# Package 'INLAjoint'

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Type Package

**Title** Multivariate Joint Modeling for Longitudinal and Time-to-Event Outcomes with 'INLA'

**Version** 24.3.25

**Description** Estimation of joint models for multivariate longitudinal markers (with various distributions available) and survival outcomes (possibly accounting for competing risks) with Integrated Nested Laplace Approximations (INLA). The flexible and user friendly function joint() facilitates the use of the fast and reliable inference technique implemented in the 'INLA' package for joint modeling. More details are given in the help page of the joint() function (accessible via 'joint in the R console) and the vignette associated to the joint() function (accessible via vignette(``INLAjoint") in the R console).

License GPL-3

URL https://github.com/DenisRustand/INLAjoint

BugReports https://github.com/DenisRustand/INLAjoint/issues

**Encoding** UTF-8

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Imports numDeriv, lme4, ggplot2, methods, Matrix, nlme, mvtnorm

Additional\_repositories https://inla.r-inla-download.org/R/testing

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BuildVignettes true

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NeedsCompilation no

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Extracts model coefficients from a given model fitted with INLAjoint

# Description

coef.INLAjoint

This function extracts model coefficients from INLAjoint objects.

#### Usage

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

family.INLAjoint 3

#### **Arguments**

object an object that contains a model fitted with INLAjoint.

... Extra arguments.

family.INLAjoint

Extracts family from a given model fitted with INLAjoint

# Description

This function extracts family from INLAjoint objects.

#### Usage

```
## S3 method for class 'INLAjoint'
family(object, ...)
```

# Arguments

object an object that contains a model fitted with INLAjoint.

... Extra arguments.

fitted.INLAjoint

Extracts fitted values from a given model fitted with INLAjoint

# Description

This function extracts fitted values from INLAjoint objects. Values are associated to a name to keep track of the outcome related to each fitted value.

# Usage

```
## S3 method for class 'INLAjoint'
fitted(object, ...)
```

# Arguments

object an object that contains a model fitted with INLAjoint.

... Extra arguments.

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fixef.INLAjoint

Extracts fixed effects values from a given model fitted with INLAjoint

# Description

This function extracts fixed effects values from INLAjoint objects.

#### Usage

```
## S3 method for class 'INLAjoint'
fixef(object, ...)
```

### **Arguments**

object an object that contains a model fitted with INLAjoint.

Extra arguments.

formula.INLAjoint

Extracts formula from a given model fitted with INLAjoint

# Description

This function extracts formula from INLAjoint objects.

# Usage

```
## S3 method for class 'INLAjoint' formula(x, \ldots)
```

#### **Arguments**

x an object that contains a model fitted with INLAjoint.

... Extra arguments.

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INLAjoint INLAjoint

#### **Description**

INLAjoint is a package that fits joint models for multivariate longitudinal markers (with various distributions available) and survival outcomes (possibly accounting for competing risks) with Integrated Nested Laplace Approximations (INLA). The flexible and user friendly function joint() facilitates the use of the fast and reliable inference technique implemented in INLA package for joint modeling. More details are given in the help page of the joint function (accessible via ?joint in the R console), the vignette associated to the joint() function (accessible via vignette("INLAjoint") in the R console).

Contact: <INLAjoint@gmail.com>

#### Usage

INLAjoint()

INLAjoint.ginv
Setup ginv

#### **Description**

Setup random walk input:

#### Usage

```
INLAjoint.ginv(x, tol = sqrt(.Machine$double.eps), rankdef = NULL)
```

#### **Arguments**

x inputtoltolerancerankdefrank output:

#### Value

ginv

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INLAjoint.object

Fitted joint object

#### **Description**

An object of class INLAjoint returned by the joint function that fits a joint model to multivariate longitudinal and time-to-event data. The following functions can apply to objects of this class: plot, print, summary and priors.used.

#### Usage

INLAjoint.object

#### **Format**

An object of class NULL of length 0.

#### Value

A list with the following components:

names.fixed a vector with the name of the fixed effects of the model. The corresponding submodel is indicated by the suffix including a letter and a number ("L" for longitudinal and "S" for survival).

summary.fixed summary statistics for the fixed effects of the model. The summary statistics sorted by longitudinal and survival components are available by applying the summary function to the INLAjoint object.

summary. fixed marginals for the fixed effects of the model.

mlik log marginal-likelihood.

cpo Conditional Predictive Ordinate.

gcpo Group-Conditional Predictive Ordinate.

po Predictive ordinate.

waic Widely applicable Bayesian information criterion

model.random a vector with the name of the random parameters of the model, possibly including the following components:

RW1 model and RW2 model Random walk of order 1 or 2 corresponding to Bayesian smoothing splines for the baseline hazard risk

IID model Univariate random effect.

IIDKD model Multivariate random effects.

Copy association parameter.

summary.random summary statistics for the random parameters of the model.

marginals.random marginals for the random parameters of the model.

size.random size of the random parameters of the model.

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summary.linear.predictor summary statistics of the linear predictors. marginals.linear.predictor marginals for the linear predictors. summary.fitted.values summary statistics of the fitted values. marginals.fitted.values marginals for the fitted values. size.linear.predictor size of the linear predictors. summary.hyperpar summary statistics for the hyperparameters of the model. The summary statistics sorted by longitudinal and survival components are available by applying the summary function to the INLAjoint object. Particularly, this is the raw output of INLA and therefore the precision of the residual errors and baseline hazard functions hyperparameters are provided. Similarly, the Cholesky matrix is given for the random-effects. The summary function can easily return either variance and covariance or standard deviations and correlations for all these hyperparameters. marginals.hyperpar marginals for the hyperparameters of the model. internal.summary.hyperpar summary of the internal hyperparameters, this is similar to the summary of the hyperparameters but here they are provided as used for the computations (logarithm scale for residual error and baseline risk hyperparameters). internal .marginals .hyperpar marginals for the internal hyperparameters of the model. misc miscellaneous (as provided in the INLA output). dic Deviance Information Criterion. mode . joint.hyper . nhyper . version Version of INLA. cpu.used Computation time of INLA. all.hyper . .args . call INLA call. selection information about parameters for sampling with inla.rjmarginal. cureVar informations about cure fraction submodel for mixture cure survival models. variant information about variant for Weibull baseline hazards. SurvInfo some information about survival submodels (names of event indicator and event time variables as well as baseline hazard). famLongi list of distributions for the longitudinal markers. corLong boolean indicating if random effects are correlated across markers. control.link informations about link function (1=default). longOutcome name of longitudinal outcomes. survOutcome name of survival outcomes. assoc vector with names of all association parameters (longi-surv). id name of the id variable.

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timeVar name of time variable.

range information about range of X-axis values for non-linear associations.

REstruc names of the grouped random effects for the longitudinal markers.

mat\_k contains the list of random effects covariance matrices when they are fixed as they are not part of the estimated parameters (used for displaying them in summary).

fixRE list of the size of number of groups of random effects, each element is a boolean indicating if the random effects of the group is fixed (TRUE) or estimated (FALSE).

lonFacChar list of factors and character covariates included in the longitudinal submodels to keep track of modalities (used internally when doing predictions to reconstruct categorical covariates).

survFacChar same as lonFacChar but for survival submodels.

corRE list indicating if groups of random effects are correlated within longitudinal submodels.

basRisk list of the baseline risk used for each survival submodel.

priors\_used informations about priors used in the model, internally used to display priors in plots (with argument priors=TRUE in the call of the plot function). Note that priors can also be displayed with the function priors.used() applied to an INLAjoint object.

dataLong name of the longitudinal dataset.

dataSurv name of the survival dataset.

#### See Also

joint.

INLAjoint.rw

Setup rw

#### Description

Setup random walk input:

#### Usage

```
INLAjoint.rw(n, order = 1L, sparse = TRUE, scale.model = FALSE, cyclic = FALSE)
```

#### **Arguments**

n number of knots

order order 1

sparse boolean, sparsity scale.model boolean, scale

cyclic boolean, cyclic output:

#### Value

random walk 1

INLAjoint.rw2

INLAjoint.rw2

Setup rw2

# Description

Setup random walk of order 2 input:

# Usage

```
INLAjoint.rw2(n, order = 2L, ...)
```

# Arguments

n number of knots

order order 2

... additional arguments passed to INLAjoint.rw output:

#### Value

random walk 2

INLAjoint.scopy.define

Setup scopy

# Description

Setup weights for non-linear effects input:

# Usage

```
INLAjoint.scopy.define(n = 5L)
```

# Arguments

n number of knots output:

# Value

Matrix with weights for scopy

joint

Fit a multivariate joint model for longitudinal and/or survival data

#### **Description**

This function fits a multivariate joint model for longitudinal and/or survival data. The longitudinal outcomes are modeled with mixed effects models and can handle various distributions. The survival outcomes (i.e., terminal event with possibly competing risks) are modeled with Cox proportional hazards regression models. Various association structures can be specified between the longitudinal and survival outcomes. The inference is based on Integrated Nested Laplace Approximations (Rue et al., 2009).

#### Usage

```
joint(
  formSurv = NULL,
  formLong = NULL,
  dataSurv = NULL,
  dataLong = NULL,
  id = NULL,
  timeVar = NULL,
  family = "gaussian",
  link = "default",
  basRisk = "rw1",
 NbasRisk = 15,
  cutpoints = NULL,
  assoc = NULL,
  assocSurv = NULL,
  corLong = FALSE,
  corRE = TRUE,
  dataOnly = FALSE,
  longOnly = FALSE,
  control = list()
)
```

#### **Arguments**

 $formSurv \hspace{1cm} the \ formula \ for \ the \ time-to-event \ outcome, \ with \ the \ response \ given \ as \ an \ inla. surv()$ 

object. Keep it as NULL if no survival part is needed and give a list of formulas

for competing risks.

formLong the formula for the longitudinal outcome, structured as with the lme4 package

(Mächler et al., 2015) for linear mixed-effects models (i.e., including random effects within parenthesis). Keep it as NULL if no longitudinal part is needed

and give a list of formulas for multivariate longitudinal.

dataSurv the dataset for the survival part. Keep it as NULL if no survival part is needed

or if the survival data is in the longitudinal dataset (it will extract the last line for

each individual as the survival dataset).

dataLong

the dataset for the longitudinal part. Keep it as NULL if no longitudinal part is needed. For multivariate longitudinal models, either give one dataset with all outcomes and covariates or a list of datasets for each longitudinal marker.

id

the name of the variable to identify individuals or grouped repeated measurements. Keep is as NULL if no longitudinal part is needed.

timeVar

a character string (or a vector) giving the name of the time-varying variable(s). Functions of time can be included in formulas, they first need to be set up as a univariate function with name fX, where X is a number between 1 and 20. Then the function can be used directly in the formula (see example below).

family

a character string (or a vector) giving the name of families for the longitudinal outcomes. The list of the available families is given by names(inla.models()\$likelihood).

link

a character string (or a vector) giving the link function associated to the families for the longitudinal outcomes. The links available for a family is given in the associated doc: inla.doc("familyName"). The link should be a vector of the same size as the family parameter and should be set to "default" for default (i.e., identity for gaussian, log for poisson, logit for bimomial,...).

basRisk

the baseline risk of event (should be a vector in case of competing risks). It can be defined as parametric with either "exponentialsurv" for exponential baseline or "weibullsurv" for Weibull baseline (note that there are two formulations of the Weibull distribution, see 'inla.doc("weibull")' for more details, default is variant = 0). Alternatively, there are two options to avoid parametric assumptions on the shape of the baseline risk: "rw1" for random walks of order one prior that corresponds to a smooth spline function based on first order differences. The second option "rw2" assigns a random walk order two prior that corresponds to a smooth spline function based on second order differences. This second option provides a smoother spline compared to order one since the smoothing is then done on the second order.

NbasRisk

the number of intervals for the baseline risk function, only one value should be provided and the same number of intervals is used for each risk submodel in case of competing risks.

cutpoints

a vector with baseline hazard cutpoints if not using equidistant (if not NULL, this replaces the NbasRisk parameter).

assoc

a character string that specifies the association between the longitudinal and survival components. The available options are "CV" for sharing the current value of the linear predictor, "CS" for the current slope, "CV\_CS" for the current value and the current slope, "SRE" for shared random effects (i.e., sharing the individual deviation from the mean at time t as defined by the random effects), "SRE\_ind" for shared random effect independent (each random effect's individual deviation is associated to an association parameter in the survival submodel) and "" (empty string) for no association. When there are either multiple longitudinal markers or multiple competing events, this should be a vector. In case of both multiple markers and events, it should be a list with one element per longitudinal marker and each element is a vector of association for each competing event. Keep it as NULL to have no association between longitudinal and survival components or if there is no survival component.

assocSurv

a boolean that indicates if a frailty term (i.e., random effect) from a survival model should be shared into another survival model. The order is important, the first model in the list of survival formulas ('formSurv') should include a random effect and it can be shared in the next formulas. Multiple survival models with random effects can be accomodated and a random effect can be shared in multiple survival models, following the same structure as 'assoc' (i.e., vector of booleans if one random effect is shared in multiple survival and list of vectors if multiple survival models with random effects share their random effects in multiple survival models).

corLong

a boolean that only applies when multiple longitudinal markers are fitted: should the random effects accross markers be correlated (TRUE) or independent (FALSE)? Default is FALSE.

corRE

list of the size of number of groups of random effects (i.e., equal to 1 if there is only one longitudinal marker or if corLong is TRUE and equal to the number of markers otherwise), each element is a boolean indicating if the random effects of the group must be correlated or independent (i.e., diagonal variance-covariance). Default is FALSE.

dataOnly

a boolean to only prepare the data with the correct format without running the model

longOnly

a boolean to only prepare the data for the longitudinal part of a longitudinalsurvival joint model with the correct format without running the model.

control

a list of control values that can be set with control=list(), with components:

priorFixed list with mean and standard deviations for the Gaussian prior distribution for the fixed effects. Default is list(mean=0, prec=0.01, mean.intercept=0, prec.intercept=0.01), where mean and prec are the mean and precision (i.e., inverse of the variance) of the fixed effects, respectively and mean.intercept and prec.intercept are the corresponding parameters for the fixed intercept.

- priorAssoc list with mean and standard deviations for the Gaussian prior distribution for the association parameters (does not apply to "SRE\_ind" association and shared random effect from survival models (frailty), see next item for those two). Default is list(mean=0, prec=0.01)
- priorSRE\_ind list with mean and standard deviations for the Gaussian prior
   distribution for the association of independent random effects ("SRE\_ind"
   and survival frailty random effects shared). Default is list(mean=0, prec=1)
- priorRandom list with prior distribution for the multivariate random effects
   (Inverse Wishart). Default is list(r=10, R=1), see "inla.doc("iidkd") for
   more details.
- initVC list of the size of number of groups of random effects giving initial values for variance-covariance of random effects, first values are variance and then covariances (as displayed in summary). All the elements of the covariance matrix must be fixed but in case of multiple groups of random effects, it is possible to fix initial values for only some groups, then elements in the list that are not initialized must be an empty string.
- initSD same as initVC but to fix standard deviations and correlations instead (only one of these two arguments can be used).

\_

strata list of the same size as the number of survival submodels, giving the name of covariates for stratified proportional hazards model (default is NULL).

fixRE list of the size of number of groups of random effects, each element is a boolean indicating if the random effects of the group must be fixed or estimated.

assocInit Initial value for all the association parameters (default is 0.1).

int.strategy a character string giving the strategy for the numerical integration used to approximate the marginal posterior distributions of the latent field. Available options are "ccd" (default), "grid" or "eb" (empirical Bayes). The empirical Bayes uses only the mode of the approximations for the integration, which speed up and simplifies computations. It can be pictured as a tradeoff between Bayesian and frequentist estimation strategies while the default full Bayesian accounts for uncertainty by using the mode and the curvature at the mode.

Ntrials Number of trials for binomial and Betabinomial distributions, default is NULL.

cpo TRUE/FALSE: Default is FALSE, set to TRUE to compute the Conditional Predictive Ordinate.

cfg TRUE/FALSE: Default is FALSE, set to TRUE to be able to sample from the posterior distribution.

safemode TRUE/FALSE: use the INLA safe mode (automatically reruns in case of negative eigenvalue(s) in the Hessian, reruns with adjusted starting values in case of crash). Default is TRUE (activated). The message "\*\*\* inla.core.safe" appears when the safe mode is running, it improves the inference of the hyperparameters and can be ignored. To remove this safe mode, switch the boolean to FALSE (it can save some computation time but may return slightly less precise estimates for some hyperparameters).

rerun TRUE/FALSE: the model reruns to improve numerical stability (default is FALSE).

tolerance accuracy in the inner optimization (default is 0.005).

h step-size for the hyperparameters (default is 0.005).

verbose TRUE/FALSE: prints details of the INLA algorithm. Default is FALSE. keep TRUE/FALSE: keep internal files. Default is FALSE. (expert option)

#### Value

An object of class INLAjoint. See INLAjoint. object for details.

#### References

Rustand, D., van Niekerk, J., Teixeira Krainski, E., Rue, H. and Proust-Lima, C. (2023). Fast and flexible inference for joint models of multivariate longitudinal and survival data using integrated nested Laplace approximations. Biostatistics, 2023, kxad019. https://doi.org/10.1093/biostatistics/kxad019 https://arxiv.org/abs/2203.06256

Rustand, D., van Niekerk, J., Rue, H., Tournigand, C., Rondeau, V. and Briollais, L. (2023). Bayesian Estimation of Two-Part Joint Models for a Longitudinal Semicontinuous Biomarker and a

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Terminal Event with R-INLA: Interests for Cancer Clinical Trial Evaluation. Biometrical Journal, 65, 2100322. https://doi.org/10.1002/bimj.202100322 https://arxiv.org/abs/2010.13704

Rue, H., Martino, S. and Chopin, N. (2009). Approximate Bayesian inference for latent Gaussian models by using integrated nested Laplace approximations. Journal of the Royal Statistical Society: Series B (Statistical Methodology), 71: 319-392. https://doi.org/10.1111/j.1467-9868.2008.00700.x

Bates, D., Mächler, M., Bolker, B., & Walker, S. (2015). Fitting Linear Mixed-Effects Models Using Ime4. Journal of Statistical Software, 67(1), 1–48. https://doi.org/10.18637/jss.v067.i01

Contact: <INLAjoint@gmail.com>

#### **Examples**

```
# joint model with 3 longitudinal / 3 competing risks of event
data(Longsim)
data(Survsim)
f1 <- function(x) x^2 # quadratic function of time for first marker
Nsplines <- splines::ns(Longsim$time, knots=2) # 2 ns splines for second marker
f2 <- function(x) predict(Nsplines, x)[,1]</pre>
f3 <- function(x) predict(Nsplines, x)[,2]
if(requireNamespace("INLA")){
 JMINLA <- joint(</pre>
  formLong = list(Y1 \sim time + f1(time) + ctsX + binX + (1 + time + f1(time) | Id),
                  Y2 \sim time + f2(time) + f3(time) + ctsX + binX + (1 | Id),
                  Y3 \sim time + ctsX + binX + (1 | Id)),
  formSurv = list(INLA::inla.surv(deathTimes, Event1) ~ binX + ctsX,
                  INLA::inla.surv(deathTimes, Event2) ~ binX,
                  INLA::inla.surv(deathTimes, Event3) ~ ctsX),
  dataLong = Longsim, dataSurv=Survsim, id = "Id", timeVar = "time", corLong=TRUE,
  family = c("gaussian", "poisson", "binomial"), basRisk = c("rw1", "rw1", "rw1"),
  assoc = list(c("CV", "CS", ""), c("CV", "", "SRE"), c("", "CV", "")),
  control=list(int.strategy="eb"))
 summary(JMINLA)
 # 'sdcor' to switch from variance-covariance to standard
 # deviation-correlation and 'hazr' to switch parameters
 # in survival submodels from mean to hazard ratios (exp(mean)).
 summary(JMINLA, sdcor=TRUE, hazr=TRUE)
}
```

joint.rerun

Rerun a model fitted with INLAjoint

#### **Description**

Reruns inla() for an object of class INLAjoint returned by the joint function. The rerun starts with posterior values from previous run and can sometimes improve the model fit (for very complex models or unstable parameter estimates due to low information in the data)

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#### Usage

```
joint.rerun(model, ...)
```

#### **Arguments**

model an object containing a model fitted with the joint() function.

Extra arguments.

#### Value

An object of class INLAjoint containing a model fitted with the joint() function.

#### See Also

joint.

logLik.INLAjoint

Extracts log-likelihood value from a given model fitted with INLAjoint

#### **Description**

This function extracts log-likelihood value from INLAjoint objects.

#### Usage

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

#### **Arguments**

object an object that contains a model fitted with INLAjoint.

... Extra arguments.

LongMS

Simulated univariate longitudinal dataset

# Description

A simulated dataset used to illustrate joint models with univariate longitudinal and multi-state survival component (see joint longitudinal and multi-state model in INLAjoint vignette). The corresponding survival dataset is named 'SurvMS'.

#### Usage

LongMS

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#### **Format**

## 'LongMS' A data frame with 96 rows and 7 columns:

id Individual id

time Visit times

X Continuous covariate

y Gaussian longitudinal outcome ...

Longsim

Simulated multivariate longitudinal dataset

#### **Description**

A simulated dataset used to illustrate some models (e.g., example of joint() function in the documentation). The corresponding survival dataset is named 'Survsim'.

# Usage

Longsim

#### **Format**

## 'Longsim' A data frame with 96 rows and 7 columns:

Id Individual id

time Visit times

ctsX Continuous covariate

binX Binary covariate

Y1, Y2, Y3 Gaussian Longitudinal outcomes ...

nobs.INLAjoint

Extracts number of observations of each composant from a given model fitted with INLAjoint

#### **Description**

This function extracts number of observations of each composant from INLAjoint objects.

#### Usage

```
## S3 method for class 'INLAjoint'
nobs(object, ...)
```

#### **Arguments**

object an object that contains a model fitted with INLAjoint.

... Extra arguments.

plot.INLAjoint 17

plot.INLAjoint	Plot the output from a multivariate joint model for longitudinal and/or survival data

# Description

This function provide plots for the output of a multivariate joint model for longitudinal and/or survival data. The output can be stored into an object and manipulated as a list of ggplot outputs, described bellow.

#### Usage

```
## S3 method for class 'INLAjoint'
plot(x, ...)
```

#### **Arguments**

x an object with the output of the the joint function

Extra arguments including: sdcor: logical indicating if the random effects correlation are to be shown. If FALSE the covariance is shown. priors: logical indicating if the priors are added to the posterior marginals plots.

#### Value

return a named list of ggplot objects containing:

Outcomes as a list of length equal the number of longitudinal outcomes plus the number of survival outcomes, each one including the plot for the posterior marginals of the associated fixed effects and residual or baseline variance (or standard error). Each element contains the plot for the posterior marginal.

Covariances the plots for the posterior marginal distribution of the covariance parameters.

Associations the plots for the posterior marginal distribution of the association parameters.

Random The plot for the fitted baseline risk functions as shown as the posterior mean and credible interval.

predict.INLAjoint Computes predictions for a given model fitted with INLAjoint

#### **Description**

This function allows to compute predictions for a given model fitted with INLAjoint, the default behavior (without arguments) returns fitted values for each component of the model. It is also possible to supply a dataset for which predictions are required, this dataset must have the same structure as the dataset used for the model fitting (i.e., same columns). The default returned predictions corresponds to the linear predictors for each outcomes.

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#### Usage

```
## S3 method for class 'INLAjoint'
predict(
  object,
  newData = NULL,
  timePoints = NULL,
 NtimePoints = 50,
  strategy = 1,
 Nsample = 300,
 NsampleRE = 50,
  loopRE = FALSE,
  id = NULL,
  Csurv = NULL,
  horizon = NULL,
  baselineHaz = "interpolation",
  return.samples = FALSE,
  survival = FALSE,
  CIF = FALSE,
  inv.link = FALSE,
)
```

#### **Arguments**

object an object that contains a model fitted with INLAjoint.

newData a dataset with the same columns as those used to fit the model. When using a lon-

> gitudinal marker to predict longitudinal and subsequent survival outcomes, only the longitudinal information (i.e., structure of the longitudinal data) is required. It is also possible to predict the average trajectories conditional on covariates by

setting the value of the longitudinal outcomes included in the model to NA.

timePoints a vector of the time points at which predictions are computed (for both longi-

> tudinal and survival outcomes), this also control the precision of the integration for time-dependent shared terms and the computation of cumulative risks (e.g., for survival or CIF curves), thus many time points will increase the accuracy of predictions. Default is NULL as these time points are automatically computed

when not defined manually.

NtimePoints number of time points at which the predictions are computed (for both longi-

> tudinal and survival outcomes), these time points are equidistant between time 0 and horizon time. This also control the precision of the integration for timedependent shared terms and the computation of cumulative risks (e.g., for survival or CIF curves), thus many time points will increase the accuracy of predic-

tions.

strategy to compute predictions. Only strategy 1 is implemented at the moment,

soon more efficient strategies are going to be implemented to allow for large

scale precictions.

number of samples for fixed effects and hyperparameters used to assess uncer-

tainty when computing predictions. Default is 300.

strategy

Nsample

print.plot.INLAjoint 19

number of random effects realizations for each sample specified in 'Nsample'.

NSalliptenE	These random effects realizations for each sample specified in 'tosample'. These random effects realizations are conditional on observed longitudinal outcomes values provided in 'newData'. When outcomes are set to NA, the realizations are sampled from the marginal distribution of random effects.
loopRE	boolean with default to FALSE. When 'NsampleRE' and 'Nsample' are large, the amount of information to store in the random access memory of the computer can be large (creation of large matrices for the computation of predictions), turning this boolean to TRUE will decompose the computation of predictions to avoid reaching the limit of RAM of the computer (which would crash the program).
id	name of the individual id variable, default is NULL as it is automatically grabbed from the fitted model but when fitting simple survival models, providing id when fitting the model is not mandatory and thus this can be useful (an explicit message is printed in this specific case).
Csurv	conditional survival, gives the starting value of the at-risk period (i.e., starting value at which risk predictions for survival models are computed). Default is the last longitudinal observation time provided in 'newData' but this is replaced by the value of 'Csurv' when provided.
horizon	horizon of the prediction.
baselineHaz	method used to evaluate the baseline hazard value, default is 'interpolation' which is currently recommended. Experimental alternatives are being developed, including 'splines' for an interpolation with splines but has not been properly validated with simulations yet.
return.samples	boolean, when set to TRUE the samples are returned instead of summary statistics over the samples. Default is FALSE.
survival	boolean, when set to TRUE the summary statistics over survival functions are computed in addition to the summary statistics over the risk functions.
CIF	boolean, when set to TRUE the summary statistics over cumulative incidence functions are computed in addition to the summary statistics over the risk functions. Only applies to competing risks.
inv.link	boolean, when set to TRUE the summary statistics are computed over the predictions of longitudinal components after applying the inverse link function for each samples in addition to the summary statistics over the linear predictors.
	Extra arguments.

 $print. plot. INLA joint \qquad \textit{Prints plot the output from a multivariate joint model for longitudinal and/or survival data}$ 

# Description

NsampleRE

The plots of a model are grouped by categories, first are the fixed effects and residual error of longitudinal and survival submodels, referred to as 'Outcomes' or 'O'. Then the variance-covariance of random effects (or standard deviations and correlations when the argument 'sdcor' is set to TRUE

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in the call of the plot function), referred to as 'Covariances' or 'C'. Association parameters referred to as 'Associations' or 'A' for linear associations and 'NL\_Associations' or 'N' for non-linear associations. Baseline hazard curves referred to as 'Baseline' or 'B' and baseline hazard related parameters referred to as 'ParamBaseline' or 'P'. It is possible to select specific plots to print by specifying the names or corresponding letters in the argument 'which'.

#### Usage

```
## S3 method for class 'plot.INLAjoint'
print(
    x,
    which = c("all", "Outcomes", "Covariances", "Associations", "Baseline"),
    ...
)
```

#### **Arguments**

x an object with the output of the the joint function

which name of required plots. Default is "all". It can be a character or named list. If it is

a list, each element can be either character or numeric to select from the elements to be visualized. Ex.: which = list(Outcomes = "L1") and list(Outcomes = 1)

will produce the same output.

... Extra arguments.

ranef.INLAjoint

Extracts random effects values from a given model fitted with INLAjoint

#### **Description**

This function extracts random effects values from INLAjoint objects.

#### Usage

```
## S3 method for class 'INLAjoint'
ranef(object, ...)
```

#### Arguments

object an object that contains a model fitted with INLAjoint.

... Extra arguments.

setup\_FE\_model 21

	setup_FE_model	Setup fixed effects part for longitudinal marker k	
--	----------------	--	--

#### **Description**

Setup fixed effects part for longitudinal marker k (internal function) input:

#### Usage

```
setup_FE_model(formula, dataset, timeVar, k, dataOnly)
```

#### **Arguments**

formula with lme4 format (fixed effects and random effects in the same object)

dataset that contains the outcome timeVar name of time variable

k identifies the longitudinal marker among 1:K markers

dataOnly boolean for internal use, indicates if only preparing data (i.e., not fitting the

model) output:

#### Value

colnames(FE) names of the fixed effects (interactions are separated by ".X." instead of ":" to facilitate their manipulation)

FE values of the fixed effects

setup_RE_model Setup random effects part for longitudinal marker k	
--	--

#### **Description**

Setup random effects part for longitudinal marker k (internal function) input:

#### Usage

```
setup_RE_model(formula, dataset, k)
```

#### **Arguments**

formula with lme4 format (fixed effects and random effects in the same object)

dataset that contains the outcome

k identifies the longitudinal marker among 1:K markers output:

22 setup\_S\_model

#### Value

```
colnames(RE_mat) names of the random effects
RE_mat values of the random effects
```

setup\_S\_model

Setup survival part for outcome m

#### **Description**

Setup survival part for outcome m (internal function) input:

#### Usage

```
setup_S_model(
  formula,
  formLong,
  dataSurv,
  LSurvdat,
  timeVar,
  assoc,
  id,
  m,
  Κ,
  Μ,
  NFT,
  corLong,
  dataOnly,
  SurvInfo,
  strata
)
```

# Arguments

formula with inla.surv() object as an outcome formLong formula from the longitudinal part, if any dataSurv dataset(s) for the survival part LSurvdat dataset for the longitudinal part converted to survival format (internal, used to get covariates if missing in the survival dataset when sharing linear predictors including covariates from longitudinal into survival) names of the variables that are time-dependent (only linear for now) timeVar assoc association parameters between K longitudinal outcomes and M survival outcomes (list of K vectors of size M) name of the variable that gives the individual id id identifies the outcome among 1:M time-to-event outcomes m

setup\_Y\_model 23

K	number of longitudinal outcomes
М	number of survival outcomes
NFT	maximum number of functions of time (fixed value)
corLong	boolean that indicates if random effects across longitudinal markers are correlated, when multiple longitudinal markers are included in the model
dataOnly	boolean for internal use, indicates if only preparing data (i.e., not fitting the model)
SurvInfo	information about survival submodels for internal use
strata	covariate for stratified proportional hazards model output:

#### Value

YS\_data includes the values of the survival outcome and covariates associated to this survival part, with the association parameters but the provided id are temporary and they will be updated after the cox expansion to make them unique and allow for time dependency

YSformF formula for this survival outcome (not including association parameters)

tup_Y_model Setup outcome for longitudinal marker
---

#### **Description**

Setup outcome for longitudinal marker (internal function) input:

### Usage

```
setup_Y_model(formula, dataset, family, k)
```

# Arguments

formula with lme4 format (fixed effects and random effects in the same object	ct)
---	-----

dataset that contains the outcome

family of the outcome (given to check if the distribution matches but the check is not

done yet)

k identifies the longitudinal marker among 1:K markers output:

# Value

YL.name name of the outcome

YL values of the outcome

24 Survsim

SurvMS

Simulated multi-state survival dataset

#### **Description**

A simulated dataset used to illustrate multi-state models (see multi-state model and joint longitudinal and multi-state model in INLAjoint vignette). The corresponding longitudinal dataset is named 'LongMS'.

#### Usage

SurvMS

#### **Format**

## 'SurvMS' A list of 3 data frames with 50 rows and 5 columns, 50 rows and 5 columns, 28 rows and 5 columns for each of the 3 transition intensities, respectively:

id Individual id

Tstart Beginning of the 'at-risk' period

Tstop Event time

status Transition indicator

X Continuous covariate ...

Survsim

Simulated competing risks survival dataset

#### **Description**

A simulated dataset used to illustrate some models (e.g., example of joint() function in the documentation). The corresponding longitudinal dataset is named 'Longsim'.

#### Usage

Survsim

#### **Format**

## 'Survsim' A data frame with 15 rows and 5 columns:

Id Individual id

deathTimes Event time

ctsX Continuous covariate

binX Binary covariate

**Event1, Event2, Event3** Event indicator for the 3 competing risks (individual is censored when the 3 events are 0) ...

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