GUTS explains dynamic mortality patterns for marine copepods exposed to dimethylnaphthalene

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Scope

Efficiently assessing pollution in the marine environment requires mechanistic models. The General Unified Threshold model for Survival (GUTS) provides a framework for deriving toxicokinetic-toxicodynamic (TKTD) models for the endpoint survival (Jager *et al* 2011). Two recurring questions in the application of GUTS are:

- What is the most appropriate death mechanism?
- Is the total body residue a proper dose metric for toxic effects?

We address these questions in a study for dimethylnaphthalene in the marine copepod *Calanus finmarchicus*. This species builds up a large lipid storage as a discrete sac in the body (Fig. 1).

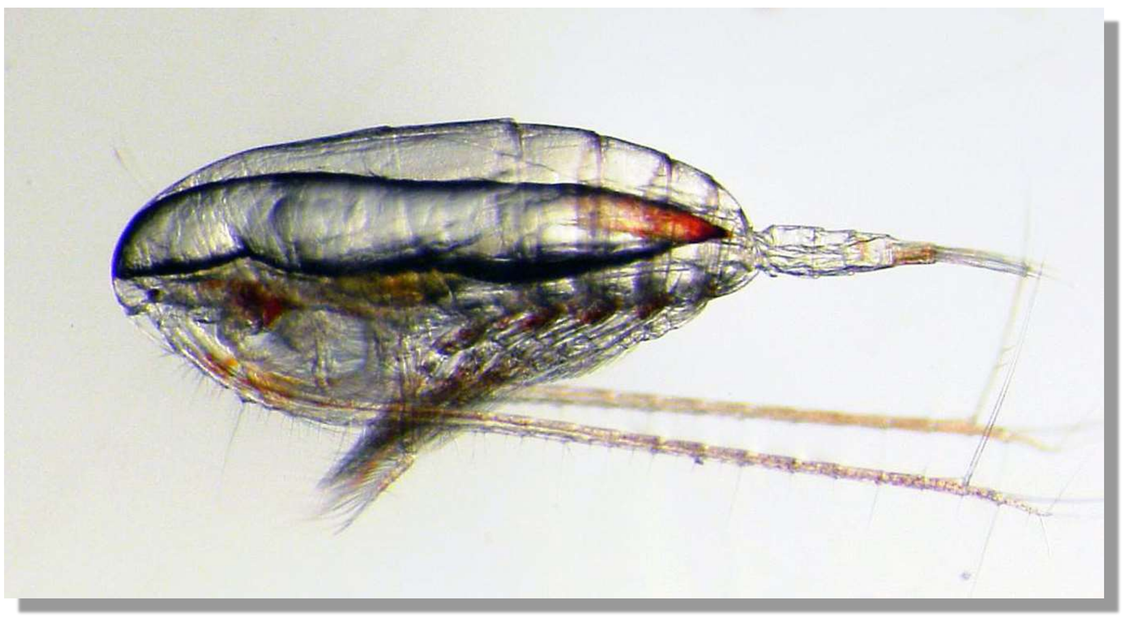

Fig. 1. Calanus finmarchicus, CV with clearly visible oil sac.

Models

Survival data: GUTS includes a TK and a TD module (Fig. 2). GUTS was fitted to the survival data by applying a scaled TK model, yielding a single rate constant. For narcotic compounds, this rate constant should represent elimination from the target tissue.

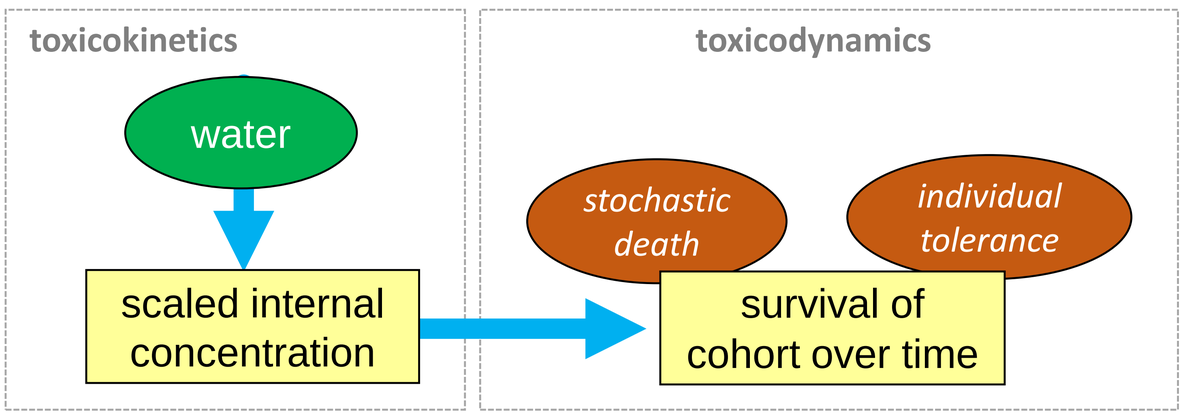

Fig. 2. Schematic representation of GUTS.

Body-residue data: We apply the standard 1-compartment model and a 2-compartment model (Fig. 3), separating structural biomass from the lipid sac (Hansen *et al* 2016). These models yield elimination rate constants, that can be compared to the rate constant derived from the survival data.

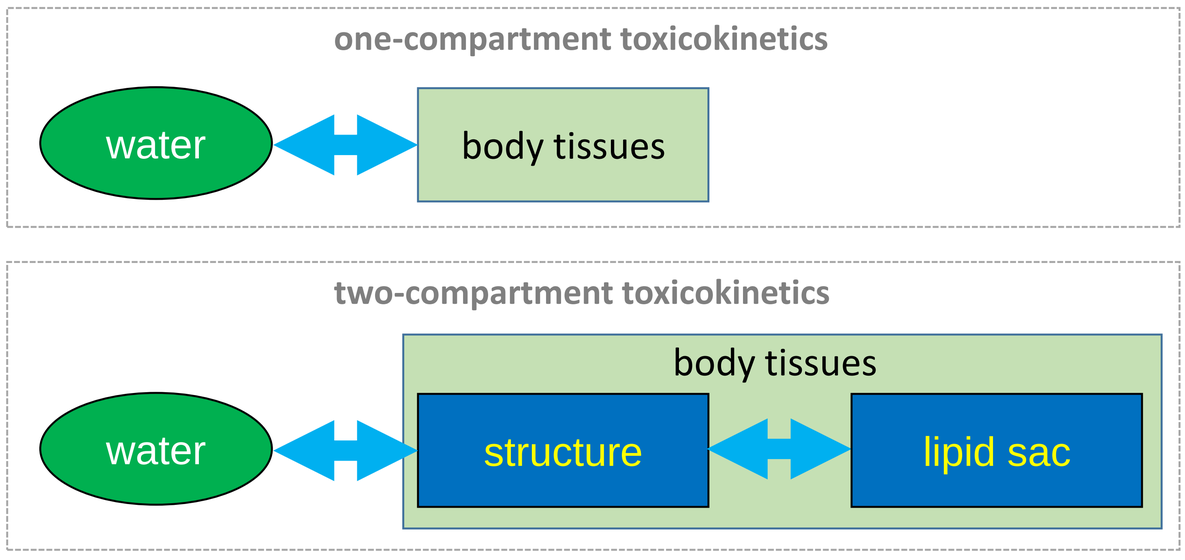

Fig. 3. Schematic representation of the 1- and 2-comp. TK models.

Conclusions

- Survival data themselves could not distinguish between SD and IT. However, the estimates for the elimination rates differ.
- Body residues were best explained by a two-compartment model. The lipid compartment is slow compared to structure.
- The elimination rate constant for structure is consistent with SD but not IT. This was confirmed by simultaneous fitting (not shown). This supports SD as the most representative death mechanism.

Model calibration

Survival data: In the simplest cases of GUTS, the death mechanism is either stochastic death (SD) or individual tolerance (IT). Both models provide a very good explanation for the data (Fig. 4), but they do so with a very different elimination rate constant (Fig. 5).

Body-residue data: For the 1-comp. model, the elimination rate constant is consistent with the IT view of the survival data (Fig. 5). However, this model provides a poor fit on the depuration phase. The 2-comp. model provides a much better fit to the data (Fig. 4). The elimination rate constant for structure (the likely target for narcotics) is consistent with SD view of the survival data (Fig. 5).

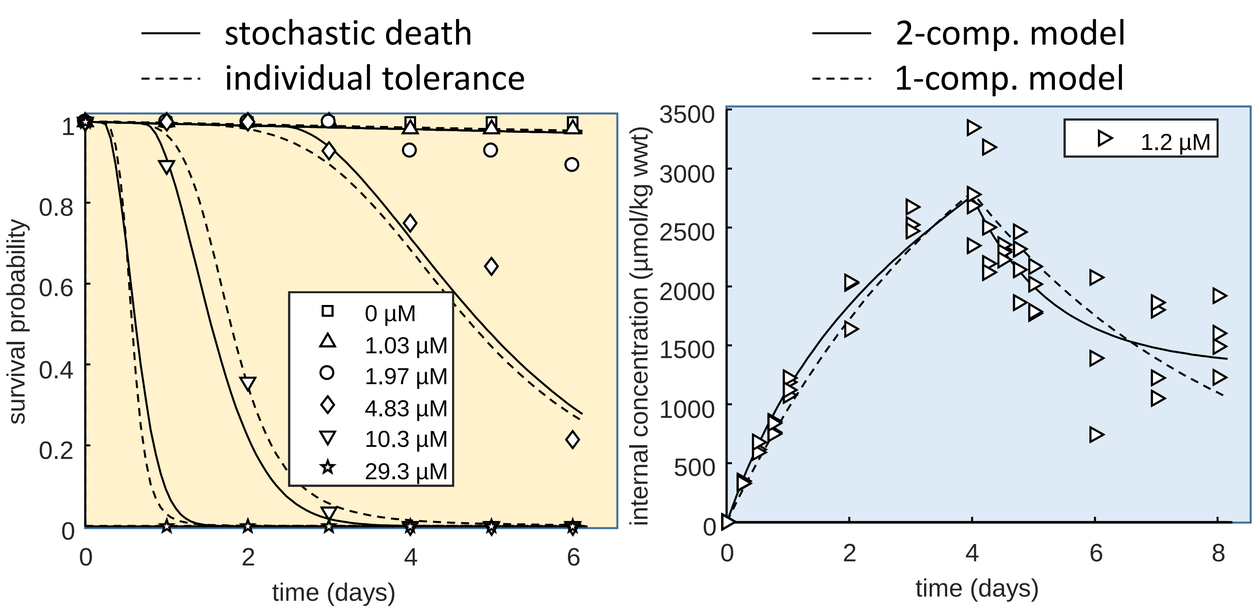

Fig. 4. Fits of GUTS to the survival data (left), and the two TK models to body-residue data (right).

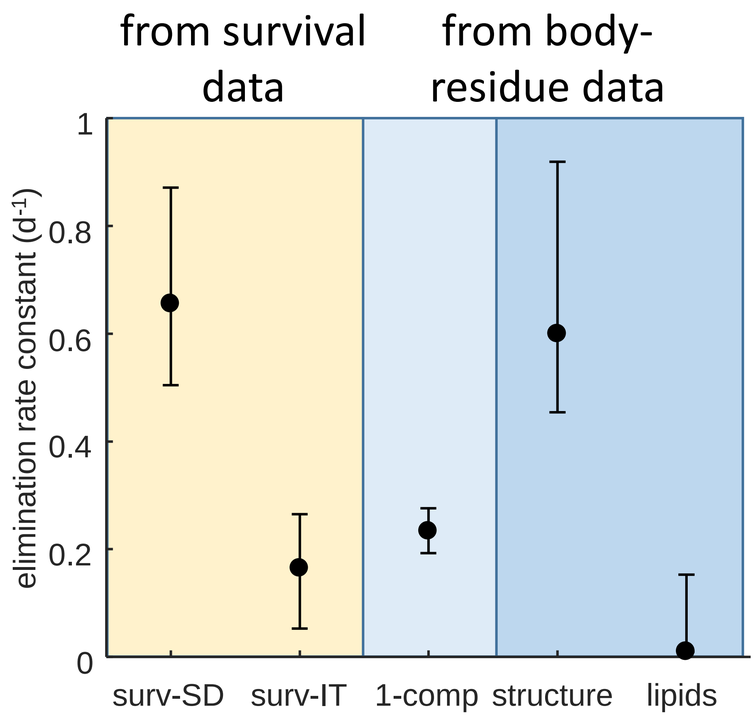

Fig. 5. Comparison of elimination rate constants from the different fits.

References

Hansen *et al* (2016). JTEH 79:549
Jager *et al* (2011). ES&T 45:2529

Acknowledgements

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