Package 'GUTS'

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Type Package

Title Fast Calculation of the Likelihood of a Stochastic Survival
Model

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Description
Given exposure and survival time series as well as parameter values, GUTS allows for the fast cal-
culation of the survival probabilities as well as the logarithm of the corresponding likeli-
hood (see Albert, C., Vogel, S. and Ashauer, R. (2016) <doi:10.1371/journal.pcbi.1004978>).

License GPL (>= 2)

Depends R (>= 3.5.0), methods, Rcpp (>= 0.12.16)

LinkingTo Rcpp

LazyLoad yes

LazyData no

Encoding UTF-8

Suggests knitr, rmarkdown, adaptMCMC, xlsx, drc, testthat, withr

VignetteBuilder knitr

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Contents

GUTS-package | *Fast Calculation of the Likelihood of a Stochastic Survival Model*

Description

GUTS (General Unified Threshold model of Survival) is a stochastic survival model for ecotoxicology. The package allows for the definition of exposure and survival time series as well as parameter values, and the fast calculation of the survival probabilities as well as the logarithm of the corresponding likelihood.

Details

A GUTS object is a special list of class "GUTS". Functions guts_setup, guts_calc_loglikelihood and guts_calc_survivalprobs are available to create and work with GUTS objects. A data set diazinon is also included. See links for more details.

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References

Albert, C., Vogel, S., and Ashauer, R. (2016). Computationally efficient implementation of a novel algorithm for the General Unified Threshold Model of Survival (GUTS). PLOS Computational Biology, 12(6), e1004978. doi:10.1371/journal.pcbi.1004978.

Jager, T., Albert, C., Preuss T., and Ashauer R. (2011). General Unified Threshold Model of Survival – a toxicokinetic toxicodynamic framework for ecotoxicology. Environmental Science & Technology, 45(7), 2529–2540, doi:10.1021/es103092a

See Also

guts_setup, guts_calc_loglikelihood, guts_calc_survivalprobs, guts_report_damage, diazinon, Rcpp

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| diazinon | *GUTS data set with Gammarus pulex exposed to diazinon* |

Description

Data of 3 pulsed toxicity tests with the freshwater crustacean Gammarus pulex and diazinon, an organophosphate insecticide.

Usage

```
data("diazinon")
```

Format

A list containing 12 data vectors.

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Source

Ashauer, R., Hintermeister, A., Caravatti, I., Kretschmann, A. and Escher, B. I. (2010) Toxicokinetic-toxicodynamic modeling explains carry-over toxicity from exposure to diazinon by slow organism recovery. *Environmental Science & Technology* 44, 3963–3971, doi:10.1021/es903478b.

See Also

GUTS

| GUTS | *Fast Calculation of the Likelihood of a Stochastic Survival Model* |

Description

GUTS (General Unified Threshold model of Survival) is a stochastic survival model for ecotoxicology. The package allows for the definition of exposure and survival time series as well as parameter values, and the fast calculation of the survival probabilities as well as the logarithm of the corresponding likelihood.

The package implements the GUTS-SIC (also called GUTS-RED) variants that assume a one-compartment model with first-order toxicokinetics.

Usage

```
guts_setup(C, Ct, y, yt, dist = "lognormal",
model = "Proper",
N = 1000L,
MF = 100L,
M = max(
5000L,
as.integer(ceiling(MF * length(union(Ct, yt)))),
as.integer(ceiling(MF * max(union(Ct, yt))))
),
SVR = 1L,
study = "", Clevel = ""
)

guts_calc_loglikelihood(gobj, par, external_dist = NULL,
  use_multinomial_coefficient = FALSE)

guts_calc_survivalprobs(gobj, par, external_dist = NULL)

guts_report_damage(gobj)

guts_report_sppe(gobj)

guts_report_squares(gobj)
```

Arguments

C	Numeric vector of concentrations. Vector must contain at least 2 values and be of the same length as Ct.
Ct	Numeric vector of concentration time points. Vector must contain at least 2 values and be of the same length as C. Time points must start at 0, and contain unique values in ascending order.
y	Integer vector (counts) of survivors. Vector must contain at least 2 values and be of the same length as yt. y must not be ascending.
yt	Numeric vector of survivor time points. Vector must contain at least 2 values and be of the same length as y. Time points must start at 0, and contain unique values in ascending order. Survivor information at time points later than the latest concentration time point will be disregarded (with a warning).
dist	Distribution as character, either "lognormal" (default), "loglogistic", "external" or "delta".
model	Model as character, either "Proper" (for full model, the default), "IT" (for individual tolerance), or "SD" (for stochastic death).
MF	Integer. Multiplication factor for M. Must be greater than 1. MF is used only if "model = 'SD'" or "model = 'Proper'" and M is not specified. Setting MF automatically ensures that the number of points for time discretization M is at least the number of measurement time steps or the measurement time (which ever is larger) multiplied by MF. A minimum of M = 5000 is ensured.

M	Integer. Desired number of points for time discretization. Must be greater than 1. M is used only if "model = 'SD'" or "model = 'Proper'"
N	Integer. Sample length of individual tolerance thresholds. Must be greater than 2. N is used only, if "model = 'Proper'"
study	string with the name of the study
Clevel	character vector with names for each of the concentraton levels
SVR	Numeric surface-volume-ratio. A multiplication factor to kd.
gobj	GUTS object. The object to be updated (and used for the calculation).
par	Numeric vector of parameters. See details below.
external_dist	Numeric vector containing the distribution of individual thresholds. Only used if dist = 'external'. See details below.
use_multinomial_coefficient	
	If "TRUE" returns loglikelihood from the correct multinomial distribution. Defaults to ignoring the constant multinomial coefficient for performance reasons.

Details

Functions:

Use `guts_setup` to define (or alter) a GUTS object. Various checks are applied to the data. On success, a GUTS object will be created.

Use `guts_calc_loglikelihood` to calculate the survival probabilities and the corresponding loglikelihood for a given set of parameters. The function is very fast and can be used in routines for parameter estimation. The function returns the loglikelihood, however it also updates the fields `par`, `S`, `D`, `SPPE`, `squares`, `zt` and `LL` of the GUTS-object.

`guts_calc_survivalprobs` is a convenience wrapper that can be used for predictions; it returns the survival probabilities, however it also updates the fields `par`, `S`, `D`, `SPPE`, `squares`, `zt` and `LL` of the GUTS-object.

`guts_report_damage` returns a data.frame with time grid points and the damage for each of these. The function reports the damage that was calculated in the previous call to `guts_calc_loglikelihood` or `guts_calc_survivalprobs`.

`guts_report_squares` returns the sum of squares. The function reports the sum of squares that was calculated in the previous call to `guts_calc_loglikelihood` or `guts_calc_survivalprobs`.

`guts_report_sppe` returns the survival-probability prediction error (SPPE). The function reports the SPPE that was calculated in the previous call to `guts_calc_loglikelihood` or `guts_calc_survivalprobs`.

Models, Parameters, and Distributions:

The GUTS package provides three model types:

- Proper: a GUTS-SIC-Proper (also called GUTS-RED-Proper) model using random individual tolerances and a stochastic death process, when individual tolerances are exceeded.
- IT: a GUTS-SIC-IT (GUTS-RED-IT) individual tolerance model using random individual tolerances. If an individual's tolerance threshold is exceeded, the individual dies.
- SD: a GUTS-SIC-SD (GUTS-RED-SD) stochastic death model using a stochastic death process above a population-wide tolerance threshold. The tolerance-threshold is the same for all individuals.

The Proper GUTS model requires the following parameters par, while variants IT and SD are based on a reduced subset (as indicated in brackets). Parameter values in par must be ordered as listed here:

- hb: background mortality rate (Proper, IT, SD)
- ke: dominant rate constant (Proper, IT, SD)
- kk: killing rate (Proper, SD)
- further parameters for the tolerance threshold (in SD) or the threshold distribution dist (in Proper and IT)

For model type "SD" (stochastic death), required parameters par[1:4] are hb, ke, kk and mn, which is the population-wide tolerance threshold. For backwards compatibility this model type can be initiated setting dist = "Delta" and model = "Proper".

For model type "IT" (individual tolerance), required parameters par[1:2] are hb, ke, as well as respective distribution parameters (from par[3] onwards). Parameter (kk) is set internally to infinity and does not need to be provided.

For model type "Proper", all parameters are needed. par[1:3] take hb, ke, kk, distribution parameters follow (from par[4] onwards).

For model types "Proper" and "IT" individual tolerance thresholds are created internally. Individual tolerances are drawn from the specified distribution dist. The parameter values required depend on the specified dist:

- "lognormal": requires the parameters mn and sd which are the mean and standard deviation of the lognormal random distribution. In contrast to parameters meanlog and sdlog of function [dlnorm], these parameters are not on the logscale. They relate in the following way:

$$sdlog = \sqrt{\ln \frac{1 + sd^2}{mn^2}}$$

$$meanlog = \ln mn - \frac{1}{2} * sdlog^2$$

- "loglogistic": requires the parameters $mn = scale = median$ and $beta = shape$.
- "external": uses random variates provided to external_dist. With this option GUTS can be run with arbitrarily distributed individual tolerance thresholds. With the option "external" only parameters hb, ke and kk (Proper only) are required. Further, the thresholds sample length N is internally adjusted to the length of the external vector of random variates external_dist. The adjustment of N is notified by a warning.

For performance reasons the implemented distributions "lognormal" and "loglogistic" are approximated using importance sampling. The option "external" generally performs well, but might require a larger thresholds sample (i.e. length(external_dist) should be large).

The number of parameters is checked according to dist and model. Wrong number of parameters invokes an error, wrong parameter values (e.g., negative values) invoke a warning, and the loglikelihood is set to -Inf.

Field and Attribute Access:

Fields and attributes of an object of class "GUTS" are read-only. It is not possible to directly modify single elements of the GUTS object. Instead use function guts_setup to create GUTS objects or modify fields on existing GUTS objects. Functions guts_calc_loglikelihood and guts_calc_survivalprobs update an object's fields par (parameters), D (damage), squares (sum of squares), SPPE (survival-probability prediction error), S (survival probabilities) and LL (the loglikelihood).

Value

`guts_setup` returns a list of class "GUTS" with the following fields:

C	Concentrations.
Ct	Concentration time points.
y	Survivors.
yt	Survivor time points.
dist	Distribution.
model	Model.
N	Sample length.
M	Time grid points.
par	Parameters.
S	Vector of survivor probabilities.
D	Vector of internal damage for each of the M time grid points.
squares	Sum of squares
SPPE	Survival-probability prediction error.
LL	The loglikelihood.

`guts_calc_loglikelihood` returns the loglikelihood.

`guts_calc_survivalprobs` returns the survival probabilities.

`guts_report_damage` returns the damage.

`guts_report_squares` returns the sum of squares.

`guts_report_sppe` returns the survival-probability prediction error (SPPE).

Note

The GUTS project web site can be found here: http://guts.r-forge.r-project.org. For questions and discussion, please subscribe to the mailing list there.

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References

Albert, C., Vogel, S., and Ashauer, R. (2016). Computationally efficient implementation of a novel algorithm for the General Unified Threshold Model of Survival (GUTS). PLOS Computational Biology, 12(6), e1004978. doi:10.1371/journal.pcbi.1004978.

Jager, T., Albert, C., Preuss, T., and Ashauer, R. (2011). General Unified Threshold Model of Survival – a toxicokinetic toxicodynamic framework for ecotoxicology. Environmental Science & Technology, 45(7), 2529–2540, doi:10.1021/es103092a.

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See Also

diazinon, GUTS-package and the package vignettes for examples on how to calibrate and project GUTS-models.

Examples

```
data(diazinon)

# create GUTS object to calculate the Proper model
#  using a log-normal distribution of tolerance thresholds
gts.lognormal <- guts_setup(
  C = diazinon$C1, Ct = diazinon$Ct1,
  y = diazinon$y1, yt = diazinon$yt1,
  dist = "lognormal", model = "Proper")

# calculate likelihood of Proper model using log-normal distribution
guts_calc_loglikelihood(
  gts.lognormal,
  c(0.051, 0.126, 1.618, 19.099, 6.495))
gts.lognormal  # show GUTS object

# repeating calculation above
#  with threshold values from an external log-normal distribution.
#  Note, we need to account for the different parametrisations
```

```
#  used in the GUTS-package and in rlnorm
sigma2 <- log( 1 + 6.495^2 / 19.099^2)
mu <- log(19.099) - 0.5 * sigma2
lognormal.thresholds <- rlnorm(1000, meanlog = mu, sdlog = sqrt(sigma2))
gts.external <- guts_setup(
  C = diazinon$C1, Ct = diazinon$Ct1,
  y = diazinon$y1, yt = diazinon$yt1,
  dist = "external", model = "Proper")
guts_calc_loglikelihood(
  gts.external,
  c(0.051, 0.126, 1.618), external_dist = lognormal.thresholds)
# -> Results using external and internal distributions are comparable


# create GUTS object to calculate the Proper model
#  using a log-logistic distribution of tolerance thresholds
gts.loglogistic <- guts_setup(
  C = diazinon$C1, Ct = diazinon$Ct1,
  y = diazinon$y1, yt = diazinon$yt1,
  dist = "loglogistic", model = "Proper")
guts_calc_survivalprobs( # returning survival probabilities
  gts.loglogistic,
  c(0.01, 0.2, 0.3, 3, 2))

str(guts_report_damage(gts.loglogistic)) # returning damage

# calculate survival probabilities with IT model
#  using a log-logistic distribution of tolerance thresholds
guts_calc_survivalprobs(
  guts_setup(
  C = diazinon$C1, Ct = diazinon$Ct1,
  y = diazinon$y1, yt = diazinon$yt1,
  dist = "loglogistic", model = "IT"),
  c(0.01, 0.2, 3, 2))

# calculate survival probabilities with an SD model with a fixed tolerance threshold
guts_calc_survivalprobs(
  guts_setup(
  C = diazinon$C1, Ct = diazinon$Ct1,
  y = diazinon$y1, yt = diazinon$yt1,
  dist = "loglogistic", model = "SD"),
  c(0.01, 0.2, 0.3, 3))


## Not run: guts_calc_survivalprobs(gts.external, rep(.5, 3))
# Warning and no result, because no external distribution was specified

## Not run: guts_calc_survivalprobs(gts.loglogistic , 1:4 ) # Error.

## Not run: gts.loglogistic[["C"]] <- 1:3 # Error.
```

Index