Package ‘gems’

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Description This package allows to simulating and analyzing multistate models with general hazard functions. It 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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ArtCohort-class

Description

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

Objects from the Class

Objects are created by calls to the function simulateCohort.

Slots

- statesNnumber: Object of class "numeric": number of states
- size: Object of class "numeric": cohort size
- baseline: Object of class "matrix": baseline matrix
- followNup: 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
- timeToTransition: Object of class "matrix": input timeToTransition matrix. logical components
- transitionFunctions: Object of class "transition.structure": input hazard functions
- timeNtoNstate: Object of class "data.frame": entry times for each patient into each of the states

Methods

- \[ \text{signature(x = "ArtCohort", i="ANY", j="ANY", drop="ANY")}: \text{extract subsets of slot time.to.state in artificial cohorts} \]
- \text{summary signature(object = "ArtCohort")}: summarize the artificial cohort
- \text{update signature(object = "ArtCohort")}: update an artificial cohort
- \text{head signature(x = "ArtCohort")}: returns the first part of the artificial cohort
- \text{tail signature(x = "ArtCohort")}: returns the last part of the artificial cohort

Author(s)

Luisa Salazar Vizcaya, Nello Blaser, Thomas Gsponer

See Also

- simulateCohort, transition.structure-class, transitionProbabilities, cumulativeIncidence

Examples

- showClass("ArtCohort")
**cumulativeIncidence**

**transition probabilities**

**Description**

Calculates the cumulative incidence and prediction intervals after first state.

**Usage**

```r
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

**See Also**

- `PosteriorProbabilities-class`, `ArtCohort-class`, `simulateCohort`

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**generateHazardMatrix**

generate template for transition functions

**Description**

This function simplifies generating the matrix of transition functions.

**Usage**

```r
generateHazardMatrix(statesNumber)
```
generateParameterCovarianceMatrix

Arguments

statesNumber  the number of states to be considered.

Value

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

See Also

transition.structure-class, 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

transition structure of dimension $N \times N$ of covariance matrices for the parameters.

Author(s)

Luisa Salazar Vizcaya, Nello Blaser, Thomas Gsponer

See Also

transition.structure-class, generateParameterMatrix, simulateCohort
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

See Also

transition.structure-class, simulateCohort

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PosteriorProbabilities-class

Class "PosteriorProbabilities"

Description

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

Objects from the Class

Objects are created by calls to the function simulateCohort.
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

Methods

[ signature(x = "PosteriorProbabilities")]: accesses the probabilities slot
plot signature(x = "PosteriorProbabilities")]: plots the posterior probabilities
head signature(x = "PosteriorProbabilities")]: returns the first part of the transition probabilities
tail signature(x = "PosteriorProbabilities")]: returns the last part of the transition probabilities

Author(s)

Luisa Salazar Vizcaya, Nello Blaser, Thomas Gsponer

See Also

transitionProbabilities, cumulativeIncidence, ArtCohort-class

Examples

showClass("PosteriorProbabilities")

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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 \( t_0 \) is reached.
Usage

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.

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 \(cohortSize \times M\) with \(M\) baseline characteristics 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 impossible 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 \(t+\text{sum(history)}\).

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
simulateCohort

should appear in the same order as in the function, leaving out \( t, b, l \) and \( history \). If the cor-
responding 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 \( \text{cohortSize} \times N \) with entry
times for each patient into each of the states.

Author(s)

Luisa Salazar Vizcaya, Nello Blaser, Thomas Gsponer

See Also

generateHazardMatrix, generateParameterMatrix, generateParameterCovarianceMatrix,
ArtCohort-class, 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,
transition.structure-class

```r
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-class

**Class** "transition.structure"

#### Description

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

#### Objects from the Class

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

#### 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

#### Methods

- `[[` signature(x = "transition.structure"): extract subsets of slot `list.matrix` of `transition.structure`
- `[[<-` signature(x = "transition.structure"): replace subsets of slot `list.matrix` of `transition.structure`
- `print` signature(x = "transition.structure"): prints the slot `list.matrix` of the `transition.structure`

#### Author(s)

Luisa Salazar Vizcaya, Nello Blaser, Thomas Gsponer

#### See Also

`generateHazardMatrix`, `generateParameterMatrix`, `generateParameterCovarianceMatrix`
transitionProbabilities

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])))

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

See Also

PosteriorProbabilities-class, ArtCohort-class, simulateCohort
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