Package ‘gems’

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Description Simulate and analyze multistate models with general hazard functions. gems provides functionality for the preparation of hazard functions and parameters, simulation from a general multistate model and predicting future events. The multistate model is not required to be a Markov model and may take the history of previous events into account. In the basic version, it allows to simulate from transition-specific hazard function, whose parameters are multivariable normally distributed.

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Description

Is a S4 class for the artificial cohort generated by simulateCohort.

Usage

## S4 method for signature 'ArtCohort,ANY,ANY,ANY'
x[i, j, ..., drop = TRUE]

## S4 method for signature 'ArtCohort'
update(object, newSize, addBaseline = matrix(NA, nrow = 
newSize - object@size), newInitialStates = rep(1, newSize - object@size))

## S4 method for signature 'ArtCohort'
head(x, ...)

## S4 method for signature 'ArtCohort'
tail(x, ...)

## S4 method for signature 'ArtCohort'
summary(object)

Arguments

- `x`: object of class 'ArtCohort'
- `i, j, drop`: same as for `data.frame`
- `...`: passed on to `data.frame` method
- `newSize`: size of the updated cohort
- `addBaseline`: baseline for new part of cohort
- `newInitialStates`: initial states for new part of cohort

Slots

- `states.number`: Object of class "numeric": number of states
- `size`: Object of class "numeric": cohort size
- `baseline`: Object of class "matrix": baseline matrix
- `follow.up`: Object of class "numeric": maximum follow-up time
- `parameters`: Object of class "transition.structure": input parameters
- `parametersCovariances`: Object of class "transition.structure": input covariance matrices
cumulativeIncidence

timeToTransition Object of class "matrix": input timeToTransition matrix. logical components
transitionFunctions Object of class "transition.structure": input hazard functions
time.to.state Object of class "data.frame": entry times for each patient into each of the states

Objects from the Class

Objects are created by calls to the function simulateCohort.

Author(s)

Luisa Salazar Vizcaya, Nello Blaser, Thomas Gsponer

See Also

simulateCohort, transition.structure, transitionProbabilities, cumulativeIncidence

Examples

showClass("ArtCohort")

---
cumulativeIncidence  transition probabilities

Description

Calculates the cumulative incidence and prediction intervals after first state

Usage

cumulativeIncidence(object, times, M = 100, stateNames = paste("State",
as.list(1:dim(cohorts)[1])))

Arguments

object

either the output of simulateCohort or the matrix with the probabilities
slot of that output.
times

a time vector.
M

number of groups for calculating confidence intervals.
stateNames

a list with the names of states.

Value

an object of class "PosteriorProbabilities", containing the statenames, timepoints and the cumulative incidence with pointwise prediction intervals over time.
Author(s)
Luisa Salazar Vizcaya, Nello Blaser, Thomas Gsponer

References

See Also
posteriorprobabilities, artcohort, simulatecohort

gems: Generalized Multistate Simulation Model

Description
Simulate and analyze multistate models with general hazard functions. gems provides functionality for the preparation of hazard functions and parameters, simulation from a general multistate model and predicting future events. The multistate model is not required to be a Markov model and may take the history of previous events into account. In the basic version, it allows to simulate from transition-specific hazard function, whose parameters are multivariable normally distributed.

References

generatehazardmatrix: generate template for transition functions

Description
This function simplifies generating the matrix of transition functions.

Usage
generatehazardmatrix(statesNumber)

Arguments
statesNumber the number of states to be considered.
generateParameterCovarianceMatrix

Value

A transition.structure of dimension \( N \times N \), where \( N \) is the number of states and with value "impossible" for all potential transitions.

Author(s)

Luisa Salazar Vizcaya, Nello Blaser, Thomas Gsponer

References


See Also

transition.structure, simulateCohort

generateParameterCovarianceMatrix

generate a template for parameter covariances

Description

This function simplifies generating the matrix of parameter covariances from a matrix of mean parameters.

Usage

generateParameterCovarianceMatrix(mu)

Arguments

mu a transition.structure of dimension \( N \times N \), whose components list the mean values for the parameters in the transitionFunction.

Value

A transition.structure of dimension \( N \times N \) of covariance matrices for the parameters.

Author(s)

Luisa Salazar Vizcaya, Nello Blaser, Thomas Gsponer

References

generateParameterMatrix

generate a template for mean parameters

Description

This function simplifies generating the matrix of mean parameters from a matrix of transition functions.

Usage

generateParameterMatrix(hf)

Arguments

hf a transition.structure of dimension $N \times N$, where $N$ is the number of states.

Value

A transition.structure of dimension $N \times N$, whose components are lists of the right length for the parameters in the corresponding hazard function hf.

Author(s)

Luisa Salazar Vizcaya, Nello Blaser, Thomas Gsponer

References


See Also

transition.structure, simulateCohort
PosteriorProbabilities

Class "PosteriorProbabilities"

Description

This S4 class summarizes the posterior probabilities over time for objects of class "ArtCohort"

Usage

## S4 method for signature 'PosteriorProbabilities,ANY,ANY,ANY'

```r
x[i, j, ..., drop = TRUE]
```

## S4 method for signature 'PosteriorProbabilities'

```r
plot(x, ci = FALSE, main = paste(x@type,
    "after starting in State", x@states[1], 
    "at time 0"),
    states = 1:dim(x@probabilities)[2], lwd = c(2, 2), col = c("blue",
    "green3"), lty = c(1, 2), xlab = "Time", ylab = "Probability", ...)
```

## S4 method for signature 'PosteriorProbabilities'

```r
head(x, ...)
```

## S4 method for signature 'PosteriorProbabilities'

```r
tail(x, ...)
```

Arguments

- **x** the PosteriorProbabilities object
- **i, j, drop** same as for a "data.frame"
- **...** arguments passed on to main method
- **ci** should confidence intervals be displayed
- **main, xlab, ylab** same as any plot
- **states** which states to display
- **lwd, col, lty** vectors of length 2, with first component for the point estimate and second component for the confidence interval

Slots

- **states** Object of class "character": names of states
- **times** Object of class "numeric": time points at which probabilities are evaluated
- **probabilities** Object of class "matrix": posterior Probabilities to be in each state at each time
- **lower** Object of class "matrix": lower prediction bound to be in each state at each time
- **upper** Object of class "matrix": upper prediction bound to be in each state at each time
- **type** Object of class "character": describes type of probability
Objects from the Class

Objects are created by calls to the function simulateCohort.

Author(s)

Luisa Salazar Vizcaya, Nello Blaser, Thomas Gsponer

See Also

transitionprobabilities, cumulativeincidence, ArtCohort

Examples

showClass("PosteriorProbabilities")

---

**simulateCohort**

*Simulate cohort*

Description

Simulates a cohort of patients from a set of functions associated to each possible transition in a multistate model. The multistate model is not required to be a Markov model and may take the history of previous events into account. In the basic version, it allows to simulate from transition-specific hazard function, whose parameters are multivariable normally distributed. For each state, all transition-specific hazard functions and their parameters need to be specified. For simulating one transition, all possible event times are simulated and the minimum is chosen. Then simulation continues from the corresponding state until an absorbing state of time to is reached.

Usage

```r
simulateCohort(transitionFunctions, parameters, cohortSize = 1000,
               parameterCovariances = FALSE, timeToTransition = array(FALSE, dim =
dim(transitionFunctions@list.matrix)),
               baseline = matrix(NA, nrow =
cohortSize),
               initialState = rep(1, cohortSize),
               absorbing = transitionFunctions@states.number, to = 100,
               report.every = 100, sampler.steps = 1000)
```

Arguments

- `transitionFunctions` a transition.structure of dimension $N \times N$ that contains the hazard functions
- `parameters` a transition.structure of dimension $N \times N$ that contains the parameters
- `cohortSize` a numeric indicating the number of patients to be simulated.
- `parameterCovariances` a transition.structure of dimension $N \times N$ of covariance matrices for the parameters.
simulateCohort

timeToTransition

   a logical matrix: TRUE for all transitions whose transitionFunction is
   specified as the time until transition instead of as a hazard function or as a
   character.

baseline

   a matrix or data.frame of dimension cohortSize x M with M baseline char-
   acteristics of subjects to be simulated.

initialState

   a numeric of length cohortSize with the initial state for each subject simulated.

absorbing

   a numeric containing all absorbing states.

to

   final time of the simulation.

report.every

   a numeric to check progress of simulation.

sampler.steps

   a numeric indicating number of steps for discretization of hazard functions

Details

The transitionFunctions contains hazard functions or time to event function associated to each
possible transition. The elements of this list can be either expressed as an explicit R function or
as a character ("impossible", "Weibull", "multWeibull", "exponential") in order to express impos-
sible transitions or parametric forms for the distributions of time to event. If the functions should
depend on time, baseline characteristics or be history-dependent, the function arguments t, bl or
history can be used. Time t refers to the time since entry into the current state. For the time since
the initial state, use t+sum(history).

The components of the parameters argument list the mean values for the parameters in the
transitionFunction. If the corresponding transitionFunction is a function, the parameters
should appear in the same order as in the function, leaving out t, bl and history. If the corre-
sponding transitionFunction is the character "Weibull", the first argument is the shape and the
second one the scale. If the corresponding transitionFunction is the character "multWeibull",
specify weights, shapes, scales in this order.

Note that when using the parameterCovariances argument it is the users responsibility to en-
sure that the functions are parametrized such that parameters for each transition are multivariate
normally distributed and mutually independent.

Value

   an object of class "ArtCohort" with time.to.state slot of dimension cohortSize x N with entry
times for each patient into each of the states.

Author(s)

   Luisa Salazar Vizcaya, Nello Blaser, Thomas Gsponer

References

   Nello Blaser, Luisa Salazar Vizcaya, Janne Estill, Cindy Zahnd, Bindu Kalesan, Matthias Egger,
   Olivia Keiser, Thomas Gsponer (2015). gems: An R Package for Simulating from Disease Progres-
See Also

generateHazardMatrix, generateParameterMatrix, generateParameterCovarianceMatrix, ArtCohort, transitionProbabilities, cumulativeIncidence

Examples

# Here is an example model with 3 states and 2 possible transitions.

# number of states in the model
statesNumber <- 3

# cohort size
cohortSize <- 100

# specification of hazard functions
hazardf <- generateHazardMatrix(statesNumber)
hazardf[[1,2]] <- function(t, r1, r2)
   {ifelse(t>=2, r1 , r2)
   }
hazardf[[2,3]] <- "Weibull"

# list of parameters for the hazard functions
mu <- generateParameterMatrix(hazardf)
mu[[1,2]] <- list(0.33, 0.03) # r1, r2
mu[[2,3]] <- list(1,0.84) # shape, scale

# time
maxTime <- 10

# simulate the cohort
cohort <- simulateCohort(
   transitionFunctions = hazardf,
   parameters = mu,
   cohortSize = cohortSize,
   to=maxTime)

# output
head(cohort)

# transition probability
tr <- transitionProbabilities(cohort, times=seq(0,4,.1))
plot(tr, ci=FALSE)

# cumulative incidence
inc <- cumulativeIncidence(cohort, times=seq(0,4,.1))
plot(inc, ci=FALSE, states=c(2,3))
transition.structure

Description

The simulated data set for each patient contains data for kidney injuries, bleeding complications and the combined endpoint of stroke or death. The data was simulated from the original data following the steps described in the package vignette.

Format

A data frame with 194 observations on the following 7 variables.

- **id**: a character vector that contains the patient id’s
- **kidney**: a numeric vector; indicator variable that show if an event has occurred
- **kidney.dur**: a numeric vector; times at which the events occurred or the patients were censored
- **bleeding**: a numeric vector; indicator variable that show if an event has occurred
- **bleeding.dur**: a numeric vector; times at which the events occurred or the patients were censored
- **death**: a numeric vector; indicator variable that show if an event has occurred
- **death.dur**: a numeric vector; times at which the events occurred or the patients were censored

References


Examples

head(data(tavi))

---

**transition.structure**  Class "transition.structure"

Description

This S4 class provides a structure to specify different characteristics of transitions, such as transition functions, parameters or parameter covariances.

Usage

```r
## S4 method for signature 'transition.structure'
x[[i, j, ..., exact = TRUE]]

## S4 replacement method for signature 'transition.structure'
x[[i, j]] <- value

possibleTransitions(object)

## S4 method for signature 'transition.structure'
```
possibleTransitions(object)

## S4 method for signature 'transition.structure'
print(x)

Arguments

x, object the transition.structure
i, j same as for matrix
exact, value,...
   passed on to list method

Slots

states.number Object of class "numeric": number of states
list.matrix Object of class "matrix": a list with two dimensions, where list element [i,j]
   correspond to transitions from i to j

Objects from the Class

Objects are created by calls to the functions generateHazardMatrix, generateParameterMatrix,
generateParameterCovarianceMatrix.

Author(s)

Luisa Salazar Vizcaya, Nello Blaser, Thomas Gsponer

See Also

generateHazardMatrix, generateParameterMatrix, generateParameterCovarianceMatrix

Examples

showClass("transition.structure")

---

transitionProbabilities

transition probabilities

Description

Calculates the probabilities and prediction intervals after first state

Usage

transitionProbabilities(object, times, M = 100, stateNames = paste("State",
   as.list(1:dim(cohorts)[1])))
transitionProbabilities

Arguments

object either the output of simulateCohort or the matrix with the probabilities slot of that output.
times a time vector.
M number of groups for calculating confidence intervals.
stateNames a list with the names of states.

Value

an object of class "PosteriorProbabilities", containing the statenames, timepoints and the transition probabilities with pointwise prediction intervals over time.

Author(s)

Luisa Salazar Vizcaya, Nello Blaser, Thomas Gsponer

References


See Also

PosteriorProbabilities, ArtCohort, simulateCohort
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