THE NETHERLANDS WORKING GROUP ON STATISTICS AND ECOTOXICOLOGY: STATISTICS AND MODELS FOR RISK ASSESSMENT

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THE NETHERLANDS WORKING GROUP ON STATISTICS AND ECOTOXICOLOGY

The Stat & Ecotox group meets twice a year and in these meetings, a member introduces some problem on the border between statistics and ecotoxicology. After the introduction, the problem will be discussed in the meeting, trying to find the right approach. All S&E-members in the meeting participate actively in that discussion.
The Stat & Ecotox group is a working group of both the Environmental Toxicology Section of the Netherlands Society of Toxicology (NVT) and of the Biometric Section of the Netherlands Society of Statistics (VVS). Members of Stat & Ecotox do not have to be a member of either of these societies. All people interested in the the application of statistics in ecotoxicological problems are invited to join the working group.
For more information, see www.ecostat.nl/wgSandE.htm, or mail to StatEcotox@ecostat.nl.

INTRODUCTION TO PROBLEMS DISCUSSED IN THE STAT & ECOTOX GROUP

Translating a limited set of observations in laboratory experiments to environmental standards a huge amount of problems are encountered. These have to be tackled by statistical estimation, modelling of relations, experiments to investigate these relations and estimate the model parameters, and, last but not least, by an arbitrary, political choice of the acceptable effect level.
In the Stat & Ecotox group current issues in statistical estimation and modelling in ecotoxicology are discussed.
The first question is how to estimate an acceptable effect level (AEL) from a laboratory experiment, that is a level (either concentration or dose) in the (laboratory) environment leading to an acceptable small effect on the species studied.
Then, knowing for a limited set of species the acceptable effect level of a single chemical in a laboratory setting, the following four questions arise

1. How can the AEL for all species in an ecosystem be estimated based on this limited set?
2. What would the AEL of this chemical be if the organism is exposed simultaneously to several other (related) chemicals?
3. How is the exposure level in the laboratory related to the exposure level in the environment?
4. Will an environmental standard based on keeping the effect small for most species, if housed in the laboratory without inter-species interaction, lead to negligibly small effects on ecosystems?

Discussion on some of these questions will be given in this poster.

HOW TO ESTIMATE AN ACCEPTABLE EFFECT LEVEL?

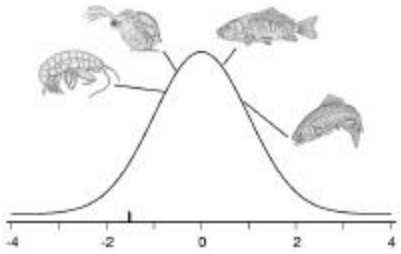
Several methods are used to estimate an acceptable effect level (AEL). The measure used most often is the NOEC. However, an NOEC does not guarantee that the effect of the chemical is acceptable small, but only that the experiment was not sufficiently accurate to show an effect at the chosen significance level. Measures which are sound estimates of a concentration inducing only a small effect, if any, are

1. inversing the NOEC procedure, that is estimating the lowest concentration for which the hypothesis of an effect of at least *x*% can be rejected;
2. estimating the concentration for which the effect is bound to be below some chosen level, the so called Bounded Effect Concentration;
3. estimating the concentration leading to an effect of *x*%, the so called **EC***x*;
4. if a concentration exists below wich the chemical does not have any effect, estimating the No Effect Concentration (NEC) with an appropriate model.

To estimate the **EC***x*, a model for the concentration-response relation has to be used. Common models are log-logistic: $E(C)=E(0)/[1+(C/\mathbf{EC}50)^{\beta}]$ and log-normal: $E(C)=E(0)\Phi([\log(C/EC50)]/\beta)$ with Φ the cumulative standard normal distribution. At the **EC***x*, the effect is *x*%, so $x=100E(C)/E(0)$. Expressing the exposure level in log concentration ($c={}_{10}\log C$), and using the log-normal dose-response relation, $\mathbf{EC}x=\mathbf{EC}50+\Phi^{-1}(x/100)\beta$, the **EC***x* can easily be calculated if both the **EC**50 and the slope parameter β are known.

EXTENDING FROM SINGLE SPECIES TO COMMUNITIES: SPECIES SENSITIVITY DISTRIBUTIONS.

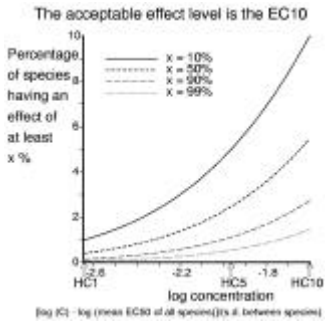
One of the methods to extend single species AELs to an AEL for complete ecosystems is to estimate the concentration at which at most p% of the species will be affected, that is exceeding the single species AEL of at most p% of the species. This concentration is called the HCp (hazardeous concentration for *p*% of the species). To estimate the HCp (often *p*=5% is used), the distribution of the sensitivities of all species is assumed to be some common probability distribution, for instance log-normal. The species for which AEL data are available are assumed to be randomly drawn from the set of all species. Given these assumptions, an estimate of the HCp can be calculated. The accuracy of this estimate depends on the number of single species AELs. To do justice to this inaccuracy, and to be sure not to overestimate the HC5, the lower limit of the (95%) confidence interval of the HCp estimate is often used as ecosystem AEL.



ARE SOME SPECIES SEVERELY AFFECTED AT THE HC*p*?

In defence of the HCp method, it is sometimes stated that although *p*% of the species may be affected if the environmental concentration is the HCp, this does not imply that these species are affected severely. The calculation of the HCp is based on AELs (mostly NOECs), and concentrations slightly above an AEL will not have a severe effect. To illustrate the fallacy of this argument, the implication is sketched of estimating the Acceptable Level (AL) with the HCp method if the ECx is used as AEL and the shape of the dose-response-relationship is the same for all species. Both the SSD and the dose-response-relationship are described by the log-normal distribution. In that case, the fraction of species having an effect of *z*% at the HCp can be calculated. If the AEL is set at an effect size of *x*%, and x/100 is indicated as x', and the hazardeous concentration for *p*% of the species is calculated (*p*'=*p*/100), then the probability that a species has an effect of *z*% (*z*'=*z*/100) at the HCp is

$$\Phi\left(\beta\sigma^{-1}\left[\Phi^{-1}(z')-\Phi^{-1}(x')\right]+\Phi^{-1}(p')\right).$$

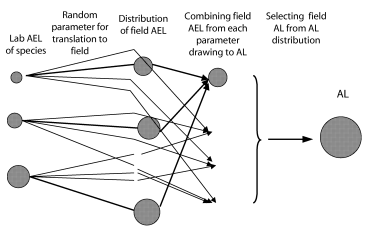


Note that this fraction only depends on the ratio of the standard deviation within species, β, and between species, σ. If the difference in sensitivity between species is much larger than that difference within each species, the HCp will be almost independent of the choice for *x* in the ECx used as AEL.

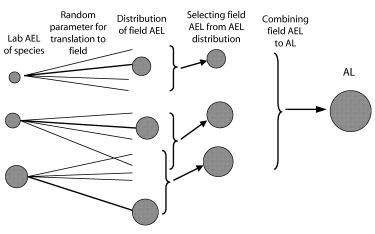
PROBABILISTIC METHODS TO ESTIMATE ACCEPTABLE LEVELS.

To calculate an AL for the environment, not only AELs for individual species are necessary but many more parameters such as partition coefficients and accumulation factors of the chemical, lipid fractions of the animals and caloric values and daily ratios of food. Data on these parameters are scarce, and their estimates are not very accurate. To investigate the effect of the uncertainty in the parameter estimates, a probabilistic approach can be used. In this approach, (part of) the parameters are not considered as fixed values, but as drawings from some probability distribution. Using Monte Carlo simulation, each of these parameters is drawn several times, and the AL is derived from the frequency distribution resulting from these drawings. For the derivation of the AL several routes can be used. Two possible routes are:

1. Calculate for each combined drawing of all parameters the corresponding acceptable level, AL(drawing), and use the frequency of these AL(drawings) to derive the AL, for instance as the lower limit of its 95% interval.



2. Calculate for each species and each set of randomly drawn parameters the corresponding environmental AEL (ALE*d*), and select per species from the AEL distribution the environmental AEL, for instance as the lower limit of its 95% interval. Then, this set of AELs can be used to calculate the AL.



Further information on these topics:

N. van der Hoeven (in press).
Current issues in statistics and models for Ecotoxicological Risk Assessment.
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