

Package ‘SmoothHazard’

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Title Estimation of Smooth Hazard Models for Interval-Censored Data
with Applications to Survival and Illness-Death Models

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Description Estimation of two-state (survival) models and irreversible illness-death models with possibly interval-censored, left-truncated and right-censored data. Proportional intensities regression models can be specified to allow for covariates effects separately for each transition. We use either a parametric approach with Weibull baseline intensities or a semi-parametric approach with M-splines approximation of baseline intensities in order to obtain smooth estimates of the hazard functions. Parameter estimates are obtained by maximum likelihood in the parametric approach and by penalized maximum likelihood in the semi-parametric approach.

Encoding UTF-8

Depends R (>= 1.9.1), prodlim (>= 1.4.9)

Imports lava (>= 1.4.1), mvtnorm (>= 1.0-3)

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idm	<i>Fit an illness-death model</i>
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Description

Fit an illness-death model using either a semi-parametric approach (penalized likelihood with an approximation of the transition intensity functions by linear combination of M-splines) or a parametric approach (specifying Weibull distributions on the transition intensities). Left-truncated, right-censored, and interval-censored data are allowed. State 0 corresponds to the initial state, state 1 to the transient one, state 2 to the absorbant one. The allowed transitions are: 0 → 1, 0 → 2 and 1 → 2.

Usage

```
idm(
  formula01,
  formula02,
  formula12,
  data,
  maxiter = 200,
  eps = c(5, 5, 3),
  n.knots = c(7, 7, 7),
  knots = "equidistant",
  CV = FALSE,
  kappa = c(1000000, 500000, 20000),
  method = "Weib",
  conf.int = 0.95,
  print.iter = FALSE,
  subset = NULL,
  na.action = na.fail
)
```

Arguments

formula01	A formula specifying a regression model for the $0 \rightarrow 1$ transition from the initial state to the transient state of the illness-death model. The right hand side of the formula specifies the covariate terms, and the left hand side must be an event history object as returned by the function Hist.
formula02	A formula specifying a regression model for the $0 \rightarrow 2$ transition from the initial state to the absorbing state. The left hand side must be equal to the left hand side of formula01. If missing it is set to formula01.
formula12	A formula specifying a regression model for the $1 \rightarrow 2$ transition from the transient state to the absorbing state. operator is not required. If missing it is set to formula01.
data	A data frame in which to interpret the variables of formula01, formula02 and formula12.
maxiter	Maximum number of iterations. The default is 200.
eps	A vector of 3 integers >0 used to define the power of three convergence criteria: 1. for the regression parameters, 2. for the likelihood, 3. for the second derivatives. The default is $c(5, 5, 3)$ which is translated into convergence if the respective values change less than 10^{-5} (for regression parameters and likelihood) and 10^{-3} for the second derivatives between two iterations.
n.knots	For method="Splines" only, a vector of length 3 specifying the number of knots, one for each transition, for the M-splines estimate of the baseline intensities in the order $0 \rightarrow 1$, $0 \rightarrow 2$, $1 \rightarrow 2$. The default is $c(7,7,7)$. When knots are specified as a list this argument is ignored. The algorithm needs least 5 knots and at most 20 knots.
knots	Argument only active for the penalized likelihood approach method="Splines". There are three ways to control the placement of the knots between the smallest and the largest of all time points: <ul style="list-style-type: none"> • knots="equidistant" Knots are placed with same distance on the time scale. • knots="quantiles" Knots are placed such that the number of observations is roughly the same between knots. • knots=list() List of 1 or 2 or three vectors. The list elements are the actual placements (timepoints) of the knots for the M-spline. The list may contain one vector of placements for each transition in the order $0 \rightarrow 1$, $0 \rightarrow 2$, $1 \rightarrow 2$. If only vector is specified the knots are used for all transitions. If only 2 vectors are specified, the knots for the $0 \rightarrow 1$ transition are also used for the $1 \rightarrow 2$ transition. <p>The algorithm needs at least 5 knots and allows no more than 20 knots.</p>
CV	Binary variable equals to 1 when search (by approximated cross validation) of the smoothing parameters kappa and 0 otherwise. Argument for the penalized likelihood approach. The default is 0.
kappa	Argument only active for the penalized likelihood approach method="Splines". A vector with 3 positive values (smoothing parameters), one for each transition, in the order $0 \rightarrow 1$, $0 \rightarrow 2$ and $1 \rightarrow 2$. If CV=1 these are used as starting values for a cross validation search to optimize kappa.

method	type of estimation method: "Splines" for a penalized likelihood approach with approximation of the transition intensities by M-splines, "Weib" for a parametric approach with a Weibull distribution on the transition intensities. Default is "Weib".
conf.int	Level of confidence pointwise confidence intervals of the transition intensities, i.e., a value between 0 and 1, the default is 0.95. The default is also used when conf.int=TRUE. To avoid computation of confidence intervals, set conf.int to FALSE or NULL.
print.iter	boolean parameter. Equals to TRUE to print the likelihood during the iteration process, FALSE otherwise. Default is FALSE. This option is not running on Windows.
subset	expression indicating the subset of the rows of data to be used in the fit. All observations are included by default.
na.action	how NAs are treated. The default is first, any na.action attribute of data, second a na.action setting of options, and third 'na.fail' if that is unset. The 'factory-fresh' default is na.omit. Another possible value is NULL.

Details

The estimated parameters are obtained using the robust Marquardt algorithm (Marquardt, 1963) which is a combination between a Newton-Raphson algorithm and a steepest descent algorithm.

Value

call	the call that produced the result.
coef	regression parameters.
loglik	vector containing the log-likelihood without and with covariate.
cv	vector containing the convergence criteria.
niter	number of iterations.
converged	integer equal to 1 when the model converged, 2, 3 or 4 otherwise.
modelPar	Weibull parameters.
N	number of subjects.
events1	number of events 0 → 1.
events2	number of events 0 → 2 or 0 → 1 → 2.
NC	vector containing the number of covariates on transitions 0 → 1, 0 → 2, 1 → 2.
responseTrans	model response for the 0 → 1 transition. Hist or Surv object.
responseAbs	model response for the 0 → 2 transition. Hist or Surv object.
time	times for which transition intensities have been evaluated for plotting. Vector in the Weibull approach. Matrix in the penalized likelihood approach for which the columns corresponds to the transitions 0 → 1, 1 → 2, 0 → 2.
intensity01	matched values of the intensities for transition 0 → 1.
lowerIntensity01	lower confidence intervals for the values of the intensities for transition 0 → 1.

upperIntensity01	upper confidence intervals for the values of the intensities for transition 0 → 1.
intensity02	matched values of the intensities for transition 0 → 2.
lowerIntensity02	lower confidence intervals for the values of the intensities for transition 0 → 2.
upperIntensity02	upper confidence intervals for the values of the intensities for transition 0 → 2.
intensity12	matched values of the intensities for transition 1 → 2.
lowerIntensity12	lower confidence intervals for the values of the intensities for transition 1 → 2.
upperIntensity12	upper confidence intervals for the values of the intensities for transition 1 → 2.
RR	vector of relative risks.
V	variance-covariance matrix derived from the Hessian of the log-likelihood if using method="Weib" or, from the Hessian of the penalized log-likelihood if using method="Splines".
se	standart errors of the regression parameters.
Xnames01	names of covariates on 0 → 1.
Xnames02	names of covariates on 0 → 2.
Xnames12	names of covariates on 1 → 2.
knots01	knots to approximate by M-splines the intensity of the 0 → 1 transition.
knots02	knots to approximate by M-splines the intensity of the 0 → 2 transition.
knots12	knots to approximate by M-splines the intensity of the 1 → 2 transition.
nknots01	number of knots on transition 0 → 1.
nknots02	number of knots on transition 0 → 2.
nknots12	number of knots on transition 1 → 2.
theta01	square root of splines coefficients for transition 0 → 1.
theta02	square root of splines coefficients for transition 0 → 2.
theta12	square root of splines coefficients for transition 1 → 2.
CV	a binary variable equals to 1 when search of the smoothing parameters kappa by approximated cross-validation, 1 otherwise. The default is 0.
kappa	vector containing the smoothing parameters for transition 0 → 1, 0 → 2, 1 → 2 used to estimate the model by the penalized likelihood approach.
CVcrit	cross validation criteria.
DoF	degrees of freedom of the model.
na.action	observations deleted if missing values.

Author(s)

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References

D. Marquardt (1963). An algorithm for least-squares estimation of nonlinear parameters. *SIAM Journal of Applied Mathematics*, 431-441.

See Also

[print.idm](#) [summary.idm](#) [predict.idm](#)

Examples

```
library(lava)
library(proplim)
set.seed(17)
d <- simulateIDM(100)
# right censored data
fitRC <- idm(formula01=Hist(time=observed.illtime,event=seen.ill)~X1+X2,
             formula02=Hist(time=observed.lifetime,event=seen.exit)~X1+X2,
             formula12=Hist(time=observed.lifetime,event=seen.exit)~X1+X2,data=d,
             conf.int=FALSE)

fitRC

## Not run:
set.seed(17)
d <- simulateIDM(300)
fitRC.splines <- idm(formula01=Hist(time=observed.illtime,event=seen.ill)~X1+X2,
                    formula02=Hist(time=observed.lifetime,event=seen.exit)~X1+X2,
                    formula12=Hist(time=observed.lifetime,event=seen.exit)~1,data=d,
                    conf.int=FALSE,method="splines")

## End(Not run)
# interval censored data
fitIC <- idm(formula01=Hist(time=list(L,R),event=seen.ill)~X1+X2,
            formula02=Hist(time=observed.lifetime,event=seen.exit)~X1+X2,
            formula12=Hist(time=observed.lifetime,event=seen.exit)~X1+X2,data=d,
            conf.int=FALSE)

fitIC

## Not run:

data(Paq1000)

# Illness-death model with certif on the 3 transitions
# Weibull parametrization and likelihood maximization

fit.weib <- idm(formula02=Hist(time=t,event=death,entry=e)~certif,
                formula01=Hist(time=list(l,r),event=dementia)~certif,
                data=Paq1000)

# Illness-death model with certif on transitions 01 and 02
# Splines parametrization and penalized likelihood maximization
fit.splines <- idm(formula02=Hist(time=t,event=death,entry=e)~certif,
                  formula01=Hist(time=list(l,r),event=dementia)~certif,
```

```

                                formula12=~1,
                                method="Splines",
                                data=Paq1000)
fit.weib
summary(fit.splines)

## End(Not run)

```

idmModel

Generate illness-death model objects

Description

Function to generate an illness-death model for simulation.

Usage

```

idmModel(
  scale.illtime = 1/100,
  shape.illtime = 1,
  scale.lifetime = 1/100,
  shape.lifetime = 1,
  scale.waittime = 1/100,
  shape.waittime = 1,
  scale.censtime = 1/100,
  shape.censtime = 1,
  n.inspections = 5,
  schedule = 10,
  punctuality = 5
)

```

Arguments

scale.illtime	Weibull scale for latent illness time
shape.illtime	Weibull shape for latent illness time
scale.lifetime	Weibull scale for latent life time
shape.lifetime	Weibull shape for latent life time
scale.waittime	Weibull scale for latent life time
shape.waittime	Weibull shape for latent life time
scale.censtime	Weibull scale for censoring time
shape.censtime	Weibull shape for censoring time
n.inspections	Number of inspection times
schedule	Mean of the waiting time between adjacent inspections.
punctuality	Standard deviation of waiting time between inspections.

Details

Based on the functionality of the lava PACKAGE the function generates a latent variable model (latent illtime, waittime and lifetime) and censoring mechanism (censtime, inspection1,inspection2,...,inspectionK).

The function `sim.idmModel` then simulates right censored lifetimes and interval censored illness times.

Value

A latent variable model object lvm

Author(s)

Thomas Alexander Gerds

Examples

```
## Not run:
library(lava)
library(prodlim)
# generate illness-death model based on exponentially
# distributed times
m <- idmModel(scale.illtime=1/70,
              shape.illtime=1.8,
              scale.lifetime=1/50,
              shape.lifetime=0.7,
              scale.waittime=1/30,
              shape.waittime=0.7)

round(sim(m,6),1)

# Estimate the parameters of the Weibull models
# based on the uncensored exact event times
# and the uncensored illstatus.
set.seed(18)
d <- sim(m,100,latent=FALSE)
d$uncensored.status <- 1
f <- idm(formula01=Hist(time=illtime,event=illstatus)~1,
         formula02=Hist(time=lifetime,event=uncensored.status)~1,
         data=d,
         conf.int=FALSE)
print(f)

# Change the rate of the 0->2 and 0->1 transitions
# also the rate of the 1->2 transition
# and also lower the censoring rate
m <- idmModel(scale.lifetime=1/2000,
              scale.waittime=1/30,
              scale.illtime=1/1000,
              scale.censtime=1/1000)

set.seed(18)
d <- sim(m,50,latent=TRUE)
d$uncensored.status <- 1
```



```

f <- idm(formula01=Hist(time=observed.illtime,event=illstatus)~1,
         formula02=Hist(time=observed.lifetime,event=uncensored.status)~1,
         data=d,
         conf.int=FALSE)
print(f)

# Estimate based on the right censored observations
fc <- idm(formula01=Hist(time=illtime,event=seen.ill)~1,
         formula02=Hist(time=observed.lifetime,event=seen.exit)~1,
         data=d,
         conf.int=FALSE)
print(fc)

# Estimate based on interval censored and right censored observations
fi <- idm(formula01=Hist(time=list(L,R),event=seen.ill)~1,
         formula02=Hist(time=observed.lifetime,event=seen.exit)~1,
         data=d,
         conf.int=FALSE)
print(fi)

# Estimation of covariate effects:
# X1, X2, X3
m <- idmModel(shape.waittime=2,
              scale.lifetime=1/2000,
              scale.waittime=1/300,
              scale.illtime=1/10000,
              scale.censtime=1/10000)
distribution(m,"X1") <- binomial.lvm(p=0.3)
distribution(m,"X2") <- normal.lvm(mean=120,sd=20)
distribution(m,"X3") <- normal.lvm(mean=50,sd=20)
regression(m,to="latent.illtime",from="X1") <- 1.7
regression(m,to="latent.illtime",from="X2") <- 0.07
regression(m,to="latent.illtime",from="X3") <- -0.1
regression(m,to="latent.waittime",from="X1") <- 1.8
regression(m,to="latent.lifetime",from="X1") <- 0.7
set.seed(28)
d <- sim(m,100,latent=TRUE)
head(d)
table(ill=d$seen.ill,death=d$seen.exit)

# Estimation based on uncensored data
d$uncensored.status <- 1
# uncensored data
F1 <- idm(formula01=Hist(time=illtime,event=illstatus)~X1+X2+X3,
         formula02=Hist(time=lifetime,event=uncensored.status)~X1+X2+X3,
         data=d,conf.int=FALSE)
print(F1)

# Estimation based on right censored data
F2 <- idm(formula01=Hist(time=illtime,event=seen.ill)~X1+X2+X3,
         formula02=Hist(time=observed.lifetime,event=seen.exit)~X1+X2+X3,
         data=d,conf.int=FALSE)

```

```

print(F2)

# Estimation based on interval censored and right censored data
F3 <- idm(formula01=Hist(time=list(L,R),event=seen.ill)~X1+X2+X3,
          formula02=Hist(time=observed.lifetime,event=seen.exit)~X1+X2+X3,
          data=d,conf.int=FALSE)
print(F3)
cbind(uncensored=F1$coef,right.censored=F2$coef,interval.censored=F3$coef)

## End(Not run)

```

intensity

M-spline estimate of the transition intensity function

Description

M-spline estimate of the transition intensity function and the cumulative transition intensity function for survival and illness-death models

Usage

```
intensity(times, knots, number.knots, theta, linear.predictor = 0)
```

Arguments

times	Time points at which to estimate the intensity function
knots	Knots for the M-spline
number.knots	Number of knots for the M-splines (and I-splines see details)
theta	The coefficients for the linear combination of M-splines (and I-splines see details)
linear.predictor	Linear predictor $\beta \cdot Z$. When it is non-zero, transition and cumulative transition are multiplied by $\exp(\text{linear.predictor})$. Default is zero.

Details

The estimate of the transition intensity function is a linear combination of M-splines and the estimate of the cumulative transition intensity function is a linear combination of I-splines (the integral of a M-spline is called I-spline). The coefficients theta are the same for the M-splines and I-splines.

Important: the theta parameters returned by `idm` and `shr` are in fact the square root of the splines coefficients. See examples.

This function is a R-translation of a corresponding Fortran function called `susp`. `susp` is used internally by `idm` and `shr`.

Value

times The time points at which the following estimates are evaluated.
intensity The transition intensity function evaluated at times.
cumulative.intensity
 The cumulative transition intensity function evaluated at times
survival The "survival" function, i.e., $\exp(-\text{cumulative.intensity})$

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See Also

[shr](#), [idm](#)

Examples

```
data(testdata)
fit.su <- shr(Hist(time=list(l, r), id) ~ cov,
             data = testdata,method = "Splines",CV = TRUE)
intensity(times = fit.su$time, knots = fit.su$knots,
          number.knots = fit.su$nknots, theta = fit.su$theta^2)

## Not run:
data(Paq1000)
fit.idm <- idm(formula02 = Hist(time = t, event = death, entry = e) ~ certif,
              formula01 = Hist(time = list(l,r), event = dementia) ~ certif,
              formula12 = ~ certif, method = "Splines", data = Paq1000)
# Probability of survival in state 0 at age 80 for a subject with no cep given
that he is in state 0 at 70
su0 <- (intensity(times = 80, knots = fit.idm$knots01,
                 number.knots = fit.idm$nknots01,
                 theta = fit.idm$theta01^2)$survival
 *intensity(times = 80, knots = fit.idm$knots02,
            number.knots = fit.idm$nknots02,
            theta = fit.idm$theta02^2)$survival)/
(intensity(times = 70, knots = fit.idm$knots01,
           number.knots = fit.idm$nknots01,
           theta = fit.idm$theta01^2)$survival
 *intensity(times = 70, knots = fit.idm$knots02,
           number.knots = fit.idm$nknots02,
           theta = fit.idm$theta02^2)$survival)
# Same result as:
predict(fit.idm, s = 70, t = 80, conf.int = FALSE) # see first element

## End(Not run)
```

Paq1000

Paquid data set

Description

Paquid data set composed of 1000 subjects selected randomly from the Paquid data set of 3675 subjects.

Format

A data frame with 1000 rows and the following 8 columns.

dementia dementia status, 0=non-demented, 1=demented

death death status, 0=alive, 1=dead

e age at entry in the study

l for demented subjects: age at the visit before the diagnostic visit; for non-demented subjects: age at the last visit (censoring age)

r for demented subjects: age at the diagnostic visit; for non-demented subjects: age at the last visit (censoring age)

t for dead subjects: age at death; for alive subject: age at the latest news

certif primary school certificate:0=with certificate, 1=without certificate

gender gender: 0=female, 1=male

Examples

```
data(Paq1000)
```

plot.idm

Plot method for an illness-death model

Description

Plot estimated baseline transition intensities from an object of class `idm` optionally with confidence limits.

Usage

```
## S3 method for class 'idm'
plot(
  x,
  conf.int = FALSE,
  citype = "shadow",
  add = FALSE,
  axes = TRUE,
  col,
  lwd,
  lty,
  xlim,
  ylim,
  xlab,
  ylab,
  legend = TRUE,
  transition = c("01", "02", "12"),
  ...
)
```

Arguments

x	a <code>idmWeib</code> class object (output from calling <code>idm</code> with the (default) option <code>intensities="Weib"</code>).
<code>conf.int</code>	If TRUE show confidence limits
<code>citype</code>	Type of confidence limits, can be "shadow" or "bars"
<code>add</code>	If TRUE add to existing plot
<code>axes</code>	If TRUE axes are drawn
<code>col</code>	Color of the lines
<code>lwd</code>	Width of the lines
<code>lty</code>	Type of the lines
<code>xlim</code>	Limits for x-axis
<code>ylim</code>	Limits for y-axis
<code>xlab</code>	Label for x-axis
<code>ylab</code>	Label for y-axis
<code>legend</code>	If TRUE a legend is drawn, which can be further controlled via SmartControl .
<code>transition</code>	Choose one of the transition intensities: <code>c("01", "02", "12")</code> .
...	Passed to SmartControl

Value

Print a plot of the baseline transition intensities of an illness-death model estimated using a Weibull approach.

See Also

```
print.idm,summary.idm,idm,
idm
```

Examples

```
library(lava)
library(prodlm)
m <- idmModel(scale.lifetime=1/10,scale.illtime=1/8)
distribution(m,"X") <- binomial.lvm()
regression(m,latent.lifetime~X) <- 0.7
set.seed(30)
d <- sim(m,100)
fit.weib <- idm(formula02=Hist(observed.lifetime,event=seen.exit)~1,
formula01=Hist(time=list(L,R),event=seen.ill)~1,data=d,conf.int=FALSE)
plot(fit.weib)

## Not run:
## FIXME: the limits for the 01 transition are a bit wide!?
## with bootstrap confidence limits
fit.weib <- idm(formula02=Hist(observed.lifetime,event=seen.exit)~1,
formula01=Hist(time=list(L,R),event=seen.ill)~1,data=d,conf.int=TRUE)
plot(fit.weib)

## End(Not run)
```

plot.shr

Plot method for a survival model.

Description

Plot estimated baseline survival function from an object of class shr. Pointwise confidence limits are available.

Usage

```
## S3 method for class 'shr'
plot(
  x,
  type = "shr",
  add = FALSE,
  newdata = NULL,
  cause = NULL,
  col,
  lty,
```

```
    lwd,  
    ylim,  
    xlim,  
    xlab = "Time",  
    ylab,  
    legend = TRUE,  
    confint = TRUE,  
    timeOrigin = 0,  
    axes = TRUE,  
    percent = TRUE,  
    ...  
  )
```

Arguments

x	a shrWeib or a shrSplines class object (output from calling <code>shr</code> function).
type	type of function to plot. The default is "shr".
add	boolean.
newdata	newdata.
cause	cause.
col	col.
lty	lty.
lwd	lwd.
ylim	ylim.
xlim	xlim.
xlab	xlab.
ylab	ylab.
legend	legend.
confint	confint.
timeOrigin	timeOrigin.
axes	axes.
percent	percent.
...	other graphical parameters.

Value

Print a plot of a survival model.

Author(s)

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See Also[plot.shr](#)**Examples**

```
# Weibull survival model
library(proplim)
data(testdata)
fit.su <- shr(Hist(time=list(l,r),id)~cov,data=testdata)

# pointwise confidence limits
plot(fit.su)

# no pointwise confidence limits
plot(fit.su,confint=FALSE)
```

predict.idm

Predictions for an illness-death model using either a penalized likelihood approach or a Weibull parametrization.

Description

Predict transition probabilities and cumulative probabilities from an object of class `idmSplines` with confidence intervals are calculated.

Usage

```
## S3 method for class 'idm'
predict(
  object,
  s,
  t,
  newdata,
  nsim = 200,
  seed = 21,
  conf.int = 0.95,
  lifeExpect = FALSE,
  maxtime,
  ...
)
```


Arguments

object	an <code>idm</code> class objects returned by a call to the <code>idm</code> function
s	time point at which prediction is made.
t	time horizon for prediction.
newdata	A data frame with covariate values for prediction.
nsim	number of simulations for the confidence intervals calculations. The default is 200.
seed	Seed passed to <code>set.seed</code> for Monte Carlo simulation of confidence intervals.
conf.int	Level of confidence, i.e., a value between 0 and 1, the default is 0.95. The default is also used when <code>conf.int=TRUE</code> . To avoid computation of confidence intervals, set <code>conf.int</code> to <code>FALSE</code> or <code>NULL</code> .
lifeExpect	Logical. If <code>TRUE</code> compute life expectancies, i.e., <code>t=Inf</code> .
maxtime	The upper limit of integration for calculations of life expectancies from Weibull parametrizations.
...	other parameters.

Value

a list containing the following predictions with pointwise confidence intervals:

p_{00}	the transition probability p_{00} .
p_{01}	the transition probability p_{01} .
p_{11}	the transition probability p_{11} .
p_{12}	the transition probability p_{12} .
p_{02_0}	the probability of direct transition from state 0 to state 2.
p_{02_1}	the probability of transition from state 0 to state 2 via state 1.
p_{02}	transition probability p_{02} . Note that $p_{02}=p_{02_0}+p_{02_1}$.
F_{01}	the lifetime risk of disease. $F_{01}=p_{01}+p_{02_1}$.
$F_{0.}$	the probability of exit from state 0. $F_{0.}=p_{02_0}+p_{01}+p_{02_1}$.

Author(s)

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 Fortran: Pierre Joly <Pierre.Joly@isped.u-bordeaux2.fr>

See Also

[idm](#)

Examples

```
## Not run:
set.seed(100)
d=simulateIDM(n = 100)
fit <- idm(formula01=Hist(time=list(L,R),event=seen.ill)~X1+X2+X3,
           formula02=Hist(time=observed.lifetime,event=seen.exit)~X1+X2+X3,
           data=d,conf.int=FALSE)
predict(fit,s=0,t=80,conf.int=FALSE,lifeExpect=FALSE)
predict(fit,s=0,t=80,nsim=4,conf.int=TRUE,lifeExpect=FALSE)
predict(fit,s=0,t=80,nsim=4,conf.int=FALSE,lifeExpect=TRUE)

data(Paq1000)
library(prodlim)
fit.paq <- idm(formula02=Hist(time=t,event=death,entry=e)~certif,
              formula01=Hist(time=list(l,r),event=dementia)~certif,data=Paq1000)

predict(fit.paq,s=70,t=80,newdata=data.frame(certif=1))
predict(fit.paq,s=70,lifeExpect=TRUE,newdata=data.frame(certif=1))

fit.splines <- idm(formula02=Hist(time=t,event=death,entry=e)~certif,
                  formula01=Hist(time=list(l,r),event=dementia)~certif,
                  formula12=~1,
                  method="Splines",
                  data=Paq1000)

predict(fit.splines,s=70,t=80,newdata=data.frame(certif=1))
predict(fit.splines,s=70,t=80,lifeExpect=TRUE,newdata=data.frame(certif=1),nsim=20)

## End(Not run)
```

print.idm

Print method for idm objects

Description

Print a summary of a fitted illness-death model

Usage

```
## S3 method for class 'idm'
print(x, conf.int = 0.95, digits = 4, pvalDigits = 4, eps = 0.0001, ...)
```

Arguments

x Class idm object, i.e. the result of a call to the `idm` function with `intensities="Weib"`.

conf.int	The level of confidence for the hazard ratios. The default is 0.95.
digits	Number of digits to print.
pvalDigits	Number of digits to print for p-values.
eps	Passed to format.pval.
...	Not used.

Author(s)

Celia Touraine <Celia.Touraine@isped.u-bordeaux2.fr>, Thomas A. Gerds <tag@biostat.ku.dk>

See Also

[summary.idm](#), [plot.idm](#)

Examples

```
## Not run:
data(Paq1000)
library(prodlim)
fit.splines <- idm(formula02=Hist(time=t,event=death,entry=t0)~certif,
formula01=Hist(time=list(l,r),event=dementia)~certif,
                 formula12=~1,
                 method="Splines",
data=Paq1000)
print(fit.splines)

## End(Not run)
```

```
print.shr
```

Print method for shrSplines objects

Description

Print a summary of a fitted illness-death model using the penalized likelihood approach.

Usage

```
## S3 method for class 'shr'
print(x, conf.int = 0.95, digits = 4, pvalDigits = 4, eps = 0.0001, ...)
```

Arguments

x	a shr object, i.e., the result of a call to the shr function with hazard="Splines".
conf.int	The level of confidence for the hazard ratios. The default is 0.95.
digits	number of digits to print.
pvalDigits	number of digits to print for p-values.
eps	convergence criterion used for p-values.
...	other unused arguments.

Author(s)

R: Celia Touraine <Celia.Touraine@isped.u-bordeaux2.fr> Fortran: Pierre Joly <Pierre.Joly@isped.u-bordeaux2.fr>

See Also

[summary.shr](#), [plot.shr](#)

Examples

```
## Not run:
# a penalized survival model
library(prodlim)
data(testdata)
fit.su <- shr(Hist(time=list(l,r),id)~cov,data=testdata,method="Splines")
print(fit.su)

## End(Not run)
```

shr

Fit a survival model

Description

Fit a survival model using either a semi-parametric approach (penalized likelihood with an approximation of the hazard function by linear combination of M-splines) or a parametric approach (specifying a Weibull distribution on the hazard function). Left-truncated, right-censored, and interval-censored data are allowed.

Usage

```
shr(
  formula,
  data,
  eps = c(5, 5, 3),
  n.knots = 7,
```

```

knots = "equidistant",
CV = FALSE,
kappa = 10000,
conf.int = 0.95,
maxiter = 200,
method = "Weib",
print.iter = FALSE,
na.action = na.omit
)

```

Arguments

formula	a formula object with the response on the left hand side and the terms on the right hand side. The response must be a survival object or Hist object as returned by the 'Surv' or 'Hist' function.
data	a data frame in which to interpret the variables named in the formula.
eps	a vector of length 3 for the convergence criteria (criterion for parameters, criterion for likelihood, criterion for second derivatives). The default is $c(5, 5, 3)$ and corresponds to criteria equals to 10^{-5} , 10^{-5} and 10^{-3} .
n.knots	Argument only active for the penalized likelihood approach <code>method="splines"</code> . Number of knots for the splines to use to approximate the hazard function. The default is 7. If knots are given as a vector this argument is ignored. The algorithm needs least 5 knots and at most 20 knots.
knots	Argument only active for the penalized likelihood approach <code>method="splines"</code> . There are three ways to control the placement of the knots between the smallest and the largest of all time points: <ul style="list-style-type: none"> • <code>knots="equidistant"</code> Knots are placed with same distance on the time scale. • <code>knots="quantiles"</code> Knots are placed such that the number of observations is roughly the same between knots. • <code>knots=list()</code> List of length 3. The list elements are the actual placements (timepoints) of the knots for the M-spline. <p>The algorithm requires at least 5 knots and allows no more than 20 knots.</p>
CV	binary variable equals to 1 when search (by approximated cross validation) of the smoothing parameter <code>kappa</code> and 0 otherwise. Argument for the penalized likelihood approach. The default is 0.
kappa	Argument only active for the penalized likelihood approach <code>method="splines"</code> . A positive number (smoothing parameter) If <code>CV=1</code> the value is used as a starting value for a cross validation search to optimize <code>kappa</code> .
conf.int	Level of confidence pointwise confidence intervals of the survival and hazard functions, i.e., a value between 0 and 1, the default is 0.95. The default is also used when <code>conf.int=TRUE</code> . To avoid computation of confidence intervals, set <code>conf.int</code> to <code>FALSE</code> or <code>NULL</code> .
maxiter	maximum number of iterations. The default is 200.

method	type of estimation method: "Splines" for a penalized likelihood approach with approximation of the hazard function by M-splines, "Weib" for a parametric approach with a Weibull distribution on the hazard function. Default is "Weib".
print.iter	boolean parameter. Equals to TRUE to print the likelihood during the iteration process, FALSE otherwise. Default is FALSE. This option is not running on Windows.
na.action	how NAs are treated. The default is first, any na.action attribute of data, second a na.action setting of options, and third 'na.fail' if that is unset. The 'factory-fresh' default is na.omit. Another possible value is NULL.

Details

The estimated parameters are obtained using the robust Marquardt algorithm (Marquardt, 1963) which is a combination between a Newton-Raphson algorithm and a steepest descent algorithm.

Value

- call
- coefregression parameters.
- loglikvector containing the log-likelihood without and with covariate.
- modelParWeibull parameters.
- Nnumber of subjects.
- NCnumber of covariates.
- neventsnumber of events.
- modelResponsemodel response: Hist or Surv object.
- convergedinteger equal to 1 when the model converged, 2, 3 or 4 otherwise.
- timetimes for which survival and hazard functions have been evaluated for plotting.
- hazardmatched values of the hazard function.
- lowerHazardlower confidence limits for hazard function.
- upperHazardupper confidence limits for hazard function.
- survmatched values of the survival function.
- lowerSurvlower confidence limits for survival function.
- upperSurvupper confidence limits for survival function.
- RRvector of relative risks.
- Vvariance-covariance matrix.
- sstandard errors.
- knotsknots of the M-splines estimate of the hazard function.
- nknotsnumber of knots.
- CVa binary variable equals to 1 when search of the smoothing parameter κ by approximated cross-validation, 1 otherwise. The default is 0.
- niternumber of iterations.
- cvvector containing the convergence criteria.
- na.actionobservations deleted if missing values.

Author(s)

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References

D. Marquardt (1963). An algorithm for least-squares estimation of nonlinear parameters. *SIAM Journal of Applied Mathematics*, 431-441.

See Also

[shr](#), [print.shr](#), [summary.shr](#), [print.shr](#),

Examples

```
# Weibull survival model
library(prodlim)
data(testdata)
fit.su <- shr(Hist(time=list(l,r),id)~cov,data=testdata)
fit.su
summary(fit.su)
## Not run:
shr.spline <- shr(Hist(time=list(l,r),id)~cov,data=testdata,method="splines",n.knots=6)
shr.spline
shr.spline.q <- shr(Hist(time=list(l,r),id)~cov,data=testdata,
                    method="splines",n.knots=6,knots="quantiles")
plot(shr.spline.q)

## manual placement of knots
shr.spline.man <- shr(Hist(time=list(l,r),id)~cov,data=testdata,method="splines",knots=seq(0,7,1))

## End(Not run)
```

sim.idmModel

Simulate illness-death model data

Description

Function to simulate illness-death model data

Usage

```
## S3 method for class 'idmModel'
sim(
  x,
  n,
  illness.known.at.death = TRUE,
  compliance = 1,
  latent = FALSE,
```

```

    keep.inspectiontimes = FALSE,
    ...
  )

```

Arguments

x	An idmModel object as obtained with idmModel
n	Number of observations
illness.known.at.death	Affects the value of variable seen.ill
compliance	Probability of missing an inspection time.
latent	if TRUE keep the latent event times
keep.inspectiontimes	if TRUE keep the inspection times.
...	Extra arguments given to sim

Details

Based on the functionality of the lava PACKAGE

Value

A data set with interval censored observations from an illness-death model

Author(s)

Thomas Alexander Gerds

Examples

```

example(idmModel)
help(idmModel)

```

sim.survIC

Simulate interval censored survival data

Description

Function to simulate interval censored survival data

Usage

```

## S3 method for class 'survIC'
sim(x, n, compliance = 1, latent = TRUE, keep.inspectiontimes = FALSE, ...)

```


Arguments

x	An survIC object as obtained with survIC
n	Number of observations
compliance	Probability of missing an inspection time.
latent	if TRUE keep the latent event times
keep.inspectiontimes	if TRUE keep the inspection times.
...	Extra arguments given to sim

Details

Based on the functionality of the lava PACKAGE

Value

A data set with interval censored observations

Author(s)

Thomas Alexander Gerds

Examples

```
library(lava)
example(survIC)
help(survIC)
o1 <- survIC()
dat.o1 <- sim(o1,10)
```

simulateIDM

Sample illness-death model data

Description

Simulate data from an illness-death model with interval censored event times and covariates

Usage

```
simulateIDM(n = 100)
```

Arguments

n	number of observations
---	------------------------

Details

Simulate data from an illness-death model with interval censored event times and covariates for the purpose of illustrating the help pages of the SmoothHazard package. See the body of the function for details, i.e., evaluate simulateIDM

See Also

idmModel sim.idmModel

Examples

```
# simulateIDM
simulateIDM(100)
```

summary.idm

Summary of a fitted illness-death model

Description

Summarize the event history data of an illness-death regression model and show regression coefficients for transition intensities

Usage

```
## S3 method for class 'idm'
summary(object, conf.int = 0.95, digits = 4, pvalDigits = 4, eps = 0.0001, ...)
```

Arguments

object	a idmSplines object, i.e., the result of a call to the <code>idm</code> function with <code>intensities="Splines"</code> .
conf.int	The level of confidence for the hazard ratios. The default is 0.95.
digits	number of digits to print.
pvalDigits	number of digits to print for p-values.
eps	convergence criterion used for p-values.
...	other unused arguments.

Author(s)

R: Celia Touraine <Celia.Touraine@isped.u-bordeaux2.fr> Fortran: Pierre Joly <Pierre.Joly@isped.u-bordeaux2.fr>

See Also

[idm](#), [print.idm](#), [plot.idm](#)

Examples

```
## Not run:
library(prodlim)
data(Paq1000)
fit.splines <- idm(formula02=Hist(time=t,event=death,entry=e)~certif,
formula01=Hist(time=list(l,r),event=dementia)~certif,
                  formula12=~1,
                  method="Splines",
data=Paq1000)
summary(fit.splines)

## End(Not run)
```

summary.shr

Summary of a fitted survival model using a penalized likelihood approach

Description

Print a short summary of a fitted illness-death model using the penalized likelihood approach.

Usage

```
## S3 method for class 'shr'
summary(object, conf.int = 0.95, digits = 4, pvalDigits = 4, eps = 0.0001, ...)
```

Arguments

object	a shr object, i.e., the result of a call to the shr function.
conf.int	The level of confidence for the hazard ratios. The default is 0.95.
digits	number of digits to print.
pvalDigits	number of digits to print for p-values.
eps	convergence criterion used for p-values.
...	other unused arguments.

Author(s)

Celia Touraine <Celia.Touraine@isped.u-bordeaux2.fr>

See Also

[shr](#), [print.shr](#), [plot.shr](#)

Examples

```
## Not run:
# a penalized survival model
data(testdata)
library(prodlim)
fit.su <- shr(Hist(time=list(1,r),id)~cov,data=testdata,method="Splines")
summary(fit.su)

# Weibull survival model
data(testdata)
fit.su <- shr(Hist(time=list(1,r),id)~cov,data=testdata)
summary(fit.su)

## End(Not run)
```

survIC

Generate survival model objects

Description

Function to generate a latent variable model for interval censored survival times.

Usage

```
survIC(
  scale.time = 1/100,
  shape.time = 1,
  n.inspections = 5,
  schedule = 10,
  punctuality = 5
)
```

Arguments

scale.time	Weilbull scale for latent time
shape.time	Weilbull shape for latent time
n.inspections	Number of inspection times
schedule	Mean of the waiting time between adjacent inspections.
punctuality	Standard deviation of waiting time between inspections.

Details

Based on the functionality of the lava PACKAGE the function generates a latent variable model with a latent time and a censoring mechanism (censtime, inspection1,inspection2,...,inspectionK).

The function `sim.survIC` then simulates interval censored times.

Value

A latent variable model object lvm

Author(s)

Thomas Alexander Gerds

Examples

```
## Not run:
library(lava)
library(prodlm)
# generate survival model based on exponentially
# distributed times
m <- survIC(scale.time=1/50, shape.time=0.7)
round(sim(m,6),1)

# Estimate the parameters of the Weibull models
# based on the uncensored exact event times
# and the uncensored illstatus.
set.seed(18)
d <- sim(m,100,latent=FALSE)
d$uncensored.status <- 1
f <- shr(Hist(time=list(L,R),event=uncensored.status)~1,
         data=d,
         conf.int=FALSE)
print(f)

## End(Not run)
```

testdata

Data set for survival models: right-censored and interval-censored data.

Description

A simulated data frame for survival models composed of right-censored and interval-censored data.

Format

A data frame with 936 observations on the following 4 variables.

l for diseased subjects: left endpoint of censoring interval; for non-diseased subjects: right censoring time

r for diseased subjects: right endpoint of censoring interval; for non-diseased subjects: right censoring time for the disease event

id disease status

cov covariate

Examples

```
data(testdata)  
head(testdata)
```

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