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stressaddition-package

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**stressaddition-package**

*stressaddition: Modelling Tri-Phasic Concentration-Response Relationships*

**Description**

The stress addition approach is an alternative to the traditional concentration addition or effect addition models. It allows the modelling of tri-phasic concentration-response relationships either as single toxicant experiments, in combination with an environmental stressor or as mixtures of two toxicants. See Liess et al. (2019) <doi:10.1038/s41598-019-51645-4> and Liess et al. (2020) <doi:10.1186/s12302-020-00394-7>.

**Details**

This R package contains the definitions of the ECx-SyS model and the Multi-TOX model. See the publications linked below for more information including equations.

Author contributions: M. Liess conceived the ECx-SyS and Multi-TOX models. S. Henz developed this R package. N. Shahid contributed to the optimization of the Multi-TOX model and provided the multiple_stress data set.

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References


See Also

Useful links:

- https://git.ufz.de/oekotox/stressaddition

ecxsys

ECx-SyS

Description

ECx-SyS is a model for tri-phasic concentration-response relationships where hormetic and sub-hormetic effects are observed at low concentrations. It expands the Stress Addition Model (SAM) by introducing system stress (SyS) which is negatively correlated with toxicant stress. A constant environmental stress can be included. See the publication for details.

Usage

ecxsys(
  concentration,
  hormesis_concentration,
  survival_tox_observed,
  survival_tox_env_observed = NULL,
  survival_max = 100,
  curves_concentration_max = NULL,
  p = 3.2,
  q = 3.2
)

Arguments

concentration A vector of concentrations. Must be sorted in ascending order and the first element must be 0 to indicate the control.
hormesis_concentration The concentration where the hormesis occurs. This is usually the concentration of the highest survival after the control.
survival_tox_observed A vector of survival values observed at the given concentrations and in absence of environmental stress. Values must be between 0 and survival_max.
survival_tox_env_observed
Survival values observed in the presence of environmental stress. Must be between 0 and survival_max.

survival_max
The maximum value the survival could possibly reach. For survival data in percent this should be 100 (the default).

curves_concentration_max
The maximum concentration of the predicted curves. This might be useful if for example your highest observed concentration is 30 but you would like to know the predicted values on a scale between 0 and 100.

p, q
The shape parameters of the beta distribution. Default is p = q = 3.2.

Details
It is advised to complete the curve down to zero for optimal prediction. Therefore survival_tox_observed in the highest concentration should be at or close to zero. If the model does not fit properly try adding a survival of 0 at ten times the maximum observed concentration.

The vectors concentration, survival_tox_observed and survival_tox_env_observed (if provided) must be of equal length and sorted by increasing concentration.

Value
A list (of class ecxsys) containing many different objects of which the most important are listed below. The survival and stress vectors correspond to the provided concentrations.

survival_tox Modeled survival resulting from toxicant stress.

survival_tox_sys Modeled survival resulting from toxicant and system stress.

survival_tox_env Modeled survival resulting from toxicant and environmental stress.

survival_tox_env_sys Modeled survival resulting from toxicant, environmental and system stress.

survival_tox_LL5 The survival predicted by the five-parameter log-logistic model derived from the observations under toxicant stress but without environmental stress.

survival_tox_env_LL5 The survival predicted by the five-parameter log-logistic model derived from the observations under toxicant stress with environmental stress.

curves A data frame containing survival and stress values as returned by predict_ecxsys. The concentrations are regularly spaced on a logarithmic scale in the given concentration range. The control is approximated by the lowest non-control concentration times 1e-7. The additional column concentration_for_plots is used by the plotting functions of this package to approximate the control and generate a nice concentration axis.

References
Examples

```r
model <- ecxsys(
  concentration = c(0, 0.05, 0.5, 5, 30),
  hormesis_concentration = 0.5,
  survival_tox_observed = c(90, 81, 92, 28, 0),
  survival_tox_env_observed = c(29, 27, 33, 5, 0)
)
```

# Use survival_max if for example the survival is given as the average number
# of surviving animals and the initial number of animals is 21:
model <- ecxsys(
  concentration = c(0, 0.03, 0.3, 3, 30),
  hormesis_concentration = 0.3,
  survival_tox_observed = c(17, 15.2, 18.8, 7, 0),
  survival_tox_env_observed = c(4.8, 4.6, 6.4, 0, 0),
  survival_max = 21
)

```

lc

Lethal Concentrations

Description

Estimate the concentration to reach a certain mortality relative to the control.

Usage

```r
lc(model, response_name, response_level, reference, warn = TRUE)
```

Arguments

- **model**: This can be one of three types of objects: Either the output of `ecxsys` or the output of `predict_ecxsys` or a data frame with a "concentration" column and a `response_name` column. In the case of the data frame the first row is assumed to be the control. See the examples.

- **response_name**: The name of the survival or stress for which you want to calculate the LC.

- **response_level**: The desired response level as a percentage between 0 and 100. For example with the value 10 the function will return the LC10, i.e. the concentration where the response falls below 90 % of the control response. In other words: where a mortality of 10 % relative to the control is reached.

- **reference**: The reference value of the response, usually the control at concentration 0. This argument is optional. If it is missing, the first value of the response is used as control. This value determines what number `response_level` actually corresponds to. For example if `response_level` is 10 and reference is 45, then the function returns the concentration where the curve is reduced by 10% relative to 45 = 40.5.

- **warn**: Logical. Should the function emit a warning if the calculation of the lethal concentration is not possible?
Details

If the response level occurs multiple times because of hormesis, which may happen for low values of \( \text{response\_level} \), then the occurrence with the smallest concentration is returned.

This function only makes sense for curves which generally go down with increasing concentration, i.e. all \( \text{survival\_*} \) curves and also \( \text{sys\_tox} \) and \( \text{sys\_tox\_env} \). Others are untested and may give unexpected results, if any.

Value

A list containing the lethal concentration and the corresponding survival. The survival will be \( \text{NA} \) if its calculation is impossible using the supplied data.

Examples

```r
# Calculate the LC10, the concentration where the survival falls
# below 90% of the survival in the control.
model <- ecxsys(
  concentration = c(0, 0.05, 0.5, 5, 30),
  hormesis_concentration = 0.5,
  survival_tox_observed = c(90, 81, 92, 28, 0)
)

# using the ecxsys() output or the curves therein directly:
lc(model, "survival_tox_sys", 10)
lc(model$curves, "survival_tox_sys", 10)

# using the output of predict_ecxsys() with custom concentrations:
conc <- 10^seq(-9, 1, length.out = 1000)
curves <- predict_ecxsys(model, conc)
lc(curves, "survival_tox_sys", 10)

# using a custom data frame:
df_custom <- data.frame(
  concentration = curves$concentration,
  foo = curves$survival_tox_sys
)
lc(df_custom, "foo", 10)

# Calculate the LC50 relative to an survival of 100
# instead of relative to the control:
lc(model, "survival_tox_sys", 50, reference = 100)
```

---

**log10_ticks**

*Logarithmic axis tick marks*

Description

Calculate the positions and labels of major and minor tick marks for a base 10 logarithmic axis.
Usage

log10_ticks(x, label_zero = TRUE)

Arguments

x  A vector of axis values. Can be arbitrarily long but only the minimum and maximum are necessary.
label_zero  Whether or not to replace the smallest major label with "0". This defaults to TRUE and is useful for some types of plots used to display concentration-response data where the leftmost data point represents the control.

Value

A list with the positions and labels of the major and minor tick marks. The labels are formatted without trailing zeros using formatC(labels, format = "fg").

Examples

x <- c(0.01, 0.2, 3, 10, 50)
plot(x, c(5, 4, 2.5, 1, 0), xaxt = "n", log = "x")
ticks <- log10_ticks(x)
axis(1, at = ticks$major, labels = ticks$major_labels)
axis(1, at = ticks$minor, labels = FALSE, tcl = -0.25)

multiple_stress  Survival of Daphnia magna exposed to multiple stressors

Description

A data set of mixture toxicity experiments. Individuals of Daphnia magna were exposed to combinations of food stress and multiple concentrations of the pesticides esfenvalerate and prochloraz. The survival was recorded at 21 days after contamination.

Usage

multiple_stress

Format

A data frame with 58 rows and 4 variables:

food  The amount of food in percent.
esfenvalerate  The concentration of esfenvalerate in µg/L.
prochloraz  The concentration of prochloraz in µg/L.
survival  The mean survival in percent.
multi_tox

Source

multi_tox Predict the survival of binary toxicant mixtures

Description
The Multi-TOX model predicts the effects of binary toxicant mixtures based on three-phasic concentration-response relationships. See the publication for details.

Usage
multi_tox(
  model_a,
  model_b,
  concentration_a,
  concentration_b,
  sa_contribution = 0.5,
  survival_max = 100
)

Arguments
model_a, model_b
  The ecxsys models of the toxicants.
concentration_a, concentration_b
  The concentrations of the toxicants in the mixture. Both vectors must either be the same length or the longer length must be a multiple of the shorter length. That’s because the shorter concentration vector gets recycled to the length of the longer one.
sa_contribution
  The proportion of stress addition contributing to the calculation of the toxicant stress in the mixture. Must be between 0 and 1 where 1 stands for 100 % stress addition.
survival_max
  Controls the scaling of the result. This represents the maximum value the survival could possibly reach. For survival data in percent this should be 100 (the default).

Details
The predictions are symmetric, i.e. it does not matter which of the toxicant models is a or b as long as the concentration arguments are supplied in the same order.
This method is only suitable for experiments without or with low environmental stress. Any environmental stress supplied as arguments to ecxsys in model_a or model_b is ignored.
**Value**

A data frame with columns of the supplied concentrations and the corresponding mixture survival and stresses.

**References**


**Examples**

```r
# Using a data set which is included in this package. See ?multiple_stress
ms <- multiple_stress
esfen <- ms[ms$food == 1 & ms$prochloraz == 0, ]
proch <- ms[ms$food == 1 & ms$esfenvalerate == 0, ]

model_esfen <- ecxsys(
  concentration = esfen$esfenvalerate,
  survival_tox_observed = esfen$survival,
  hormesis_concentration = 0.1
)
model_proch <- ecxsys(
  concentration = proch$prochloraz,
  survival_tox_observed = proch$survival,
  hormesis_concentration = 100
)

# Predict the survival at 8 different esfenvalerate concentrations
# but keep the prochloraz concentration constant at 32:
mt <- multi_tox(
  model_esfen,
  model_proch,
  c(0, 0.0001, 0.001, 0.01, 0.1, 0.316, 1, 3.16),
  32,
  sa_contribution = 0.8
)
mt[1:3]  # The concentrations and survival of the 8 mixtures.

# Predict the survival at 4 different combinations
# of esfenvalerate and prochloraz:
mt <- multi_tox(
  model_esfen,
  model_proch,
  c(0.1, 0.2, 0.3, 0.4),
  c(0, 1, 32, 100),
  sa_contribution = 0.8
)
mt[1:3]  # The concentrations and survival of the 4 mixtures.
```
**plot_ecxs</noset>ys**

Plot the results of the ECx-SyS model

**Description**

Plot the observed and modeled survivals and stresses.

**Usage**

```r
plot_stress(
  model,
  which = c("sys_tox", "sys_tox_observed", "sys_tox_env", "sys_tox_env_observed"),
  show_legend = FALSE,
  xlab = "concentration",
  ylab = "stress",
  main = NULL
)
```

```r
plot_survival(
  model,
  which = c("survival_tox", "survival_tox_sys", "survival_tox_observed",
            "survival_tox_env", "survival_tox_env_sys", "survival_tox_env_observed"),
  show_legend = FALSE,
  xlab = "concentration",
  ylab = "survival",
  main = NULL
)
```

**Arguments**

- `model` The model object returned from `ecxsys`.
- `which` A vector of curve names to plot. Allowed are all values of `names(model$curves)` except "concentration". See the Value section of `predict_ecxs`ys for descriptions of these names. Additionally, you can use "survival_tox_observed" and "survival_tox_env_observed" for the observed survival and "sys_tox_observed" and "sys_tox_env_observed" for the observed Sys. Use "all" to plot everything or NA to only draw the axis and labels. Invalid names will be silently ignored.
- `show_legend` Should the plot include a legend? Defaults to FALSE because it may cover some parts of the plot depending on the plot size and the number of elements shown.
- `xlab`, `ylab`, `main` Axis labels and title.

**Value**

None
predict_ecxsyst

Examples

```r
model <- ecxsys(
    concentration = c(0, 0.05, 0.5, 5, 30),
    hormesis_concentration = 0.5,
    survival_tox_observed = c(90, 81, 92, 28, 0),
    survival_tox_env_observed = c(29, 27, 33, 5, 0)
)
plot_survival(model, show_legend = TRUE)
plot_stress(model, show_legend = TRUE)

# Plot all curves:
plot_survival(model, which = "all")
plot_stress(model, which = "all")

# Plot only some selected curves:
plot_survival(model, which = c("survival_tox_sys", "survival_tox_env_sys"))
plot_stress(model, which = c("sys_tox", "sys_tox_env"))

# Plot only the observed values:
plot_survival(model, which = c("survival_tox_observed", "survival_tox_env_observed"))
plot_stress(model, which = c("sys_tox_observed", "sys_tox_env_observed"))
```

Description

Calculate the survivals and stresses of an ECx-SyS model at arbitrary concentrations.

Usage

```r
predict_ecxsyst(model, concentration)
```

Arguments

- `model`: An ECx-SyS model as returned by `ecxsys`.
- `concentration`: A numeric vector of concentrations.

Value

A data frame (of class "ecxsys_predicted") with the following columns:

- `concentration`: The supplied concentrations.
- `survival_tox_LL5`: The survival predicted by the five-parameter log-logistic model derived from the observations under toxicant stress but without environmental stress.
- `survival_tox`: Modeled survival resulting from toxicant stress.
- `survival_tox_sys`: Modeled survival resulting from toxicant and system stress.
stress_tox  The toxicant stress.
sys_tox  System stress under toxicant stress conditions without environmental stress.
stress_tox_sys  The sum of stress_tox and sys_tox.
survival_tox_env_LL5  The survival predicted by the five-parameter log-logistic model derived from the observations under toxicant stress with environmental stress.
survival_tox_env  Modeled survival resulting from toxicant and environmental stress.
survival_tox_env_sys  Modeled survival resulting from toxicant, environmental and system stress.
stress_env  Environmental stress.
stress_tox_env  The sum of toxicant and environmental stress.
sys_tox_env  System stress under toxicant and environmental stress conditions.
stress_tox_env_sys  The sum of stress_tox_env and sys_tox_env.

Examples

model <- ecxsys(
  concentration = c(0, 0.05, 0.5, 5, 30),
  hormesis_concentration = 0.5,
  survival_tox_observed = c(90, 81, 92, 28, 0),
  survival_tox_env_observed = c(29, 27, 33, 5, 0)
)
p <- predict_ecxsys(model, c(0.001, 0.01, 0.1, 1, 10))

---

**Stressconversion**  *Convert Between Stress and Survival*

**Description**

Functions to convert survival to general stress or vice versa using the beta distribution.

**Usage**

```
survival_to_stress(survival, p = 3.2, q = 3.2)
stress_to_survival(stress, p = 3.2, q = 3.2)
```

**Arguments**

- `survival`: One or more survival values to convert to general stress. Should be a value between 0 and 1. Smaller or bigger values are treated as 0 or 1 respectively.
- `p, q`: The shape parameters of the beta distribution. Default is 3.2.
- `stress`: One or more stress values to convert to survival.
Details

These are simple wrappers around the beta distribution function pbeta and the beta quantile function qbeta.

Value

stress_to_survival returns a vector the same length as stress giving the survival caused by each amount of stress.

survival_to_stress returns a vector the same length as survival containing the stress values associated with each survival.

Examples

stress <- 0.3
survival <- stress_to_survival(stress)
survival_to_stress(survival)
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