GLOBAL SENSITIVITY ANALYSIS OF THE LEMNA MODEL BY SCHMITT ET AL. (2013) USING R

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The R script will be made available on request Contact: judith.klein@ime.fraunhofer.de

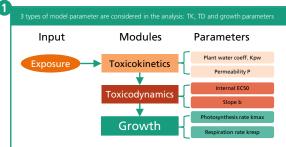


Introduction

- Lemna model by Schmitt et al. 2013 is considered ready for use in the risk assessment of plant protection products in EFSA SO TKTD 2018 but a more generic sensitivity analysis was requested
- General behavior of the model parameters is investigated by conducting a <u>global sensitivity analysis</u>

Materials & Methods

- Analysis is restricted to the simulation of <u>laboratory growth</u> tests (Tier 2C approach in EU risk assessment scheme)
- Different exposure patterns within the standard test duration of 7 days are covered:
 - a. constant exposure
 - b. two pulse exposure and
 - c. one pulse exposure
- As relevant endpoint the inhibition of growth rate over 7 days is used
- Analysis is done in R and compatible with the original published model R code



One-at-a time (OAT) analysis for all parameters and exposure scenarios is conducted

Procedure: Sensitivity Analysis

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For each exposure scenario		
ſ	For each parameter	
	Γ	For each simulation
		Set parameter value
		Run model (orig. R script)
		Save result (effect on growth rate)
ſ	Plo	ot results

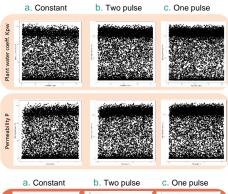
Results & Discussions

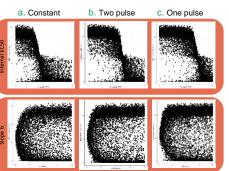
<u>Contribution to variance</u> with respect to the considered growth, TK and TD parameters in sensitivity analysis

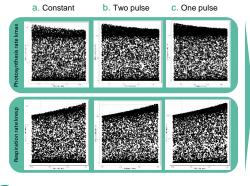


 Based on linear correlation of inhibition of growth rate (but: nonlinear model)
Parameter EC50int contributes mostly to variance on the inhibition of growth rate

Scatter plots: Parameter values are plotted with respect to the effect on growth rate after 7 days in % for all three exposure scenarios: constant exposure (a), 2 peak exposure (b), 1 peak exposure (c)

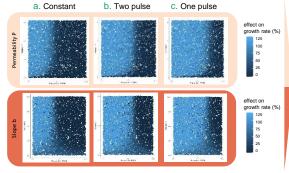






Difference within the exposure scenarios for growth parameters is small

<u>Scatter plots</u>: Parameter EC50int is plotted versus the model parameter with respect to the effect on growth rate after 7 days in % for all three exposure scenarios: constant exposure (a), 2 peak exposure (b), 1 peak exposure (c)



 For high permeability values, effect on growth rate is not sensitive for changes in P
For small values of P, effect on growth rate is sensitive to changes in P
Parameter b

Parameter b has an effect, however not a directed effect

Conclusions

 A sigmoid pattern for the TD parameter EC50int is observed

At first sight, effect

on growth rate is

not sensitive to a

change in TK

parameters

- Parameter b has an effect, however not a directed effect: it depends on the values of the other parameters whether an increase of b increases or decreases effect on growth rate
- The by far most sensitive parameter in the global sensitivity analysis over a broad parameter space is EC50int which explained about 95 % of the variability of the inhibition of the growth rate in all three exposure scenarios
- Scatter plots show that permeability P and slope b also need to be considered
- The value of EC50int, P and b are obtained by calibrating the model to experimental data

References

EFSA PPR Panel, 2014. Scientific Opinion on good modelling practice in the context of mechanistic effect models for risk assessment of plant protection products. EFSA Journal 2014; 12(3):3589, 92 pp. doi:10.2003/j.efsa.2014.3589

EFSA PPR Panel, 2018. 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 2018; 16(8):5377, 188 pp. doi:10.2903/jefsa.2018.5377 Schmitt WH, Bruns E, Dollinger M and Sowig P, 2013. Mechanistic TK/TD-model simulating the effect of growth inhibitors on Lemna populations Ecological Modelling, 255, 1–10.