Package ‘FastJM’

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Title Semi-Parametric Joint Modeling of Longitudinal and Survival Data
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Description Maximum likelihood estimation for the semi-parametric joint modeling of competing risks and longitudinal data applying customized linear scan algorithms, proposed by Li and colleagues (2022) <doi:10.1155/2022/1362913>. The time-to-event data is modelled using a (cause-specific) Cox proportional hazards regression model with time-fixed covariates. The longitudinal outcome is modelled using a linear mixed effects model. The association is captured by shared random effects. The model is estimated using an Expectation Maximization algorithm.
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anova

Anova Method for Fitted Joint Models

Description

Performs a likelihood ratio test between two nested joint models.

Usage

```r
## S3 method for class 'jmcs'
anova(object, object2, digits = 4, ...)
```

Arguments

- `object` an object inheriting from class `jmcs`, nested in `object2`.
- `object2` an object inheriting from class `jmcs`.
- `digits` the number of significant digits to use when printing. Default is 4.
- `...` further arguments passed to or from other methods.

Value

A table to summarize the likelihood ratio test.

Author(s)

Shanpeng Li <lishanpeng@ucla.edu>
cdata

See Also
jmcs

Examples

# Fit a joint model
fit <- jmcs(ydata = ydata, cdata = cdata,
            long.formula = response ~ time + x1,
            surv.formula = Surv(surv, failure_type) ~ x1 + x2,
            random = ~ time| ID)

fit2 <- jmcs(ydata = ydata, cdata = cdata,
             long.formula = response ~ time + gender + x1 + race,
             surv.formula = Surv(surv, failure_type) ~ x1 + gender + x2 + race,
             random = ~ time| ID)

anova(fit, fit2)

cdata

Simulated competing risks data

Description
The cdata data frame has 1000 rows and 7 columns.

Usage
data(cdata)

Format
This data frame contains the following columns:

ID patient identifier.
surv event time.
failure_type event indicator. 0 denotes censoring, 1 risk 1, and 2 risk 2.
x1 continuous variable.
x2 treatment indicator. 0 denotes the placebo group and 1 the treatment group.
gender gender indicator.
race race indicator.
Fitted values for joint models

Description
Extract fitted values for joint models.

Usage
## S3 method for class 'jmcs'
fitted(
  object,
  type = c("Marginal", "Subject"),
  process = c("Longitudinal", "Event"),
  ...
)

Arguments
- object: an object inheriting from class jmcs.
- type: for which type of fitted values to calculate.
- process: for which sub-model to calculate the fitted values.
- ...: further arguments passed to or from other methods.

Value
a numeric vector of fitted values.

Author(s)
Shanpeng Li <lishanpeng0913@ucla.edu>

Examples

```r
fit <- jmcs(ydata = ydata, cdata = cdata,
  long.formula = response ~ time + gender + x1 + race,
  surv.formula = Surv(surv, failure_type) ~ x1 + gender + x2 + race,
  random = ~ time| ID)

# fitted for the longitudinal process
head(cbind(
  "Marg" = fitted(fit, type = "Marginal", process = "Longitudinal"),
  "Subj" = fitted(fit, type = "Subject", process = "Longitudinal")
))

# fitted for the event process - marginal survival function
head(fitted(fit, type = "Marginal", process = "Event"))
```
Description

Extracts the fixed effects for a fitted joint model.

Usage

fixef(object, process = c("Longitudinal", "Event"), ...)

Arguments

object an object inheriting from class jmcs.
process for which sub-model to extract the estimated coefficients.
... further arguments passed to or from other methods.

Value

A numeric vector or a list of the estimated parameters for the fitted model.

Author(s)

Shanpeng Li <lishanpeng0913@ucla.edu>

Examples

# a joint model fit
fit <- jmcs(ydata = ydata, cdata = cdata,
            long.formula = response ~ time + gender + x1 + race,
            surv.formula = Surv(surv, failure_type) ~ x1 + gender + x2 + race,
            random = ~ time| ID)

# fixed effects for the longitudinal process
fixef(fit, process = "Longitudinal")
# fixed effects for the event process
fixef(fit, process = "Event")
**jmcs**

**Joint modeling of longitudinal continuous data and competing risks**

**Description**

Joint modeling of longitudinal continuous data and competing risks

**Usage**

```r
jmcs(
  ydata,
  cdata,
  long.formula,
  random = NULL,
  surv.formula,
  REML = TRUE,
  quadpoint = NULL,
  maxiter = 10000,
  print.para = FALSE,
  survinitial = TRUE,
  tol = 1e-04,
  method = "pseudo-adaptive",
  opt = "nlminb"
)
```

**Arguments**

- **ydata**: a longitudinal data frame in long format.
- **cdata**: a survival data frame with competing risks or single failure. Each subject has one data entry.
- **long.formula**: a formula object with the response variable and fixed effects covariates to be included in the longitudinal sub-model.
- **random**: a one-sided formula object describing the random effects part of the longitudinal sub-model. For example, fitting a random intercept model takes the form ~ 1|ID. Alternatively, fitting a random intercept and slope model takes the form ~ x1 + ... + xn|ID.
- **surv.formula**: a formula object with the survival time, event indicator, and the covariates to be included in the survival sub-model.
- **REML**: a logic object that indicates the use of REML estimator. Default is TRUE.
- **quadpoint**: the number of pseudo-adaptive Gauss-Hermite quadrature points to be chosen for numerical integration. Default is 6 which produces stable estimates in most dataframes.
- **maxiter**: the maximum number of iterations of the EM algorithm that the function will perform. Default is 10000.
**jmcs**

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>print.para</td>
<td>Print detailed information of each iteration. Default is FALSE, i.e., not to print the iteration details.</td>
</tr>
<tr>
<td>survinitial</td>
<td>Fit a Cox model to obtain initial values of the parameter estimates. Default is TRUE.</td>
</tr>
<tr>
<td>tol</td>
<td>Tolerance parameter. Default is 0.0001.</td>
</tr>
<tr>
<td>opt</td>
<td>Optimization method to fit a linear mixed effects model, either nlminb (default) or optim.</td>
</tr>
</tbody>
</table>

**Value**

Object of class jmcs with elements

- **beta**: the vector of fixed effects for the linear mixed effects model.
- **gamma1**: the vector of fixed effects for type 1 failure for the survival model.
- **gamma2**: the vector of fixed effects for type 2 failure for the survival model. Valid only if CompetingRisk = TRUE.
- **nu1**: the vector of association parameter(s) for type 1 failure.
- **nu2**: the vector of association parameter(s) for type 2 failure. Valid only if CompetingRisk = TRUE.
- **H01**: the matrix that collects baseline hazards evaluated at each uncensored event time for type 1 failure. The first column denotes uncensored event times, the second column the number of events, and the third columns the hazards obtained by Breslow estimator.
- **H02**: the matrix that collects baseline hazards evaluated at each uncensored event time for type 2 failure. The data structure is the same as H01. Valid only if CompetingRisk = TRUE.
- **Sig**: the variance-covariance matrix of the random effects.
- **sigma**: the variance of the measurement error for the linear mixed effects model.
- **iter**: the total number of iterations until convergence.
- **convergence**: convergence identifier: 1 corresponds to successful convergence, whereas 0 to a problem (i.e., when 0, usually more iterations are required).
- **vcov**: the variance-covariance matrix of all the fixed effects for both models.
- **sebeta**: the standard error of beta.
- **segamma1**: the standard error of gamma1.
- **segamma2**: the standard error of gamma2. Valid only if CompetingRisk = TRUE.
- **senu1**: the standard error of nu1.
- **senu2**: the standard error of nu2. Valid only if CompetingRisk = TRUE.
- **seSig**: the vector of standard errors of covariance of random effects.
- **sesigma**: the standard error of variance of measurement error for the linear mixed effects model.
loglike      the log-likelihood value.
fitted      a list with the fitted values:
  resid      the vector of estimated residuals for the linear mixed effects model.
fitted      the vector of fitted values for the linear mixed effects model.
fittedmar   the vector of marginal fitted values for the linear mixed effects model.
residmar     the vector of estimated marginal residuals for the linear mixed effects model.
fittedSurv  the estimated survival rate evaluated at each uncensored event time.
FUNB        the estimated random effects for each subject.
CompetingRisk logical value; TRUE if a competing event are accounted for.
quadpoint    the number of Gauss Hermite quadrature points used for numerical integration.
ydata       the input longitudinal dataset for fitting a joint model. It has been re-ordered in accordance with descending observation times in cdata.
cdata       the input survival dataset for fitting a joint model. It has been re-ordered in accordance with descending observation times.
PropEventType a frequency table of number of events.
LongitudinalSubmodel the component of the long.formula.
SurvivalSubmodel  the component of the surv.formula.
random       the component of the random.
call         the matched call.
Quad.method  the quadrature rule used for integration. If pseudo-adaptive quadrature rule is used, then return pseudo-adaptive. Otherwise return standard.
id          the grouping vector for the longitudinal outcome.

Author(s)
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See Also
ranef, fixef, fitted.jmcs, residuals.jmcs, survfitjmcs, plot.jmcs, plot.survfitjmcs, vcov.jmcs

Examples

require(FastJM)
# Load a simulated longitudinal dataset
data(ydata)
# Load a simulated survival dataset with two competing events
data(cdata)

# Fit a joint model
fit <- jmcs(ydata = ydata, cdata = cdata,
long.formula = response ~ time + gender + x1 + race,
surv.formula = Surv(surv, failure_type) ~ x1 + gender + x2 + race,
random = ~ time| ID)

fit
# Extract the parameter estimates of longitudinal sub-model fixed effects
fixef(fit, process = "Longitudinal")
# Extract the parameter estimates of survival sub-model fixed effects
fixef(fit, process = "Event")
# Obtain the random effects estimates for first 6 subjects
head(ranef(fit))
# Obtain the variance-covariance matrix of all parameter estimates
vcov(fit)
# Prediction of cumulative incidence for competing risks data
# Predict the conditional probabilities for two patients who are alive (censored)
ND <- ydata[ydata$ID %in% c(419, 218), ]
ID <- unique(ND$ID)
NDc <- cdata[cdata$ID %in% ID, ]
survfit <- survfitjmcs(fit,
    ynewdata = ND,
    cnewdata = NDc,
    u = seq(3, 4.8, by = 0.2),
    M = 100,
    seed = 100)

oldpar <- par(mfrow = c(2, 2))
plot(survfit, estimator = "both", include.y = TRUE)
par(oldpar)

---

plot.jmcs

Fitted values for joint models

Description
Plot Diagnostics for Joint Models.

Usage
## S3 method for class 'jmcs'
plot(x, add.smooth = getOption("add.smooth"), ...)

Arguments
x
x of class 'jmcs'.

add.smooth
logical; if TRUE a smooth line is superimposed in the "Residuals vs Fitted" plot.

... further arguments passed to or from other methods.
Value

The first two plots are longitudinal sub-model diagnostics and the last two are marginal survival function and marginal cumulative hazard.

Author(s)

Shanpeng Li <lishanpeng0913@ucla.edu>

Examples

```r
fit <- jmcs(ydata = ydata, cdata = cdata,
    long.formula = response ~ time + gender + x1 + race,
    surv.formula = Surv(surv, failure_type) ~ x1 + gender + x2 + race,
    random = ~ time| ID)

oldpar <- par(mfrow = c(2, 2))
plot(fit)
par(oldpar)
```

Description

Plot conditional probabilities for new subjects. If CompetingRisk = FALSE, print the survival probabilities. Otherwise, print the cumulative incidence probabilities for each failure type.

Usage

```r
## S3 method for class 'survfitjmcs'
plot(
    x,
    estimator = c("both", "mean", "median"),
    conf.int = TRUE,
    include.y = FALSE,
    ...
)
```

Arguments

- `x`: x of class survfitjmcs.
- `estimator`: character string specifying, whether to include in the plot the mean of the conditional probabilities of survival, the median or both. The mean and median are taken as estimates of these conditional probabilities over the M replications of the Monte Carlo scheme described in survfitjmcs.
`plot.survfitjmcs`  

```
conf.int logical; if TRUE, then a pointwise confidence interval is included in the plot. Default is TRUE.
include.y include longitudinal responses of this subject versus time. Default is FALSE.
... further arguments passed to or from other methods.
```

Value

plots of conditional probabilities over different pre-specified time points for subjects. If single failure type, then survival probabilities will be returned. Otherwise, cumulative incidence probabilities for each failure type will be returned.

Author(s)

Shanpeng Li <lishanpeng0913@ucla.edu>

See Also

`survfitjmcs`

Examples

# a joint model fit
fit <- jmcs(ydata = ydata, cdata = cdata,
    long.formula = response ~ time + gender + x1 + race,
    surv.formula = Surv(surv, failure_type) ~ x1 + gender + x2 + race,
    random = ~ time| ID)

# Prediction of cumulative incidence for competing risks data
ND <- ydata[ydata$ID %in% c(419, 218), ]
ID <- unique(ND$ID)
NDc <- cdata[cdata$ID %in% ID, ]
survfit <- survfitjmcs(fit,
    ynewdata = ND,
    cnewdata = NDc,
    u = seq(3, 4.8, by = 0.2),
    M = 100,
    seed = 100)

oldpar <- par(mfrow = c(2, 2), mar = c(5, 4, 4, 4))
plot(survfit, estimator = "both", include.y = TRUE)
par(oldpar)
print.jmcs

Description
Print jmcs

Usage
## S3 method for class 'jmcs'
print(x, digits = 4, ...)

Arguments

  x  Object of class 'jmcs'.
  digits  the number of significant digits to use when printing.
  ...  Further arguments passed to or from other methods.

Value
a summary of data, joint model, log likelihood, and parameter estimates.

Author(s)
Shanpeng Li <lishanpeng0913@ucla.edu>

See Also
jmcs

print.survfitjmcs

Description
Print survfitjmcs

Usage
## S3 method for class 'survfitjmcs'
print(x, ...)

Arguments

  x  x of class 'survfitjmcs'.
  ...  Further arguments passed to or from other methods.
ranef

Value

a list of matrices with conditional probabilities for subjects.

Author(s)

Shanpeng Li <lishanpeng0913@ucla.edu>

See Also

jmcs, survfitjmcs

Description

Extracts the posterior mean of the random effects for a fitted joint model.

Usage

ranef(object, ...)

Arguments

object an object inheriting from class jmcs.
... further arguments passed to or from other methods.

Value

a matrix of random effects estimates.

Author(s)

Shanpeng Li <lishanpeng0913@ucla.edu>

See Also

jmcs
Examples

# a joint model fit
fit <- jmcs(ydata = ydata, cdata = cdata,
            long.formula = response ~ time + gender + x1 + race,
            surv.formula = Surv(surv, failure_type) ~ x1 + gender + x2 + race,
            random = ~ time| ID)

# extract random effects estimates
head(ranef(fit))

residuals

Residuals for joint models

Description

Extract residuals for joint models.

Usage

## S3 method for class 'jmcs'
residuals(object, type = c("Marginal", "Subject"), ...)

Arguments

object      an object inheriting from class jmcs.
type       what type of residuals to calculate.
...         further arguments passed to or from other methods.

Value

a vector of residuals of the longitudinal sub-model.

Author(s)

Shanpeng Li <lishanpeng0913@ucla.edu>

See Also

jmcs
Examples

# a joint model fit
fit <- jmcs(ydata = ydata, cdata = cdata,
            long.formula = response ~ time + gender + x1 + race,
            surv.formula = Surv(surv, failure_type) ~ x1 + gender + x2 + race,
            random = ~ time | ID)

# residuals of the longitudinal sub-model
head(cbind(
    "Marg" = residuals(fit, type = "Marginal"),
    "Subj" = residuals(fit, type = "Subject")
))

survfitjmcs

Prediction in Joint Models

Description

This function computes the conditional probability of surviving later times than the last observed
time for which a longitudinal measurement was available.

Usage

survfitjmcs(
  object,
  seed = 100,
  ynewdata = NULL,
  cnewdata = NULL,
  u = NULL,
  M = 200,
  simulate = TRUE,
  quadpoint = NULL,
  ...
)

Arguments

  object          an object inheriting from class jmcs.
  seed            a random seed number to proceed Monte Carlo simulation. Default is 100.
  ynewdata        a data frame that contains the longitudinal and covariate information for the
                  subjects for which prediction of survival probabilities is required.
  cnewdata        a data frame that contains the survival and covariate information for the subjects
                  for which prediction of survival probabilities is required.
  u               a numeric vector of times for which prediction survival probabilities are to be
                  computed.
the number of Monte Carlo samples to be generated. Default is 200.

simulate

logical; if TRUE, a Monte Carlo approach is used to estimate conditional probabilities. Otherwise, Gauss-Hermite quadrature rule is used for numerical integration to estimate instead. Default is TRUE.

quadpoint

number of quadrature points used for estimating conditional probabilities when simulate = FALSE. Default is 20.

... further arguments passed to or from other methods.

Value

a list of matrices with conditional probabilities for subjects.

Author(s)

Shanpeng Li <lishanpeng0913@ucla.edu>

See Also

jmcs

vcov

Variance-covariance matrix of the estimated parameters for joint models

Description

Extract variance-covariance matrix for joint models.

Usage

## S3 method for class 'jmcs'
vcov(object, ...)

Arguments

object an object inheriting from class jmcs.

... further arguments passed to or from other methods.

Value

a matrix of variance covariance of all parameter estimates.

Author(s)

Shanpeng Li <lishanpeng0913@ucla.edu>

See Also

jmcs
**Description**

The `ydata` data frame has 3067 rows and 6 columns.

**Usage**

```r
data(ydata)
```

**Format**

This data frame contains the following columns:

- **ID** patient identifier.
- **response** response variable.
- **time** visit time.
- **x1** treatment indicator. 0 denotes the placebo group and 1 the treatment group.
- **gender** gender indicator.
- **race** race indicator.
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