Assessment Factors for Toxicity Based Risk Assessment in the Presence of Non-Exchangeable Species

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Outline of presentation:

Risk Assessment
   Ecological Risk Assessment
   Modelling: Current Envisagement

Non-Exchangeability
   Background
   (Re-) Modelling

Decision Rules

Acknowledgement & References
Assessment Factors

- Assessment Factors (AFs) = Uncertainty Factor; Safety Factor; Extrapolation Factor

- Used to extrapolate species tolerance data $x_1, x_2, \ldots, x_n$ (e.g. LC$_{50}$s) to multi-species ecosystems and address associated uncertainties in order to derive ‘safe’ concentration levels for regulatory purposes, e.g. pesticide registration, via:

  \[
  \text{Safe Conc.} = f(x_1, \ldots, x_n; \text{AF})
  \]
Current Practices & Problem Redefinition

- Current EU practice is deterministic
  \[ f(x_1, \ldots, x_n; AF) = \frac{\min\{x_1, \ldots, x_n\}}{AF} \]

- It gives a lower concentration which is 'safe' to most species.
  – Doesn’t quantify risk!

- Solution: use probabilistic modelling which accounts for species tolerance variability and uncertainty to extrapolate to concentration hazardous to \( p\% \) of the ecological community (HC\(_p\))

- Problem is analogous to estimating \( p\)-th percentile of a distribution

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The Species Sensitivity Distribution (SSD)

- A probabilistic model is fitted to the log transformed data $y_1, \ldots, y_n$ – The SSD
- Typically assumed $y_1, y_2, \ldots, y_n \sim iid \sim N(\mu, \sigma^2)$
- If $\mu$ and $\sigma^2$ known then $\log\text{-HC}_{p} = \mu - K_p \sigma$ where $K_p = \Phi^{-1}(1 - p/100)$
- Literature focuses on $p = 5$; driven by Dutch Government
- Decision rules (on log-scale) tend to be of the form $\bar{y} - \kappa_p s$ where $\kappa_p$ is the Assessment Shift-Factor (ASF)
Species Non-Exchangeability

- SSD assumes all data is \textit{i.i.d.}
- Recent report (EFSA, 2005) noted that the Rainbow Trout may be a \textit{typically} more sensitive species; i.e. tends to lie in the lower half of the SSD
- The Rainbow Trout is a typical dossier species (for logistical reasons)
Background

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Rainbow trout more sensitive than average fish species

Average species more sensitive than rainbow trout
A Hypothesis Test

- $H_0$: species $i$ exchangeable; $H_1$: species $i$ non-exchangeable
- For each species $i$ calculate
  \[
  \hat{R}_i = \sum_{\text{all substances in database}} \text{rank}(\text{species}_i)
  \]
- Generate the true distribution of $R_i$ using Monte Carlo
- Determine a $p$-value by applying a continuous approximation via the Law of Large Numbers
- Rainbow trout significantly rejected null hypothesis.
Re-Modelling for a Future Risk Assessment (1)

- Let $y^*$ be the special species’ log-toxicity value
- Assume $y_i \sim N(\mu, \sigma^2)$ for $i = 1, \ldots, n - 1$ and $y^* \sim N(\mu - k, [\phi \sigma]^2)$ (Craig & Hickey, 2008)
- $k$ and $\phi$ are the non-exchangeability parameters – they are properties of the species, not the substance
- We estimate them from a large toxicity database as MAP-estimators, e.g. $k_{\text{trout}} = 0.195, \phi_{\text{trout}} = 0.702$
Re-Modelling for a Future Risk Assessment (2)

- An intuitively better model would include:
  \[ y^* \sim N \left( \mu - k'\sigma, [\phi\sigma]^2 \right) \] (EFSA, 2005)

- Costs tractability

- Bayes factor analysis indicates simpler model is not too much worse
(Re-) Modelling

**NB.** Bayes factor is per chemical in the database.

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- Apply re-modelled SSD to suitable loss functions: e.g. Generalised Absolute Loss (Aldenberg and Jaworska, 2000); LINEX (Hickey et al., 2008)

- Retrieve optimal $p$-th percentile estimators of the form:

$$\hat{\mu} - \kappa_p^* \hat{s}$$

where $\hat{\mu}$, $\hat{s}^2$ are found to be new estimators of $\mu$, $\sigma^2$; and $\kappa_p^*$ is a function independent of the data and depends on $n$, $p$ and $\phi$. 

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THE END


