 methods including `summary`, `print`, `plot`, `lines`, `coef`, `logLik`, `AIC`, `BIC`, `fitted`, `predict`.

Source

Tao Sun, Yi Liu, Richard J. Cook, Wei Chen and Ying Ding (2019). Copula-based Score Test for Bivariate Time-to-event Data, with Application to a Genetic Study of AMD Progression. *Lifetime Data Analysis* 25(3), 546-568.

Tao Sun and Ying Ding (In Press). Copula-based Semiparametric Regression Model for Bivariate Data under General Interval Censoring. *Biostatistics*. DOI: 10.1093/biostatistics/kxz032.

Examples

```
# fit a Copula2-Semiparametric model
data(AREDS)
copula2_sp <- ic_spTran_copula(data = AREDS, copula = "Copula2",
                             l = 0, u = 15, m = 3, r = 3,
                             var_list = c("ENROLLAGE", "rs2284665", "SevScaleBL"))
summary(copula2_sp)
```

 Kidney

Kidney

Description

A real dataset of bivariate right-censored data with 38 subjects and 3 covariates. The data are the recurrence times to infection, at the point of insertion of the catheter, for kidney patients using portable dialysis equipment. Catheters may be removed for reasons other than infection, in which case the observation is censored. Each patient has exactly 2 observations.

Usage

```
data("Kidney")
```

Format

A data frame with 76 observations on the following 7 variables.

```
id subject id
ind margin indicator
obs_time observed time
status event status
age in years
sex 1=male, 2=female
disease disease type with 4 levels Other GN AN PKD
```

Note

This data has often been used to illustrate the use of random effects (frailty) in a survival model. However, one of the males (id 21) is a large outlier, with much longer survival than his peers. If this observation is removed no evidence remains for a random subject effect.

Source

<https://github.com/therneau/survival>

References

CA McGilchrist, CW Aisbett (1991), Regression with frailty in survival analysis. *Biometrics* **47**, 461-66.

Examples

```
data(Kidney)
clayton_cox <- rc_spCox_copula(data = Kidney,
  var_list = c("age", "sex", "disease"),
  copula = "Clayton",
  method = "BFGS",
  B = 2)
summary(clayton_cox)
```

lines.CopulaCenR *Plotting for CopulaCenR fits*

Description

Plotting for CopulaCenR fits from `ic_spTran_copula`, `rc_spCox_copula`, `ic_par_copula` and `rc_par_copula`.

Usage

```
## S3 method for class 'CopulaCenR'
lines(x, y, class = "joint", newdata,
  evalPoints = 50, evalTimes1 = NULL, evalTimes2 = NULL,
  plot_margin = 1, cond_time = NULL, cond_margin = 2,
  plotly_object = NULL, ...)
```

Arguments

<code>x</code>	an object of <code>ic_spTran_copula</code> , <code>rc_spCox_copula</code> , <code>ic_par_copula</code> , <code>rc_par_copula</code>
<code>y</code>	new data frame with colname names <code>id</code> , <code>ind</code> and <code>covariate</code>
<code>class</code>	one of "joint", "conditional" or "marginal"
<code>newdata</code>	new data frame (ignored if <code>y</code> is included)
<code>evalPoints</code>	number of time points to be evaluated; default is 50
<code>evalTimes1</code>	a vector of times for margin 1 to be evaluated; default is NULL; will override <code>evalPoints</code> if non-NULL
<code>evalTimes2</code>	a vector of times for margin 2 to be evaluated
<code>plot_margin</code>	for <code>class = "marginal"</code> only; indicator of which margin to plot (either 1 or 2); default is 1 for margin 1
<code>cond_time</code>	for <code>class = "conditional"</code> only; the time by which event has occurred in the margin indicated by <code>cond_margin</code> ; must be smaller than the largest observed time

<code>cond_margin</code>	for <code>class = "conditional"</code> only; indicator of the margin where event has occurred (either 1 or 2); default is 2 for margin 2
<code>plotly_object</code>	only for <code>class = "joint"</code> , an object of <code>plot.CopulaCenR</code>
<code>...</code>	further arguments

Details

`y` must be a data frame with columns `id` (subject id), `ind` (1,2 for two margins) and `covariates`. The argument `class` determines the plot: "joint" for joint survival probabilities, "conditional" for conditional probabilities and "marginal" for marginal probabilities.

The function evaluates on a series of time points (given by `evalPoints` or `evalTimes`; `evalTimes` will override `evalPoints`). By default, the time points are automatically selected by specifying the number of points (`evalPoints = 50`). Users can also provide the specific time points through `evalTimes1` and `evalTimes2` for the two margins, respectively. When `class = "conditional"`, only `evalTimes1` is needed and the evaluation times are actually `evalTimes1` plus `cond_time`.

If `class = "conditional"`, one needs to specify the margin that has the event (by `cond_margin`) and time when the event has occurred (by `cond_time`). For example, if `cond_margin = 2` and `cond_time = 5`, then the function produces the conditional survival probability (after time 5) in margin 1 given that margin 2 has got an event by time 5. This measurement is useful for predicting the second event given the first event has occurred. See the example for details.

If `class = "marginal"`, one needs to specify which margin to plot through the argument `plot_margin`. See the example for details.

If `class = "joint"`, one needs to include a `plot_ly` object (from `plot.CopulaCenR` with `class = "joint"`) through the argument `plotly_object`. See the example for details.

Value

a 3D joint survival distribution plot if `class = "joint"`; a 2D survival distribution plot if `class = "marginal"` or "conditional".

Examples

```
data(AREDS)
# fit a Copula2-Sieve model
copula2_sp <- ic_spTran_copula(data = AREDS, copula = "Copula2",
                             l = 0, u = 15, m = 3, r = 3,
                             var_list = c("ENROLLAGE", "rs2284665", "SevScaleBL"))
newdata = data.frame(id = rep(1:3, each=2), ind = rep(c(1,2),3),
                    SevScaleBL = rep(3,6), ENROLLAGE = rep(60,6),
                    rs2284665 = c(0,0,1,1,2,2))
# Plot marginal survival probabilities
plot(x = copula2_sp, class = "marginal",
     newdata = newdata[newdata$id==1,],
     plot_margin = 1, ylim = c(0.6,1),
```

```

      ylab = "Marginal Survival Probability")
lines(x = copula2_sp, class = "marginal",
      newdata = newdata[newdata$id==2,],
      plot_margin = 1, lty = 2)
legend("bottomleft", c("id: 1","id: 2"), lty = c(1,2))

# Plot conditional survival probabilities
plot(x = copula2_sp, class = "conditional",
     newdata = newdata[newdata$id==1,],
     cond_margin = 2, cond_time = 5, ylim = c(0.25,1),
     xlab = "years", ylab = "Conditional Survival Probability")
lines(x = copula2_sp, class = "conditional",
     newdata = newdata[newdata$id==2,],
     cond_margin = 2, cond_time = 5, lty = 2)
legend("bottomleft", c("id: 1","id: 2"), lty = c(1,2))

# Plot joint survival probabilities
plot3d <- plot(x = copula2_sp, class = "joint",
              newdata = newdata[newdata$id==1,])
plot3d <- lines(x = copula2_sp, class = "joint",
               newdata = newdata[newdata$id==2,], plotly_object = plot3d)

```

logLik.CopulaCenR *the log-likelihood of a CopulaCenR object*

Description

the log-likelihood of a CopulaCenR object

Usage

```
## S3 method for class 'CopulaCenR'
logLik(object, ...)
```

Arguments

object	a CopulaCenR object
...	further arguments

lrt_copula *Likelihood-ratio test for covariate effect(s) in copula models*

Description

This function (`lrt_copula`) is used to perform the likelihood ratio test (LRT) between two nested copula models

Usage

```
lrt_copula(model1, model2)
```

Arguments

```
model1      The output of the larger model
model2      The output of the smaller model
```

Value

the LRT statistics, p value

Examples

```
#' # Likelihood-ratio test for "rs2284665" in AREDS data
data(AREDS)
# Fit null model without "rs2284665"
copula2_sp_null <- ic_spTran_copula(data = AREDS, copula = "Copula2",
                                   l = 0, u = 15, m = 3, r = 3,
                                   var_list = c("SevScaleBL"))
# Fit full model
copula2_sp <- ic_spTran_copula(data = AREDS, copula = "Copula2",
                               l = 0, u = 15, m = 3, r = 3,
                               var_list = c("rs2284665", "SevScaleBL"))
lrt_copula(model1 = copula2_sp, model2 = copula2_sp_null)
```

plot.CopulaCenR

Plotting for CopulaCenR fits

Description

Plotting for CopulaCenR fits from `ic_spTran_copula`, `rc_spCox_copula`, `ic_par_copula` and `rc_par_copula`.

Usage

```
## S3 method for class 'CopulaCenR'
plot(x, y, class = "joint", newdata,
     evalPoints = 50, evalTimes1 = NULL, evalTimes2 = NULL,
     plot_margin = 1, cond_time = NULL, cond_margin = 2, type = "l",
     xlab = "years", ylab = "survival probability", cex.main = 1.4,
     cex.lab = 1.4, cex.axis = 1.4, legend = TRUE, ...)
```

Arguments

x	an object of ic_spTran_copula or rc_spCox_copula or ic_par_copula or rc_par_copula
y	new data frame with colname names id, ind and covariate
class	one of "joint", "conditional" or "marginal"
newdata	new data frame (ignored if y is included)
evalPoints	number of time points to be evaluated in both margins; default is 50
evalTimes1	a vector of times for margin 1 to be evaluated; default is NULL; will override evalPoints if non-NULL
evalTimes2	a vector of times for margin 2 to be evaluated
plot_margin	for class = "marginal" only; indicator of which margin to plot (either 1 or 2); default is 1 for margin 1
cond_time	for class = "conditional" only; the time by which event has occurred in the margin indicated by cond_margin; must be smaller than the largest observed time
cond_margin	for class = "conditional" only; indicator of the margin where event has occurred (either 1 or 2); default is 2 for margin 2
type	type of plot with default type = "l".
xlab	a title for the x axis.
ylab	a title for the x axis.
cex.main	cex for main.
cex.lab	cex for lab.
cex.axis	cex for axis.
legend	whether to show legend with default legend = TRUE.
...	further arguments

Details

y must be a data frame with columns id (subject id), ind (1,2 for two margins) and covariates. The argument class determines the plot: "joint" for joint survival probabilities, "conditional" for conditional probabilities and "marginal" for marginal probabilities.

The function evaluates on a series of time points (given by evalPoints or evalTimes; evalTimes will override evalPoints). By default, the time points are automatically selected by specifying the number of points (evalPoints = 50). Users can also provide the specific time points through evalTimes1 and evalTimes2 for the two margins, respectively. When class = "conditional", only evalTimes1 is needed and the evaluation times are actually evalTimes1 plus cond_time.

If class = "conditional", one needs to specify the margin that has the event (by cond_margin) and time when the event has occurred (by cond_time). For example, if cond_margin = 2 and cond_time = 5, then the function produces the conditional survival probability (after time 5) in margin 1 given that margin 2 has got an event by time 5. This measurement is useful for predicting the second event given the first event has occurred. See the example for details.

If class = "marginal", one needs to specify which margin to plot through the argument plot_margin. See the example for details.

Value

a 3D joint survival distribution plot if class = "joint"; a 2D survival distribution plot if class = "marginal" or "conditional".

Examples

```
data(AREDS)
# fit a Copula2-Sieve model
copula2_sp <- ic_spTran_copula(data = AREDS, copula = "Copula2",
                             l = 0, u = 15, m = 3, r = 3,
                             var_list = c("ENROLLAGE", "rs2284665", "SevScaleBL"))
newdata = data.frame(id = rep(1, each=2), ind = rep(c(1,2),1),
                     SevScaleBL = rep(3,2), ENROLLAGE = rep(60,2),
                     rs2284665 = c(0,0))
# Plot joint survival probabilities
plot(x = copula2_sp, class = "joint", newdata = newdata)

# Plot conditional survival probabilities
plot(x = copula2_sp, class = "conditional", newdata = newdata,
     cond_margin = 2, cond_time = 5, ylim = c(0.25,1),
     ylab = "Conditional Survival Probability")

# Plot marginal survival probabilities
plot(x = copula2_sp, class = "marginal", newdata = newdata,
     plot_margin = 1, ylim = c(0.6,1),
     ylab = "Marginal Survival Probability")
```

predict.CopulaCenR *Predictions from CopulaCenR regression models*

Description

Predictions for new observations based on ic_spTran_copula, rc_spCox_copula, ic_par_copula and rc_par_copula.

Usage

```
## S3 method for class 'CopulaCenR'
predict(object, newdata, type = "lp", ...)
```

Arguments

object	a CopulaCenR object from <code>ic_spTran_copula</code> , <code>rc_spCox_copula</code> , <code>ic_par_copula</code> and <code>rc_par_copula</code>
newdata	a data frame (see details)
type	"lp" for linear predictors or "survival" for marginal and joint survival probabilities
...	further arguments

Details

For the newdata, when `type = "survival"`, it must be a data frame with columns `id` (subject id), `ind` (1,2 for two margins), `time` (to be evaluated) and `covariates`; when `type = "lp"`, the newdata needs to have `id`, `ind` and `covariates`, but `time` is not needed.

When the argument `type = "lp"`, it gives a linear predictor for each margin (i.e., log hazards ratio in the proportional hazards model, log proportional odds in the proportional odds model).

When the argument `type = "survival"`, the marginal and joint survival values will be evaluated at the given time points in the newdata.

Value

If `type = "lp"`, it returns a data frame with `id`, `lp1` (linear predictor for margin 1), `lp2`. If `type = "survival"`, it returns a data frame with `id`, `t1` (evaluated times for the margin 1), `t2`, `S1` (predicted marginal survival probabilities for margin 1), `S2` and `S12` (the predicted joint survival probabilities at `t1`, `t2`)

Examples

```
data(AREDS)
# fit a Copula2-Sieve model
copula2_sp <- ic_spTran_copula(data = AREDS, copula = "Copula2",
                             l = 0, u = 15, m = 3, r = 3,
                             var_list = c("ENROLLAGE", "rs2284665", "SevScaleBL"))
# Predicted probabilities for newdata
newdata = data.frame(id = rep(1:3, each=2), ind = rep(c(1,2),3),
                    time = c(2,3,5,6,7,8),
                    SevScaleBL = rep(3,6),
                    ENROLLAGE = rep(60,6),
                    rs2284665 = c(0,0,1,1,2,2))
output <- predict(object = copula2_sp, newdata = newdata)
```

`print.CopulaCenR` *Printing outputs of a CopulaCenR object*

Description

Printing outputs of a CopulaCenR object

Usage

```
## S3 method for class 'CopulaCenR'  
print(x, ...)
```

Arguments

`x` a CopulaCenR object
`...` further arguments

`print.summary.CopulaCenR`
Print the summary of a CopulaCenR object

Description

Print the summary of a CopulaCenR object

Usage

```
## S3 method for class 'summary.CopulaCenR'  
print(x, ...)
```

Arguments

`x` a summary.CopulaCenR object
`...` further arguments

rc_par_copula	<i>Copula regression models with parametric margins for bivariate right-censored data</i>
---------------	---

Description

Fits a copula model with parametric margins for bivariate right-censored data.

Usage

```
rc_par_copula(data, var_list, copula = "Clayton", m.dist = "Weibull",
  method = "BFGS", iter = 500, stepsize = 1e-06, control = list())
```

Arguments

data	a data frame; must have id (subject id), ind (1,2 for two margins), obs_time, status (0 for right-censoring, 1 for event).
var_list	the list of covariates to be fitted into the model.
copula	specify the copula family.
m.dist	specify the marginal baseline distribution.
method	optimization method (see ?optim); default is "BFGS"; also can be "Newton" (see ?nlm).
iter	number of iterations when method = "Newton"; default is 500.
stepsize	size of optimization step when method = "Newton"; default is 1e-6.
control	a list of control parameters for methods other than "Newton"; see ?optim.

Details

The input data must be a data frame with columns id (subject id), ind (1,2 for two margins; each id must have both ind = 1 and 2), obs_time, status (0 for right-censoring, 1 for event) and covariates.

The supported copula models are "Clayton", "Gumbel", "Frank", "AMH", "Joe" and "Copula2". The "Copula2" model is a two-parameter copula model that incorporates Clayton and Gumbel as special cases. The parametric generator functions of copula functions are list below:

The Clayton copula has a generator

$$\phi_{\eta}(t) = (1 + t)^{-1/\eta},$$

with $\eta > 0$ and Kendall's $\tau = \eta/(2 + \eta)$.

The Gumbel copula has a generator

$$\phi_{\eta}(t) = \exp(-t^{1/\eta}),$$

with $\eta \geq 1$ and Kendall's $\tau = 1 - 1/\eta$.

The Frank copula has a generator

$$\phi_{\eta}(t) = -\eta^{-1} \log\{1 + e^{-t}(e^{-\eta} - 1)\},$$

with $\eta \geq 0$ and Kendall's $\tau = 1 + 4\{D_1(\eta) - 1\}/\eta$, in which $D_1(\eta) = \frac{1}{\eta} \int_0^{\eta} \frac{t}{e^t - 1} dt$.

The AMH copula has a generator

$$\phi_{\eta}(t) = (1 - \eta)/(e^t - \eta),$$

with $\eta \in [0, 1)$ and Kendall's $\tau = 1 - 2\{(1 - \eta)^2 \log(1 - \eta) + \eta\}/(3\eta^2)$.

The Joe copula has a generator

$$\phi_{\eta}(t) = 1 - (1 - e^{-t})^{1/\eta},$$

with $\eta \geq 1$ and Kendall's $\tau = 1 - 4 \sum_{k=1}^{\infty} \frac{1}{k(\eta k + 2)\{\eta(k-1) + 2\}}$.

The Two-parameter copula (Copula2) has a generator

$$\phi_{\eta}(t) = \{1/(1 + t^{\alpha})\}^{\kappa},$$

with $\alpha \in (0, 1]$, $\kappa > 0$ and Kendall's $\tau = 1 - 2\alpha\kappa/(2\kappa + 1)$.

The supported marginal distributions are "Weibull" (proportional hazards), "Gompertz" (proportional hazards) and "Loglogistic" (proportional odds). These marginal distributions are listed below and we also assume the same baseline parameters between two margins.

The Weibull (PH) survival distribution is

$$\exp\{-(t/\lambda)^k e^{Z^T \beta}\},$$

with $\lambda > 0$ as scale and $k > 0$ as shape.

The Gompertz (PH) survival distribution is

$$\exp\{-\frac{b}{a}(e^{at} - 1)e^{Z^T \beta}\},$$

with $a > 0$ as shape and $b > 0$ as rate.

The Loglogistic (PO) survival distribution is

$$\{1 + (t/\lambda)^k e^{Z^T \beta}\}^{-1},$$

with $\lambda > 0$ as scale and $k > 0$ as shape.

Optimization methods can be all methods (except "Brent") from `optim`, such as "Nelder-Mead", "BFGS", "CG", "L-BFGS-B", "SANN". Users can also use "Newton" (from `nlm`).

Value

a `CopulaCenR` object summarizing the model. Can be used as an input to general S3 methods including `summary`, `print`, `plot`, `lines`, `coef`, `logLik`, `AIC`, `BIC`, `fitted`, `predict`.

Source

Tao Sun, Yi Liu, Richard J. Cook, Wei Chen and Ying Ding (2019). Copula-based Score Test for Bivariate Time-to-event Data, with Application to a Genetic Study of AMD Progression. *Lifetime Data Analysis* 25(3), 546-568.

Tao Sun and Ying Ding (In Press). Copula-based Semiparametric Regression Model for Bivariate Data under General Interval Censoring. *Biostatistics*. DOI: 10.1093/biostatistics/kxz032.

Examples

```
# fit a Clayton-Weibull model
data(DRS)
clayton_wb <- rc_par_copula(data = DRS, var_list = "treat",
                           copula = "Clayton",
                           m.dist = "Weibull")
summary(clayton_wb)
```

rc_spCox_copula	<i>Copula regression models with Cox semiparametric margins for bivariate right-censored data</i>
-----------------	---

Description

Fits a copula model with Cox semiparametric margins for bivariate right-censored data.

Usage

```
rc_spCox_copula(data, var_list, copula = "Clayton", method = "BFGS",
               iter = 500, stepsize = 1e-06, control = list(), B = 100,
               seed = 1)
```

Arguments

data	a data frame; must have id (subject id), ind (1,2 for two margins), obs_time, status (0 for right-censoring, 1 for event).
var_list	the list of covariates to be fitted into the model.
copula	specify the copula family.
method	optimization method (see ?optim); default is "BFGS"; also can be "Newton" (see ?nlm).
iter	number of iterations when method = "Newton"; default is 500.
stepsize	size of optimization step when method = "Newton"; default is 1e-6.
control	a list of control parameters for methods other than "Newton"; see ?optim.
B	number of bootstraps for estimating standard errors with default 100;
seed	the bootstrap seed; default is 1

Details

The input data must be a data frame with columns `id` (subject id), `ind` (1,2 for two margins; each id must have both `ind = 1` and `2`), `obs_time`, `status` (0 for right-censoring, 1 for event) and `covariates`.

The supported copula models are "Clayton", "Gumbel", "Frank", "AMH", "Joe" and "Copula2". The "Copula2" model is a two-parameter copula model that incorporates Clayton and Gumbel as special cases. The parametric generator functions of copula functions are list below:

The Clayton copula has a generator

$$\phi_{\eta}(t) = (1 + t)^{-1/\eta},$$

with $\eta > 0$ and Kendall's $\tau = \eta/(2 + \eta)$.

The Gumbel copula has a generator

$$\phi_{\eta}(t) = \exp(-t^{1/\eta}),$$

with $\eta \geq 1$ and Kendall's $\tau = 1 - 1/\eta$.

The Frank copula has a generator

$$\phi_{\eta}(t) = -\eta^{-1} \log\{1 + e^{-t}(e^{-\eta} - 1)\},$$

with $\eta \geq 0$ and Kendall's $\tau = 1 + 4\{D_1(\eta) - 1\}/\eta$, in which $D_1(\eta) = \frac{1}{\eta} \int_0^{\eta} \frac{t}{e^t - 1} dt$.

The AMH copula has a generator

$$\phi_{\eta}(t) = (1 - \eta)/(e^t - \eta),$$

with $\eta \in [0, 1)$ and Kendall's $\tau = 1 - 2\{(1 - \eta)^2 \log(1 - \eta) + \eta\}/(3\eta^2)$.

The Joe copula has a generator

$$\phi_{\eta}(t) = 1 - (1 - e^{-t})^{1/\eta},$$

with $\eta \geq 1$ and Kendall's $\tau = 1 - 4 \sum_{k=1}^{\infty} \frac{1}{k(\eta k + 2)\{\eta(k-1) + 2\}}$.

The Two-parameter copula (Copula2) has a generator

$$\phi_{\eta}(t) = \{1/(1 + t^{\alpha})\}^{\kappa},$$

with $\alpha \in (0, 1]$, $\kappa > 0$ and Kendall's $\tau = 1 - 2\alpha\kappa/(2\kappa + 1)$.

The marginal distribution is a Cox semiparametric proportional hazards model. The copula parameter and coefficient standard errors are estimated from bootstrap.

Optimization methods can be all methods (except "Brent") from `optim`, such as "Nelder-Mead", "BFGS", "CG", "L-BFGS-B", "SANN". Users can also use "Newton" (from `nlm`).

Value

a `CopulaCenR` object summarizing the model. Can be used as an input to general S3 methods including `summary`, `print`, `plot`, `lines`, `coef`, `logLik`, `AIC`, `BIC`, `fitted`, `predict`.

Source

Tao Sun, Yi Liu, Richard J. Cook, Wei Chen and Ying Ding (2019). Copula-based Score Test for Bivariate Time-to-event Data, with Application to a Genetic Study of AMD Progression. *Lifetime Data Analysis* 25(3), 546-568.

Tao Sun and Ying Ding (In Press). Copula-based Semiparametric Regression Model for Bivariate Data under General Interval Censoring. *Biostatistics*. DOI: 10.1093/biostatistics/kxz032.

Examples

```
# fit a Clayton-Cox model
data(DRS)
clayton_cox <- rc_spCox_copula(data = DRS, var_list = "treat",
                             copula = "Clayton", B = 2)
summary(clayton_cox)
```

score_copula

*Generalized score test for covariate effect(s)***Description**

Generalized score test on covariate effect(s) under a fitted copula model.

Usage

```
score_copula(object, var_score)
```

Arguments

object	The output object from the main functions (rc_par_copula, rc_spCox_copula, ic_spTran_copula, ic_par_copula) under the null hypothesis
var_score	the list of covariates to be tested by the score test

Value

the score statistics, p value

Examples

```
# Score test for "rs2284665" in AREDS data
# fit a Copula2-semiparametric model under NULL
data(AREDS)
copula2_sp_null <- ic_spTran_copula(data = AREDS, copula = "Copula2",
                                   l = 0, u = 15, m = 3, r = 3,
                                   var_list = c("ENROLLAGE", "SevScaleBL"))
score_copula(object = copula2_sp_null, var_score = "rs2284665")
```

summary.CopulaCenR *Summarizing outputs of a CopulaCenR object*

Description

Summarizing outputs of a CopulaCenR object

Usage

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

Arguments

object	a CopulaCenR object
...	further arguments

tau_copula *Calculate Kendall's tau*

Description

To obtain Kendall's tau from copula parameter(s)

Usage

```
tau_copula(eta, copula)
```

Arguments

eta	copula parameter(s); if copula = "Copula2", input α and κ
copula	specify the type of copula model

Details

The supported copula models are "Clayton", "Gumbel", "Frank", "AMH", "Joe" and "Copula2". The "Copula2" model is a two-parameter copula model that incorporates Clayton and Gumbel as special cases.

The Kendall's τ formulas are list below:

The Clayton copula Kendall's $\tau = \eta/(2 + \eta)$.

The Gumbel copula Kendall's $\tau = 1 - 1/\eta$.

The Frank copula Kendall's $\tau = 1 + 4\{D_1(\eta) - 1\}/\eta$, in which $D_1(\eta) = \frac{1}{\eta} \int_0^\eta \frac{t}{e^t - 1} dt$.

The AMH copula Kendall's $\tau = 1 - 2\{(1 - \eta)^2 \log(1 - \eta) + \eta\}/(3\eta^2)$.

The Joe copula Kendall's $\tau = 1 - 4 \sum_{k=1}^{\infty} \frac{1}{k(\eta^k+2)\{\eta^{(k-1)+2}\}}$.

The Two-parameter copula (Copula2) Kendall's $\tau = 1 - 2\alpha\kappa/(2\kappa + 1)$.

Value

Kendall's τ

Source

Ali MM, Mikhail NN, Haq MS (1978). A Class of Bivariate Distributions Including the Bi- variate Logistic. *Journal of Multivariate Analysis* doi:10.1016/0047-259X(78)90063-5.

Clayton DG (1978). A Model for Association in Bivariate Life Tables and Application in Epidemiological Studies of Familial Tendency in Chronic Disease Incidence. *Biometrika* doi:10.2307/2335289.

Gumbel EJ (1960). Bivariate Exponential Distributions. *Journal of the American Statistical Association* doi:10.2307/2281591.

Joe H (1993). Parametric Families of Multivariate Distributions with Given Margins. *Journal of Multivariate Analysis* doi:10.1006/jmva.1993.1061.

Joe H (1997). Multivariate Models and Dependence Concepts. *Chapman & Hall, London*.

Frank MJ (1979). On the Simultaneous Associativity of $F(x, y)$ and $x + y - F(x, y)$. *Aequationes Mathematicae*.

Examples

```
# fit a Copula2-Semiparametric model
data(AREDS)
copula2_sp <- ic_spTran_copula(data = AREDS, copula = "Copula2",
  l = 0, u = 15, m = 3, r = 3,
  var_list = c("ENROLLAGE", "rs2284665", "SevScaleBL"))
tau_copula(eta = as.numeric(coef(copula2_sp)[c("alpha", "kappa")]),
  copula = "Copula2")
```

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