Modelling Multiple Endpoints in Life-Cycle Toxicity Tests

Tjalling Jager[1], Trudie Crommentuijn[2], Kees van Gestel[3], Bas Kooijman[1]
[1] Theoretical Biology, Vrije Universiteit De Boelelaan 1085, NL-1081 HV, Amsterdam, The Netherlands,
email: tjalling@bio.vu.nl - http://www.bio.vu.nl/thb/
[2] Ministry of VROM, The Hague [3] Animal Ecology, Vrije Universiteit, Amsterdam

1. FROM STANDARD TESTS TO LIFE-CYCLE TESTING

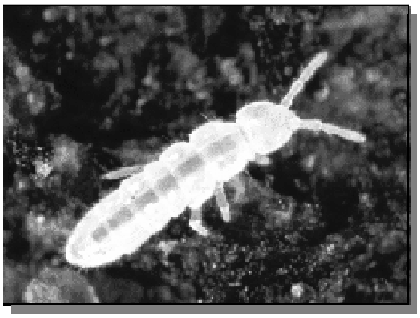
Standard toxicity testing evolved in the seventies from the need for summary statistics for chemical risk assessment. Although standardisation has been useful, unsatisfactory choices remain:

- NOEC is an extremely poor summary statistic.
- ECx is calculated from a purely empirical curve.
- A fixed and arbitrary exposure time is used.
- Tests focus on a single endpoint only.

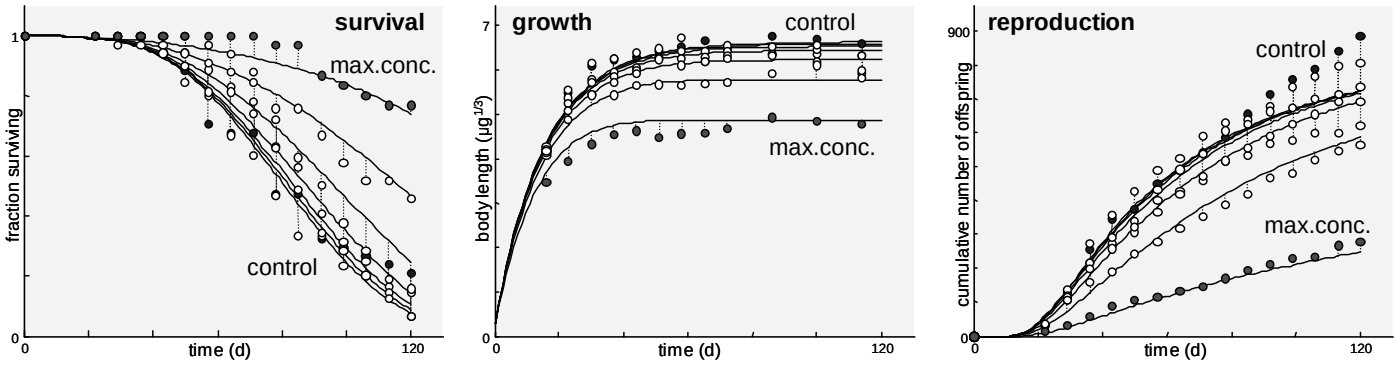
Life-cycle testing can overcome some of these problems, by following more endpoints over a longer exposure period. The disadvantage is that these tests are notoriously hard to analyse.

To describe life-cycle data, we use the DEBtox model, adapted to accommodate this form of testing. The changes include the simultaneous fit on all endpoints, and a module describing ageing of the animals.

The springtail Folsomia candida



Simultaneous fits for the effects of cadmium on F. candida



2. MODEL FITS FOR CADMIUM IN *F. CANDIDA*

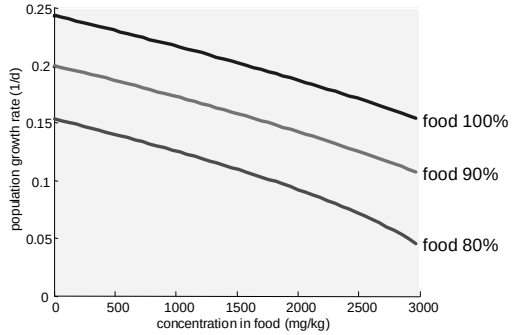
We demonstrate the extended model on a life-cycle test with the springtail *Folsomia candida*, exposed to cadmium in their food (Crommentuijn *et al.*, 1997, in: Van Straalen & Løkke). Parameter estimates are given in the table. The No-Effect Concentration (NEC) is the concentration producing no effects, even after long exposure.

The mode of action that best describes the data is that Cd decreases the energy assimilated from food, thereby decreasing growth and reproduction. Exposure to Cd in fact *increases* the lifespan, which is described by the ageing model. Both survival and reproduction follow the same ageing mechanism.

Parameter estimates from the model fits, n.e. is not estimated

Physiological		Ageing		Toxicological	
Growth rate	0.064 d^{-1}	Maintenance rate coeff.	$2.9.10^{-6}$ d^{-1}	Elimination rate	0.12 d^{-1}
Initial length	0.262 $\mu g^{1/3}$ n.e.	Damage amplification	0.023 d^{-1}	NEC for survival	>3000 mg/kg n.e.
Length at puberty	4.0 $\mu g^{1/3}$	Damage increases respiration	5.0 μg^{-1}	NEC for growth/repro	0.00017 mg/kg
Maximum length	6.6 $\mu g^{1/3}$	Damage to hazard rate	0.00021 $(\mu g\ d)^{-1}$	Tolerance concentration	11000 mg/kg
Maximum reproduction	30 eggs/d	Damage to reproduction	26 µg		

Population growth as function of the Cd concentration, estimated for different food levels



3. POPULATION GROWTH RATE

The estimated parameters can be used to calculate the population growth rate for any concentration, and for different food levels. The decrease in growth rate is slow as Cd decreases reproduction but increases survival.

4. CONCLUSIONS

- The extended DEBtox model provides a good fit on all data simultaneously, using few relevant parameters per curve.
- The ageing model requires further verification, but results indicate that survival and reproduction are affected through a similar mechanism.
- The model fits can also be used to predict effects at the population level for different scenarios.
- More information on DEBtox can be found at our website.