Reference model for sub-lethal effects of mixtures

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Introduction

Typical approaches for analyzing mixture toxicity are descriptive and do not yield insight into underlying mechanisms. E.g., they cannot explain why mixture interactions change in time and differ between endpoints. To understand mixtures, we need biology-based approaches [1]. This was already presented for survival [2]; here we continue with sub-lethal effects [3].

Theory

The scheme shows the causality chain from external stimulus to effect, and how it translates into a Dynamic Energy Budget (DEB) context. Each chemical has its own toxicokinetics and affects the same or different target sites. Targets are linked to subsystems; the physiological processes in DEB. These processes interact to produce effects on body size and reproduction in time.

Interactions

Interactions are inevitable in a DEB context. Metabolic processes interact in their effect on growth and reproduction, a.o., because body size affects reproduction and toxicokinetics. These physiological interactions already give deviations from classic CA and IA. The nature of the misfit to experimental data will provide mechanistic information on other interactions.



Simulations

As data for mixture effects in time are scarce, we illustrate our approach using simulations representing Daphnia magna. Two hypothetical compounds, with different toxicokinetics affect different processes (assimilation and maintenance).





Conclusions

We present a biology-based approach for sub-lethal mixture toxicity, which is far more useful than descriptive approaches.

The model acknowledges that body size and reproduction are tightly linked processes in time.

Interactions need to be explained by biological mechanisms, not statistical terms.

The DEB framework makes certain interactions inevitable.

References

[1] Jager, T, EHW Heugens, SALM Kooijman (2006). Ecotoxicology 15:305-314.

[2] Baas, J, BPP van Houte, CAM van Gestel, SALM Kooijman (2007). ETC 26:1320-1327.

[3] Jager, T, J Baas, SALM Kooijman (subm.).

More information

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