Package 'survPen'

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Title Multidimensional Penalized Splines for Survival and Net Survival Models

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Description
Fits hazard and excess hazard models with multidimensional penalized splines allowing for time-dependent effects, non-linear effects and interactions between several continuous covariates. In survival and net survival analysis, in addition to modelling the effect of time (via the baseline hazard), one has often to deal with several continuous covariates and model their functional forms, their time-dependent effects, and their interactions. Model specification becomes therefore a complex problem and penalized regression splines represent an appealing solution to that problem as splines offer the required flexibility while penalization limits overfitting issues. Current implementations of penalized survival models can be slow or unstable and sometimes lack some key features like taking into account expected mortality to provide net survival and excess hazard estimates. In contrast, survPen provides an automated, fast, and stable implementation (thanks to explicit calculation of the derivatives of the likelihood) and offers a unified framework for multidimensional penalized hazard and excess hazard models. survPen may be of interest to those who 1) analyse any kind of time-to-event data: mortality, disease relapse, machinery breakdown, unemployment, etc 2) wish to describe the associated hazard and to understand which predictors impact its dynamics.
See Fauvernier et al. (2019a) <doi:10.21105/joss.01434> for an overview of the package and Fauvernier et al. (2019b) <doi:10.1111/rssc.12368> for the method.

Depends R (>= 3.4.0)

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Imports statmod, stats, Rcpp (>= 1.0.2)

LinkingTo Rcpp, RcppEigen

URL `https://github.com/fauvernierma/survPen`

BugReports `https://github.com/fauvernierma/survPen/issues`

Encoding UTF-8

LazyData true

RoxygenNote 7.1.1

Suggests knitr, rmarkdown, testthat

VignetteBuilder knitr

NeedsCompilation yes

Repository CRAN

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R topics documented:

`colSums2` *colSums of a matrix*

Description

colSums of a matrix

Usage

```
colSums2(Mat)
```

Arguments

`Mat`	a matrix.

Value

colSums(Mat)

`constraint` *Sum-to-zero constraint*

Description

Applies the sum-to-zero constraints to design and penalty matrices.

Usage

```
constraint(X, S, Z = NULL)
```

Arguments

`X`	A design matrix
`S`	A penalty matrix or a list of penalty matrices
`Z`	A list of sum-to-zero constraint matrices; default is NULL

Value

List of objects with the following items:

`X`	Design matrix
`S`	Penalty matrix or list of penalty matrices
`Z`	List of sum-to-zero constraint matrices

Examples

```
library(survPen)

set.seed(15)

X <- matrix(rnorm(10*3),nrow=10,ncol=3)
S <- matrix(rnorm(3*3),nrow=3,ncol=3) ; S <- 0.5*( S + t(S))

# applying sum-to-zero constraint to a desgin matrix and a penalty matrix
constr <- constraint(X,S)
```

`cor.var` *Implementation of the corrected variance Vc*

Description

Takes the model at convergence and calculates the variance matrix corrected for smoothing parameter uncertainty

Usage

```
cor.var(model)
```

Arguments

`model`	survPen object, see `survPen.fit` for details

Value

survPen object with corrected variance Vc

`crs` *Bases for cubic regression splines (equivalent to "cr" in `mgcv`)*

Description

Builds the design matrix and the penalty matrix for cubic regression splines.

Usage

```
crs(x, knots = NULL, df = 10, intercept = TRUE)
```

Arguments

`x`	Numeric vector
`knots`	Numeric vectors that specifies the knots of the splines (including boundaries); default is NULL
`df`	numeric value that indicates the number of knots desired (or degrees of freedom) if knots=NULL; default is 10
`intercept`	if FALSE, the intercept is excluded from the basis; default is TRUE

Details

See package `mgcv` and section 4.1.2 of Wood (2006) for more details about this basis

Value

List of three elements

`bs`	design matrix
`pen`	penalty matrix
`knots`	vector of knots (specified or calculated from `df`)

References

Wood, S. N. (2006), Generalized additive models: an introduction with R. London: Chapman & Hall/CRC.

Examples

```
x <- seq(1,10,length=100)
# natural cubic spline with 3 knots
crs(x,knots=c(1,5,10))
```

`crs.FP` *Penalty matrix constructor for cubic regression splines*

Description

constructs the penalty matrix associated with cubic regression splines basis. This function is called inside `crs`.

Usage

```
crs.FP(knots, h)
```

Arguments

`knots`	Numeric vectors that specifies the knots of the splines (including boundaries)
`h`	vector of knots differences (corresponds to `diff(sort(knots))`)

Value

List of two elements:

`F.mat`	matrix used in function `crs` for basis construction
`P.mat`	penalty matrix

Examples

```
library(survPen)

# construction of the penalty matrix using a sequence of knots
knots <- c(0,0.25,0.5,0.75,1)
diff.knots <- diff(knots)

crs.FP(knots,diff.knots)
```

`datCancer` *Patients diagnosed with cervical cancer*

Description

A simulated dataset containing the follow-up times of 2000 patients diagnosed with cervical cancer between 1990 and 2010. End of follow-up is June 30th 2013. The variables are as follows:

- begin. beginning of follow-up. For illustration purposes about left truncation only (0–1)
- fu. follow-up time in years (0–5)
- age. age at diagnosis in years, from 21.39 to 99.33
- yod. decimal year of diagnosis, from 1990.023 to 2010.999
- dead. censoring indicator (1 for dead, 0 for censored)
- rate. expected mortality rate (from overall mortality of the general population) (0–0.38)

Usage

`data(datCancer)`

Format

A data frame with 2000 rows and 6 variables

`deriv_R` *Derivative of a Choleski factor*

Description

Derivative of a Choleski factor

Usage

```
deriv_R(deriv_Vp, p, R1)
```

Arguments

`deriv_Vp`	derivatives of the Bayesian covariance matrix wrt rho (log smoothing parameters).
`p`	number of regression parameters
`R1`	Choleski factor of Vp

Value

a list containing the derivatives of R1 wrt rho (log smoothing parameters)

`design.matrix` *Design matrix for the model needed in Gauss-Legendre quadrature*

Description

Builds the design matrix for the whole model when the sum-to-zero constraints are specified. The function is called inside `model.cons` for Gauss-Legendre quadrature.

Usage

```
design.matrix(
  formula,
  data.spec,
  Z.smf,
  Z.tensor,
  Z.tint,
  list.smf,
  list.tensor,
  list.tint,
  list.rd
)
```

Arguments

`formula`	formula object identifying the model
`data.spec`	data frame that represents the environment from which the covariate values and knots are to be calculated
`Z.smf`	List of matrices that represents the sum-to-zero constraint to apply for `smf` splines
`Z.tensor`	List of matrices that represents the sum-to-zero constraint to apply for `tensor` splines
`Z.tint`	List of matrices that represents the sum-to-zero constraint to apply for `tint` splines
`list.smf`	List of all smf.smooth.spec objects contained in the model
`list.tensor`	List of all tensor.smooth.spec objects contained in the model
`list.tint`	List of all tint.smooth.spec objects contained in the model
`list.rd`	List of all rd.smooth.spec objects contained in the model

Value

design matrix for the model

Examples

```
library(survPen)

# standard spline of time with 4 knots

data <- data.frame(time=seq(0,5,length=100),event=1,t0=0)

form <- ~ smf(time,knots=c(0,1,3,5))

t1 <- eval(substitute(time), data)
t0 <- eval(substitute(t0), data)
event <- eval(substitute(event), data)

# Setting up the model
model.c <- model.cons(form,lambda=0,data.spec=data,t1=t1,t1.name="time",
t0=rep(0,100),t0.name="t0",event=event,event.name="event",
expected=NULL,expected.name=NULL,type="overall",n.legendre=20,
cl="survPen(form,data,t1=time,event=event)",beta.ini=NULL)

# Retrieving the sum-to-zero constraint matrices and the list of knots
Z.smf <- model.c$Z.smf ; list.smf <- model.c$list.smf

# Calculating the design matrix
design.M <- design.matrix(form,data.spec=data,Z.smf=Z.smf,list.smf=list.smf,
Z.tensor=NULL,Z.tint=NULL,list.tensor=NULL,list.tint=NULL,list.rd=NULL)
```

`grad_rho`	*Gradient vector of LCV and LAML wrt rho (log smoothing parameters)*

Description

Gradient vector of LCV and LAML wrt rho (log smoothing parameters)

Usage

```
grad_rho(
  X_GL,
  GL_temp,
  haz_GL,
  deriv_rho_beta,
  weights,
  tm,
  nb_smooth,
  p,
  n_legendre,
  S_list,
  temp_LAML,
  Vp,
  S_beta,
  beta,
  inverse_new_S,
  X,
  temp_deriv3,
  event,
  expected,
  type,
  Ve,
  mat_temp,
  method
)
```

Arguments

`X_GL`	list of matrices (`length(X.GL)=n.legendre`) for Gauss-Legendre quadrature
`GL_temp`	list of vectors used to make intermediate calculations and save computation time
`haz_GL`	list of all the matrix-vector multiplications X.GL[[i]]%*%beta for Gauss Legendre integration in order to save computation time
`deriv_rho_beta`	firt derivative of beta wrt rho (implicit differentiation)
`weights`	vector of weights for Gauss-Legendre integration on [-1;1]
`tm`	vector of midpoints times for Gauss-Legendre integration; tm = 0.5*(t1 - t0)

`nb_smooth`	number of smoothing parameters
`p`	number of regression parameters
`n_legendre`	number of nodes for Gauss-Legendre quadrature
`S_list`	List of all the rescaled penalty matrices multiplied by their associated smoothing parameters
`temp_LAML`	temporary matrix used when method="LAML" to save computation time
`Vp`	Bayesian covariance matrix
`S_beta`	List such that S_beta[[i]]=S_list[[i]]%*%beta
`beta`	vector of estimated regression parameters
`inverse_new_S`	inverse of the penalty matrix
`X`	design matrix for the model
`temp_deriv3`	temporary matrix for third derivatives calculation when type="net" to save computation time
`event`	vector of right-censoring indicators
`expected`	vector of expected hazard rates
`type`	"net" or "overall"
`Ve`	frequentist covariance matrix
`mat_temp`	temporary matrix used when method="LCV" to save computation time
`method`	criterion used to select the smoothing parameters. Should be "LAML" or "LCV"; default is "LAML"

Value

List of objects with the following items:

`grad_rho`	gradient vector of LCV or LAML
`deriv_rho_inv_Hess_beta`	List of first derivatives of Vp wrt rho
`deriv_rho_Hess_unpen_beta`	List of first derivatives of the Hessian of the unpenalized log-likelihood wrt rho

---

`Hess_rho` *Hessian matrix of LCV and LAML wrt rho (log smoothing parameters)*

Description

Hessian matrix of LCV and LAML wrt rho (log smoothing parameters)

Usage

```
Hess_rho(
  X_GL,
  X_GL_Q,
  GL_temp,
  haz_GL,
  deriv2_rho_beta,
  deriv_rho_beta,
  weights,
  tm,
  nb_smooth,
  p,
  n_legendre,
  deriv_rho_inv_Hess_beta,
  deriv_rho_Hess_unpen_beta,
  S_list,
  minus_eigen_inv_Hess_beta,
  temp_LAML,
  temp_LAML2,
  Vp,
  S_beta,
  beta,
  inverse_new_S,
  X,
  X_Q,
  temp_deriv3,
  temp_deriv4,
  event,
  expected,
  type,
  Ve,
  deriv_rho_Ve,
  mat_temp,
  deriv_mat_temp,
  eigen_mat_temp,
  method
)
```

Arguments

`X_GL`	list of matrices (`length(X.GL)=n.legendre`) for Gauss-Legendre quadrature
`X_GL_Q`	list of transformed matrices from X_GL in order to calculate only the diagonal of the fourth derivative of the likelihood
`GL_temp`	list of vectors used to make intermediate calculations and save computation time
`haz_GL`	list of all the matrix-vector multiplications X.GL[[i]]%*%beta for Gauss Legendre integration in order to save computation time
`deriv2_rho_beta`	second derivatives of beta wrt rho (implicit differentiation)

`deriv_rho_beta`	firt derivatives of beta wrt rho (implicit differentiation)
`weights`	vector of weights for Gauss-Legendre integration on [-1;1]
`tm`	vector of midpoints times for Gauss-Legendre integration; tm = 0.5*(t1 - t0)
`nb_smooth`	number of smoothing parameters
`p`	number of regression parameters
`n_legendre`	number of nodes for Gauss-Legendre quadrature
`deriv_rho_inv_Hess_beta`	list of first derivatives of Vp wrt rho
`deriv_rho_Hess_unpen_beta`	list of first derivatives of Hessian of unpenalized log likelihood wrt rho
`S_list`	List of all the rescaled penalty matrices multiplied by their associated smoothing parameters
`minus_eigen_inv_Hess_beta`	vector of eigenvalues of Vp
`temp_LAML`	temporary matrix used when method="LAML" to save computation time
`temp_LAML2`	temporary matrix used when method="LAML" to save computation time
`Vp`	Bayesian covariance matrix
`S_beta`	List such that S_beta[[i]]=S_list[[i]]%*%beta
`beta`	vector of estimated regression parameters
`inverse_new_S`	inverse of the penalty matrix
`X`	design matrix for the model
`X_Q`	transformed design matrix in order to calculate only the diagonal of the fourth derivative of the likelihood
`temp_deriv3`	temporary matrix for third derivatives calculation when type="net" to save computation time
`temp_deriv4`	temporary matrix for fourth derivatives calculation when type="net" to save computation time
`event`	vector of right-censoring indicators
`expected`	vector of expected hazard rates
`type`	"net" or "overall"
`Ve`	frequentist covariance matrix
`deriv_rho_Ve`	list of derivatives of Ve wrt rho
`mat_temp`	temporary matrix used when method="LCV" to save computation time
`deriv_mat_temp`	list of derivatives of mat_temp wrt rho
`eigen_mat_temp`	vector of eigenvalues of mat_temp
`method`	criterion used to select the smoothing parameters. Should be "LAML" or "LCV"; default is "LAML"

Value

Hessian matrix of LCV or LAML wrt rho

`instr` *Position of the nth occurrence of a string in another one*

Description

Returns the position of the nth occurrence of str2 in str1. Returns 0 if str2 is not found

Usage

```
instr(str1, str2, startpos = 1, n = 1)
```

Arguments

`str1`	main string in which str2 is to be found
`str2`	substring contained in str1
`startpos`	starting position in str1; default is 1
`n`	which occurrence is to be found; default is 1

Value

number representing the nth position of str2 in str1

Examples

```
library(survPen)

instr("character test to find the position of the third letter r","r",n=3)
```

`inv.repam` *Reverses the initial reparameterization for stable evaluation of the log determinant of the penalty matrix*

Description

Transforms the final model by reversing the initial reparameterization performed by `repam`. Derives the corrected version of the Bayesian covariance matrix

Usage

```
inv.repam(model, X.ini, S.pen.ini)
```

Arguments

`model`	survPen object, see `survPen.fit` for details
`X.ini`	initial design matrix (before reparameterization)
`S.pen.ini`	initial penalty matrices

Value

survPen object with standard parameterization

`model.cons` *Design and penalty matrices for the model*

Description

Sets up the model before optimization. Builds the design matrix, the penalty matrix and all the design matrices needed for Gauss-Legendre quadrature.

Usage

```
model.cons(
  formula,
  lambda,
  data.spec,
  t1,
  t1.name,
  t0,
  t0.name,
  event,
  event.name,
  expected,
  expected.name,
  type,
  n.legendre,
  cl,
  beta.ini
)
```

Arguments

`formula`	formula object identifying the model
`lambda`	vector of smoothing parameters
`data.spec`	data frame that represents the environment from which the covariate values and knots are to be calculated
`t1`	vector of follow-up times
`t1.name`	name of `t1` in `data.spec`

`t0`	vector of origin times (usually filled with zeros)
`t0.name`	name of `t0` in `data.spec`
`event`	vector of censoring indicators
`event.name`	name of event in `data.spec`
`expected`	vector of expected hazard
`expected.name`	name of expected in `data.spec`
`type`	"net" or "overall"
`n.legendre`	number of nodes for Gauss-Legendre quadrature
`cl`	original `survPen` call
`beta.ini`	initial set of regression parameters

Value

List of objects with the following items:

`cl`	original `survPen` call
`type`	"net" or "overall"
`n.legendre`	number of nodes for Gauss-Legendre quadrature
`n`	number of individuals
`p`	number of parameters
`X.para`	design matrix associated with fully parametric parameters (unpenalized)
`X.smooth`	design matrix associated with the penalized parameters
`X`	design matrix for the model
`leg`	list of nodes and weights for Gauss-Legendre integration on [-1;1] as returned by `gauss.quad`
`X.GL`	list of matrices (`length(X.GL)=n.legendre`) for Gauss-Legendre quadrature
`S`	penalty matrix for the model. Sum of the elements of `S.list`
`S.scale`	vector of rescaling factors for the penalty matrices
`rank.S`	rank of the penalty matrix
`S.F`	balanced penalty matrix as described in section 3.1.2 of (Wood,2016). Sum of the elements of `S.F.list`
`U.F`	Eigen vectors of S.F, useful for the initial reparameterization to separate penalized ad unpenalized subvectors. Allows stable evaluation of the log determinant of S and its derivatives
`S.smf`	List of penalty matrices associated with all "smf" calls
`S.tensor`	List of penalty matrices associated with all "tensor" calls
`S.tint`	List of penalty matrices associated with all "tint" calls
`S.rd`	List of penalty matrices associated with all "rd" calls
`smooth.name.smf`	List of names for the "smf" calls associated with S.smf

`smooth.name.tensor`	List of names for the "tensor" calls associated with S.tensor
`smooth.name.tint`	List of names for the "tint" calls associated with S.tint
`smooth.name.rd`	List of names for the "rd" calls associated with S.rd
`S.pen`	List of all the rescaled penalty matrices redimensioned to df.tot size. Every element of `pen` noted `pen[[i]]` is made from a penalty matrix returned by `smooth.cons` and is multiplied by the factor S.scale=norm(X,type="I")^2/norm(pen[[i]],type="I")
`S.list`	Equivalent to S.pen but with every element multiplied by its associated smoothing parameter
`S.F.list`	Equivalent to S.pen but with every element divided by its Frobenius norm
`lambda`	vector of smoothing parameters
`df.para`	degrees of freedom associated with fully parametric terms (unpenalized)
`df.smooth`	degrees of freedom associated with penalized terms
`df.tot`	`df.para` + `df.smooth`
`list.smf`	List of all `smf.smooth.spec` objects contained in the model
`list.tensor`	List of all `tensor.smooth.spec` objects contained in the model
`list.tint`	List of all `tint.smooth.spec` objects contained in the model
`nb.smooth`	number of smoothing parameters
`Z.smf`	List of matrices that represents the sum-to-zero constraints to apply for `smf` splines
`Z.tensor`	List of matrices that represents the sum-to-zero constraints to apply for `tensor` splines
`Z.tint`	List of matrices that represents the sum-to-zero constraints to apply for `tint` splines
`beta.ini`	initial set of regression parameters

Examples

```
library(survPen)

# standard spline of time with 4 knots

data <- data.frame(time=seq(0,5,length=100),event=1,t0=0)

form <- ~ smf(time,knots=c(0,1,3,5))

t1 <- eval(substitute(time), data)
t0 <- eval(substitute(t0), data)
event <- eval(substitute(event), data)

# The following code sets up everything we need in order to fit the model
model.c <- model.cons(form,lambda=0,data.spec=data,t1=t1,t1.name="time",
t0=rep(0,100),t0.name="t0",event=event,event.name="event",
expected=NULL,expected.name=NULL,type="overall",n.legendre=20,
cl="survPen(form,data,t1=time,event=event)",beta.ini=NULL)
```

NR.beta — *Inner Newton-Raphson algorithm for regression parameters estimation*

Description

Applies Newton-Raphson algorithm for beta estimation. Two specific modifications aims at guaranteeing convergence : first the hessian is perturbed whenever it is not positive definite and second, at each step, if the penalized log-likelihood is not maximized, the step is halved until it is.

Usage

```
NR.beta(build, beta.ini, detail.beta, max.it.beta = 200, tol.beta = 1e-04)
```

Arguments

`build`	list of objects returned by `model.cons`
`beta.ini`	vector of initial regression parameters; default is NULL, in which case the first beta will be `log(sum(event)/sum(t1))` and the others will be zero (except if there are "by" variables in which case all betas are set to zero)
`detail.beta`	if TRUE, details concerning the optimization process in the regression parameters are displayed; default is FALSE
`max.it.beta`	maximum number of iterations to reach convergence in the regression parameters; default is 200
`tol.beta`	convergence tolerance for regression parameters; default is `1e-04`

Details

If we note `ll.pen` and `beta` respectively the current penalized log-likelihood and estimated parameters and `ll.pen.old` and `betaold` the previous ones, the algorithm goes on while (abs(ll.pen-ll.pen.old)>tol.beta) or any(abs((beta-betaold)/betaold)>tol.beta)

Value

List of objects:

`beta`	estimated regression parameters
`ll.unpen`	log-likelihood at convergence
`ll.pen`	penalized log-likelihood at convergence
`haz.GL`	list of all the matrix-vector multiplications X.GL[[i]]%*%beta for Gauss Legendre integration. Useful to avoid repeating operations in `survPen.fit`
`iter.beta`	number of iterations needed to converge

Examples

```
library(survPen)

# standard spline of time with 4 knots

data <- data.frame(time=seq(0,5,length=100),event=1,t0=0)

form <- ~ smf(time,knots=c(0,1,3,5))

t1 <- eval(substitute(time), data)
t0 <- eval(substitute(t0), data)
event <- eval(substitute(event), data)

# Setting up the model before fitting
model.c <- model.cons(form,lambda=0,data.spec=data,t1=t1,t1.name="time",
t0=rep(0,100),t0.name="t0",event=event,event.name="event",
expected=NULL,expected.name=NULL,type="overall",n.legendre=20,
cl="survPen(form,data,t1=time,event=event)",beta.ini=NULL)

# Estimating the regression parameters at given smoothing parameter (here lambda=0)
Newton1 <- NR.beta(model.c,beta.ini=rep(0,4),detail.beta=TRUE)
```

`NR.rho` *Outer Newton-Raphson algorithm for smoothing parameters estimation via LCV or LAML optimization*

Description

Applies Newton-Raphson algorithm for smoothing parameters estimation. Two specific modifications aims at guaranteeing convergence : first the hessian is perturbed whenever it is not positive definite and second, at each step, if LCV or -LAML is not minimized, the step is halved until it is.

Usage

```
NR.rho(
  build,
  rho.ini,
  data,
  formula,
  max.it.beta = 200,
  max.it.rho = 30,
  beta.ini = NULL,
  detail.rho = FALSE,
  detail.beta = FALSE,
  nb.smooth,
  tol.beta = 1e-04,
  tol.rho = 1e-04,
  step.max = 5,
  method = "LAML"
)
```

Arguments

`build`	list of objects returned by `model.cons`
`rho.ini`	vector of initial log smoothing parameters; if it is NULL, all log lambda are set to -1
`data`	an optional data frame containing the variables in the model
`formula`	formula object specifying the model
`max.it.beta`	maximum number of iterations to reach convergence in the regression parameters; default is 200
`max.it.rho`	maximum number of iterations to reach convergence in the smoothing parameters; default is 30
`beta.ini`	vector of initial regression parameters; default is NULL, in which case the first beta will be `log(sum(event)/sum(t1))` and the others will be zero (except if there are "by" variables in which case all betas are set to zero)
`detail.rho`	if TRUE, details concerning the optimization process in the smoothing parameters are displayed; default is FALSE
`detail.beta`	if TRUE, details concerning the optimization process in the regression parameters are displayed; default is FALSE
`nb.smooth`	number of smoothing parameters
`tol.beta`	convergence tolerance for regression parameters; default is `1e-04`
`tol.rho`	convergence tolerance for smoothing parameters; default is `1e-04`
`step.max`	maximum absolute value possible for any component of the step vector (on the log smoothing parameter scale); default is 5
`method`	LCV or LAML; default is LAML

Details

If we note `val` the current LCV or LAML value, `val.old` the previous one and `grad` the gradient vector of LCV or LAML with respect to the log smoothing parameters, the algorithm goes on `while(abs(val-val.old)>tol.rho|any(abs(grad)>tol.rho))`

Value

object of class survPen (see `survPen.fit` for details)

Examples

```
library(survPen)

# standard spline of time with 4 knots
```

```
data <- data.frame(time=seq(0,5,length=100),event=1,t0=0)

form <- ~ smf(time,knots=c(0,1,3,5))

t1 <- eval(substitute(time), data)
t0 <- eval(substitute(t0), data)
event <- eval(substitute(event), data)

# Setting up the model before fitting
model.c <- model.cons(form,lambda=0,data.spec=data,t1=t1,t1.name="time",
t0=rep(0,100),t0.name="t0",event=event,event.name="event",
expected=0,expected.name=NULL,type="overall",n.legendre=20,
cl="survPen(form,data,t1=time,event=event)",beta.ini=NULL)

# Estimating the smoothing parameter and the regression parameters
# we need to apply a reparameterization to model.c before fitting
Newton2 <- NR.rho(repam(model.c)$build,rho.ini=-1,data,form,nb.smooth=1,detail.rho=TRUE)
```

predict.survPen — *Hazard and Survival prediction from fitted* survPen *model*

Description

Takes a fitted survPen object and produces hazard and survival predictions given a new set of values for the model covariates.

Usage

```
## S3 method for class 'survPen'
predict(
  object,
  newdata,
  newdata.ref = NULL,
  n.legendre = 50,
  conf.int = 0.95,
  do.surv = TRUE,
  type = "standard",
  exclude.random = FALSE,
  get.deriv.H = FALSE,
  ...
)
```

Arguments

object	a fitted survPen object as produced by survPen.fit
newdata	data frame giving the new covariates value

`newdata.ref`	data frame giving the new covariates value for the reference population (used only when type="HR")
`n.legendre`	number of nodes to approximate the cumulative hazard by Gauss-Legendre quadrature; default is 50
`conf.int`	numeric value giving the precision of the confidence intervals; default is 0.95
`do.surv`	If TRUE, the survival and its lower and upper confidence values are computed. Survival computation requires numerical integration and can be time-consuming so if you only want the hazard use do.surv=FALSE; default is TRUE
`type,`	if type="lpmatrix" returns the design matrix (or linear predictor matrix) corresponding to the new values of the covariates; if equals "HR", returns the predicted HR and CIs between newdata and newdata.ref; default is "standard" for classical hazard and survival estimation
`exclude.random`	if TRUE all random effects are set to zero; default is FALSE
`get.deriv.H`	if TRUE, the derivatives wrt to the regression parameters of the cumulative hazard are returned; default is FALSE
`...`	other arguments

Details

The confidence intervals noted CI.U are built on the log cumulative hazard scale U=log(H) (efficient scale in terms of respect towards the normality assumption) using Delta method. The confidence intervals on the survival scale are then `CI.surv = exp(-exp(CI.U))`

Value

List of objects:

`haz`	hazard predicted by the model
`haz.inf`	lower value for the confidence interval on the hazard based on the Bayesian covariance matrix Vp (Wood et al. 2016)
`haz.sup`	Upper value for the confidence interval on the hazard based on the Bayesian covariance matrix Vp
`surv`	survival predicted by the model
`surv.inf`	lower value for the confidence interval on the survival based on the Bayesian covariance matrix Vp
`surv.sup`	Upper value for the confidence interval on the survival based on the Bayesian covariance matrix Vp
`deriv.H`	derivatives wrt to the regression parameters of the cumulative hazard. Useful to calculate standardized survival
`HR`	predicted hazard ratio ; only when type = "HR"
`HR.inf`	lower value for the confidence interval on the hazard ratio based on the Bayesian covariance matrix Vp ; only when type = "HR"
`HR.sup`	Upper value for the confidence interval on the hazard ratio based on the Bayesian covariance matrix Vp ; only when type = "HR"

References

Wood, S.N., Pya, N. and Saefken, B. (2016), Smoothing parameter and model selection for general smooth models (with discussion). Journal of the American Statistical Association 111, 1548-1575

Examples

```
library(survPen)

data(datCancer) # simulated dataset with 2000 individuals diagnosed with cervical cancer

# model : unidimensional penalized spline for time since diagnosis with 5 knots
f1 <- ~smf(fu,df=5)

# hazard model
mod1 <- survPen(f1,data=datCancer,t1=fu,event=dead,expected=NULL,method="LAML")

# predicting hazard and survival at time 1
pred <- predict(mod1,data.frame(fu=1))
pred$haz
pred$surv

# predicting hazard ratio between age 70 and age 30
pred.HR <- predict(mod1,data.frame(fu=1,age=70),newdata.ref=data.frame(fu=1,age=30),type="HR")
pred.HR$HR
pred.HR$HR.inf
pred.HR$HR.sup
```

`print.summary.survPen` *print summary for a* `survPen` *fit*

Description

print summary for a `survPen` fit

Usage

```
## S3 method for class 'summary.survPen'
print(
  x,
  digits = max(3, getOption("digits") - 2),
  signif.stars = getOption("show.signif.stars"),
  ...
)
```

Arguments

`x`	an object of class `summary.survPen`
`digits`	controls number of digits printed in output.
`signif.stars`	Should significance stars be printed alongside output.
`...`	other arguments

Value

print of summary

`rd` *Defining random effects in survPen formulae*

Description

Used inside a formula object to define a random effect.

Usage

```
rd(...)
```

Arguments

`...`	Any number of covariates separated by ","

Value

object of class `rd.smooth.spec`

Examples

```
# cubic regression spline of time with 10 unspecified knots + random effect at the cluster level
formula.test <- ~smf(time,df=10) + rd(cluster)
```

`repam` *Applies initial reparameterization for stable evaluation of the log determinant of the penalty matrix*

Description

Transforms the object from `model.cons` by applying the matrix reparameterization (matrix U.F). The reparameterization is reversed at convergence by `inv.repam`.

Usage

```
repam(build)
```

Arguments

`build`	object as returned by `model.cons`

Value

`build`	an object as returned by `model.cons`
`X.ini`	initial design matrix (before reparameterization)
`S.pen.ini`	initial penalty matrices

Examples

```
library(survPen)

# standard spline of time with 4 knots

data <- data.frame(time=seq(0,5,length=100),event=1,t0=0)

form <- ~ smf(time,knots=c(0,1,3,5))

t1 <- eval(substitute(time), data)
t0 <- eval(substitute(t0), data)
event <- eval(substitute(event), data)

# Setting up the model before fitting
model.c <- model.cons(form,lambda=0,data.spec=data,t1=t1,t1.name="time",
t0=rep(0,100),t0.name="t0",event=event,event.name="event",
expected=NULL,expected.name=NULL,type="overall",n.legendre=20,
cl="survPen(form,data,t1=time,event=event)",beta.ini=NULL)

# Reparameterization allows separating the parameters into unpenalized and
# penalized ones for maximum numerical stability
re.model.c <- repam(model.c)
```

smf *Defining smooths in survPen formulae*

Description

Used inside a formula object to define a smooth, a tensor product smooth or a tensor product interaction. Natural cubic regression splines (linear beyond the knots, equivalent to `ns` from package `splines`) are used as marginal bases. While `tensor` builds a tensor product of marginal bases including the intercepts, `tint` applies a tensor product of the marginal bases without their intercepts. Unlike `tensor`, the marginal effects of the covariates should also be present in the formula when using `tint`. For a conceptual difference between tensor products and tensor product interactions see Section 5.6.3 from Wood (2017)

Usage

```
smf(..., knots = NULL, df = NULL, by = NULL, same.rho = FALSE)

tensor(..., knots = NULL, df = NULL, by = NULL, same.rho = FALSE)

tint(..., knots = NULL, df = NULL, by = NULL, same.rho = FALSE)
```

Arguments

`...`	Any number of covariates separated by ","
`knots`	numeric vector that specifies the knots of the splines (including boundaries); default is NULL, in which case the knots are spread through the covariate values using quantiles. Precisely, for the term "smf(x,df=df1)", the vector of knots will be: quantile(unique(x),seq(0,1,length=df1))
`df`	numeric value that indicates the number of knots (or degrees of freedom) desired; default is NULL. If knots and df are NULL, df will be set to 10
`by`	numeric or factor variable in order to define a varying coefficient smooth
`same.rho`	if the specified by variable is a factor, specifies whether the smoothing parameters should be the same for all levels; default is FALSE.

Value

object of class `smf.smooth.spec`, `tensor.smooth.spec` or `tint.smooth.spec` (see `smooth.spec` for details)

References

Wood, S. N. (2017), Generalized additive models: an introduction with R. Second Edition. London: Chapman & Hall/CRC.

Examples

```
# penalized cubic regression spline of time with 5 unspecified knots
formula.test <- ~smf(time,df=5)

# suppose that we want to fit a model from formula.test
library(survPen)
data(datCancer)

mod.test <- survPen(~smf(fu,df=5) ,data=datCancer,t1=fu,event=dead)

# then the knots can be retrieved like this:
mod.test$list.smf[[1]]$knots
# or calculated like this
quantile(unique(datCancer$fu),seq(0,1,length=5))


# penalized cubic regression splines of time and age with respectively 5 and 7 unspecified knots
formula.test2 <- ~smf(time,df=5)+smf(age,df=7)

# penalized cubic regression splines of time and age with respectively 3 and 4 specified knots
formula.test3 <- ~smf(time,knots=c(0,3,5))+smf(age,knots=c(30,50,70,90))

# penalized tensor product for time and age with respectively 5 and 4 unspecified knots leading
# to 5*4 = 20 regression parameters
formula.test <- ~tensor(time,age,df=c(5,4))

# penalized tensor product for time and age with respectively 3 and 4 specified knots
formula.test3 <- ~tensor(time,agec,knots=list(c(0,3,5),c(30,50,70,90)))

# penalized tensor product for time, age and year with respectively 6, 5 and 4 unspecified knots
formula.test <- ~tensor(time,age,year,df=c(6,5,4))

# penalized tensor product interaction for time and age with respectively 5 and 4 unspecified knots
# main effects are specified as penalized cubic regression splines
formula.test <- ~smf(time,df=5)+smf(age,df=4)+tint(time,age,df=c(5,4))
```

`smooth.cons` *Design and penalty matrices of penalized splines in a smooth.spec object*

Description

Builds the design and penalty matrices from the result of `smooth.spec`.

Usage

```
smooth.cons(
  term,
  knots,
  df,
  by = NULL,
  option,
  data.spec,
  same.rho = FALSE,
  name
)
```

Arguments

`term`	Vector of strings that generally comes from the value "term" of a `smooth.spec` object.
`knots`	List of numeric vectors that specifies the knots of the splines (including boundaries).
`df`	Degrees of freedom: numeric vector that indicates the number of knots desired for each covariate.
`by`	numeric or factor variable in order to define a varying coefficient smooth; default is NULL.
`option`	"smf", "tensor" or "tint".
`data.spec`	data frame that represents the environment from which the covariate values and knots are to be calculated; default is NULL.
`same.rho`	if there is a factor by variable, should the smoothing parameters be the same for all levels; default is FALSE.
`name`	simplified name of the smooth.spec call.

Value

List of objects with the following items:

`X`	Design matrix
`pen`	List of penalty matrices
`term`	Vector of strings giving the names of each covariate
`knots`	list of numeric vectors that specifies the knots for each covariate
`dim`	Number of covariates
`all.df`	Numeric vector giving the number of knots associated with each covariate
`sum.df`	Sum of all.df
`Z.smf`	List of matrices that represents the sum-to-zero constraint to apply for "smf" splines
`Z.tensor`	List of matrices that represents the sum-to-zero constraint to apply for "tensor" splines
`Z.tint`	List of matrices that represents the sum-to-zero constraint to apply for "tint" splines
`lambda.name`	name of the smoothing parameters

Examples

```
library(survPen)

# standard spline of time with 4 knots (so we get a design matrix with 3 columns
# because of centering constraint)

data <- data.frame(time=seq(0,5,length=100))
smooth.c <- smooth.cons("time",knots=list(c(0,1,3,5)),df=4,option="smf",
data.spec=data,name="smf(time)")
```

`smooth.cons.integral` *Design matrix of penalized splines in a smooth.spec object for Gauss-Legendre quadrature*

Description

Almost identical to `smooth.cons`. This version is dedicated to Gauss-Legendre quadrature. Here, the sum-to-zero constraints must be specified so that they correspond to the ones that were calculated with the initial dataset.

Usage

```
smooth.cons.integral(
  term,
  knots,
  df,
  by = NULL,
  option,
  data.spec,
  Z.smf,
  Z.tensor,
  Z.tint,
  name
)
```

Arguments

`term`	Vector of strings that generally comes from the value "term" of a smooth.spec object
`knots`	List of numeric vectors that specifies the knots of the splines (including boundaries).
`df`	Degrees of freedom : numeric vector that indicates the number of knots desired for each covariate.
`by`	numeric or factor variable in order to define a varying coefficient smooth; default is NULL.

`option`	"smf", "tensor" or "tint".
`data.spec`	data frame that represents the environment from which the covariate values and knots are to be calculated; default is NULL.
`Z.smf`	List of matrices that represents the sum-to-zero constraint to apply for `smf` splines.
`Z.tensor`	List of matrices that represents the sum-to-zero constraint to apply for `tensor` splines.
`Z.tint`	List of matrices that represents the sum-to-zero constraint to apply for `tint` splines.
`name`	simplified name of the smooth.spec call.

Value

design matrix

Examples

```
library(survPen)

# standard spline of time with 4 knots (so we get a design matrix with 3 columns
# because of centering constraint)

data <- data.frame(time=seq(0,5,length=100))

# retrieving sum-to-zero constraint matrices
Z.smf <- smooth.cons("time",knots=list(c(0,1,3,5)),df=4,option="smf",
data.spec=data,name="smf(time)")$Z.smf

# constructing the design matrices for Gauss-Legendre quadrature
smooth.c.int <- smooth.cons.integral("time",knots=list(c(0,1,3,5)),df=4,option="smf",data.spec=data,
name="smf(time)",Z.smf=Z.smf,Z.tensor=NULL,Z.tint=NULL)
```

`smooth.spec` *Covariates specified as penalized splines*

Description

Specifies the covariates to be considered as penalized splines.

Usage

```
smooth.spec(
  ...,
  knots = NULL,
  df = NULL,
  by = NULL,
  option = NULL,
  same.rho = FALSE
)
```

Arguments

`...`	Numeric vectors specified in `smf`, `tensor` or `tint`
`knots`	List of numeric vectors that specifies the knots of the splines (including boundaries); default is NULL
`df`	Degrees of freedom: numeric vector that indicates the number of knots desired for each covariate; default is NULL
`by`	numeric or factor variable in order to define a varying coefficient smooth; default is NULL
`option`	"smf", "tensor" or "tint". Depends on the wrapper function; default is "smf"
`same.rho`	if there is a factor by variable, should the smoothing parameters be the same for all levels; default is FALSE.

Value

object of class smooth.spec

`term`	Vector of strings giving the names of each covariate specified in ...
`dim`	Numeric value giving the number of covariates associated with this spline
`knots`	list of numeric vectors that specifies the knots for each covariate
`df`	Numeric vector giving the number of knots associated with each covariate
`by`	numeric or factor variable in order to define a varying coefficient smooth
`same.rho`	if there is a factor by variable, should the smoothing parameters be the same for all levels; default is FALSE
`name`	simplified name of the call to function smooth.spec

Examples

```
library(survPen)

# standard spline of time with 10 unspecified knots
smooth.spec(time)

# tensor of time and age with 5*5 specified knots
smooth.s <- smooth.spec(time,age,knots=list(time=seq(0,5,length=5),age=seq(20,80,length=5)),
option="tensor")
```

`summary.survPen` *Summary for a* `survPen` *fit*

Description

Takes a fitted `survPen` object and produces various useful summaries from it.

Usage

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

Arguments

`object`	a fitted `survPen` object as produced by `survPen.fit`
`...`	other arguments

Value

List of objects:

`call`	the original survPen call
`formula`	the original survPen formula
`coefficients`	reports the regression parameters estimates for unpenalized terms with the associated standard errors
`edf.per.smooth`	reports the edf associated with each smooth term
`random`	TRUE if there are random effects in the model
`random.effects`	reports the estimates of the log standard deviation (log(sd)) of every random effects plus the estimated standard error (also on the log(sd) scale)
`likelihood`	unpenalized likelihood of the model
`penalized.likelihood`	penalized likelihood of the model
`nb.smooth`	number of smoothing parameters
`smoothing.parameter`	smoothing parameters estimates
`parameters`	number of regression parameters
`edf`	effective degrees of freedom
`method`	smoothing selection criterion used (LAML or LCV)
`val.criterion`	minimized value of criterion. For LAML, what is reported is the negative log marginal likelihood
`converged`	convergence indicator, TRUE or FALSE. TRUE if Hess.beta.modif=FALSE and Hess.rho.modif=FALSE (or NULL)

Examples

```
library(survPen)

data(datCancer) # simulated dataset with 2000 individuals diagnosed with cervical cancer

# model : unidimensional penalized spline for time since diagnosis with 5 knots
f1 <- ~smf(fu,df=5)

# fitting hazard model
mod1 <- survPen(f1,data=datCancer,t1=fu,event=dead,expected=NULL,method="LAML")

# summary
summary(mod1)
```

survPen — *(Excess) hazard model with (multidimensional) penalized splines and integrated smoothness estimation*

Description

Fits an (excess) hazard model with (multidimensional) penalized splines allowing for time-dependent effects, non-linear effects and interactions between several continuous covariates. The linear predictor is specified on the logarithm of the (excess) hazard. Smooth terms are represented using cubic regression splines with associated quadratic penalties. For multidimensional smooths, tensor product splines or tensor product interactions are available. Smoothness is estimated automatically by optimizing one of two criteria: Laplace approximate marginal likelihood (LAML) or likelihood cross-validation (LCV). When specifying the model's formula, no distinction is made between the part relative to the form of the baseline hazard and the one relative to the effects of the covariates. Thus, time-dependent effects are naturally specified as interactions with some function of time via "*" or ":". See the examples below for more details. The main functions of the survPen package are `survPen`, `smf`, `tensor`, `tint` and `rd`. The first one fits the model while the other four are constructors for penalized splines.

The user must be aware that the `survPen` package does not depend on `mgcv`. Thus, all the functionalities available in `mgcv` in terms of types of splines (such as thin plate regression splines or P-splines) are not available in `survPen` (yet).

Usage

```
survPen(
  formula,
  data,
  t1,
  t0 = NULL,
  event,
  expected = NULL,
  lambda = NULL,
  rho.ini = NULL,
  max.it.beta = 200,
  max.it.rho = 30,
  beta.ini = NULL,
  detail.rho = FALSE,
  detail.beta = FALSE,
  n.legendre = 20,
  method = "LAML",
  tol.beta = 1e-04,
  tol.rho = 1e-04,
  step.max = 5
)
```

Arguments

`formula`	formula object specifying the model. Penalized terms are specified using `smf` (comparable to `s(...,bs="cr")` in `mgcv`), `tensor` (comparable to `te(...,bs="cr")` in `mgcv`), `tint` (comparable to `ti(...,bs="cr")` in `mgcv`), or `rd` (comparable to `s(...,bs="re")` in `mgcv`).
`data`	an optional data frame containing the variables in the model
`t1`	vector of follow-up times or name of the column in `data` containing follow-up times
`t0`	vector of origin times or name of the column in `data` containing origin times; allows to take into account left truncation; default is NULL, in which case it will be a vector of zeroes
`event`	vector of right-censoring indicators or name of the column in `data` containing right-censoring indicators; 1 if the event occurred and 0 otherwise
`expected`	(for net survival only) vector of expected hazard or name of the column in `data` containing expected hazard; default is NULL, in which case overall survival will be estimated
`lambda`	vector of smoothing parameters; default is NULL when it is to be estimated by LAML or LCV
`rho.ini`	vector of initial log smoothing parameters; default is NULL, in which case every initial log lambda will be -1
`max.it.beta`	maximum number of iterations to reach convergence in the regression parameters; default is 200
`max.it.rho`	maximum number of iterations to reach convergence in the smoothing parameters; default is 30
`beta.ini`	vector of initial regression parameters; default is NULL, in which case the first beta will be `log(sum(event)/sum(t1))` and the others will be zero (except if there are "by" variables in which case all betas are set to zero)
`detail.rho`	if TRUE, details concerning the optimization process in the smoothing parameters are displayed; default is FALSE
`detail.beta`	if TRUE, details concerning the optimization process in the regression parameters are displayed; default is FALSE

`n.legendre`	number of Gauss-Legendre quadrature nodes to be used to compute the cumulative hazard; default is 20
`method`	criterion used to select the smoothing parameters. Should be "LAML" or "LCV"; default is "LAML"
`tol.beta`	convergence tolerance for regression parameters; default is `1e-04`. See `NR.beta` for details
`tol.rho`	convergence tolerance for smoothing parameters; default is `1e-04`. See `NR.rho` for details
`step.max`	maximum absolute value possible for any component of the step vector (on the log smoothing parameter scale) in LCV or LAML optimization; default is 5. If necessary, consider lowering this value to achieve convergence

Details

In time-to-event analysis, we may deal with one or several continuous covariates whose functional forms, time-dependent effects and interaction structure are challenging. One possible way to deal with these effects and interactions is to use the classical approximation of the survival likelihood by a Poisson likelihood. Thus, by artificially splitting the data, the package `mgcv` can then be used to fit penalized hazard models (Remontet et al. 2018). The problem with this option is that the setup is rather complex and the method can fail with huge datasets (before splitting). Wood et al. (2016) provided a general penalized framework that made available smooth function estimation to a wide variety of models. They proposed to estimate smoothing parameters by maximizing a Laplace approximate marginal likelihood (LAML) criterion and demonstrate how statistical consistency is maintained by doing so. The `survPen` function implements the framework described by Wood et al. (2016) for modelling time-to-event data without requiring data splitting and Poisson likelihood approximation. The effects of continuous covariates are represented using low rank spline bases with associated quadratic penalties. The `survPen` function allows to account simultaneously for time-dependent effects, non-linear effects and interactions between several continuous covariates without the need to build a possibly demanding model-selection procedure. Besides LAML, a likelihood cross-validation (LCV) criterion (O Sullivan 1988) can be used for smoothing parameter estimation. First and second derivatives of LCV with respect to the smoothing parameters are implemented so that LCV optimization is computationally equivalent to the LAML optimization proposed by Wood et al. (2016). In practice, LAML optimization is generally both a bit faster and a bit more stable so it is used as default. For m covariates $(x_1, \ldots, x_m)$, if we note $h(t, x_1, \ldots, x_m)$ the hazard at time t, the hazard model is the following :

$$log[h(t, x_1, \ldots, x_m)] = \sum_j g_j(t, x_1, \ldots, x_m)$$

where each g_j is either the marginal basis of a specific covariate or a tensor product smooth of any number of covariates. The marginal bases of the covariates are represented as natural (or restricted) cubic splines (as in function `ns` from library `splines`) with associated quadratic penalties. Full parametric (unpenalized) terms for the effects of covariates are also possible (see the examples below). Each g_j is then associated with zero, one or several smoothing parameters. The estimation procedure is based on outer Newton-Raphson iterations for the smoothing parameters and on inner Newton-Raphson iterations for the regression parameters (see Wood et al. 2016). Estimation of the regression parameters in the inner algorithm is by direct maximization of the penalized likelihood of the survival model, therefore avoiding data augmentation and Poisson likelihood approximation.

The cumulative hazard included in the log-likelihood is approximated by Gauss-Legendre quadrature for numerical stability.

Value

Object of class "survPen" (see `survPenObject` for details)

by variables

The `smf`, `tensor` and `tint` terms used to specify smooths accept an argument `by`. This `by` argument allows for building varying-coefficient models i.e. for letting smooths interact with factors or parametric terms. If a `by` variable is numeric, then its ith element multiples the ith row of the model matrix corresponding to the smooth term concerned. If a `by` variable is a factor then it generates an indicator vector for each level of the factor, unless it is an ordered factor. In the non-ordered case, the model matrix for the smooth term is then replicated for each factor level, and each copy has its rows multiplied by the corresponding rows of its indicator variable. The smoothness penalties are also duplicated for each factor level. In short a different smooth is generated for each factor level. The main interest of by variables over separated models is the `same.rho` argument (for `smf`, `tensor` and `tint`) which allows forcing all smooths to have the same smoothing parameter(s). Ordered `by` variables are handled in the same way, except that no smooth is generated for the first level of the ordered factor. This is useful if you are interested in differences from a reference level.

See the survival_analysis_with_survPen vignette for more details.

Random effects

i.i.d random effects can be specified using penalization. Indeed, the ridge penalty is equivalent to an assumption that the regression parameters are i.i.d. normal random effects. Thus, it is easy to fit a frailty hazard model. For example, consider the model term `rd(clust)` which will result in a model matrix component corresponding to `model.matrix(~clust-1)` being added to the model matrix for the whole model. The associated regression parameters are assumed i.i.d. normal, with unknown variance (to be estimated). This assumption is equivalent to an identity penalty matrix (i.e. a ridge penalty) on the regression parameters. The unknown smoothing parameter λ associated with the term `rd(clust)` is directly linked to the unknown variance σ^2: $\sigma^2 = \frac{1}{\lambda * S.scale}$. Then, the estimated log standard deviation is: $log(\hat{\sigma}) = -0.5 * log(\hat{\lambda}) - 0.5 * log(S.scale)$. And the estimated variance of the log standard deviation is: $Var[log(\hat{\sigma})] = 0.25 * Var[log(\hat{\lambda})] = 0.25 * inv.Hess.rho$. See the survival_analysis_with_survPen vignette for more details. This approach allows implementing commonly used random effect structures. For example if `g` is a factor then `rd(g)` produces a random parameter for each level of `g`, the random parameters being i.i.d. normal. If `g` is a factor and `x` is numeric, then `rd(g,x)` produces an i.i.d. normal random slope relating the response to `x` for each level of `g`. Thus, random effects treated as penalized splines allow specifying frailty (excess) hazard models (Charvat et al. 2016). For each individual i from cluster (usually geographical unit) j, a possible model would be:

$$log[h(t_{ij}, x_{ij1}, \ldots, x_{ijm})] = \sum_k g_k(t_{ij}, x_{ij1}, \ldots, x_{ijm}) + w_j$$

where `w_j` follows a normal distribution with mean 0. The random effect associated with the cluster variable is specified with the model term `rd(cluster)`. We could also specify a random effect depending on age for example with the model term `rd(cluster,age)`. `u_j = exp(w_j)` is known as the shared frailty.

See the survival_analysis_with_survPen vignette for more details.

Excess hazard model

When studying the survival of patients who suffer from a common pathology we may be interested in the concept of excess mortality that represents the mortality due to that pathology. For example, in cancer epidemiology, individuals may die from cancer or from another cause. The problem is that the cause of death is often either unavailable or unreliable. Supposing that the mortality due to other causes may be obtained from the total mortality of the general population (called expected mortality for cancer patients), we can define the concept of excess mortality. The excess mortality is directly linked to the concept of net survival, which would be the observed survival if patients could not die from other causes. Therefore, when such competing events are present, one may choose to fit an excess hazard model instead of a classical hazard model. Flexible excess hazard models have already been proposed (for examples see Remontet et al. 2007, Charvat et al. 2016) but none of them deals with a penalized framework (in a non-fully Bayesian setting). Excess mortality can be estimated supposing that, in patients suffering from a common pathology, mortality due to others causes than the pathology can be obtained from the (all cause) mortality of the general population; the latter is referred to as the expected mortality h_P. The mortality observed in the patients (h_O) is actually decomposed as the sum of h_P and the excess mortality due to the pathology (h_E). This may be written as:

$$h_O(t,x) = h_E(t,x) + h_P(a+t,z)$$

In that equation, t is the time since cancer diagnosis, a is the age at diagnosis, h_P is the mortality of the general population at age $a+t$ given demographical characteristics z (h_P is considered known and available from national statistics), and x a vector of variables that may have an effect on h_E. Including the age in the model is necessary in order to deal with the informative censoring due to other causes of death. Thus, for m covariates $(x_1,\ldots,x_m)$, if we note $h_E(t,x_1,\ldots,x_m)$ the excess hazard at time t, the excess hazard model is the following:

$$log[h_E(t,x_1,\ldots,x_m)] = \sum_j g_j(t,x_1,\ldots,x_m)$$

Convergence

No convergence indicator is given. If the function returns an object of class `survPen`, it means that the algorithm has converged. If convergence issues occur, an error message is displayed. If convergence issues occur, do not refrain to use detail.rho and/or detail.beta to see exactly what is going on in the optimization process. To achieve convergence, consider lowering step.max and/or changing rho.ini and beta.ini. If your excess hazard model fails to converge, consider fitting a hazard model and use its estimated parameters as initial values for the excess hazard model. Finally, do not refrain to change the "method" argument (LCV or LAML) if convergence issues occur.

Other

Be aware that all character variables are transformed to factors before fitting.

References

Charvat, H., Remontet, L., Bossard, N., Roche, L., Dejardin, O., Rachet, B., ... and Belot, A. (2016), A multilevel excess hazard model to estimate net survival on hierarchical data allowing for non linear and non proportional effects of covariates. Statistics in medicine, 35(18), 3066-3084.

Fauvernier, M., Roche, L., Uhry, Z., Tron, L., Bossard, N., Remontet, L. and the CENSUR Working Survival Group. Multidimensional penalized hazard model with continuous covariates: applications for studying trends and social inequalities in cancer survival, in revision in the Journal of the Royal Statistical Society, series C.

O Sullivan, F. (1988), Fast computation of fully automated log-density and log-hazard estimators. SIAM Journal on scientific and statistical computing, 9(2), 363-379.

Remontet, L., Bossard, N., Belot, A., & Esteve, J. (2007), An overall strategy based on regression models to estimate relative survival and model the effects of prognostic factors in cancer survival studies. Statistics in medicine, 26(10), 2214-2228.

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Wood, S.N., Pya, N. and Saefken, B. (2016), Smoothing parameter and model selection for general smooth models (with discussion). Journal of the American Statistical Association 111, 1548-1575

Examples

```
library(survPen)
data(datCancer) # simulated dataset with 2000 individuals diagnosed with cervical cancer

#-------------------------------------------------------- example 0
# Comparison between restricted cubic splines and penalized restricted cubic splines

library(splines)

# unpenalized
f <- ~ns(fu,knots=c(0.25, 0.5, 1, 2, 4),Boundary.knots=c(0,5))

mod <- survPen(f,data=datCancer,t1=fu,event=dead)

# penalized
f.pen <- ~ smf(fu,knots=c(0,0.25, 0.5, 1, 2, 4,5)) # careful here: the boundary knots are included

mod.pen <- survPen(f.pen,data=datCancer,t1=fu,event=dead)
```

```
# predictions

new.time <- seq(0,5,length=100)
pred <- predict(mod,data.frame(fu=new.time))
pred.pen <- predict(mod.pen,data.frame(fu=new.time))

par(mfrow=c(1,1))
plot(new.time,pred$haz,type="l",ylim=c(0,0.2),main="hazard vs time",
xlab="time since diagnosis (years)",ylab="hazard",col="red")
lines(new.time,pred.pen$haz,col="blue3")
legend("topright",legend=c("unpenalized","penalized"),
col=c("red","blue3"),lty=rep(1,2))



#-------------------------------------------------------- example 1
# hazard models with unpenalized formulas compared to a penalized tensor product smooth

library(survPen)
data(datCancer) # simulated dataset with 2000 individuals diagnosed with cervical cancer

# constant hazard model
f.cst <- ~1
mod.cst <- survPen(f.cst,data=datCancer,t1=fu,event=dead)

# piecewise constant hazard model
f.pwcst <- ~cut(fu,breaks=seq(0,5,by=0.5),include.lowest=TRUE)
mod.pwcst <- survPen(f.pwcst,data=datCancer,t1=fu,event=dead,n.legendre=200)
# we increase the number of points for Gauss-Legendre quadrature to make sure that the cumulative
# hazard is properly approximated

# linear effect of time
f.lin <- ~fu
mod.lin <- survPen(f.lin,data=datCancer,t1=fu,event=dead)

# linear effect of time and age with proportional effect of age
f.lin.age <- ~fu+age
mod.lin.age <- survPen(f.lin.age,data=datCancer,t1=fu,event=dead)

# linear effect of time and age with time-dependent effect of age (linear)
f.lin.inter.age <- ~fu*age
mod.lin.inter.age <- survPen(f.lin.inter.age,data=datCancer,t1=fu,event=dead)

# cubic B-spline of time with a knot at 1 year, linear effect of age and time-dependent effect
# of age with a quadratic B-spline of time with a knot at 1 year
library(splines)
f.spline.inter.age <- ~bs(fu,knots=c(1),Boundary.knots=c(0,5))+age+
age:bs(fu,knots=c(1),Boundary.knots=c(0,5),degree=2)
# here, bs indicates an unpenalized cubic spline

mod.spline.inter.age <- survPen(f.spline.inter.age,data=datCancer,t1=fu,event=dead)
```

```
# tensor of time and age
f.tensor <- ~tensor(fu,age)
mod.tensor <- survPen(f.tensor,data=datCancer,t1=fu,event=dead)


# predictions of the models at age 60

new.time <- seq(0,5,length=100)
pred.cst <- predict(mod.cst,data.frame(fu=new.time))
pred.pwcst <- predict(mod.pwcst,data.frame(fu=new.time))
pred.lin <- predict(mod.lin,data.frame(fu=new.time))
pred.lin.age <- predict(mod.lin.age,data.frame(fu=new.time,age=60))
pred.lin.inter.age <- predict(mod.lin.inter.age,data.frame(fu=new.time,age=60))
pred.spline.inter.age <- predict(mod.spline.inter.age,data.frame(fu=new.time,age=60))
pred.tensor <- predict(mod.tensor,data.frame(fu=new.time,age=60))

lwd1 <- 2

par(mfrow=c(1,1))
plot(new.time,pred.cst$haz,type="l",ylim=c(0,0.2),main="hazard vs time",
xlab="time since diagnosis (years)",ylab="hazard",col="blue3",lwd=lwd1)
segments(x0=new.time[1:99],x1=new.time[2:100],y0=pred.pwcst$haz[1:99],col="lightblue2",lwd=lwd1)
lines(new.time,pred.lin$haz,col="green3",lwd=lwd1)
lines(new.time,pred.lin.age$haz,col="yellow",lwd=lwd1)
lines(new.time,pred.lin.inter.age$haz,col="orange",lwd=lwd1)
lines(new.time,pred.spline.inter.age$haz,col="red",lwd=lwd1)
lines(new.time,pred.tensor$haz,col="black",lwd=lwd1)
legend("topright",
legend=c("cst","pwcst","lin","lin.age","lin.inter.age","spline.inter.age","tensor"),
col=c("blue3","lightblue2","green3","yellow","orange","red","black"),
lty=rep(1,7),lwd=rep(lwd1,7))


# you can also calculate the hazard yourself with the lpmatrix option.
# For example, compare the following predictions:
haz.tensor <- pred.tensor$haz

X.tensor <- predict(mod.tensor,data.frame(fu=new.time,age=60),type="lpmatrix")
haz.tensor.lpmatrix <- exp(X.tensor%mult%mod.tensor$coefficients)

summary(haz.tensor.lpmatrix - haz.tensor)

#---------------- The 95% confidence intervals can be calculated like this:

# standard errors from the Bayesian covariance matrix Vp
std <- sqrt(rowSums((X.tensor%mult%mod.tensor$Vp)*X.tensor))

qt.norm <- stats::qnorm(1-(1-0.95)/2)
haz.inf <- as.vector(exp(X.tensor%mult%mod.tensor$coefficients-qt.norm*std))
haz.sup <- as.vector(exp(X.tensor%mult%mod.tensor$coefficients+qt.norm*std))

# checking that they are similar to the ones given by the predict function
summary(haz.inf - pred.tensor$haz.inf)
summary(haz.sup - pred.tensor$haz.sup)


#--------------------------------------------------------- example 2

library(survPen)
data(datCancer) # simulated dataset with 2000 individuals diagnosed with cervical cancer

# model : unidimensional penalized spline for time since diagnosis with 5 knots
f1 <- ~smf(fu,df=5)
# when knots are not specified, quantiles are used. For example, for the term "smf(x,df=df1)",
# the vector of knots will be: quantile(unique(x),seq(0,1,length=df1))

# you can specify your own knots if you want
# f1 <- ~smf(fu,knots=c(0,1,3,6,8))

# hazard model
mod1 <- survPen(f1,data=datCancer,t1=fu,event=dead,expected=NULL,method="LAML")
summary(mod1)

# to see where the knots were placed
mod1$list.smf

# with LCV instead of LAML
mod1bis <- survPen(f1,data=datCancer,t1=fu,event=dead,expected=NULL,method="LCV")
summary(mod1bis)

# hazard model taking into account left truncation (not representative of cancer data,
# the begin variable was simulated for illustration purposes only)
mod2 <- survPen(f1,data=datCancer,t0=begin,t1=fu,event=dead,expected=NULL,method="LAML")
summary(mod2)

# excess hazard model
mod3 <- survPen(f1,data=datCancer,t1=fu,event=dead,expected=rate,method="LAML")
summary(mod3)

# compare the predictions of the models
new.time <- seq(0,5,length=50)
pred1 <- predict(mod1,data.frame(fu=new.time))
pred1bis <- predict(mod1bis,data.frame(fu=new.time))
pred2 <- predict(mod2,data.frame(fu=new.time))
pred3 <- predict(mod3,data.frame(fu=new.time))

# LAML vs LCV
par(mfrow=c(1,2))
plot(new.time,pred1$haz,type="l",ylim=c(0,0.2),main="LCV vs LAML",
xlab="time since diagnosis (years)",ylab="hazard")
lines(new.time,pred1bis$haz,col="blue3")
legend("topright",legend=c("LAML","LCV"),col=c("black","blue3"),lty=c(1,1))

plot(new.time,pred1$surv,type="l",ylim=c(0,1),main="LCV vs LAML",
xlab="time since diagnosis (years)",ylab="survival")
lines(new.time,pred1bis$surv,col="blue3")
```

```
# hazard vs excess hazard
par(mfrow=c(1,2))
plot(new.time,pred1$haz,type="l",ylim=c(0,0.2),main="hazard vs excess hazard",
xlab="time since diagnosis (years)",ylab="hazard")
lines(new.time,pred3$haz,col="green3")
legend("topright",legend=c("overall","excess"),col=c("black","green3"),lty=c(1,1))

plot(new.time,pred1$surv,type="l",ylim=c(0,1),main="survival vs net survival",
xlab="time",ylab="survival")
lines(new.time,pred3$surv,col="green3")
legend("topright",legend=c("overall survival","net survival"), col=c("black","green3"), lty=c(1,1))

# hazard vs excess hazard with 95% Bayesian confidence intervals (based on Vp matrix,
# see predict.survPen)
par(mfrow=c(1,1))
plot(new.time,pred1$haz,type="l",ylim=c(0,0.2),main="hazard vs excess hazard",
xlab="time since diagnosis (years)",ylab="hazard")
lines(new.time,pred3$haz,col="green3")
legend("topright",legend=c("overall","excess"),col=c("black","green3"),lty=c(1,1))

lines(new.time,pred1$haz.inf,lty=2)
lines(new.time,pred1$haz.sup,lty=2)

lines(new.time,pred3$haz.inf,lty=2,col="green3")
lines(new.time,pred3$haz.sup,lty=2,col="green3")



#-------------------------------------------------------- example 3

library(survPen)
data(datCancer) # simulated dataset with 2000 individuals diagnosed with cervical cancer

# models: tensor product smooth vs tensor product interaction of time since diagnosis and
# age at diagnosis. Smoothing parameters are estimated via LAML maximization
f2 <- ~tensor(fu,age,df=c(5,5))

f3 <- ~tint(fu,df=5)+tint(age,df=5)+tint(fu,age,df=c(5,5))

# hazard model
mod4 <- survPen(f2,data=datCancer,t1=fu,event=dead)
summary(mod4)

mod5 <- survPen(f3,data=datCancer,t1=fu,event=dead)
summary(mod5)

# predictions
new.age <- seq(50,90,length=50)
new.time <- seq(0,7,length=50)
```

```
Z4 <- outer(new.time,new.age,function(t,a) predict(mod4,data.frame(fu=t,age=a))$haz)
Z5 <- outer(new.time,new.age,function(t,a) predict(mod5,data.frame(fu=t,age=a))$haz)

# color settings
col.pal <- colorRampPalette(c("white", "red"))
colors <- col.pal(100)

facet <- function(z){

facet.center <- (z[-1, -1] + z[-1, -ncol(z)] + z[-nrow(z), -1] + z[-nrow(z), -ncol(z)])/4
cut(facet.center, 100)

}

# plot the hazard surfaces for both models
par(mfrow=c(1,2))
persp(new.time,new.age,Z4,col=colors[facet(Z4)],main="tensor",theta=30,
xlab="time since diagnosis",ylab="age at diagnosis",zlab="excess hazard",ticktype="detailed")
persp(new.time,new.age,Z5,col=colors[facet(Z5)],main="tint",theta=30,
xlab="time since diagnosis",ylab="age at diagnosis",zlab="excess hazard",ticktype="detailed")

#--------------------------------------------------------- example 4

library(survPen)
data(datCancer) # simulated dataset with 2000 individuals diagnosed with cervical cancer

# model : tensor product spline for time, age and yod (year of diagnosis)
# yod is not centered here since it does not create unstability but be careful in practice
# and consider centering your covariates if you encounter convergence issues
f4 <- ~tensor(fu,age,yod,df=c(5,5,5))

# excess hazard model
mod6 <- survPen(f4,data=datCancer,t1=fu,event=dead,expected=rate)
summary(mod6)


# predictions of the surfaces for ages 50, 60, 70 and 80
new.year <- seq(1990,2010,length=30)
new.time <- seq(0,5,length=50)

Z_50 <- outer(new.time,new.year,function(t,y) predict(mod6,data.frame(fu=t,yod=y,age=50))$haz)
Z_60 <- outer(new.time,new.year,function(t,y) predict(mod6,data.frame(fu=t,yod=y,age=60))$haz)
Z_70 <- outer(new.time,new.year,function(t,y) predict(mod6,data.frame(fu=t,yod=y,age=70))$haz)
Z_80 <- outer(new.time,new.year,function(t,y) predict(mod6,data.frame(fu=t,yod=y,age=80))$haz)


# plot the hazard surfaces for a given age
par(mfrow=c(2,2))
persp(new.time,new.year,Z_50,col=colors[facet(Z_50)],main="age 50",theta=20,
xlab="time since diagnosis",ylab="yod",zlab="excess hazard",ticktype="detailed")
persp(new.time,new.year,Z_60,col=colors[facet(Z_60)],main="age 60",theta=20,
xlab="time since diagnosis",ylab="yod",zlab="excess hazard",ticktype="detailed")
persp(new.time,new.year,Z_70,col=colors[facet(Z_70)],main="age 70",theta=20,
xlab="time since diagnosis",ylab="yod",zlab="excess hazard",ticktype="detailed")
persp(new.time,new.year,Z_80,col=colors[facet(Z_80)],main="age 80",theta=20,
xlab="time since diagnosis",ylab="yod",zlab="excess hazard",ticktype="detailed")

########################################
```

survPen.fit — *(Excess) hazard model with multidimensional penalized splines for given smoothing parameters*

Description

Fits an (excess) hazard model. If penalized splines are present, the smoothing parameters are specified.

Usage

```
survPen.fit(
  build,
  data,
  formula,
  max.it.beta = 200,
  beta.ini = NULL,
  detail.beta = FALSE,
  method = "LAML",
  tol.beta = 1e-04
)
```

Arguments

`build`	list of objects returned by `model.cons`
`data`	an optional data frame containing the variables in the model
`formula`	formula object specifying the model
`max.it.beta`	maximum number of iterations to reach convergence in the regression parameters; default is 200
`beta.ini`	vector of initial regression parameters; default is NULL, in which case the first beta will be `log(sum(event)/sum(t1))` and the others will be zero (except if there are "by" variables in which case all betas are set to zero)
`detail.beta`	if TRUE, details concerning the optimization process in the regression parameters are displayed; default is FALSE
`method`	criterion used to select the smoothing parameters. Should be "LAML" or "LCV"; default is "LAML"
`tol.beta`	convergence tolerance for regression parameters; default is `1e-04`. See `NR.beta` for details

Value

Object of class "survPen" (see survPenObject for details)

Examples

```
library(survPen)

# standard spline of time with 4 knots

data <- data.frame(time=seq(0,5,length=100),event=1,t0=0)

form <- ~ smf(time,knots=c(0,1,3,5))

t1 <- eval(substitute(time), data)
t0 <- eval(substitute(t0), data)
event <- eval(substitute(event), data)

# Setting up the model before fitting
model.c <- model.cons(form,lambda=0,data.spec=data,t1=t1,t1.name="time",
t0=rep(0,100),t0.name="t0",event=event,event.name="event",
expected=NULL,expected.name=NULL,type="overall",n.legendre=20,
cl="survPen(form,data,t1=time,event=event)",beta.ini=NULL)

# fitting
mod <- survPen.fit(model.c,data,form)
```

survPenObject *Fitted survPen object*

Description

A fitted survPen object returned by function survPen and of class "survPen". Method functions predict and summary are available for this class.

Value

A survPen object has the following elements:

call	original survPen call
formula	formula object specifying the model
t0.name	name of the vector of origin times
t1.name	name of the vector of follow-up times
event.name	name of the vector of right-censoring indicators
expected.name	name of the vector of expected hazard
haz	fitted hazard

`coefficients`	estimated regression parameters. Unpenalized parameters are first, followed by the penalized ones
`type`	"net" for net survival estimation with penalized excess hazard model or "overall" for overall survival with penalized hazard model
`df.para`	degrees of freedom associated with fully parametric terms (unpenalized)
`df.smooth`	degrees of freedom associated with penalized terms
`p`	number of regression parameters
`edf`	effective degrees of freedom
`edf1`	alternative effective degrees of freedom ; used as an upper bound for edf2
`edf2`	effective degrees of freedom corrected for smoothing parameter uncertainty
`aic`	Akaike information criterion with number of parameters replaced by edf when there are penalized terms. Corresponds to 2*edf - 2*ll.unpen
`aic2`	Akaike information criterion corrected for smoothing parameter uncertainty. Be careful though, this is still a work in progress, especially when one of the smoothing parameters tends to infinity.
`iter.beta`	vector of numbers of iterations needed to estimate the regression parameters for each smoothing parameters trial. It thus contains `iter.rho+1` elements.
`X`	design matrix of the model
`S`	penalty matrix of the model
`S.scale`	vector of rescaling factors for the penalty matrices
`S.list`	Equivalent to pen but with every element multiplied by its associated smoothing parameter
`S.smf`	List of penalty matrices associated with all "smf" calls
`S.tensor`	List of penalty matrices associated with all "tensor" calls
`S.tint`	List of penalty matrices associated with all "tint" calls
`S.rd`	List of penalty matrices associated with all "rd" calls
`smooth.name.smf`	List of names for the "smf" calls associated with S.smf
`smooth.name.tensor`	List of names for the "tensor" calls associated with S.tensor
`smooth.name.tint`	List of names for the "tint" calls associated with S.tint
`smooth.name.rd`	List of names for the "rd" calls associated with S.rd
`S.pen`	List of all the rescaled penalty matrices redimensioned to df.tot size. Every element of `S.pen` noted `S.pen[[i]]` is made from a penalty matrix `pen[[i]]` returned by `smooth.cons` and is multiplied by S.scale
`grad.unpen.beta`	gradient vector of the log-likelihood with respect to the regression parameters
`grad.beta`	gradient vector of the penalized log-likelihood with respect to the regression parameters
`Hess.unpen.beta`	hessian of the log-likelihood with respect to the regression parameters

`Hess.beta`	hessian of the penalized log-likelihood with respect to the regression parameters
`Hess.beta.modif`	if TRUE, the hessian of the penalized log-likelihood has been perturbed at convergence
`ll.unpen`	log-likelihood at convergence
`ll.pen`	penalized log-likelihood at convergence
`deriv.rho.beta`	transpose of the Jacobian of beta with respect to the log smoothing parameters
`deriv.rho.inv.Hess.beta`	list containing the derivatives of the inverse of `Hess` with respect to the log smoothing parameters
`deriv.rho.Hess.unpen.beta`	list containing the derivatives of `Hess.unpen` with respect to the log smoothing parameters
`lambda`	estimated or given smoothing parameters
`nb.smooth`	number of smoothing parameters
`iter.rho`	number of iterations needed to estimate the smoothing parameters
`optim.rho`	identify whether the smoothing parameters were estimated or not; 1 when exiting the function `NR.rho`; default is NULL
`method`	criterion used for smoothing parameter estimation
`criterion.val`	value of the criterion used for smoothing parameter estimation at convergence
`LCV`	Likelihood cross-validation criterion at convergence
`LAML`	negative Laplace approximate marginal likelihood at convergence
`grad.rho`	gradient vector of criterion with respect to the log smoothing parameters
`Hess.rho`	hessian matrix of criterion with respect to the log smoothing parameters
`inv.Hess.rho`	inverse of `Hess.rho`
`Hess.rho.modif`	if TRUE, the hessian of LCV or LAML has been perturbed at convergence
`Ve`	Frequentist covariance matrix
`Vp`	Bayesian covariance matrix
`Vc`	Bayesian covariance matrix corrected for smoothing parameter uncertainty (see Wood et al. 2016)
`Vc.approx`	Kass and Steffey approximation of `Vc` (see Wood et al. 2016)
`Z.smf`	List of matrices that represents the sum-to-zero constraint to apply for `smf` splines
`Z.tensor`	List of matrices that represents the sum-to-zero constraint to apply for `tensor` splines
`Z.tint`	List of matrices that represents the sum-to-zero constraint to apply for `tint` splines
`list.smf`	List of all `smf.smooth.spec` objects contained in the model
`list.tensor`	List of all `tensor.smooth.spec` objects contained in the model
`list.tint`	List of all `tint.smooth.spec` objects contained in the model

`list.rd`	List of all `rd.smooth.spec` objects contained in the model
`U.F`	Eigen vectors of S.F, useful for the initial reparameterization to separate penalized ad unpenalized subvectors. Allows stable evaluation of the log determinant of S and its derivatives
`factor.structure`	List containing the levels and classes of all factor variables present in the data frame used for fitting
`converged`	convergence indicator, TRUE or FALSE. TRUE if Hess.beta.modif=FALSE and Hess.rho.modif=FALSE (or NULL)

References

Wood, S.N., Pya, N. and Saefken, B. (2016), Smoothing parameter and model selection for general smooth models (with discussion). Journal of the American Statistical Association 111, 1548-1575

`tensor.in` *tensor model matrix for two marginal bases*

Description

Function called recursively inside `tensor.prod.X`.

Usage

```
tensor.in(X1, X2)
```

Arguments

`X1`	first marginal design matrix with n rows and p1 columns
`X2`	first marginal design matrix with n rows and p2 columns

Value

Matrix of dimensions n*(p1*p2) representing the row tensor product of the matrices X1 and X2

Examples

```
library(survPen)

# row-wise tensor product between two design matrices
set.seed(15)

X1 <- matrix(rnorm(10*3),nrow=10,ncol=3)
X2 <- matrix(rnorm(10*2),nrow=10,ncol=2)
tensor.in(X1,X2)
```

`tensor.prod.S` *Tensor product for penalty matrices*

Description

Computes the penalty matrices of a tensor product smooth from the marginal penalty matrices. The code is from function `tensor.prod.penalties` in `mgcv` package.

Usage

```
tensor.prod.S(S)
```

Arguments

`S`	list of m marginal penalty matrices

Value

`TS`	List of the penalty matrices associated with the tensor product smooth

Examples

```
library(survPen)

# tensor product between three penalty matrices
set.seed(15)

S1 <- matrix(rnorm(3*3),nrow=3,ncol=3)
S2 <- matrix(rnorm(2*2),nrow=2,ncol=2)

S1 <- 0.5*(S1 + t(S1) ) ; S2 <- 0.5*(S2 + t(S2) )

tensor.prod.S(list(S1,S2))
```

`tensor.prod.X` *tensor model matrix*

Description

Computes the model matrix of tensor product smooth from the marginal bases.

Usage

```
tensor.prod.X(X)
```

Arguments

`X`	list of m design matrices with n rows and p1, p2, ... pm columns respectively

Value

`T`	Matrix of dimensions n*(p1*p2*...*pm) representing the row tensor product of the matrices in X

Examples

```
library(survPen)

# row-wise tensor product between three design matrices
set.seed(15)

X1 <- matrix(rnorm(10*3),nrow=10,ncol=3)
X2 <- matrix(rnorm(10*2),nrow=10,ncol=2)
X3 <- matrix(rnorm(10*2),nrow=10,ncol=2)
tensor.prod.X(list(X1,X2,X3))
```

`%cross%` *Matrix cross-multiplication between two matrices*

Description

Matrix cross-multiplication between two matrices

Usage

```
Mat1 %cross% Mat2
```

Arguments

`Mat1`	a matrix.
`Mat2`	another matrix.

Value

prod the product t(Mat1)

`%mult%` *Matrix multiplication between two matrices*

Description

Matrix multiplication between two matrices

Usage

```
Mat1 %mult% Mat2
```

Arguments

`Mat1`	a matrix.
`Mat2`	another matrix.

Value

prod the product Mat1

`%vec%` *Matrix multiplication between a matrix and a vector*

Description

Matrix multiplication between a matrix and a vector

Usage

```
Mat %vec% vec
```

Arguments

`Mat`	a matrix.
`vec`	a vector.

Value

prod the product Mat

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