Applying AOPs to Environmental Toxicity: Source to Outcome

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The current approach to assessing adverse effects of chemicals in the environment is largely based on a battery of in-vivo study methods supported by a limited number of accepted in-silico approaches. Application Factors (AFs) are applied to the most sensitive in-vivo endpoints to derive Predicted No Effect Concentrations (PNECs). Thus AFs are currently the link between effects observed in short-term single-species studies and effects on ecosystem communities (and the associated protection goals). However, there is no clear mechanistic justification to support the defined levels of the AFs. New tools are beginning to emerge that can address some of these deficiencies. These tools include mechanistic effect models that can (begin to) account for some of the complexity of communities and ecosystems, and models that can extrapolate from individual level effects to population effects. Within the Adverse Outcome Pathway (AOP) framework, mechanistic effect models can be used to link chemical effects at different levels of biological organisation based on an understanding of the chemical Mode of Action (MoA).

One of the most prevalent MoAs in the aquatic compartment is narcosis, which is thought to encompass between 50 and 70% of all industrial chemicals. The narcosis MoA is characterised by a strong correlation between toxicity and hydrophobicity. This suggests that the toxicity is related to bulk partitioning into lipid rich compartments such as cellular membranes with “membrane perturbation/disruption” as an early key event. However, the exact nature of the Molecular Initiating Event(s) in narcosis is unknown. There is evidence for subclasses of narcosis. At a basic level the classification scheme of Verhaar et al. (1992) recognises both Class 1 (general narcotic) and Class 2 (polar narcotic) compounds, and there is additional evidence that other subclasses also exist such as ester and amine narcosis (Russom 1997, Schultz et al, 1998).

There are different approaches to calculating the toxicity of narcotic chemicals. One approach is the Critical Body Burden (CBB) approach, where an effect in an individual occurs when a critical concentration in the organism is exceeded. For narcosis a CBB range of 2-8mmol/kg has been established for acute lethality (van Wesel & Opperhuizen, 1995). Another approach for predicting the toxicity of narcotic chemicals was developed by Mackay et al. (2009) based on the concepts of chemical activity and toxic potency.

Despite significant gaps in the chain of events leading to adverse outcome, an initial AOP for narcotic chemicals has been outlined by Ankley et al., 2010. Mechanistic effect models can potentially help elucidate every step of this AOP. Concentrations at target sites can be predicted using either CBB or activity-based models. Toxicodynamic/toxicokinetic models can predict how effects propagate from lower to higher levels of biological organisation using endpoints such as damage accrual, damage recovery, energy allocation, physiological compensation and thresholds. Finally population dynamics can be modelled based on ecological and life history traits to predict responses on the population level.

The implementation of such models, however, may require a higher level of understanding than currently available. Whilst AOPs provide a useful framework for making robust links between key events at a
molecular/sub-individual level and apical endpoints, considerable work is needed before they are fully applicable in supporting more ecologically relevant risk assessment decisions.