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Why a *Lemna* TKTD model can also be applied to sediment rooted macrophytes

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Introduction

- The EFSA PPR panel (2018) has evaluated TKTD models for primary producers
- *Lemna* model of Schmitt et al. (2013) is considered as ready to use in risk assessment while a more complex model for *Myriophyllum spicatum* was found to need further refinements and testing
- We propose that the basic principles of the *Lemna* TKTD growth model can also be used to model growth inhibition tests with sediment rooted macrophytes

The underlying idea

- EFSA PPR panel (2018) guidance for the use of TKTD models is given for Tier 2C conditions, i.e., variable exposure under laboratory conditions.
- In this setting, constant growth conditions can be assumed, and the tests are designed to allow for exponential growth.
- Where the same basic principles (here: exponential growth) apply, one model may be used to describe them, despite different morphology and physiology. This is analogous to the reduced GUTS model (Jager & Ashauer 2018) used for modelling lethal effects on invertebrates and vertebrates.
- Consequently, the same growth model as for *Lemna* can also be applied for other macrophytes under Tier 2C.
- This results in a simple TKTD model that can be generically applied to all macrophyte species under Tier 2C conditions.
- Refinements may be required where this simple approach does not describe the data. This may, e.g., be the case if considerable uptake occurs from both the water and the sediment compartment.

The model

- is similar to the Tier 2C version of the *Lemna* model of Schmitt et al. (2013) but restricted to growth under laboratory test conditions (Tier 2C tool)
- is kept as simple as possible to allow calibration based on growth inhibition tests
- combines a one-compartment toxicokinetic (TK) model and relates growth inhibition to internal (scaled) concentration

Toxicokinetics (TK) describes uptake, elimination, distribution and metabolisation

Toxicodynamics (TD) describes the effects of growth inhibiting substances

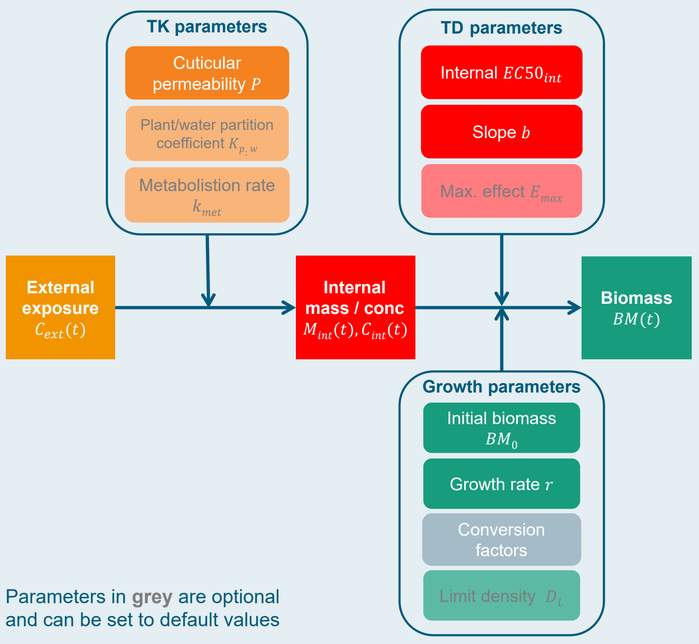
Growth is considered as exponential or logistic increase of biomass in time

Conversion parameters are species specific parameters

Summary

- The resulting generic model is analogous to the reduced GUTS model (Jager & Ashauer 2018) regarding the description of basic principles applicable to organisms of different morphology and physiology, in this case, exponentially growing macrophytes in the laboratory
- Parameterisation can be done by calibration to based on growth inhibition tests and the model can be validated by additional laboratory tests
- For an exemplary use of the model, see poster 8658 by Hommen et al.

Conceptual diagram



Parameters in **grey** are optional and can be set to default values

Equation system

TK

$$\frac{d}{dt}M_{int}(t) = \boldsymbol{P} \cdot A(t) \cdot \left(C_{ext}(t) - C_{int}(t)\right)$$

$$A(t) = \boldsymbol{A_{perBM}} \cdot BM(t)$$

TD

$$\hat{f}_{C_{int}}(C_{int}) = 1 - \frac{C_{int}^{\boldsymbol{b}}}{\boldsymbol{EC50_{int}^{b}} + C_{int}^{\boldsymbol{b}}}$$

$$M_{int}(t) = C_{int}(t) \cdot (BM(t) \cdot \boldsymbol{k_{fw}})$$

Growth

$$\frac{d}{dt}BM(t) = \boldsymbol{r_{control}} \cdot f_{C_{int}}(t) \cdot BM(t)$$

How to parametrise the model?

- TKTD parameters are substance and species specific and are fitted based on growth inhibition tests
- Permeability P of the cuticle determines the speed of uptake and elimination
- Plant-water partitioning coefficient Kpw introduced by Schmitt et al. (2013) to calculate the internal unbound concentration. Only relevant for substances with high K_{ow} or when internal concentrations are measured and thus, fixed to 1 by default
- Metabolisation rate k_{met} can be ignored (k_{met} = 0) as a worst case assumption
- $EC50_{int}$ represents internal concentration yielding 50% effect
- Slope parameter b defines the slope of the internal concentration-response function (Hill coefficient)
- Maximum effect $E_{\max}$ reduces the maximum possible effect but should be set to 1 by default
- Thus, in its simplest version, the model needs 3 TKTD parameters (*P, EC50int, b*) to be calibrated
- Control growth rate r and initial biomass BM_0 are study specific parameters and can be taken from a given test or set to typical values
- OECD 239 assumes exponential growth for the calculation of effects. Thus, usually, exponential growth over the test duration is assumed for the control plants ($r_{control}$)
- For longer time periods logistic growth can be used (additional parameter D_L, derived from control data)
- In addition, some species specific factors for conversion between fresh and dry weight, volume and surface area are needed
- The model does not consider effects on morphology of the plants
- Conversion factors do not affect the goodness of fit, but affect the calibrated parameter values
- These species specific parameters can be taken from measurements in growth inhibition tests or can be estimated based on literature data

Model parameters of the generic TKTD model for macrophytes

Parameter	Domain	Unit	Description
Growth			
$\boldsymbol{r_{control}}$	$\mathbb{R}_+ \setminus \{0\}$	d^{-1}	Growth rate of control, can be taken from control data
D_L	$\mathbb{R}_+ \setminus \{0\}$	g	Limit density (only if logistic growth of control)
Toxicokinetics			
$\boldsymbol{P}$	$\mathbb{R}_+ \setminus \{0\}$	$cm\ d^{-1}$	Permeability of cuticle, corresponds to dominant rate constant
Toxicodynamics			
E_{max}	$[0,1]$	-	Maximum effect (default setting is fixed to one)
$\boldsymbol{EC50_{int}}$	$\mathbb{R}_+$	µg/L	Scaled internal concentration leading to 50% effect
$\boldsymbol{b}$	$\mathbb{R}_+$	-	Shape parameter of reverse concentration response curve
General (conversion factors – do not affect model outcome)			
$\boldsymbol{d_{fw}}$	$\mathbb{R}_+ \setminus \{0\}$	g/cm³	Plant density (with respect to fresh weight) (set to 1 g/mL)
$\boldsymbol{k_{fw}}$	$\mathbb{R}_+ \setminus \{0\}$	g fw / g dw	Conversion factor dry weight to fresh weight (e.g. from control data)
$\boldsymbol{A_{perBM}}$	$\mathbb{R}_+ \setminus \{0\}$	cm²/g	Plant surface area per dry biomass
$\boldsymbol{k_{dw}}$	$\mathbb{R}_+ \setminus \{0\}$	g/cm	Conversion factor shoot length to dry weight

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