Legislation around emission of chemicals in the environment aims at minimizing ecological effects. Because of our poor understanding of ecosystem dynamics it is usually unclear how effects on particular species translate into ecological effects. The interpretation of results from experiments with mesocosms is also far from obvious. This explains why No-Observed Effect Concentrations (NOECs) are frequently used in environmental risk assessments. This use is, however, under increased criticism, due to substantial statistical problems that are inherent to this concept: the problem of recognizing small effects in scattery data. A statistically nonsignificant effect does not imply that biologically significant effects are absent.

Small effect concentrations have been proposed to replace NOECs in risk analysis. This approach suffers from several problems, such as, What is small?; How do small effects on species relate to ecosystem dynamics?; To what extend does the resulting value depend on model details that do not have a mechanistic basis? How do we extrapolate acute effects to chronic effects?

Recently we solved the problem of estimating the No-Effect Concentration (NEC) as a model parameter from data of standardized aquatic toxicity tests (Kooijman 1993): acute and chronic survival (Bedaux & Kooijman 1994, Kooijman & Bedaux 1996a,d), body growth (fish, Kooijman & Bedaux 1996c,d), reproduction (daphnia, Kooijman & Bedaux 1996b,d) and (algal) population growth (Kooijman et al, 1996, Kooijman & Bedaux 1996d). This alternative for the NOEC does not suffer from statistical problems, while its use in risk assessments still avoids the difficulty of translating observed effects into consequences for ecosystems dynamics. Being a model parameter, the point estimate of the NEC can be provided with a confidence interval. This allows positive identification of a concentration range where no effects are to be expected, which is not possible in the NOEC approach. If, on the other hand, the null hypothesis NEC=0 (implying that the toxicant has effects in all concentrations) cannot be rejected, one might consider additional research about the effects of the compound.

The method to estimate NECs is a by-product of a new process-based characterization of toxic effects. The basic idea is that the hazard rate and the parameters that quantify the energy budget of the individual are proportional to the concentration in the animal that exceeds the no-effect concentration. The inverse of the proportionality constant, which is called the tolerance concentration, quantifies the toxicity of the compound. The energy budget parameters are defined by the Dynamic Energy Budget (DEB) theory (Kooijman, 1993), which specifies the rules that organisms use for the energy uptake of resources (food) and the ensuing allocations to maintenance, growth, development and propagation. The DEB theory has been tested against a wide variety of ecophysiological data (Kooijman, 1996).
1993). At high concentrations, toxicants will affect many physiological processes simultaneously and we would need many parameters to quantify all these effects. The various physiological processes can be ordered with respect to their sensitivity for the toxicant, however, so that just one process (i.e. one parameter) is affected in the lower concentration range.

The characterization of toxic effects is build up in two steps: (i) the uptake and elimination behaviour of the compound and (ii) the translation of internal concentrations into effects. As the most simple option, one compartment first-order toxicokinetics can be assumed. This results in a NEC, a tolerance concentration and an elimination rate as characterizations of the various sublethal effects. The tolerance concentration is replaced by the killing rate for lethal effects. These simple characterizations are independent of exposure time and depend in a simple way on the octanol-water partition coefficient. The possibility to remove the elimination rate as an essential parameter, classifies the model with just two toxicity parameters as the simplest possible. The results of aquatic toxicity bioassays as standardized by the OECD are suitable substrates for the models.

Figure 1 gives an example for a typical bioassay for survival, where the environmental concentration was constant and growth during exposure is negligibly small. In that case, the hazard rate at tissue-concentration \( Q(t) \) reduces to

\[
\dot{\lambda} + \dot{k}_a P_v^{-1}(Q(t) - Q_0) = \dot{\lambda} + \dot{k}_a (c - c_0) + \dot{k} \exp(-tk_a) - c_0 + \dot{k}_a \exp(-tk_a) - c_0 + c_0 \]

where \( \dot{\lambda} \) is the control hazard rate, \( \dot{k}_a \) the elimination rate, \( t \) the exposure time, \( c \) the environmental concentration and \( c_0 \) the no-effect concentration. The notation \( ()_+ \) indicates that negative values are replaced by 0. The bioconcentration coefficient \( P_v \equiv Q(\infty)/c \) is introduced to relate the toxicity to environmental concentrations, rather than tissue concentrations, which are generally not known. So, the killing rate \( \dot{k}_a \) has dimension per environmental concentration per time.

Sublethal effects on parameter \( p_0 \) are modelled as

\[
p_c = p_0 (1 + Q_p^{-1}(Q(t) - Q_0)_+) = p_0 (1 + c_p^{-1}(c - c_0) \exp(-tk_a) - c_0)_+
\]

where \( p_0 \) is the value of the target parameter of the DEB-model in the control and \( c_p \) the tolerance concentration for parameter \( p \). Examples of such DEB parameters are volume-specific maintenance costs, volume-specific growth costs, or costs per egg. If the environmental concentration equals the NEC plus the tolerance concentration, the value of the affected parameter is two times that of the control. This property provides an easy interpretation of the tolerance concentration. The linear relationship between \( p_c \) and \( Q(t) \) can be justified mathematically as an approximation that holds for small effects.

It can be shown (Kooijman & Bedaux 1996d) that simple relationships between toxicity parameters and the octanol-water partition coefficient \( P_{ow} \) result from first principles and are consistent with empirical relationships that have been found between the LC50 and \( P_{ow} \). The relationships are \( c_0 \propto P_{ow}^{-1}, \dot{k}_a \propto P_{ow} \) and \( \dot{k}_a \propto P_{ow}^{-0.5} \).

Being process-based, the model allows for the evaluation of effects under complex exposure regimes, where environmental concentrations are not constant. Modules, such as the one-compartment toxicokinetics, can, if necessary, be replaced by more realistic (and more
Figure 1: The time and concentration profiles for the effect of dieldrin on survival of guppies *Poecilia reticulata*. Data from Ms. D.D.M. Adema (TNO-IMW). The resulting parameter values are: The no-effect concentration $c_0 = 5.20 \ (0.47) \ \mu g l^{-1}$, the killing rate $\dot{k}_l = 0.0376 \ (0.0078) \ \text{l (d } \mu g)^{-1}$, the elimination rate $\dot{k}_a = 0.791 \ (0.218) \ \text{d}^{-1}$ and the control mortality rate $\dot{\lambda} = 0.00835 \ (0.00490) \ \text{d}^{-1}$. Values between brackets refer to asymptotic standard errors. The profile ln likelihood for the NEC is given in the third graph, from which we can deduce an estimate for the 95% confidence set: from 2.72 till 2.85 $\mu g l^{-1}$ and from 4.09 till 6.2 $\mu g l^{-1}$. Results and graphs are obtained with software package DEBtox, which is provided in Kooijman & Bedaux (1996).
complex) kinetics that allow for changes in physiological conditions, for instance. This makes sense in more detailed studies for scientific purposes or for chemicals that require special attention. The approach is also suitable for evaluating the consequences of effects on individuals for population dynamics. This boils down to a parameter perturbation technique that has a wider applicability.

We think that the link between scientifically sound models and models that are used for routine risk assessment should be as close as possible. The range of consistent models, varying from very simple to very complex, avoids the problem of compromising between different modelling purposes that require conflicting properties of models (realism vs simplicity; compound-specific vs generic). The observation that the values for NECs prove to be insensitive for the mode of action of the compound is encouraging.

References


