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genSurv-package

Generating Multi-State Survival Data

# Description

The **genSurv** software permits to generate data with one binary time-dependent covariate and data stemming from a progressive illness-death model.

#### **Details**

Package: genSurv
Type: Package
Version: 1.0.4
Date: 2021-10-19
License: GPL-3
LazyLoad: yes

#### Author(s)

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# References

Anderson, P.K., Gill, R.D. (1982). Cox's regression model for counting processes: a large sample study. *Annals of Statistics*, **10**(4), 1100-1120. doi: 10.1214/aos/1176345976

Cox, D.R. (1972). Regression models and life tables. *Journal of the Royal Statistical Society: Series B*, **34**(2), 187-202. doi: 10.1111/j.25176161.1972.tb00899.x

Jackson, C. (2011). Multi-State Models for Panel Data: The msm Package for R. *Journal of Statistical Software*, **38**(8), 1–28. doi: 10.18637/jss.v038.i08

Johnson, M. E. (1987). Multivariate Statistical Simulation, John Wiley and Sons.

Johnson, N., Kotz, S. (1972). *Distribution in statistics: continuous multivariate distributions*, John Wiley and Sons.

Lu J., Bhattacharya G. (1990). Some new constructions of bivariate weibull models. *Annals of Institute of Statistical Mathematics*, **42**(3), 543-559. doi: 10.1007/BF00049307

Meira-Machado, L., Cadarso-Suárez, C., De Uña- Álvarez, J., Andersen, P.K. (2009). Multi-state models for the analysis of time to event data. *Statistical Methods in Medical Research*, **18**(2), 195-222. doi: 10.1177/0962280208092301

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Meira-Machado L., Faria S. (2014). A simulation study comparing modeling approaches in an illness-death multi-state model. *Communications in Statistics - Simulation and Computation*, **43**(5), 929-946. doi: 10.1080/03610918.2012.718841

Meira-Machado, L., Roca-Pardiñas, J. (2011). p3state.msm: Analyzing Survival Data from an Illness-Death Model. *Journal of Statistical Software*, **38**(3), 1-18. doi: 10.18637/jss.v038.i03

Meira-Machado, L., Sestelo M. (2019). Estimation in the progressive illness-death model: a nonexhaustive review. *Biometrical Journal*, **61**(2), 245–263. doi: 10.1002/bimj.201700200

Therneau, T.M., Grambsch, P.M. (2000). *Modelling survival data: Extending the Cox Model*, New York: Springer.

as.CMM

Coerce to an object of class CMM

#### Description

Function to coerce objects of class TDCM and THMM to objects of class CMM.

# Usage

as.CMM(x)
is.CMM(x)

#### **Arguments**

Х

Any R object.

# Value

An object with two classes one being data. frame and the other CMM.

# Author(s)

Artur Araújo, Luís Meira Machado and Susana Faria

#### References

Cox, D.R. (1972). Regression models and life tables. *Journal of the Royal Statistical Society: Series B*, **34**(2), 187-202. doi: 10.1111/j.25176161.1972.tb00899.x

Jackson, C. (2011). Multi-State Models for Panel Data: The msm Package for R. *Journal of Statistical Software*, **38**(8), 1–28. doi: 10.18637/jss.v038.i08

Meira-Machado, L., Cadarso-Suárez, C., De Uña-Álvarez, J., Andersen, P.K. (2009). Multi-state models for the analysis of time to event data. *Statistical Methods in Medical Research*, **18**(2), 195-222.

Meira-Machado L., Faria S. (2014). A simulation study comparing modeling approaches in an illness-death multi-state model. *Communications in Statistics - Simulation and Computation*, **43**(5), 929-946. doi: 10.1080/03610918.2012.718841

as.TDCM

Meira-Machado, L., Roca-Pardiñas, J. (2011). p3state.msm: Analyzing Survival Data from an Illness-Death Model. *Journal of Statistical Software*, **38**(3), 1-18. doi: 10.18637/jss.v038.i03

Meira-Machado, L., Sestelo M. (2019). Estimation in the progressive illness-death model: a nonexhaustive review. *Biometrical Journal*, **61**(2), 245–263. doi: 10.1002/bimj.201700200

Therneau, T.M., Grambsch, P.M. (2000). *Modelling survival data: Extending the Cox Model*, New York: Springer.

#### See Also

```
as.TDCM, as.THMM, genCMM, genTDCM, genTHMM.
```

#### **Examples**

```
# generate TDCM data
tdcmdata <- genTDCM(n=100, dist="exponential", corr=0, dist.par=c(1,1),
model.cens="uniform", cens.par=1, beta=c(-3,2), lambda=10)

# coerce TDCM data to CMM data
cmmdata0 <- as.CMM(tdcmdata)
head(cmmdata0, n=20L)

# generate THMM data
thmmdata <- genTHMM( n=100, model.cens="uniform", cens.par=80, beta= c(0.09,0.08,-0.09),
covar=80, rate= c(0.05,0.04,0.05) )

# coerce THMM data to CMM data
cmmdata1 <- as.CMM(thmmdata)
head(cmmdata1, n=20L)</pre>
```

as.TDCM

Coerce to an object of class TDCM

### Description

Function to coerce objects of class CMM and THMM to objects of class TDCM.

#### Usage

```
as.TDCM(x)
is.TDCM(x)
```

# Arguments x

# Value

An object with two classes one being data. frame and the other TDCM.

Any R object.

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#### Author(s)

Artur Araújo, Luís Meira Machado and Susana Faria

#### References

Cox, D.R. (1972). Regression models and life tables. *Journal of the Royal Statistical Society: Series B*, **34**(2), 187-202. doi: 10.1111/j.25176161.1972.tb00899.x

Jackson, C. (2011). Multi-State Models for Panel Data: The msm Package for R. *Journal of Statistical Software*, **38**(8), 1–28. doi: 10.18637/jss.v038.i08

Meira-Machado, L., Cadarso-Suárez, C., De Uña-Álvarez, J., Andersen, P.K. (2009). Multi-state models for the analysis of time to event data. *Statistical Methods in Medical Research*, **18**(2), 195-222. doi: 10.1177/0962280208092301

Meira-Machado L., Faria S. (2014). A simulation study comparing modeling approaches in an illness-death multi-state model. *Communications in Statistics - Simulation and Computation*, **43**(5), 929-946. doi: 10.1080/03610918.2012.718841

Meira-Machado, L., Roca-Pardiñas, J. (2011). p3state.msm: Analyzing Survival Data from an Illness-Death Model. *Journal of Statistical Software*, **38**(3), 1-18. doi: 10.18637/jss.v038.i03

Meira-Machado, L., Sestelo M. (2019). Estimation in the progressive illness-death model: a nonexhaustive review. *Biometrical Journal*, **61**(2), 245–263. doi: 10.1002/bimj.201700200

Therneau, T.M., Grambsch, P.M. (2000). *Modelling survival data: Extending the Cox Model*, New York: Springer.

#### See Also

```
as.CMM, as.THMM, genCMM, genTDCM, genTHMM.
```

#### **Examples**

```
# generate CMM data
cmmdata <- genCMM( n=1000, model.cens="uniform", cens.par=2.5, beta=c(2,1,-1),
covar=10, rate=c(1,5,1,5,1,5) )

# coerce CMM data to TDCM data
tdcmdata0 <- as.TDCM(cmmdata)
head(tdcmdata0, n=20L)

# generate THMM data
thmmdata <- genTHMM( n=100, model.cens="uniform", cens.par=80, beta= c(0.09,0.08,-0.09),
covar=80, rate= c(0.05,0.04,0.05) )

# coerce THMM data to TDCM data
tdcmdata1 <- as.TDCM(thmmdata)
head(tdcmdata1, n=20L)</pre>
```

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as.THMM

Coerce to an object of class THMM

### Description

Function to coerce objects of class CMM and TDCM to objects of class THMM.

# Usage

```
as.THMM(x)
is.THMM(x)
```

# **Arguments**

Χ

Any R object.

#### Value

An object with two classes one being data. frame and the other THMM.

#### Author(s)

Artur Araújo, Luís Meira Machado and Susana Faria

#### References

Cox, D.R. (1972). Regression models and life tables. *Journal of the Royal Statistical Society: Series B*, **34**(2), 187-202. doi: 10.1111/j.25176161.1972.tb00899.x

Jackson, C. (2011). Multi-State Models for Panel Data: The msm Package for R. *Journal of Statistical Software*, **38**(8), 1–28. doi: 10.18637/jss.v038.i08

Meira-Machado, L., Cadarso-Suárez, C., De Uña-Álvarez, J., Andersen, P.K. (2009). Multi-state models for the analysis of time to event data. *Statistical Methods in Medical Research*, **18**(2), 195-222. doi: 10.1177/0962280208092301

Meira-Machado L., Faria S. (2014). A simulation study comparing modeling approaches in an illness-death multi-state model. *Communications in Statistics - Simulation and Computation*, **43**(5), 929-946. doi: 10.1080/03610918.2012.718841

Meira-Machado, L., Roca-Pardiñas, J. (2011). p3state.msm: Analyzing Survival Data from an Illness-Death Model. *Journal of Statistical Software*, **38**(3), 1-18. doi: 10.18637/jss.v038.i03

Meira-Machado, L., Sestelo M. (2019). Estimation in the progressive illness-death model: a nonexhaustive review. *Biometrical Journal*, **61**(2), 245–263. doi: 10.1002/bimj.201700200

Therneau, T.M., Grambsch, P.M. (2000). *Modelling survival data: Extending the Cox Model*, New York: Springer.

### See Also

```
as.CMM, as.TDCM, genCMM, genTDCM, genTHMM.
```

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# **Examples**

```
# generate CMM data
cmmdata <- genCMM( n=1000, model.cens="uniform", cens.par=2.5, beta=c(2,1,-1),
covar=10, rate=c(1,5,1,5,1,5) )

# coerce CMM data to THMM data
thmmdata0 <- as.THMM(cmmdata)
head(thmmdata0, n=20L)

# generate TDCM data
tdcmdata <- genTDCM(n=100, dist="exponential", corr=0, dist.par=c(1,1),
model.cens="uniform", cens.par=1, beta=c(-3,2), lambda=10)

# coerce TDCM data to THMM data
thmmdata1 <- as.THMM(tdcmdata)
head(thmmdata1, n=20L)</pre>
```

genCMM

Generation of Cox Markov data from an illness-death model

# Description

Generation of Cox Markov data from an illness-death model.

# Usage

```
genCMM(n, model.cens, cens.par, beta, covar, rate)
```

# **Arguments**

n	Sample size.
model.cens	Model for censorship. Possible values are "uniform" and "exponential".
cens.par	Parameter for the censorship distribution. Must be greater than 0.
beta	Vector of three regression parameters for the three transitions: (beta_12,beta_13,beta_23).
covar	Parameter for generating the time-fixed covariate. An uniform distribution is used.
rate	Vector of dimension six: (shape1, scale1, shape2, scale2, shape3, scale3). A Weibull baseline hazard function is assumed (with two parameters) for each transition (see details below).

# **Details**

The Weibull distribution with shape parameter  $\lambda$  and scale parameter  $\theta$  has hazard function given by:

$$\alpha(t) = \lambda \theta t^{\theta - 1}$$

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#### Value

An object with two classes, data.frame and CMM. The data structure used for generating survival data from the Cox Markov Model (CMM) is similar as for the time-dependent Cox model (TDCM). In this case the data structure has one more variable representing the transition (variable trans). trans=1 denotes the transition from State 1 to State 3 (without observing the intermediate event; State 2); trans=2 denotes the transition from State 1 to State 2; and trans=3 denotes the transition from State 2 to State 3 (absorbing).

# Author(s)

Artur Araújo, Luís Meira Machado and Susana Faria

#### References

Meira-Machado, L., Cadarso-Suárez, C., De Uña-Álvarez, J., Andersen, P.K. (2009). Multi-state models for the analysis of time to event data. *Statistical Methods in Medical Research*, **18**(2), 195-222. doi: 10.1177/0962280208092301

Meira-Machado L., Faria S. (2014). A simulation study comparing modeling approaches in an illness-death multi-state model. *Communications in Statistics - Simulation and Computation*, **43**(5), 929-946. doi: 10.1080/03610918.2012.718841

Meira-Machado, L., Roca-Pardiñas, J. (2011). p3state.msm: Analyzing Survival Data from an Illness-Death Model. *Journal of Statistical Software*, **38**(3), 1-18. doi: 10.18637/jss.v038.i03

Meira-Machado, L., Sestelo M. (2019). Estimation in the progressive illness-death model: a nonexhaustive review. *Biometrical Journal*, **61**(2), 245–263. doi: 10.1002/bimj.201700200

Therneau, T.M., Grambsch, P.M. (2000). *Modelling survival data: Extending the Cox Model*, New York: Springer.

#### See Also

genCPHM, genTDCM, genTHMM.

# **Examples**

```
cmmdata <- genCMM( n=1000, model.cens="uniform", cens.par=2.5, beta=c(2,1,-1),
covar=10, rate=c(1,5,1,5,1,5) )
head(cmmdata, n=20L)
library(survival)
fit_13<-coxph(Surv(start,stop,event)~covariate, data=cmmdata, subset=c(trans==1))
fit_13
fit_12<-coxph(Surv(start,stop,event)~covariate, data=cmmdata, subset=c(trans==2))
fit_12
fit_23<-coxph(Surv(start,stop,event)~covariate, data=cmmdata, subset=c(trans==3))
fit_23</pre>
```

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genCPHM	Generation of survival data from a Cox Proportional Hazard Model

# Description

Generation of survival data from a Cox Proportional Hazard Model.

# Usage

```
genCPHM(n, model.cens, cens.par, beta, covar)
```

#### **Arguments**

n	Sample size.
model.cens	Model for censorship. Possible values are "uniform" and "exponential".
cens.par	Parameter for the censorship distribution. Must be greater than 0.
beta	Regression parameter for the time-fixed covariate.
covar	Parameter for generating the time-fixed covariate. An uniform distribution is used.

#### Value

An object with two classes, data. frame and CPHM.

#### Author(s)

Artur Araújo, Luís Meira Machado and Susana Faria

# References

Cox, D.R. (1972). Regression models and life tables. *Journal of the Royal Statistical Society: Series B*, **34**(2), 187-202. doi: 10.1111/j.25176161.1972.tb00899.x

Meira-Machado L., Faria S. (2014). A simulation study comparing modeling approaches in an illness-death multi-state model. *Communications in Statistics - Simulation and Computation*, **43**(5), 929-946. doi: 10.1080/03610918.2012.718841

Meira-Machado, L., Sestelo M. (2019). Estimation in the progressive illness-death model: a nonexhaustive review. *Biometrical Journal*, **61**(2), 245–263. doi: 10.1002/bimj.201700200

#### See Also

```
genCMM, genTDCM, genTHMM.
```

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# **Examples**

```
cphmdata <- genCPHM(n=1000, model.cens="exponential", cens.par=2, beta= 2, covar=1)
head(cphmdata, n=20L)
library(survival)
fit<-coxph(Surv(time,status)~covariate,data=cphmdata)
summary(fit)</pre>
```

genTDCM

Generating data from a Cox model with time-dependent covariates

# **Description**

Generating data from a Cox model with time-dependent covariates.

### Usage

```
genTDCM(n, dist, corr, dist.par, model.cens, cens.par, beta, lambda)
```

# **Arguments**

n	Sample size.
dist	Bivariate distribution assumed for generating the two covariates (time-fixed and time-dependent). Possible bivariate distributions are "exponential" and "weibull" (see details below).
corr	Correlation parameter. Possible values for the bivariate exponential distribution are between -1 and 1 (0 for independency). Any value between 0 (not included) and 1 (1 for independency) is accepted for the bivariate weibull distribution.
dist.par	Vector of parameters for the allowed distributions. Two (scale) parameters for the bivariate exponential distribution and four (2 shape parameters and 2 scale parameters) for the bivariate weibull distribution: (shape1, scale1, shape2, scale2). See details below.
model.cens	Model for censorship. Possible values are "uniform" and "exponential".
cens.par	Parameter for the censorship distribution. Must be greater than 0.
beta	Vector of two regression parameters for the two covariates.
lambda	Parameter for an exponential distribution. An exponential distribution is assumed for the baseline hazard function.

# **Details**

The bivariate exponential distribution, also known as Farlie-Gumbel-Morgenstern distribution is given by

$$F(x,y) = F_1(x)F_2(y)[1 + \alpha(1 - F_1(x))(1 - F_2(y))]$$

for  $x \ge 0$  and  $y \ge 0$ . Where the marginal distribution functions  $F_1$  and  $F_2$  are exponential with scale parameters  $\theta_1$  and  $\theta_2$  and correlation parameter  $\alpha, -1 \le \alpha \le 1$ .

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The bivariate Weibull distribution with two-parameter marginal distributions. It's survival function is given by

 $S(x,y) = P(X > x, Y > y) = e^{-\left[\left(\frac{x}{\theta_1}\right)^{\frac{\beta_1}{\delta}} + \left(\frac{y}{\theta_2}\right)^{\frac{\beta_2}{\delta}}\right]^{\delta}}$ 

Where  $0 < \delta \le 1$  and each marginal distribution has shape parameter  $\beta_i$  and a scale parameter  $\theta_i$ , i = 1, 2.

#### Value

An object with two classes, data.frame and TDCM. To accommodate time-dependent effects, we used a counting process data-structure, introduced by Andersen and Gill (1982). In this data-structure, apart the time-fixed covariates (named covariate), an individual's survival data is expressed by three variables: start, stop and event. Individuals without change in the time-dependent covariate (named tdcov) are represented by only one line of data, whereas patients with a change in the time-dependent covariate must be represented by two lines. For these patients, the first line represents the time period until the change in the time-dependent covariate; the second line represents the time period that passes from that change to the end of the follow-up. For each line of data, variables start and stop mark the time interval (start, stop) for the data, while event is an indicator variable taking on value 1 if there was a death at time stop, and 0 otherwise. More details about this data-structure can be found in papers by (Meira-Machado et al., 2009).

#### Author(s)

Artur Araújo, Luís Meira Machado and Susana Faria

#### References

Anderson, P.K., Gill, R.D. (1982). Cox's regression model for counting processes: a large sample study. *Annals of Statistics*, **10**(4), 1100-1120. doi: 10.1214/aos/1176345976

Cox, D.R. (1972). Regression models and life tables. *Journal of the Royal Statistical Society: Series B*, **34**(2), 187-202. doi: 10.1111/j.25176161.1972.tb00899.x

Johnson, M. E. (1987). Multivariate Statistical Simulation, John Wiley and Sons.

Johnson, N., Kotz, S. (1972). *Distribution in statistics: continuous multivariate distributions*, John Wiley and Sons.

Lu J., Bhattacharya G. (1990). Some new constructions of bivariate weibull models. *Annals of Institute of Statistical Mathematics*, **42**(3), 543-559. doi: 10.1007/BF00049307

Meira-Machado, L., Cadarso-Suárez, C., De Uña-Álvarez, J., Andersen, P.K. (2009). Multi-state models for the analysis of time to event data. *Statistical Methods in Medical Research*, **18**(2), 195-222. doi: 10.1177/0962280208092301

Meira-Machado L., Faria S. (2014). A simulation study comparing modeling approaches in an illness-death multi-state model. *Communications in Statistics - Simulation and Computation*, **43**(5), 929-946. doi: 10.1080/03610918.2012.718841

Meira-Machado, L., Sestelo M. (2019). Estimation in the progressive illness-death model: a nonexhaustive review. *Biometrical Journal*, **61**(2), 245–263. doi: 10.1002/bimj.201700200

Therneau, T.M., Grambsch, P.M. (2000). *Modelling survival data: Extending the Cox Model*, New York: Springer.

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#### See Also

```
genCMM, genCPHM, genTHMM.
```

### **Examples**

```
tdcmdata <- genTDCM(n=1000, dist="weibull", corr=0.8, dist.par=c(2,3,2,3),
model.cens="uniform", cens.par=2.5, beta=c(-3.3,4), lambda=1)
head(tdcmdata, n=20L)
library(survival)
fit1<-coxph(Surv(start,stop,event)~tdcov+covariate,data=tdcmdata)
summary(fit1)

tdcmdata2 <- genTDCM(n=1000, dist="exponential", corr=0, dist.par=c(1,1),
model.cens="uniform", cens.par=1, beta=c(-3,2), lambda=0.5)
head(tdcmdata2, n=20L)
fit2<-coxph(Surv(start,stop,event)~tdcov+covariate,data=tdcmdata2)
summary(fit2)</pre>
```

genTHMM

Generation of survival data from a time-homogeneous Markov model

#### **Description**

Generation of survival data from a time-homogeneous Markov model.

# Usage

```
genTHMM(n, model.cens, cens.par, beta, covar, rate)
```

# **Arguments**

n Sample size.

model.cens Model for censorship. Possible values are "uniform" and "exponential". cens.par Parameter for the censorship distribution. Must be greater than 0.

beta Vector of three regression parameters for the three transitions: (beta\_12,beta\_13,beta\_23).

covar Parameter for generating the time-fixed covariate. An uniform distribution is

used.

rate Vector of dimension three. We assume an exponential baseline hazard function

with constant hazard rate for each transition.

#### Value

An object with two classes, data.frame and THMM. For generating survival data from the THMM model, the counting process data structure must contain the following variables: id, time, state, covariate. Each patient is identified by id. The variable time represents time for each interval of follow-up while variable state denotes the state of the individual. Variable covariate is the (time-fixed) covariate to be studied in the regression model. Individuals without change in the time dependent covariate are represented by two lines of data, whereas patients with a change in the time-dependent covariate must be represented by three lines.

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#### Author(s)

Artur Araújo, Luís Meira Machado and Susana Faria

#### References

Jackson, C. (2011). Multi-State Models for Panel Data: The msm Package for R. *Journal of Statistical Software*, **38**(8), 1–28. doi: 10.18637/jss.v038.i08

Meira-Machado, L., Cadarso-Suárez, C., De Uña-Álvarez, J., Andersen, P.K. (2009). Multi-state models for the analysis of time to event data. *Statistical Methods in Medical Research*, **18**(2), 195-222. doi: 10.1177/0962280208092301

Meira-Machado L., Faria S. (2014). A simulation study comparing modeling approaches in an illness-death multi-state model. *Communications in Statistics - Simulation and Computation*, **43**(5), 929-946. doi: 10.1080/03610918.2012.718841

Meira-Machado, L., Sestelo M. (2019). Estimation in the progressive illness-death model: a nonexhaustive review. *Biometrical Journal*, **61**(2), 245–263. doi: 10.1002/bimj.201700200

Therneau, T.M., Grambsch, P.M. (2000). *Modelling survival data: Extending the Cox Model*, New York: Springer.

#### See Also

```
genCMM, genTDCM, genCPHM.
```

#### **Examples**

```
thmmdata <- genTHMM( n=100, model.cens="uniform", cens.par=80, beta= c(0.09,0.08,-0.09), covar=80, rate= c(0.05,0.04,0.05) ) head(thmmdata, n=20L)
```

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