

modeling and statistical tools for ecotoxicology

## http://mosaic.univ-lyon1.fr





















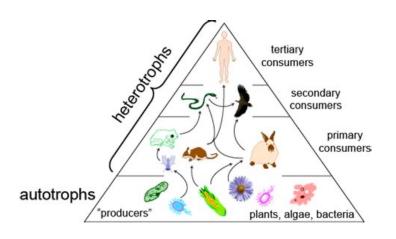


## **Environmental risk assesment**

## An evidence





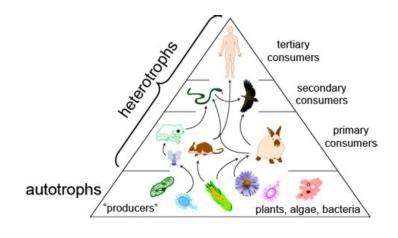


## **Environmental risk assesment**

## An evidence







## A priority







## **Environmental risk assessment**







One substance =



One registration

## **Environmental risk assessment**







One substance =

One registration







0.21 0.62 0.17 0.59 0.56 0.33 0.77 0.84 0.91 0.93 0.65 0.31 0.32 0.46 0.13 0.67 0.08 0.21 0.24 0.79 0.39 0.55 0.50 0.07 0.90 0.06 0.37 0.18 0.31 0.86 0.59 0.88 0.22 0.55 0.69 0.90 0.55 0.74 0.19 0.03 0.84 0.43 0.52 0.98 0.80 0.46 0.99 0.84 0.80 0.36 0.37 0.27 0.70 0.80 0.67 0.61 0.52 0.98 0.17 0.27 0.70 0.80 0.67 0.61 0.52 0.98 0.47 0.52 0.66 0.25 0.24 0.28 0.98 0.17 0.78 0.31





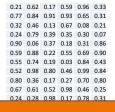


## **Environmental risk assessment**



Collect Analyze Evaluate Decide







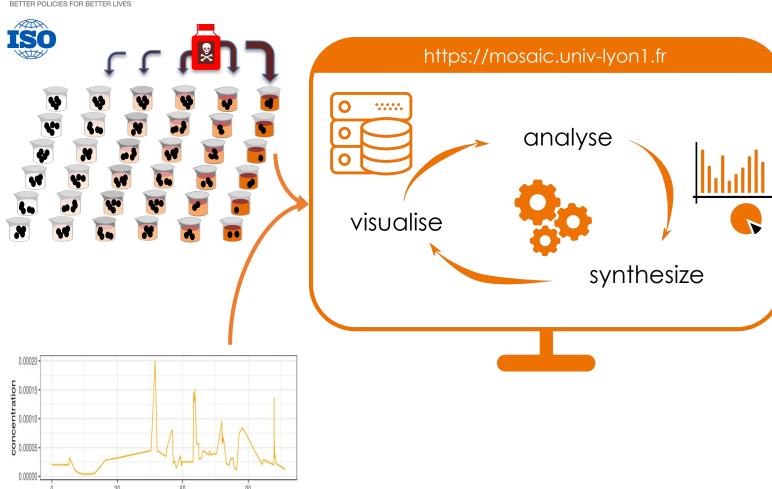




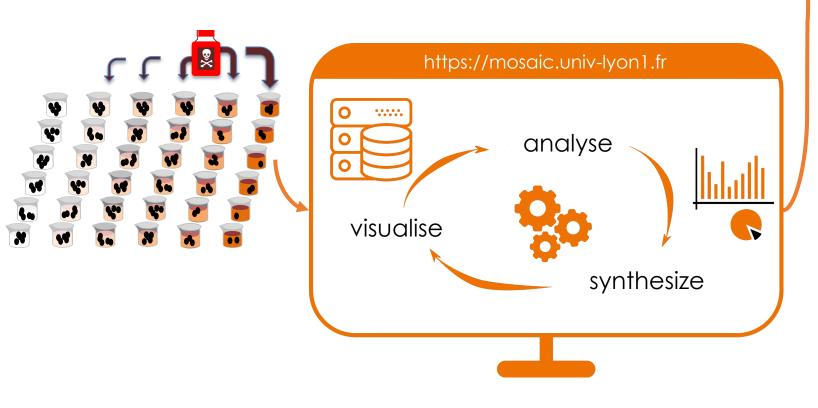


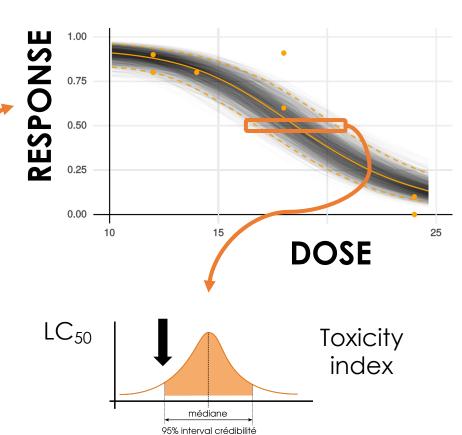


time

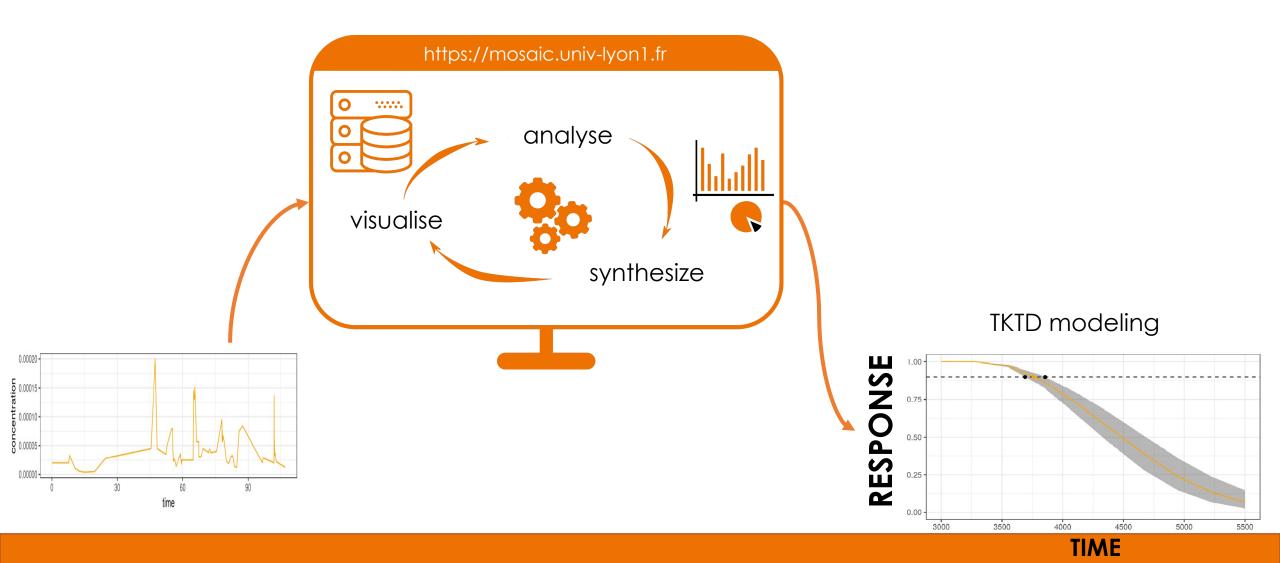








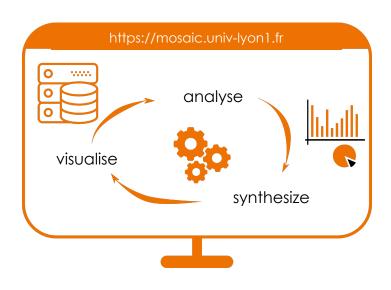






Transparency and reproducibility

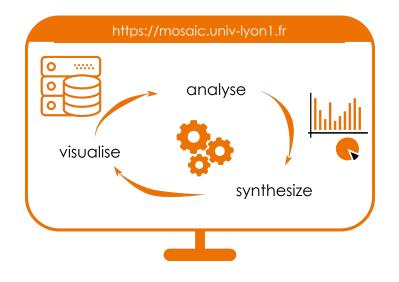






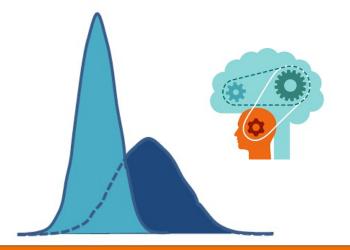
Transparency and reproducibility





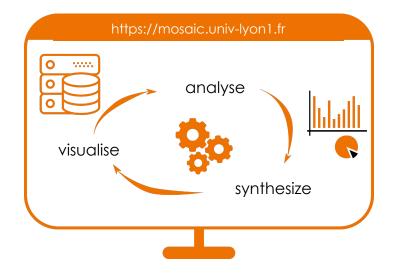
■Bayesian statistics









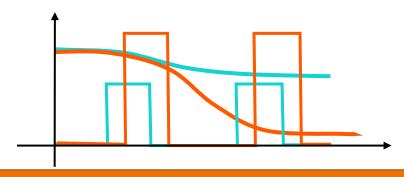


- Mechanistic modeling approach
- Bayesian statistics



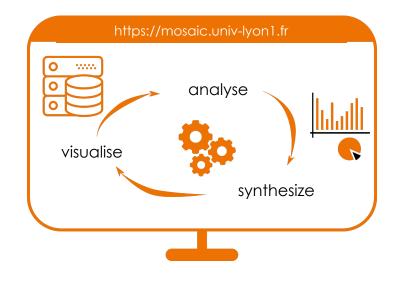


Predict to better prevent











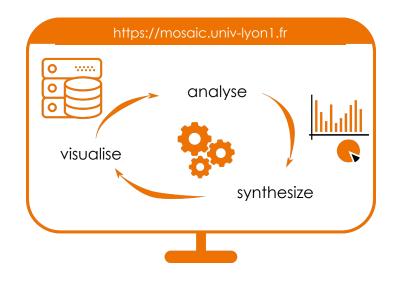
**243**Adopted: 29 July 2016

### **OECD GUIDELINE FOR THE TESTING OF CHEMICALS**

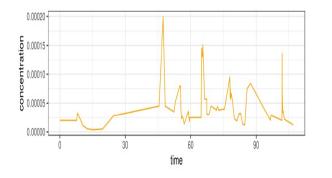
### Lymnaea stagnalis Reproduction Test

52. EC<sub>x</sub> values, including their associated lower and upper credible/confidence limits, are estimated using any appropriate statistical method based on a regression analysis of the number of clutches (or eggs) per individual-day. Even if any statistical software can be used for regression analysis (3), the user-friendly web-platform MOSAIC\_repro, freely available at <a href="http://pbil.univ-lyon1.fr/software/mosaic/reproduction/">http://pbil.univ-lyon1.fr/software/mosaic/reproduction/</a>, is recommended because the procedures implemented within this software were developed during the validation process of the *L. stagnalis* Reproduction Test (see details in ANNEX 7).

 $EC_{r}$ 







→ TKTD modeling

# MOSAIC

**MOSAIC** is a turnkey decision-making tool for ecotoxicologists, regulators and industrials.

Without the need to immerse into extensive mathematical and statistical technicalities, users are given advanced and **innovative methods** for a valuable quantitative environmental risk assessment.





## MOSAIC

- Free usage
- User-friendly interface
- Data privacy
- Reproducible results
- Open methods







## Usage statistics (overview) —

Showing 3351 entries

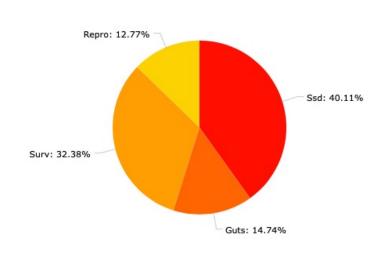
Unique users

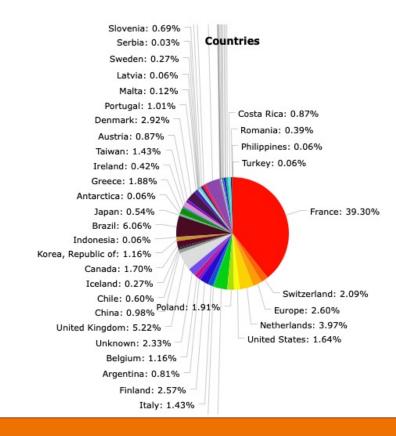
553

**New users** 

553









### Usage statistics (last month) —

Showing 271 entries

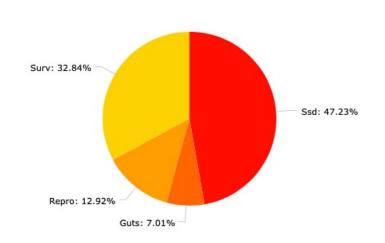
**Unique users** 

**78** 

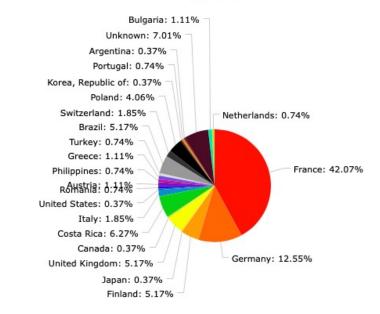
**New users** 

78

#### Modules

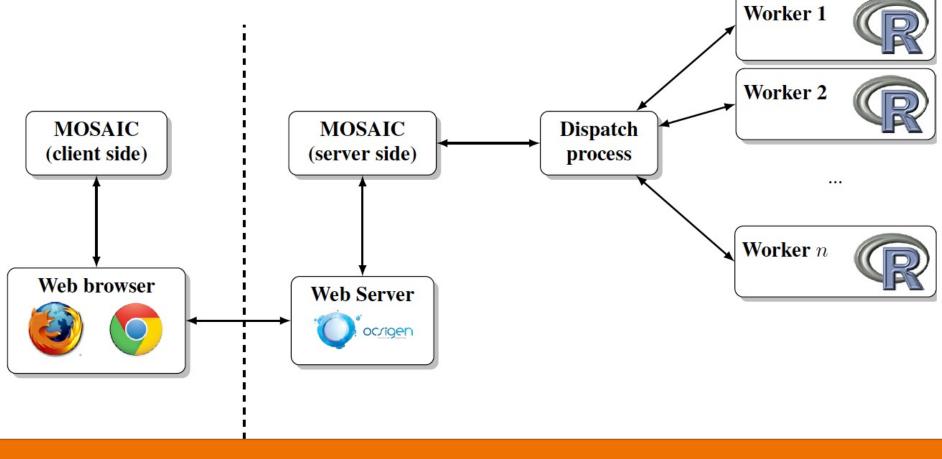


#### Countries



# MOSAIC

### The dark side —









# **Two modules**for survival

## MOSAIC SURV

Classical dose-response analysis of bioassay survival data, with descriptive summaries of the data and x% lethal concentrations (LCx) estimates under a Bayesian framework.

## MOSAIC GUTS

Toxicokinetic-toxicodynamic (TKTD) analysis of survival data, fitted with a General Unified Threshold model of Survival (GUTS) model to estimate threshold concentrations and x% lethal concentrations (LCx) under a Bayesian framework.



## MOSAIC repro

Classical dose-response analysis of bioassay reproduction data, in addition with descriptive summaries of the data and estimates of x% effective concentrations (ECx) under a Bayesian framework.

# **Two modules**for reproduction and SSD

## MOSAIC

**Species Sensitivity Distribution** fitted to estimate **hazardous concentration for p%** (HCp) of the species.

Parameters of the probability distribution are estimated from toxicity thresholds under a **frequentist framework**.

# MOS/IC<sub>REPRO</sub>



### OECD/OCDE

243

Adopted: 29 July 2016

### **OECD GUIDELINE FOR THE TESTING OF CHEMICALS**

 $EC_x$ 

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#### SCIENTIFIC OPINION



ADOPTED: 27 June 2018

doi: 10.2903/j.efsa.2018.5377



### Scientific Opinion on the state of the art of Toxicokinetic/Toxicodynamic (TKTD) effect models for regulatory risk assessment of pesticides for aquatic organisms

EFSA Panel on Plant Protection Products and their Residues (PPR),
Colin Ockleford, Paulien Adriaanse, Philippe Berny, Theodorus Brock, Sabine Duquesne,
Sandro Grilli, Antonio F Hernandez-Jerez, Susanne Hougaard Bennekou, Michael Klein,
Thomas Kuhl, Ryszard Laskowski, Kyriaki Machera, Olavi Pelkonen, Silvia Pieper,
Robert H Smith, Michael Stemmer, Ingvar Sundh, Aaldrik Tiktak, Christopher J. Topping,
Gerrit Wolterink, Nina Cedergreen, Sandrine Charles, Andreas Focks, Melissa Reed,
Maria Arena, Alessio Ippolito, Harry Byers and Ivana Teodorovic

It is acknowledged that standard software suitable for general (non-expert) use is not yet at hand, although for GUTS there are some options available. MOSAIC (MOdeling and StAtistical tools for ecotoxicology) developed at the University of Lyon contains a GUTS tool (http://pbil.univ-lyon1.fr/sof tware/mosaic/guts) which can be used for calibration. Moreover, GUTS-ShinyApp (http://lbbe-shiny.univ-lyon1.fr/guts-shinyapp/) can be used to simulate predictions of survival for different exposure profiles with different TKTD parameter values for both GUTS-RED-SD and GUTS-RED-IT models.



# Two new modules — 2020

## MOSAIC growth

Classical dose-response analysis of bioassay data of **growth-type**, in addition with descriptive summaries of the data and estimates of **x% effective concentrations** (ECx) under a **Bayesian framework**.

## MOSAIC bioacc

Provides bioaccumulation factors (BCF/BMF/BAF) from the fitting of a toxicokinetic (TK) model on accumulation-depuration data under a **Bayesian framework**. Fulfils all requirements of regulators when examining applications for market authorization of active substances.

## MOSAIC

### How to cite MOSAIC?

- Ratier A, Lopes C, Multari G, et al (2020) Brief communication: new perspectives on the calculation of bioaccumulation factors for active substances in living organisms. *bioRxiv*. https://doi.org/10.1101/2020.07.07.185835
- Charles S, Wu D, Ducrot V (2021) How to account for the uncertainty from standard toxicity tests in species sensitivity distributions: an example in non-target plants. *PLOS ONE* 16:e0245071.
- Charles S, Veber P, Delignette-Muller ML. 2018. MOSAIC: a web-interface for statistical analyses in ecotoxicology. *Environ. Sci. Pollut. Res.* 25:11295–11302.
- Kon Kam King G, Veber P, Charles S, Delignette-Muller ML. 2014. MOSAIC\_SSD: a new web tool for species sensitivity distribution to include censored data by maximum likelihood. *Environ. Toxicol. Chem.* 33:2133–9.
- Baudrot V, Veber P, Gence G, Charles S. 2018. Fit GUTS reduced models online: from theory to practice. *Integr. Environ. Assess. Manag.* 14:625–630.







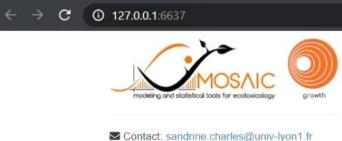
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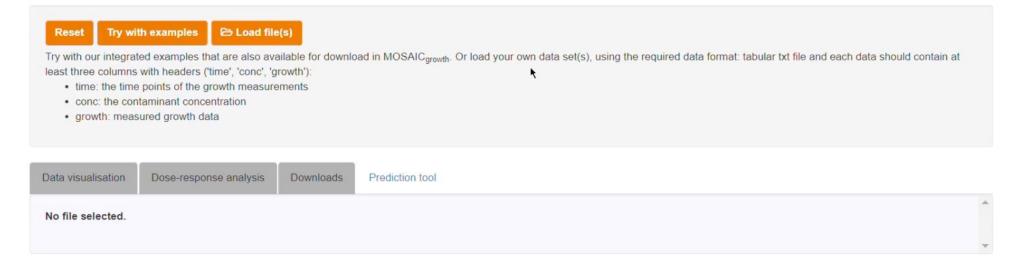


Growth

### MOSAIC growth

This tool provides a dose-response (DR) analysis of growth toxicity test data under a Bayesian framework, including an estimation of the x% effective toxicity value, that can be an x% effective rate  $(ER_x)$ , an x% effective concentration  $(EC_x)$  or any other expression of your choice. For clarity reasons, we will use in the application the abbreviation  $ER_x$ . Growth measurement might be any quantitative continuous variable describing the growth of organisms ( e.g., shoot length and dry weight for plants). This tool makes it possible to analyse one single or multiple data sets and to get various outputs, such as a summary table of  $ER_x$  estimates. MOSAIC growth does not expect any input besides growth data sets. All calculations are based on JAGS software and a companion R-package rjags. More details about the underlying modelling and guidelines for the application can be found in the vignette and tutorial.

Alpha version (updated on 18/09/2020)



## https://mosaic.univ-lyon1.fr/growth

#### References

[1] Manar, R., Bessi, H., Vasseur, P. 2009. Reproductive effects and bioaccumulation of chlordane in Daphnia magna. Environnemental Toxicology and Chemistry 28:2150–2159. https://doi.org/10.1897/08-564.1.

[2] Billoir, E., Delignette-Muller, M.L., Péry, A.R.R., Charles, S. 2008. A Bayesian Approach to Analyzing Ecotoxicological Data. Environnemental Science and Technology 42:8978-84. https://doi.org/10.1021/es801418x.

[3] Ducrot, V., et al., 2014. Development and validation of an OECD reproductive toxicity test guideline with the pond snail Lymnaea stagnalis (Mollusca, Gastropoda). Regulatory Toxicology and Pharmacology 70:605–614.







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Alpha version (updated on 18/09/2020)

Try with our integrated examples that are also available for download in MOSAIC<sub>growth</sub>. Or load your own data set(s), using the required data format: tabular txt file and each data should contain at least three columns with headers ('time', 'conc', 'growth'):

- · time: the time points of the growth measurements
- conc: the contaminant concentration
- · growth: measured growth data

Data visualisation Dose-response analysis Downloads Prediction tool

No file selected.

#### References

- [1] Manar, R., Bessi, H., Vasseur, P. 2009. Reproductive effects and bioaccumulation of chlordane in Daphnia magna. Environnemental Toxicology and Chemistry 28:2150-2159. https://doi.org/10.1897/08-564.1.
- [2] Billoir, E., Delignette-Muller, M.L., Péry, A.R.R., Charles, S. 2008. A Bayesian Approach to Analyzing Ecotoxicological Data. Environnemental Science and Technology 42:8978-84. https://doi.org/10.1021/es801418x.
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