Package 'FastJM'

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Type Package

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.

License GPL (>= 3)

NeedsCompilation yes

Imports Rcpp (>= 1.0.7), dplyr, nlme, caret, survival, timeROC

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LazyData true

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Contents

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anova   *Anova Method for Fitted Joint Models*

Description

Performs a likelihood ratio test between two nested joint models.

Usage

```
## 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 <lishanpeng0913@ucla.edu>

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)
```

AUCjmcs   *Time-dependent AUC for joint models*

Description

Time-dependent AUC for joint models

Usage

```
AUCjmcs(
  seed = 100,
  object,
  landmark.time = NULL,
  horizon.time = NULL,
  obs.time = NULL,
  method = c("Laplace", "GH"),
  quadpoint = NULL,
  maxiter = NULL,
  n.cv = 3,
  survinitial = TRUE,
  ...
)
```

Arguments

`seed`	a numeric value of seed to be specified for cross validation.
`object`	object of class 'jmcs'.
`landmark.time`	a numeric value of time for which dynamic prediction starts..
`horizon.time`	a numeric vector of future times for which predicted probabilities are to be computed.
`obs.time`	a character string of specifying a longitudinal time variable.
`method`	estimation method for predicted probabilities. If `Laplace`, then the empirical empirical estimates of random effects is used. If `GH`, then the pseudo-adaptive Gauss-Hermite quadrature is used.
`quadpoint`	the number of pseudo-adaptive Gauss-Hermite quadrature points if `method = "GH"`.
`maxiter`	the maximum number of iterations of the EM algorithm that the function will perform. Default is 10000.
`n.cv`	number of folds for cross validation. Default is 3.
`survinitial`	Fit a Cox model to obtain initial values of the parameter estimates. Default is TRUE.
`...`	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](), [survfitjmcs]()

---

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   *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

```
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 levent process - marginal survival function
head(fitted(fit, type = "Marginal", process = "Event"))
```

---

fixef   *Estimated coefficients estimates for joint models*

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

```
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.
print.para	Print detailed information of each iteration. Default is FALSE, i.e., not to print the iteration details.
survinitial	Fit a Cox model to obtain initial values of the parameter estimates. Default is TRUE.
tol	Tolerance parameter. Default is 0.0001.
method	Method for proceeding numerical integration in the E-step. Default is pseudo-adaptive.
opt	Optimization method to fit a linear mixed effects model, either nlminb (default) or optim.

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)

Shanpeng Li <lishanpeng0913@ucla.edu>

See Also

[ranef](), [fixef](), [fitted.jmcs](),[residuals.jmcs](), [survfitjmcs](), [plot.jmcs](),[vcov.jmcs]()

Examples

```
require(FastJM)
require(survival)
# 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)
# Obtain the result summaries of the joint model fit
summary(fit, process = "Longitudinal")
summary(fit, process = "Event")
# 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),
                       method = "GH",
                       obs.time = "time")
survfit
PE <- PEjmcs(fit, seed = 100, landmark.time = 3, horizon.time = c(3.6, 4, 4.4),
             obs.time = "time", method = "GH",
             quadpoint = NULL, maxiter = 1000, n.cv = 3,
             survinitial = TRUE)
Brier <- summary(PE, error = "Brier")
Brier

MAEQ <- MAEQjmcs(fit, seed = 100, landmark.time = 3, horizon.time = c(3.6, 4, 4.4),
                 obs.time = "time", method = "GH",
                 quadpoint = NULL, maxiter = 1000, n.cv = 3,
                 survinitial = TRUE)
APE <- summary(MAEQ, digits = 3)
APE

## evaluate prediction accuracy of fitted joint model using cross-validated mean AUC
```

```
AUC <- AUCjmcs(fit, seed = 100, landmark.time = 3, horizon.time = c(3.6, 4, 4.4),
               obs.time = "time", method = "GH",
               quadpoint = NULL, maxiter = 1000, n.cv = 3)
summary(AUC, digits = 3)
```

MAEQjmcs   *A metric of prediction accuracy of joint model by comparing the pre-*
                        dicted risk with the empirical risks stratified on different predicted risk
                        group.

Description

A metric of prediction accuracy of joint model by comparing the predicted risk with the empirical
risks stratified on different predicted risk group.

Usage

```
MAEQjmcs(
  seed = 100,
  object,
  landmark.time = NULL,
  horizon.time = NULL,
  obs.time = NULL,
  method = c("Laplace", "GH"),
  quadpoint = NULL,
  maxiter = 1000,
  n.cv = 3,
  survinitial = TRUE,
  quantile.width = 0.25,
  ...
)
```

Arguments

`seed`	a numeric value of seed to be specified for cross validation.
`object`	object of class 'jmcs'.
`landmark.time`	a numeric value of time for which dynamic prediction starts..
`horizon.time`	a numeric vector of future times for which predicted probabilities are to be computed.
`obs.time`	a character string of specifying a longitudinal time variable.
`method`	estimation method for predicted probabilities. If `Laplace`, then the empirical empirical estimates of random effects is used. If `GH`, then the pseudo-adaptive Gauss-Hermite quadrature is used.

quadpoint	the number of pseudo-adaptive Gauss-Hermite quadrature points if `method = "GH"`.
maxiter	the maximum number of iterations of the EM algorithm that the function will perform. Default is 10000.
n.cv	number of folds for cross validation. Default is 3.
survinitial	Fit a Cox model to obtain initial values of the parameter estimates. Default is TRUE.
quantile.width	a numeric value of width of quantile to be specified. Default is 0.25.
...	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](), [survfitjmcs]()

| PEjmcs | *A metric of prediction accuracy of joint model by comparing the predicted risk with the counting process.* |

Description

A metric of prediction accuracy of joint model by comparing the predicted risk with the counting process.

Usage

```
PEjmcs(
  object,
  seed = 100,
  landmark.time = NULL,
  horizon.time = NULL,
  obs.time = NULL,
  method = c("Laplace", "GH"),
  quadpoint = NULL,
  maxiter = NULL,
  n.cv = 3,
  survinitial = TRUE,
  ...
)
```

Arguments

`object`	object of class 'jmcs'.
`seed`	a numeric value of seed to be specified for cross validation.
`landmark.time`	a numeric value of time for which dynamic prediction starts..
`horizon.time`	a numeric vector of future times for which predicted probabilities are to be computed.
`obs.time`	a character string of specifying a longitudinal time variable.
`method`	estimation method for predicted probabilities. If `Laplace`, then the empirical empirical estimates of random effects is used. If `GH`, then the pseudo-adaptive Gauss-Hermite quadrature is used.
`quadpoint`	the number of pseudo-adaptive Gauss-Hermite quadrature points if `method = "GH"`.
`maxiter`	the maximum number of iterations of the EM algorithm that the function will perform. Default is 10000.
`n.cv`	number of folds for cross validation. Default is 3.
`survinitial`	Fit a Cox model to obtain initial values of the parameter estimates. Default is TRUE.
`...`	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, survfitjmcs

`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

```
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)
```

---

print	*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   *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.

Value

a list of matrices with conditional probabilities for subjects.

Author(s)

Shanpeng Li <lishanpeng0913@ucla.edu>

See Also

[jmcs](#), [survfitjmcs](#)

---

ranef   *Random effects estimates for joint models*

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")
))
```

summary	*Anova Method for Fitted Joint Models*

Description

Produce result summaries of a joint model fit.

Usage

```
## S3 method for class 'jmcs'
summary(object, process = c("Longitudinal", "Event"), digits = 4, ...)
```

Arguments

object	an object inheriting from class jmcs.
process	for which model (i.e., longitudinal model or survival model) to extract the estimated coefficients.
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 model results.

See Also

[jmcs](#)

summary.AUCjmcs	*Print AUCjmcs*

Description

Print AUCjmcs

Usage

```
## S3 method for class 'AUCjmcs'
summary(object, digits = 4, ...)
```

Arguments

object	object of class 'AUCjmcs'.
digits	number of digits of decimal to be printed.
...	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, survfitjmcs

---

summary.MAEQjmcs   *Print MAEQjmcs*

Description

Print MAEQjmcs

Usage

```
## S3 method for class 'MAEQjmcs'
summary(object, digits = 3, ...)
```

Arguments

object	object of class 'MAEQjmcs'.
digits	number of decimal points to be rounded.
...	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, survfitjmcs

---

summary.PEjmcs   *Print PEjmcs*

Description

Print PEjmcs

Usage

```
## S3 method for class 'PEjmcs'
summary(object, error = c("MAE", "Brier"), ...)
```

Arguments

object	object of class 'PEjmcs'.
error	a character string that specifies the loss function.
...	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, survfitjmcs

---

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,
  Last.time = NULL,
  obs.time = NULL,
  method = c("Laplace", "GH"),
  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.
Last.time	a numeric vector or character string. This specifies the known time at which each of the subjects in cnewdata was known to be alive. If NULL, then this is automatically taken as the survival time of each subject. If a numeric vector, then it is assumed to be greater than or equals to the last available longitudinal time point for each subject. If a character string, then it should be a variable in cnewdata.
obs.time	a character string of specifying a longitudinal time variable in ynewdata.
method	a character string specifying the type of probability approximation; if Laplace, then a first order estimator is computed. If GH, then the standard Gauss-Hermite quadrature is used instead.
quadpoint	number of quadrature points used for estimating conditional probabilities when method = "GH". Default is NULL. If method = "GH", then use the same amount of quadrature points obtained from object.
...	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

---

ydata	*Simulated longitudinal data*

Description

The ydata data frame has 3067 rows and 6 columns.

Usage

```
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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