Package 'jlctree'

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Title Joint Latent Class Trees for Joint Modeling of Time-to-Event and Longitudinal Data

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Description Implements the tree-based approach to joint modeling of time-to-event and longitudinal data. This approach looks for a tree-based partitioning such that within each estimated latent class defined by a terminal node, the time-to-event and longitudinal responses display a lack of association. See Zhang and Simonoff (2018) <arXiv:1812.01774>.

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jlctree-package   *Fits Joint Latent Class Tree (JLCT) model.*

Description

Fits Joint Latent Class Tree (JLCT) model. The main function of this package is jlctree.

Problem setup: The dataset contains three types of variables about each subject: the time-to-event, the longitudinal outcome, and additional covariates. The goal is to jointly model the time-to-event by a survival model and the longitudinal outcomes by a linear mixed-effects model, and using the additional covariates. The longitudinal outcomes consist of repeated measurements, thus are expected to be time-varying for a given subject. The additional covariates can be either time-invariant or time-varying. Nevertheless, jlctree also allows data with time-invariant longitudinal outcome and covariates.

JLCT model: This package implements the Joint Latent Class Tree (JLCT) modeling approach. JLCT assumes that the population consists of homogeneous latent classes; within a latent class subjects follow the same survival and linear mixed-effects model, but those differ from class to class. In addition, JLCT assumes that conditioning on latent class membership, time-to-event and longitudinal outcomes are independent. JLCT looks for a tree-based partitioning such that within each estimated latent class defined by a terminal node, the time-to-event and longitudinal responses display a lack of association. Once the tree is constructed, JLCT assigns each observation to a latent class (i.e. terminal node), and independently fits survival and linear mixed-effects models, using the class membership information.

Time-to-event data format: The time-to-event data format required by jlctree depends on the time-varying nature of the variables to use: if longitudinal outcome, or any of the covariates specified in survival, classmb, fixef, and ranef is time-varying, then the time-to-event data must be in left-truncated right-censored (LTRC) format. Otherwise, when longitudinal outcome and all of the covariates are time-invariant, there should be only one observation per subject, and the time-to-event data can either be in LTRC format (when there exits subject-specific entry time) or in standard right-censored format.

To construct time-to-event data in left-truncated right-censored format, consider using function tmerge in R package survival. See the simulated data_timevar and data_timeinv for examples of LTRC format and right-censored format respectively.

References

Ningshan Zhang and Jeffrey S. Simonoff: Joint Latent Class Trees: A Tree-Based Approach to Joint Modeling of Time-to-event and Longitudinal Data. arXiv:1812.01774 (2018).

See Also

jlctree, data_timeinv, data_timevar

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data_timeinv	*A simulated dataset with time-invariant longitudinal outcome and co-variates.*

Description

A simulated dataset with time-invariant longitudinal outcome, time-to-event, and time-invariant covariates. Since longitudinal outcome and all of the covariates are time-invariant, there is only one observation per subject. The time-to-event data is right-censored.

Usage

```
data(data_timeinv)
```

Format

A data frame with 500 rows and 10 variables.

ID subject identifier (1 - 500)

X1 continuous covariate between 0 and 1; time-invariant

X2 continuous covariate between 0 and 1; time-invariant

X3 binary covariate; time-invariant

X4 continuous covariate between 0 and 1; time-invariant

X5 categorical covariate taking values from 1, 2, 3, 4, 5; time-invariant

time_Y right-censored event time

delta censoring indicator, 1 if censored and 0 otherwise

y longitudinal outcome; time-invariant

g true latent class identifier 1, 2, 3, 4, which is determined by the outcomes of $1\{X1 > 0.5\}$ and $1\{X2 > 0.5\}$, with some noise

Examples

```
# The data for the first five subjects (ID = 1 - 5):
#
#  ID   X1   X2 X3  X4 X5    time_Y delta          y g
#   1 0.27 0.53  1 0.8  1 10.703940     0 0.8923776 2
#   2 0.37 0.68  1 0.5  3  9.153915     1 0.6871529 2
#   3 0.57 0.38  1 0.2  1  4.489658     1 0.8410745 3
#   4 0.91 0.95  0 0.4  3  1.009941     1 2.1058681 4
#   5 0.20 0.12  0 0.8  5 11.125094     0 0.1383508 1
```

---

data_timevar	*A simulated dataset with time-varying longitudinal outcome and co-variates.*

Description

A simulated dataset with time-varying longitudinal outcome, time-to-event, and time-varying co-variates. The dataset is already converted into left-truncated right-censored (LTRC) format, so that the Cox model with time-varying longitudinal outcome as a covariate can be fit. See, for example, Fu and Simonoff (2017).

Usage

```
data(data_timevar)
```

Format

A data frame with 866 rows and 11 variables. The variables are as follows:

ID subject identifier (1 - 500)

X1 continuous covariate between 0 and 1; time-varying

X2 continuous covariate between 0 and 1; time-varying

X3 binary covariate; time-varying

X4 continuous covariate between 0 and 1; time-varying

X5 categorical covariate taking values from 1, 2, 3, 4, 5; time-varying

time_L left-truncated time

time_Y right-censored time

delta censoring indicator, 1 if censored and 0 otherwise

y longitudinal outcome; time-varying

g true latent class identifier 1, 2, 3, 4, which is determined by the outcomes of $1\{X1 > 0.5\}$ and $1\{X2 > 0.5\}$, with some noise

References

Fu, W. and Simonoff, J. S. (2017). Survival trees for left-truncated and right-censored data, with application to time-varying covariate data. Biostatistics, 18(2), 352-369.

Examples

```
# The data for the first five subjects (ID = 1 - 5):
#
#  ID   X1   X2 X3  X4 X5      time_L   time_Y delta          y g
#   1 0.27 0.53  0 0.0  4 0.09251632 1.536030     0 -0.2191137 1
#   1 0.49 0.71  1 0.0  5 1.53603028 4.366769     1  0.6429496 2
```

```
#  2 0.37 0.68  1 0.4  4 0.44674406 1.203560   0  0.5473454 2
#  2 0.65 0.67  0 0.2  5 1.20355968 1.330767   1  1.5515773 4
#  3 0.57 0.38  0 0.2  4 0.82944637 1.267248   0  1.1410397 3
#  3 0.79 0.19  1 0.4  4 1.26724819 5.749602   1  1.0888787 3
#  4 0.91 0.95  0 0.9  1 0.81237396 1.807741   1  2.2105303 4
#  5 0.20 0.12  1 0.3  5 0.80510669 1.029981   0 -0.1167814 1
#  5 0.02 0.31  0 0.4  5 1.02998145 6.404183   1 -0.1747389 1
```

---

get_lrt   *Computes the likelihood ratio test statistic.*

Description

Computes the likelihood ratio test statistic. Not to be called directly by the user.

Usage

```
get_lrt(f1, f2, data, stable = TRUE, cov.max = 1e+05)
```

Arguments

f1	a two-sided formula of the fitted survival model, without the longitudinal outcome in the right side of the formula.
f2	a two-sided formula of the fitted survival model, same as f1 but with the longitudinal outcome being the first covariate on the right side of the formula.
data	a data.frame containing the covariates in both f1 and f2.
stable	a parameter, see also jlctree.control.
cov.max	a parameter, see also jlctree.control.

Value

The likelihood ratio test statistic.

See Also

[get_node_val](#)

Examples

```
data(data_timevar);
f1 <- Surv(time_L, time_Y, delta)~X3+X4+X5;
f2 <- Surv(time_L, time_Y, delta)~y+X3+X4+X5;
get_lrt(f1, f2, data_timevar);
```

---

get_node_val   *Computes the test statistic at the current node.*

Description

Computes the test statistic at the current node. Not to be called directly by the user.

Usage

```
get_node_val(f1, f2, data, lrt = TRUE, ...)
```

Arguments

f1	a two-sided formula of the fitted survival model, without the longitudinal outcome in the right side of the formula. Only needed when lrt=TRUE.
f2	a two-sided formula of the fitted survival model, same as f1 but with the longitudinal outcome being the first covariate on the right side of the formula.
data	a data.frame containing covariates in f2.
lrt	if TRUE, use likelihood ratio test, otherwise use Wald test. Default is TRUE.
...	further arguments to pass to or from other methods.

Value

The test statistic at the current node.

See Also

[get_lrt](#),[get_wald](#)

Examples

```
data(data_timevar);
f1 <- Surv(time_L, time_Y, delta)~X3+X4+X5;
f2 <- Surv(time_L, time_Y, delta)~y+X3+X4+X5;
get_node_val(f1, f2, data_timevar, lrt=TRUE);
```

---

get_wald   *Computes the Wald test statistic.*

Description

Computes the Wald test statistic. Not to be called directly by the user.

Usage

```
get_wald(f, data)
```

Arguments

f   a two-sided formula of the fitted survival model, with the longitudinal outcome
            being the first covariate on the right side of the formula.

data   a data.frame containing covariates in f.

Value

The Wald test statistic.

See Also

get_node_val

Examples

```
data(data_timevar);
f <- Surv(time_L, time_Y, delta)~y+X3+X4+X5;
get_wald(f, data_timevar);
```

---

jlctree   *Fits Joint Latent Class Tree (JLCT) model.*

Description

Fits Joint Latent Class Tree model. This is the main function that is normally called by the user.
See jlctree-package for more details.

Usage

```
jlctree(survival, classmb, fixed, random, subject, data, parms = list(),
  control = list())
```

Arguments

survival	a two-sided formula object; required. The left side of the formula corresponds to a Surv() object of type "counting" for left-truncated right-censored (LTRC) data, or of type "right" for right-censored data. The right side of the formula specifies the names of covariates to include in the survival model, excluding the longitudinal outcome.
classmb	one-sided formula describing the covariates in the class-membership tree construction; required. Covariates used for tree construction are separated by + on the right of ~.
fixed	two-sided linear formula object for the fixed-effects in the linear mixed-effects model for longitudinal outcomes; required. The longitudinal outcome is on the left of ~ and the covariates are separated by + on the right of ~.
random	one-sided formula for the node-specific random effects in the linear mixed-effects model for longitudinal outcomes; optional. If missing, there are no node-specific random effects in the fitted linear mixed-effects model. Covariates with a random effect are separated by + on the right of ~.
subject	name of the covariate representing the subject identifier; optional. If missing, there are no subject-specific random intercepts in the fitted linear mixed-effects model for longitudinal outcomes.
data	the dataset; required.
parms	parameter list of Joint Latent Class Tree model parameters. See also jlctree.control.
control	rpart control parameters. See also rpart.control.

Value

A list with components:

tree	an rpart object, containing the constructed Joint Latent Class tree.
control	the rpart.control parameters.
parms	the jlctree.control parameters.
lmmmodel	an lme4 object, containing the linear mixed-effects effects model with fixed effects, node-specific random effects (if valid), and subject-specific random intercepts (if valid). Returned when fity is TRUE.
coxphmodel_diffh_diffs	
	a coxph object, containing a Cox PH model with different hazards and different slopes across terminal nodes. Returned when fits is TRUE.
coxphmodel_diffh	
	a coxph object, containing a Cox PH model with different hazards but same slopes across terminal nodes. Returned when fits is TRUE.
coxphmodel_diffs	
	a coxph object, containing a Cox PH model with same hazards but different slopes across terminal nodes. Returned when fits is TRUE.

See Also

[jlctree-package](#), [jlctree.control](#), [rpart.control](#)

Examples

```
# Time-to-event in LTRC format:
data(data_timevar)
tree <- jlctree(survival=Surv(time_L, time_Y, delta)~X3+X4+X5,
                classmb=~X1+X2, fixed=y~X1+X2+X3+X4+X5, random=~1,
                subject='ID',data=subset(data_timevar, ID<=30),
                parms=list(maxng=4, fity=FALSE, fits=FALSE))

# Time-to-event in right-censored format:
data(data_timeinv)
tree <- jlctree(survival=Surv(time_Y, delta)~X3+X4+X5,
                classmb=~X1+X2, fixed=y~X1+X2+X3+X4+X5, random=~1,
                subject='ID', data=subset(data_timeinv, ID<=30),
                parms=list(maxng=4, fity=FALSE, fits=FALSE))
```

---

jlctree.control   *Sets the control parameters for* jlctree*.*

Description

Sets the control parameters for jlctree.

Usage

```
jlctree.control(test.stat = "lrt", stop.thre = 3.84, stable = TRUE,
  maxng = 6, min.nevents = 5, split.add = 20, cov.max = 1e+05,
  fity = TRUE, fits = TRUE, ...)
```

Arguments

test.stat	test statistic to use, "lrt" for likelihood ratio test, and "wald" for Wald test. Default is "lrt".
stop.thre	stops splitting if current node has test statistic less than stop.thre. Default is 3.84.
stable	if TRUE, check the variance of the estimated coefficients in survival models fit at tree nodes. If a node has variance larger than cov.max, the splitting function will not consider splits leading to that node. Default is TRUE.
maxng	maximum number of terminal nodes. Default is 6.
min.nevents	minimum number of events in any terminal node. By default, this parameter is set to the number of covariates used in the survival model.
split.add	when computing the difference between parent node's test statistic and sum of child nodes' test statistics, add split.add to the difference. When split.add > 0, tree may still split even if current split leads to negative improvement. Set split.add to a large positive value for the purpose of greedy splitting. Default is 20.

cov.max	upper bound on the variance of the estimated coefficients in survival models at tree nodes. Default is 1e5.
fity	if TRUE, once a tree is constructed, fit a linear mixed-effects model using tree nodes as group indicators. Default is TRUE.
fits	if TRUE, once a tree is constructed, fit survival models using tree nodes as group indicators. Default is TRUE.
...	further arguments to pass to or from other methods.

Value

A list of all these parameters.

See Also

[jlctree](), [jlctree-package]()

---

prune_tree   *Prunes an* rpart *tree to have the desired number of nodes.*

Description

Prunes an rpart tree to have the desired number of nodes.

Usage

```
prune_tree(tree, maxn)
```

Arguments

tree	the tree to prune, an rpart object.
maxn	desired number of terminal nodes.

Value

The pruned tree, an rpart object.

---

surve   *Defines the evaluation function for a new splitting method of* rpart.

Description

Defines the evaluation function for a new splitting method of rpart. Not to be called directly by the user.

Usage

```
surve(y, wt, parms)
```

Arguments

y	the response value as found in the formula that is passed in by rpart. Note that rpart will normally have removed any observations with a missing response.
wt	the weight vector from the call, if any.
parms	the vector or list (if any) supplied by the user as a parms argument to the call.

Value

See reference.

References

<https://cran.r-project.org/package=rpart/vignettes/usercode.pdf>

See Also

[survs,survi](#)

---

survi   *Defines the initialization function for a new splitting method of* rpart.

Description

Defines the initialization function for a new splitting method of rpart. Not to be called directly by the user.

Usage

```
survi(y, offset, parms, wt)
```

Arguments

y	the response value as found in the formula that is passed in by `rpart`. Note that `rpart` will normally have removed any observations with a missing response.
offset	the offset term, if any, found on the right hand side of the formula that is passed in by `rpart`.
parms	the vector or list (if any) supplied by the user as a `parms` argument to the call.
wt	the weight vector from the call, if any.

Value

See reference.

References

<https://cran.r-project.org/package=rpart/vignettes/usercode.pdf>

See Also

[survs,](#)[surve](#)

---

survs	*Defines the splitting function for a new splitting method of* `rpart`.

Description

Defines the splitting function for a new splitting method of `rpart`. Not to be called directly by the user.

Usage

```
survs(y, wt, x, parms, continuous)
```

Arguments

y	the response value as found in the formula that is passed in by `rpart`. Note that `rpart` will normally have removed any observations with a missing response.
wt	the weight vector from the call, if any.
x	vector of x values.
parms	the vector or list (if any) supplied by the user as a `parms` argument to the call.
continuous	if TRUE the x variable should be treated as continuous. The value of this parameter is determined by `rpart` automatically.

Value

See reference.

References

https://cran.r-project.org/package=rpart/vignettes/usercode.pdf

See Also

surve, survi

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