Package 'reReg'

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Title Recurrent Event Regression

Version 1.3.0

Description A collection of regression models for recurrent event process and failure time data. Available methods in-

clude these from Xu et al. (2017) <doi:10.1080/01621459.2016.1173557>, Lin et al. (2000) <doi:10.1111/1467-9868.00259>, Wang et al. (2001) <doi:10.1198/016214501753209031>, Ghosh and Lin (2003) <doi:10.1111/j.0006-341X.2003.00102.x>, and Huang and Wang (2004) <doi:10.1198/016214504000001033>.

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BugReports http://github.com/stc04003/reReg/issues

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Author Sy Han (Steven) Chiou [aut, cre],

Chiung-Yu Huang [aut]

Maintainer Sy Han (Steven) Chiou <schiou@utdallas.edu>

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reReg-package reReg: Recurrent Event Regression

Description

The package provides an easy access to fit semiparametric regression models to recurrent event data. The available implementations allow users to explore recurrent data through event plot and the cumulative sample mean function plot, simulate recurrent event data, and fit semiparametric regression models under different assumptions.

Author(s)

Maintainer: Sy Han (Steven) Chiou <schiou@utdallas.edu>

Authors:

• Chiung-Yu Huang <ChiungYu.Huang@ucsf.edu>

References

Lin, D., Wei, L., Yang, I. and Ying, Z. (2000). Semiparametric Regression for the Mean and Rate Functions of Recurrent Events. *Journal of the Royal Statistical Society: Series B (Methodological)*, **62**: 711–730.

Wang, M.-C., Qin, J., and Chiang, C.-T. (2001). Analyzing Recurrent Event Data with Informative Censoring. *Journal of the American Statistical Association*, **96**(455): 1057–1065.

Ghosh, D. and Lin, D.Y. (2002). Marginal Regression Models for Recurrent and Terminal Events. *Statistica Sinica*: 663–688.

Ghosh, D. and Lin, D.Y. (2003). Semiparametric Analysis of Recurrent Events Data in the Presence of Dependent Censoring. *Biometrics*, **59**: 877–885.

Huang, C.-Y. and Wang, M.-C. (2004). Joint Modeling and Estimation for Recurrent Event Processes and Failure Time Data. *Journal of the American Statistical Association*, **99**(468): 1153–1165.

Xu, G., Chiou, S.H., Huang, C.-Y., Wang, M.-C. and Yan, J. (2017). Joint Scale-change Models for Recurrent Events and Failure Time. *Journal of the American Statistical Association*, **112**(518): 796–805.

Xu, G., Chiou, S.H., Yan, J., Marr, K., and Huang, C.-Y. (2019). Generalized Scale-Change Models for Recurrent Event Processes under Informative Censoring. *Statistica Sinica*: pre-print.

plot.Recur

See Also

Useful links:

- http://github.com/stc04003/reReg
- Report bugs at http://github.com/stc04003/reReg/issues

```
plot.Recur
```

Produce Event Plot or Mean Cumulative Function Plot

Description

Plot the event plot or the mean cumulative function (MCF) from an Recur object.

Usage

```
## S3 method for class 'Recur'
plot(
    x,
    mcf = FALSE,
    event.result = c("increasing", "decreasing", "asis"),
    mcf.adjrisk = TRUE,
    mcf.smooth = FALSE,
    control = list(),
    ...
)
```

Arguments

x	an object of class Recur returned by the Recur() function. See ?Recur for creating Recur objects.
mcf	an optional logical value indicating whether the mean cumulative function (MCF) will be plotted instead of the event plot (default).
event.result	an optional character string that is passed to the plotEvents() function as the result argument. See plotEvents. This argument is used to specify whether the event plot is sorted by the subjects' terminal time. The available options are
	increasing sort the terminal time from in ascending order (default). This places longer terminal times on top.
	decreasing sort the terminal time from in descending order (default). This places shorter terminal times on top.
	asis present the as is, without sorting.
mcf.adjrisk	an optional logical value that is passed to the plotMCF() function as the adjrisk argument. See plotMCF. This argument indicates whether risk set size will be adjusted. If mcf.adjrisk = TRUE, subjects leave the risk set after terminal times as in the Nelson-Aalen estimator. If mcf.adjrisk = FALSE, subjects remain in the risk set after terminal time.

mcf.smooth	an optional logical value that is passed to the plotMCF() function as the smooth
	argument. See plotMCF. This argument indicates whether to add a smooth curve
	obtained from a monotone increasing P-splines implemented in package scam.
control	a list of control parameters. See Details.
	additional graphical parameters to be passed to methods.

Details

The argument control consists of options with argument defaults to a list with the following values:

xlab customizable x-label, default value is "Time".

- ylab customizable y-label, default value is "Subject" for event plot and "Cumulative mean" for MCF plot.
- **main** customizable title, the default value is "Recurrent event plot" when mcf = FALSE and "Sample cumulative mean function plot" when mcf = TRUE.
- terminal.name customizable label for terminal event, default value is "Terminal event".
- recurrent.name customizable legend title for recurrent event, default value is "Recurrent events".

recurrent.types customizable label for recurrent event type, default value is NULL.

alpha between 0 and 1, controls the transparency of points.

The xlab, ylab and main parameters can also be passed down without specifying a control list. See **Examples**.

Value

A ggplot object.

References

Nelson, W. B. (1995) Confidence Limits for Recurrence Data-Applied to Cost or Number of Product Repairs. *Technometrics*, **37**(2): 147–157.

See Also

Recur, plotEvents, plotMCF

```
data(simDat)
reObj <- with(simDat, Recur(Time, id, event, status))</pre>
```

```
## Event plots:
plot(re0bj)
plot(re0bj, event.result = "decreasing")
```

```
## MCF plots
plot(reObj, mcf = TRUE)
plot(reObj, mcf = TRUE, mcf.adjrisk = FALSE)
```

plot.reReg

```
## With (hypothetical) multiple event types
set.seed(1)
reObj2 <- with(simDat, Recur(Time, id, event * sample(1:3, nrow(simDat), TRUE), status))
plot(reObj2)</pre>
```

plot.reReg

Plot the Baseline Cumulative Rate Function and the Baseline Cumulative Hazard Function

Description

Plot the baseline cumulative rate function and the baseline cumulative hazard function (if applicable) for an reReg object.

Usage

```
## S3 method for class 'reReg'
plot(
    x,
    baseline = c("both", "rate", "hazard"),
    smooth = FALSE,
    control = list(),
    ...
)
```

Arguments

х	an object of class reReg, returned by the reReg function.
baseline	a character string specifying which baseline function to plot.
	<pre>baseline = "both" plot both the baseline cumulative rate and the baseline cu- mulative hazard function (if applicable) in separate panels within the same display (default).</pre>
	baseline = "rate" plot the baseline cumulative rate function.
	baseline = "hazard" plot the baseline cumulative hazard function.
smooth	an optional logical value indicating whether to add a smooth curve obtained from a monotone increasing P-splines implemented in package scam.
control	a list of control parameters. See Details .
	additional graphical parameters to be passed to methods.

Details

The argument control consists of options with argument defaults to a list with the following values:

xlab customizable x-label, default value is "Time".

- ylab customizable y-label, default value is empty.
- main customizable title, default value are "Baseline cumulative rate and hazard function" when baseline = "both", "Baseline cumulative rate function" when baseline = "rate", and "Baseline cumulative hazard function" when baseline = "hazard".

Value

A ggplot object.

See Also

reReg

Examples

```
data(simDat)
fm <- Recur(Time, id, event, status) ~ x1 + x2
fit <- reReg(fm, data = simDat, method = "cox", B = 0)
plot(fit)
plot(fit, baseline = "rate")
plot(fit, baseline = "rate", xlab = "Time (days)", smooth = TRUE)</pre>
```

plotEvents

Produce Event Plots

Description

Plot the event plot for an Recur object. The usage of the function is similar to that of plot.Recur() but with more flexible options.

Usage

```
plotEvents(
  formula,
  data,
  result = c("increasing", "decreasing", "asis"),
  control = list(),
  ...
)
```

Arguments

formula	a formula object, with the response on the left of a "~" operator, and the pre- dictors on the right. The response must be a recurrent event survival object as returned by function Recur().
data	an optional data frame in which to interpret the variables occurring in the "formula".
result	an optional character string specifying whether the event plot is sorted by the subjects' terminal time. The available options are
	increasing sort the terminal time from in ascending order (default). This places longer terminal times on top.

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plotEvents

	decreasing sort the terminal time from in descending order (default). This places shorter terminal times on top.
	asis present the as is, without sorting.
control	a list of control parameters.
	graphical parameters to be passed to methods. These include xlab, ylab, main, and more. See Details .

Details

The argument control consists of options with argument defaults to a list with the following values:

xlab customizable x-label, default value is "Time".

ylab customizable y-label, default value is "Subject".

main customizable title, default value is "Recurrent event plot".

terminal.name customizable label for terminal event, default value is "Terminal event".

recurrent.name customizable legend title for recurrent event, default value is "Recurrent events".

recurrent.types customizable label for recurrent event type, default value is NULL.

alpha between 0 and 1, controls the transparency of points.

legend a character string specifying the position of the legend (if any). The available options are "right", "left", "top", "bottom", and "none". The default value is "right".

Value

A ggplot object.

See Also

Recur, plot.Recur

plotHaz

Description

Plot the baseline cumulative hazard function for an reReg object. The 95% confidence interval on the baseline cumulative rate function

Usage

plotHaz(x, smooth = FALSE, control = list(), ...)

Arguments

х	an object of class reReg, returned by the reReg function.
smooth	an optional logical value indicating whether to add a smooth curve obtained from a monotone increasing P-splines implemented in package scam.
control	a list of control parameters.
	graphical parameters to be passed to methods. These include xlab, ylab, main, and more. See Details .

Details

The argument control consists of options with argument defaults to a list with the following values:

xlab customizable x-label, default value is "Time".

ylab customizable y-label, default value is empty.

main customizable title, default value is "Baseline cumulative hazard function".

These arguments can also be passed down without specifying a control list. See Examples.

Value

A ggplot object.

See Also

reReg plot.reReg

```
data(simDat)
fm <- Recur(Time, id, event, status) ~ x1 + x2
fit <- reReg(fm, data = simDat, method = "cox", B = 0)
## Plot both the baseline cumulative rate and hazard function
plot(fit)</pre>
```

plotMCF

```
## Plot baseline cumulative hazard function
plotHaz(fit)
plotHaz(fit, smooth = TRUE)
```

plotMCF

Produce Cumulative Sample Mean Function Plots

Description

Plot the mean cumulative function (MCF) for an Recur object. The usage of the function is similar to that of plot.Recur() but with more flexible options.

Usage

```
plotMCF(
   formula,
   data,
   onePanel = FALSE,
   adjrisk = TRUE,
   smooth = FALSE,
   control = list(),
   ...
)
```

Arguments

formula	a formula object, with the response on the left of a "~" operator, and the predic- tors on the right. The response must be a recurrent event survival object returned by the Recur() function.
data	an optional data frame in which to interpret the variables occurring in the "formula"
onePanel	an optional logical value indicating whether the mean cumulative functions will be plotted in the same panel. This is only useful when there are multiple recur- rent event types or in the presence of (discrete) covariates.
adjrisk	an optional logical value that is passed to the plotMCF() function as the adjrisk argument. See plotMCF. This argument indicates whether risk set size will be adjusted. If mcf.adjrisk = TRUE, subjects leave the risk set after terminal times as in the Nelson-Aalen estimator. If mcf.adjrisk = FALSE, subjects remain in the risk set after terminal time.
smooth	an optional logical value indicating whether to add a smooth curve obtained from a monotone increasing P-splines implemented in package scam. This feature only works for data with one recurrent event type.
control	a list of control parameters.
	graphical parameters to be passed to methods. These include xlab, ylab, main, and more. See Details .

Details

When adjrisk = TRUE, the plotMCF() is equivalent to the Nelson-Aalen estimator for the intensity function of the recurrent event process. When adjrisk = FALSE, the plotMCF() does not adjust for the risk set and assumes all subjects remain at risk after the last observed recurrent event. This is known as the survivor rate function. The argument control consists of options with argument defaults to a list with the following values:

xlab customizable x-label, default value is "Time".

ylab customizable y-label, default value is "Cumulative mean".

main customizable title, default value is "Sample cumulative mean function plot".

The xlab, ylab and main parameters can also be passed down without specifying a control list.

Value

A ggplot object.

See Also

Recur, plot.Recur

Examples

```
data(simDat)
plotMCF(Recur(Time, id, event, status) ~ 1, data = simDat)
plotMCF(Recur(Time, id, event, status) ~ x1, data = simDat, onePanel = TRUE)
```

plotRate	Plotting th	e Baseline	Cumulative	Rate	Function	for	the	Recurrent
	Event Proc	ess						

Description

Plot the baseline rate function for an reReg object.

Usage

```
plotRate(
    x,
    type = c("unrestricted", "scaled", "raw"),
    smooth = FALSE,
    control = list(),
    ...
)
```

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plotRate

Arguments

х	an object of class reReg, usually returned by the reReg function.
type	a character string specifying the type of rate function to be plotted. Options are "unrestricted", "scaled", "raw". See Details .
smooth	an optional logical value indicating whether to add a smooth curve obtained from a monotone increasing P-splines implemented in package scam.
control	a list of control parameters.
	graphical parameters to be passed to methods. These include xlab, ylab, main, and more. See Details .

Details

The plotRate() plots the estimated baseline cumulative rate function depending on the identifiability assumption. When type = "unrestricted" (default), the baseline cumulative rate function is plotted under the assumption E(Z) = 1. When type = "scaled", the baseline cumulative rate function is plotted under the assumption $\Lambda(\min(Y^*, \tau)) = 1$. When type = "raw", the baseline cumulative rate function is plotted under the assumption $\Lambda(\tau) = 1$. See ?reReg for the specification of the notations and underlying models.

The argument control consists of options with argument defaults to a list with the following values:

xlab customizable x-label, default value is "Time".

ylab customizable y-label, default value is empty.

main customizable title, default value is "Baseline cumulative rate function".

These arguments can also be passed down without specifying a control list. See **Examples**.

Value

A ggplot object.

See Also

reReg plot.reReg

```
data(simDat)
fm <- Recur(Time, id, event, status) ~ x1 + x2</pre>
```

```
fit <- reReg(fm, data = simDat, method = "cox", B = 0)
## Plot both the baseline cumulative rate and hazard function
plot(fit)
## Plot baseline cumulative rate function
plotRate(fit)
plotRate(fit, smooth = TRUE)</pre>
```

Recur

Description

Create a recurrent event survival object, used as a response variable in reReg. This function is replacing the original reSurv() in version 1.1.6. See ?reda::Recur for more details.

See Also

%2%

Examples

Recur(2:6, id = c(1, 1, 1, 2, 2)) Recur(2:6, id = c(1, 1, 1, 2, 2)) Recur(1:5 %2% 2:6, id = c(1, 1, 1, 2, 2))

Recur-pipe

The %to% function is imported from reda

Description

This pipe operator specifies the time segments or recurrent episodes by endpoints. See reda for more details.

Examples

```
Recur(2:6, id = c(1, 1, 1, 2, 2))
Recur(2:6, id = c(1, 1, 1, 2, 2))
Recur(1:5 %2% 2:6, id = c(1, 1, 1, 2, 2))
```

reReg

Fits Semiparametric Regression Models for Recurrent Event Data

Description

Fits a general (joint) semiparametric regression model for the recurrent event data, where the rate function of the underlying recurrent event process and the hazard function of the terminal event can be specified as a Cox-type model, an accelerated mean model, an accelerated rate model, or a generalized scale-change model. See details for model specifications.

reReg

Usage

```
reReg(
  formula,
  data,
  B = 200,
  method = "cox",
  se = c("resampling", "bootstrap", "NULL"),
  control = list()
)
```

Arguments

formula	a formula object, with the response on the left of a "~" operator, and the pre- dictors on the right. The response must be a recurrent event survival object as returned by function Recur.
data	an optional data frame in which to interpret the variables occurring in the "formula"
В	a numeric value specifies the number of resampling for variance estimation. When $B = 0$, variance estimation will not be performed.
method	a character string specifying the underlying model. See Details.
se	a character string specifying the method for standard error estimation. See De-tails .
control	a list of control parameters.

Details

Suppose the recurrent event process and the failure events are observed in the time interval $t \in [0, \tau]$, for some constant τ . We formulate the recurrent event rate function, $\lambda(t)$, and the terminal event hazard function, h(t), in the form of

$$\lambda(t) = Z\lambda_0(te^{X^\top \alpha})e^{X^\top \beta}, h(t) = Zh_0(te^{X^\top \eta})e^{X^\top \theta},$$

where $\lambda_0(t)$ is the baseline rate function, $h_0(t)$ is the baseline hazard function, X is a n by p covariate matrix and α , Z is an unobserved shared frailty variable, and (α, η) and (β, θ) correspond to the shape and size parameters of the rate function and the hazard function, respectively. The model includes several popular semiparametric models as special cases, which can be specified via the method argument with the rate function and hazard function separated by "|". For examples, Wang, Qin and Chiang (2001) ($\alpha = \eta = \theta = 0$) can be called with method = "cox|."; Huang and Wang (2004) ($\alpha = \eta = 0$) can be called with method = "cox|cox"; Xu et al. (2017) ($\alpha = \beta$ and $\eta = \theta$) can be called with method = "am|am"; Xu et al. (2019) ($\eta = \theta = 0$) can be called with method = "sc|.". Users can mix the models depending on the application. For example, method = "cox|ar" postulate a Cox proportional model for the recurrent event rate function and an accelerated rate model for the terminal event hazard function ($\alpha = \theta = 0$). If only one method is specified without an "|", it is used for both the rate function and the hazard function. For example, specifying method = "cox" is equivalent to method = "cox|cox". Some methods that assumes Z = 1 and requires independent censoring are also implemented in reReg; these includes method = "cox.LWYY" for Lin et al. (2000), method = "cox.GL" for Ghosh and Lin (2002), and method = "am.GL" for Ghosh and Lin (2003).

The available methods for variance estimation are:

NULL variance estimation will not be performed. This is equivalent to setting B = 0.

resampling performs the efficient resampling-based variance estimation.

bootstrap performs nonparametric bootstrap.

The control list consists of the following parameters:

- tol absolute error tolerance.
- **a0, b0** initial guesses used for root search.
- solver the equation solver used for root search. The available options are BB::BBsolve, BB::dfsane, BB:BBoptim, and optim.
- **baseSE** an logical value indicating whether the 95% confidence bounds for the baseline functions will be computed.
- **parallel** an logical value indicating whether parallel computation will be applied when se = "bootstrap" is called.
- **parCl** an integer value specifying the number of CPU cores to be used when parallel = TRUE. The default value is half the CPU cores on the current host.

References

Lin, D., Wei, L., Yang, I. and Ying, Z. (2000). Semiparametric Regression for the Mean and Rate Functions of Recurrent Events. *Journal of the Royal Statistical Society: Series B (Methodological)*, **62**: 711–730.

Wang, M.-C., Qin, J., and Chiang, C.-T. (2001). Analyzing Recurrent Event Data with Informative Censoring. *Journal of the American Statistical Association*, **96**(455): 1057–1065.

Ghosh, D. and Lin, D.Y. (2002). Marginal Regression Models for Recurrent and Terminal Events. *Statistica Sinica*: 663–688.

Ghosh, D. and Lin, D.Y. (2003). Semiparametric Analysis of Recurrent Events Data in the Presence of Dependent Censoring. *Biometrics*, **59**: 877–885.

Huang, C.-Y. and Wang, M.-C. (2004). Joint Modeling and Estimation for Recurrent Event Processes and Failure Time Data. *Journal of the American Statistical Association*, **99**(468): 1153–1165.

Xu, G., Chiou, S.H., Huang, C.-Y., Wang, M.-C. and Yan, J. (2017). Joint Scale-change Models for Recurrent Events and Failure Time. *Journal of the American Statistical Association*, **112**(518): 796–805.

Xu, G., Chiou, S.H., Yan, J., Marr, K., and Huang, C.-Y. (2019). Generalized Scale-Change Models for Recurrent Event Processes under Informative Censoring. *Statistica Sinica*: pre-print.

See Also

Recur, simSC

reSurv

Examples

reSurv

Create an reSurv Object

Description

Create a recurrent event survival object, used as a response variable in reReg. This function is deprecated in Version 1.1.6. A recurrent event object is now being created with Recur(). See '?Recur()' for details.

Usage

```
reSurv(time1, time2, id, event, status, origin = 0)
```

Arguments

time1	when "time2" is provided, this vector is treated as the starting time for the gap time between two successive recurrent events. In the absence of "time2", this is the observation time of recurrence on calendar time scale, in which, the time corresponds to the time since entry/inclusion in the study.
time2	an optional vector for ending time for the gap time between two successive re- current events.
id	subject's id.
event	a binary vector used as the recurrent event indicator. event = 1 for recurrent times.
status	a binary vector used as the status indicator for the terminal event. status = 0 for censored times.
origin	a numerical vector indicating the time origin of subjects. When origin is a scalar, reSurv assumes all subjects have the same origin. Otherwise, origin needs to be a numerical vector, with length equals to the number of subjects. In this case, each element corresponds to different origins for different subjects. This argument is only needed when "time2" is missing.

simDat

Examples

```
## Not run:
    data(simDat)
    ## being deprecated in Verson 1.1.7
    with(dat, reSurv(Time, id, event, status))
    ## Use Recur() instead
    with(dat, Recur(Time, id, event, status))
## End(Not run)
```

simDat

Simulated dataset for demonstration

Description

A simulated data frame with variables

id subjects identification

Time observation time

status terminal event indicator; 1 if a terminal event is recorded

event recurrent event indicator; 1 if a recurrent event is recorded

x1 baseline covariate generated from a standard uniform distribution

x2 baseline covariate generated from a standard uniform distribution (independent from z1

Usage

data(simDat)

Format

A data frame with 274 rows and 6 variables.

Details

The sample dataset is generated by set.seed(1); simSC(30, c(-1, 1), c(-1, 1)). See simSC for instruction on simulating recurrent event data from scale-change models.

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Description

The function simSC() generates simulated recurrent event data from either a Cox-type model, an accelerated mean model, an accelerated rate model, or a scale-change model.

Usage

```
simSC(
    n,
    a1 = a2,
    b1 = b2,
    a2 = a1,
    b2 = b1,
    type = "cox",
    zVar = 0.25,
    tau = 60,
    summary = FALSE
)
```

Arguments

n	number of observation.
a1, a2, b1, b2	are numeric vectors of length 2. These correspond to the α , β , η , and θ in the joint model. See Details
type	is a character string specifying the underlying model. The rate function type and the hazard function type are separated by a vertical bar "I", with the rate function on the left. For example, type = " $cox am$ " generates the recurrent process from a Cox model and the terminal event from an accelerated mean model. Setting type = " cox " gives type = " $cox cox$ ".
zVar	a numeric variable specifying the variance of the fraility variable, Z, when zVar > 0. When zVar = 0, Z is set to a fixed constant 1. The default value is 0.25.
tau	a numeric value specifying the maximum observation time.
summary	a logical value indicating whether a brief data summary will be printed.

Details

The function simSC() generates simulated recurrent event data over the interval $(0, \tau)$ based on the specification of the recurrent process and the terminal events. Specifically, the rate function, $\lambda(t)$, of the recurrent process can be specified as one of the following model:

$$\lambda(t) = Z\lambda_0(te^{X^{\top}\alpha})e^{X^{\top}\beta}, h(t) = Zh_0(te^{X^{\top}\eta})e^{X^{\top}\theta},$$

where $\lambda_0(t)$ is the baseline rate function, $h_0(t)$ is the baseline hazard function, X is a n by p covariate matrix and α , Z is an unobserved shared frailty variable, and (α, η) and (β, θ) correspond to the shape and size parameters of the rate function and the hazard function, respectively.

For all scenarios, two covariates are considered; $X = (X_1, X_2)$, where X_1 follows a Bernoulli distribution with probability 0.5 and X_2 follows a standard normal distribution. The censoring time could be either independent (given covariates) or informative. The simulated data is used for illustration. An informative censoring time, C, is generated separately from an exponential distribution with a rate parameter of 1 / 60 if X_1 is 1, or $Z^2/30$ if X_1 is 0. The observed recurrent events is then observed up to the minimum of C, terminal event, and τ . Lastly, we assume the baseline functions

$$\lambda_0(t) = \frac{2}{1+t}, h_0(t) = \frac{1}{8(1+t)}.$$

See Also

reReg

Examples

set.seed(123)
simSC(100, c(-1, 1), c(-1, 1), summary = TRUE)

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