Exploring GUTS in the environmental risk assessment of pesticides

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Background

Pesticide regulations are based on environmental risk assessment (ERA) that incorporates information on the fate and transport (exposure) and ecotoxicological effects of a chemical on exposed organisms. At Tier 1, effects data are based on standardized laboratory which do not take into account the time-variable exposure profile of the chemicals.

Toxicokinetic-toxicodynamic (TKTD) models have been developed to improve the ERA of chemicals by describing the effects of chemical substances on organisms over time. Recently, the **General Unified Threshold model for Survival** (**GUTS**) has been judged to be "ready to be used in risk assessment" by EFSA[1]. However, despite the advantage of TKTD modelling, this approach is still underutilized within the context of environmental risk assessment.

Aims

- Firstly, we used a <u>case study with cypermethrin</u> to investigate whether literature data might be used to address the requirements of the EFSA guidelines for GUTS in pesticide regulations with an aim to potentially avoid some of the costly validation work that is currently required and makes GUTS "uncompetitive" against other Tier 2 refinement options.

- Secondly, given the potential for GUTS to model a whole range of exposure profiles, we <u>explored how ACRE could be combined with GUTS</u> to make an *efficient risk characterisation of exposure and risk*.

Methods

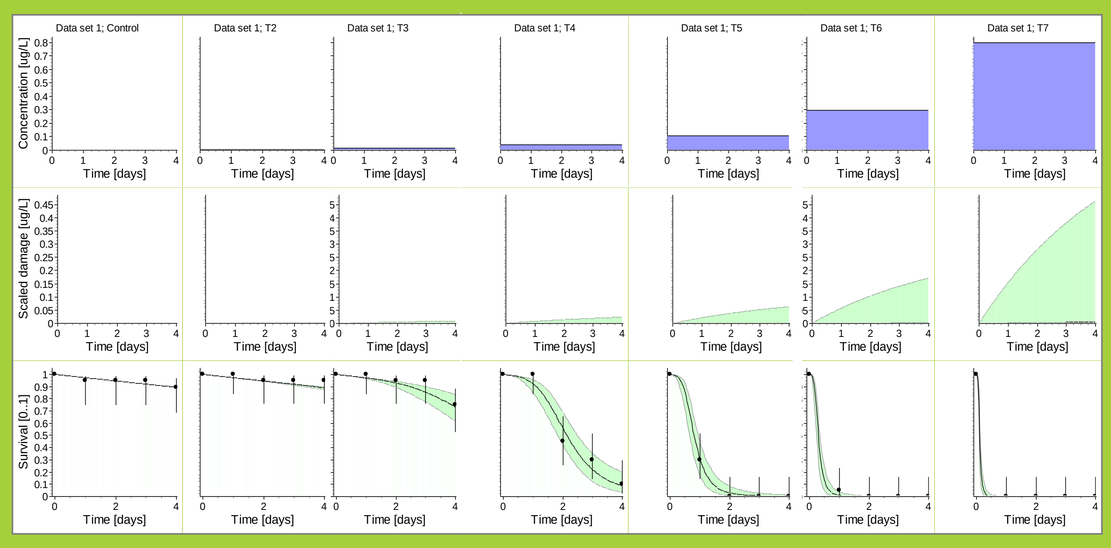
Cypermethrin was selected as case study. Raw survival data from *Gammarus pulex* from a number of constant- and pulsed-exposure experiments[2] were used to calibrate and validate GUTS parameters using the user-friendly software OpenGUTS (https://openguts.info).

Finally, cypermethrin concentration-time exposures calculated with ACRE for their representatives uses and using endpoints from the EFSA conclusion document[3] were used as input data for GUTS model prediction to estimate the LP_{50} (the factor by which an entire exposure profile needs to be multiplied to yield 50% mortality by the end of the profile). Whilst some criteria of the evaluation may meet current requirements (e.g. data quality, use of appropriate exposure profiles), others do not (e.g. model performance in validation).

GUTS in the risk assessment of pesticides

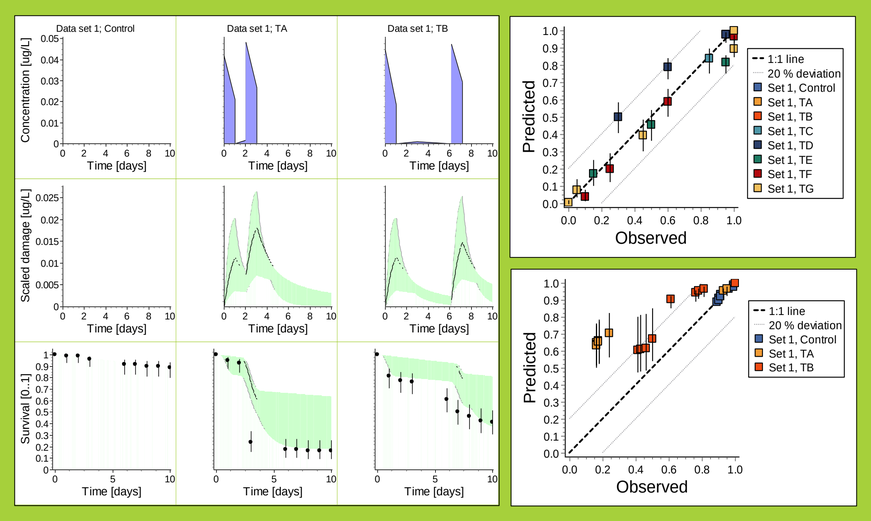
1) MODEL CALIBRATION

constant-exposure toxicity test, 5 time points



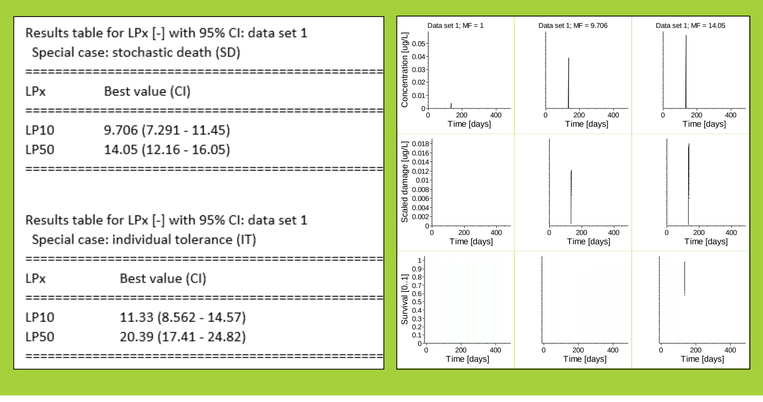
2) MODEL VALIDATION

two pulses toxicity tests, 7 time points and 3 concentrations



3) MODEL PREDICTIONS:

use the calibrated model for survival predictions on the entered exposure profile to produce LP_{50} values that can be used in the risk assessment.



Automated extraction of exposure profile data

ACRE is a fully automated process developed by Enviresearch that allows the running of FOCUS surface water models for all Step 3 scenarios and Step 4 mitigation measures by a single click of a button. ACRE works with the same SWASH files and models as the standard risk assessment tools, but is **more efficient**, **less error prone**, much **faster** and with the potential to perform refinements that previously were simply too time/resource intensive to consider.

These benefits can be exploited further by using ACRE modelling outputs as GUTS modelling inputs in the Step 3 and Step 4 Model Predictions.

ACRE tool coupled by a custom-written R code allow the quick and easy extraction of concentrations in surface water listed in the *.out* file created by TOXSWA. As result, a large number of data sets with exposure profile for all application usage patterns are efficiently created and can be entered in GUTS.

CONCLUSION

- GUTS has the potential to be an efficient approach to refine the aquatic risk assessment of pesticide. However, the exposure experiments to generate calibration and validation data need to be carefully designed to comply with EFSA guidelines.

- The use of data from published literature is potentially an option, but practically they rarely provide quality data.

- ACRE tool developed by Enviresearch is a quick and efficient way of getting multiple FOCUS exposure profile data without repetitious manual data entry and minimising the risks of errors.

Reference:
[1] EFSA PPR, et al. "Scientific Opinion on the state of the art of Toxicokinetic/Toxicodynamic (TKTD) effect models for regulatory risk assessment of pesticides for aquatic organisms." EFSA Journal 16.8 (2018): e05377.
[2] Ashauer, R. et al. (2016). Modelling survival: exposure pattern, species sensitivity and uncertainty. Scientific Reports, 6(1), pp.1-11.
[3] EFSA (2018). Peer review of the pesticide risk assessment of the active substance cypermethrin.

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