Modelling survival under chemical stress
A comprehensive guide to the GUTS framework

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The GUTS e-book

Making sense of toxic effects over time requires mechanistic models, and thus explicit consideration of toxicokinetics and toxicodynamics (TKTD). For the endpoint survival, all existing TKTD models can now be viewed as special cases of an overarching framework: GUTS, the General Unified Threshold model for Survival (Jager et al, 2011).

Since its inception in 2010, interest in GUTS has been rapidly increasing, creating a need for a detailed treatise. In a CEFIC-LRI funded project, we prepared an extensive e-book on GUTS. The book contains a detailed description of the model framework (concepts, assumptions, mathematics, historical roots), worked-out case studies, results of a ring test for software implementations, and much more.

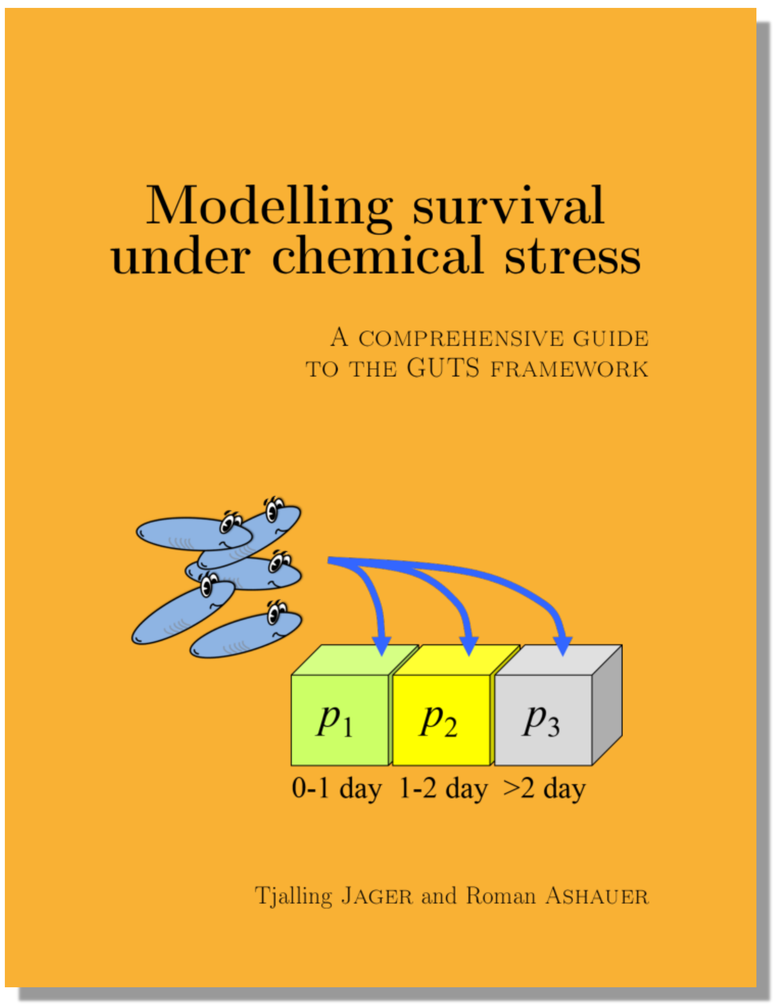


Fig. 1. The GUTS e-book can be downloaded (free of charge) from https://leanpub.com/guts_book (or use the QR code)

Structure of GUTS

The structure of GUTS is schematically shown in Figure 2. A toxicokinetics module translates external concentrations to internal ones. Internal concentrations lead to damage. Damage triggers the death mechanism, which combines two mechanisms: stochastic death and individual tolerance. In practice, special (reduced) cases of GUTS will be used; the simplest forms are able to deal with data from standard acute toxicity tests.

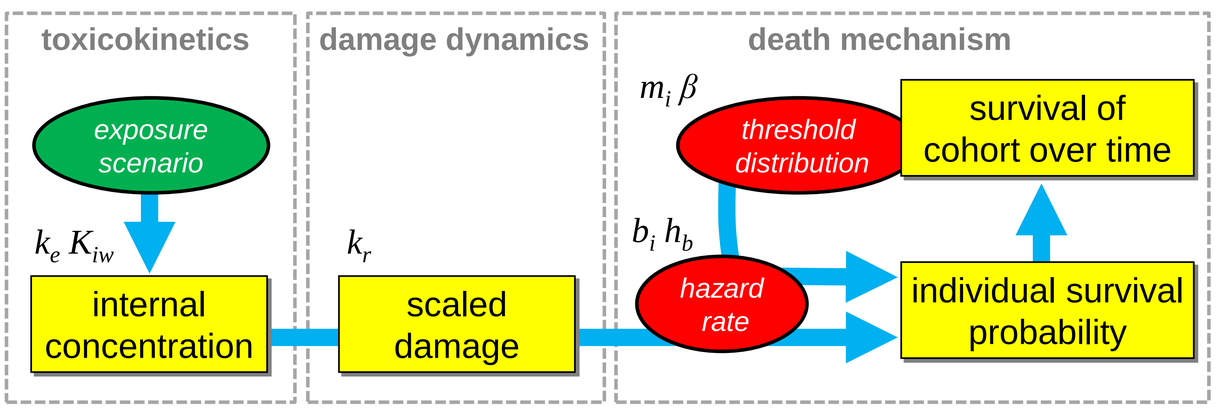


Fig. 2. Schematic representation of the complete GUTS framework. In practice, reduced models will be used.

Example fit and prediction

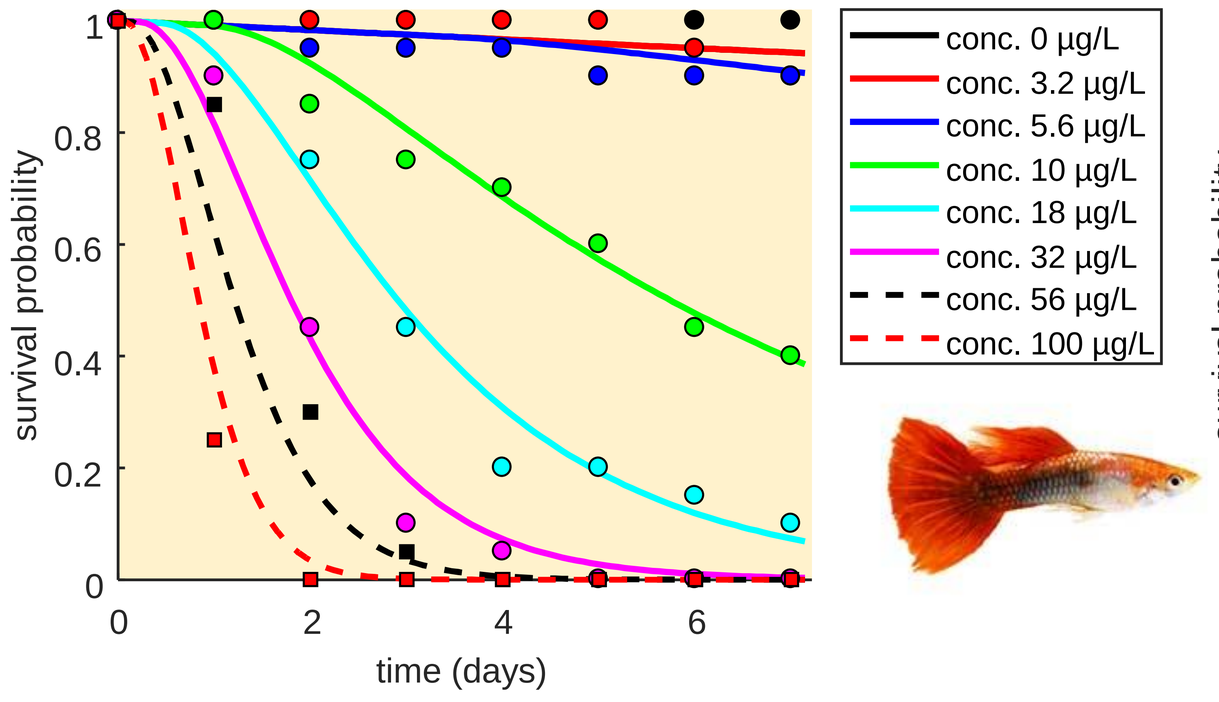
Figure 3 shows an example of a fit and a subsequent prediction for dieldrin in guppies, using a special case of GUTS: the reduced model with stochastic death. This case study is worked out in detail in the e-book.

Applications of GUTS

GUTS can be used for various purposes:

1. Analysis of toxicity data from standard and non-standard toxicity test. Model parameters can be used for robust estimation of LC*x*,*t* (for any effect level *x*, and any time point *t*) or a no-effect level.
2. Extrapolation to untested conditions. E.g., predicting survival for time-varying exposure such as the output of a fate model.
3. Building block in population models to deal with survival at the individual level.
4. Supporting extrapolation between chemicals and between species. Model parameters from mechanistic models are better suited for this purpose than descriptive LC50s.

Web support:
http://www.debtox.info/book_guts.html
https://www.ecotoxmodels.org/guts/
http://cefic-lri.org/projects/eco39-review-ring-test-and-guidance-for-tktd-modelling/



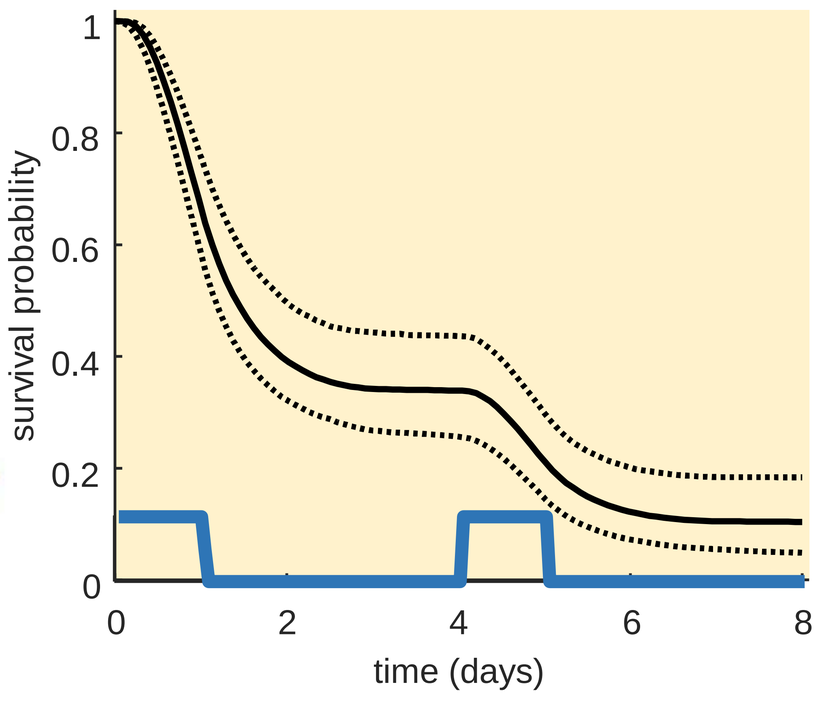


Fig. 3. Left panel: fit of the GUTS-RED-SD model to survival data for dieldrin in guppies. Right panel: prediction, based on the fit, for a pulse-exposure with two pulses of 50 µg/L (scenario in blue).

References

Jager T, Albert C, Preuss TG, Ashauer R (2011). General Unified Threshold model of Survival - a toxicokinetic-toxicodynamic framework for ecotoxicology. Environ Sci Technol 45:2529-2540.

Acknowledgements

The development of the GUTS e-book was financially supported by CEFIC-LRI, project ECO39.