Environment International 91 (2016) 215–219

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Next-generation ecological risk assessment: Predicting risk from molecular initiation to ecosystem service delivery

Valery E. Forbes *, Nika Galic

Department of Ecology, Evolution, and Behavior, College of Biological Sciences, 123 Snyder Hall, 1475 Gortner Ave, St. Paul, MN 55018, USA

ARTICLE INFO

Article history:
Received 6 January 2016
Received in revised form 4 March 2016
Accepted 5 March 2016
Available online xxxx

Keywords:
Adverse outcome pathways
Ecological protection goals
Ecosystem services
Environmental management
Mechanistic effect models
Predictive systems models

ABSTRACT

Ecological risk assessment is the process of evaluating how likely it is that the environment may be impacted as the result of exposure to one or more chemicals and/or other stressors. It is not playing as large a role in environmental management decisions as it should be. A core challenge is that risk assessments often do not relate directly or transparently to protection goals. There have been exciting developments in in vitro testing and high-throughput systems that measure responses to chemicals at molecular and biochemical levels of organization, but the linkage between such responses and impacts of regulatory significance – whole organisms, populations, communities, and ecosystems – are not easily predictable. This article describes some recent developments that are directed at bridging this gap and providing more predictive models that can make robust links between what we typically measure in risk assessments and what we aim to protect.

1. Challenges for ecological risk assessment

Ecological risk assessment is the process of evaluating how likely it is that the environment may be impacted as the result of exposure to one or more chemicals and/or other stressors. This process should be playing a central role in environmental protection since basing regulatory decisions on evidence ought to be in the interests of all stakeholders. Yet there are concerns that risk assessments are not being used as much as they should in risk management especially given the level of investment in them. There are a number of related reasons for this mismatch between risk assessment and risk management that have been identified in the Silver Book (NRC, 2009) from the USA and in recent Opinions from scientific advisory committees of the European Commission (SCHER/SCHENIHR/SCCS, 2013a; SCHER/SCHENIHR/SCCS, 2013b). The core challenge is that the risk assessments often do not relate directly or transparently to protection goals. For example, most toxicity tests used for ecological risk assessment (ERA) are based on a handful of model species and measure chemical impacts on individual organism performance (e.g., survival, growth, reproduction) (Van Leewen and Vermeire, 2007). This is despite the fact that ecological protection goals are generally at population, community, and ecosystem levels (Nienstedt et al., 2012; NRC, 2013), and impacts on organism performance are not directly proportional to impacts on populations or higher levels of organization. Methods that have been used in ERAs for extrapolating among species and across levels of biological organization (i.e., application of standard uncertainty factors, species sensitivity distributions) are overly simplistic and likely to lead to both over-estimates and under-estimates of risk (Forbes and Calow, 2002). Another major challenge is the requirement to reduce the use of vertebrate animals in toxicity tests and – at the same time – to test more chemicals (Ankley et al., 2010). Here we briefly discuss responses to both of these challenges and propose an integration of currently disparate levels and fields of research for a more integrated and predictive chemical risk assessment.

2. New developments in sub-organismal modeling

One response to pressure to reduce the use of vertebrates while testing more chemicals has been the development of various in vitro and high throughput test systems (Schroeder et al., 2016). Although in vitro tests can readily assess important modes of action such as receptor agonism/antagonism, it can be difficult to convert in vitro results to whole animal estimates of toxicity because of the potential for multiple modes of toxic action and feedback loops that exist within intact organisms (Nichols et al., 2011). In an effort to establish credible links between responses to toxic chemical exposure at the cell or tissue level with responses at the whole organism level, a conceptual framework that describes adverse outcome pathways (AOPs) has received much attention in recent years (Ankley et al., 2010; Schroeder et al., 2016). AOPs aim to assemble, portray, and evaluate toxicity information across different levels of biological organization with the aim of establishing causal relationships between the interaction of chemicals with their

* Corresponding author.
E-mail addresses: veforbes@umn.edu (V.E. Forbes), ngalic@umn.edu (N. Galic).

http://dx.doi.org/10.1016/j.envint.2016.03.002
0160-4120/

molecular targets and adverse outcomes of regulatory relevance through a series of key biological events (Groh and Tollefsen, 2015).

Much of the AOP literature describes conceptual links between molecular initiating events and metrics of organism performance. Surprisingly few studies modeling suborganismal processes yet provide quantitative, mechanistic links to organism-level performance metrics, such as fecundity, growth and survival. There are, however, efforts underway to develop AOPs that go beyond descriptive linkages. One example are models capturing the essential features of the female fish reproductive system with vitellogenin production as the model output (Kim et al., 2006; Sundling et al., 2014; Li et al., 2011). Computational models of the hypothalamic-pituitary-gonadal axis in fish simulate a series of events in the endocrine regulation of vitellogenin (Murphy et al., 2005; Li et al., 2011; Sundling et al., 2014). Some of these models have been applied to test effects of different endocrine-disrupting chemicals on vitellogenin production (Murphy et al., 2005; Li et al., 2011). Although vitellogenin is necessary for egg production, mechanistic and quantitative links between vitellogenin and fecundity are lacking, and the best data available to describe the relationship are correlative (Miller et al., 2007). Although establishment of correlations between molecular, biochemical, or other suborganismal responses and whole organism performance can provide useful first steps for the development of mechanistic models, they do not provide evidence of causation and cannot be extrapolated with confidence to other situations.

There is little doubt that framing the study of chemical effects using the AOP concept can be helpful for gaining mechanistic insight into how chemicals cause harm. Although the potential of AOPs to be developed into predictive tools for risk assessment is widely appreciated, transforming the approach from a conceptual framework into a robust predictor of risk to endpoints of regulatory concern is not without its challenges (Groh and Tollefsen, 2015). It is recognized that the development of more quantitative AOPs will require toxicokinetic and toxicodynamic modeling that can translate exposure and effects measured in in vitro systems to those in intact organisms and that can extrapolate effects across species (Phillips et al., 2015) and to endpoints that matter from a regulatory perspective. For instance, recent studies demonstrate that there are real possibilities of using in vitro cell cultures in combination with toxicity modeling to predict impacts on organism growth (Stadnicka-Michalak et al., 2015). However, the question of whether and to what extent responses at the individual level translate into effects at higher levels still remains. In short, there are currently no well-defined risk-assessment frameworks that mechanistically link responses from molecular initiating events to impacts on protection goals.

3. New developments in modeling higher levels of biological organization

For the most part, regulatory risk assessments are based on simple measures of whole organism lethal and sublethal toxicity and do not explicitly consider influences of life history or species ecology on risk (Van Leewen and Vermeire, 2007). It is still unclear how the most typically measured toxic responses at the organismal level (i.e., survival, reproduction, growth) translate into effects on populations, communities and ecosystem services. In the US, the Endangered Species Act requires that populations of threatened and endangered species are not jeopardized by pesticide exposure (NRC, 2013). In European pesticide risk assessment, there is a growing tendency to define protection goals at the ecosystem service level (Nienstedt et al., 2012). Ecosystem services are provided by various levels of biological organization, from individual organisms to networks of species in trophic and non-trophic interactions in ecosystems. Assessing risks to populations and networks of species in the field based on measurements on test organisms in a laboratory setting is prone to error as it neglects various constraints that organisms experience (e.g., density-dependent resource limitation) as well as feedbacks between different levels of biological organization (Barnthouse, 2004; Forbes et al., 2011). In addition, this approach ignores natural variability in environmental conditions as well as impacts of a changing climate and other stressors.

A recent response to dealing with the limitations of current risk assessment methods has been the development of mechanistic effect models (MEMs). MEMs are dynamic models that quantify impacts of chemicals on individuals, populations or ecosystems and are based on mechanistic understanding. They are designed to produce outputs more directly related to protection goals, they can incorporate necessary ecological complexities at relevant scales, and they can address influences of spatial and temporal heterogeneity in exposure scenarios (Forbes and Calow, 2012). The majority of MEMs developed to date have focused primarily on organism- to population-level processes, with frequent inclusion of relevant physiological processes, e.g., resource acquisition and allocation (Preuss et al., 2009; Martin et al., 2013; Johnston et al., 2014; Reed et al., 2015), spatially-explicit movement impacting exposure (Meli et al., 2013; Liu et al., 2013) or detailed toxicological processes, e.g., toxicokinetics and toxicodynamics (Ashauer et al., 2007; Galic et al., 2014; Dohmen et al., 2015; Liu et al., 2014). Several reviews have assessed the availability of various modeling approaches for use in chemical risk assessment (Pastorok et al., 2002; Galic et al., 2010; Schmolke et al., 2010; Forbes et al., accepted). These reviews demonstrate that a range of modeling approaches has been developed and that the models differ in the amount of biological and spatial detail they incorporate, as well as in terms of techniques used for parameterizing, analyzing and testing the models' validity. Choice of modeling approach largely depends on the objective and desired output, as well as on the availability and type of data needed for parameterization and validation. Fairly simple models have few data requirements and may be useful for quantitatively integrating toxic effects on multiple individual-level responses (that may have different dose-response relationships) to impacts on populations (Calow et al., 1997) and may help to assess the relative vulnerability of different species or life-cycle types (Hanson and Stark, 2011; Ibrahim et al., 2014). More detailed, species-specific models require more information (Topping et al., 2003; Becher et al., 2014), but allow refined assessment of more realistic scenarios (Topping et al., 2015). They can also make the sources of uncertainty in risk assessment explicit; whereas these are hidden in simpler approaches (Forbes et al., 2015).

In the past an important barrier to creating a comprehensive MEM framework for ERA was a lack of acceptance of models by the community of stakeholders involved in ERAs (Hunka et al., 2013). Two of the most important reasons for this were a lack of guidance for model users (i.e., risk assessors and risk managers) on how to evaluate and interpret models and a lack of guidance for model developers to ensure that models fulfill necessary criteria for their practical application in regulatory risk assessments. These barriers have largely been addressed through a series of international stakeholder workshops (Thorbek et al., 2009; Forbes et al., 2011; Hommen et al., 2015), comprehensive research and training programs (i.e., CREAM; Grimm et al., 2009), and published guidance (Grimm et al., 2010; 2014; Augusiak et al., 2014; EFSA, 2014).

Despite the many advances in MEMs in recent years, most available models do not make predictions beyond the population level. To the extent that protection goals are at the population level (e.g., endangered species risk assessments under the US Endangered Species Act), it may not be necessary to extrapolate impacts to higher levels of biological organization. However, single species population models could underestimate long-term impacts of chemicals if factors such as competition or predation are neglected (Gergs et al., 2013; Kattwinkel and Liess, 2014). Intraspecific competition is most commonly included as a density-dependent mechanism of population regulation (Forbes et al., accepted). Additional drivers of population dynamics, such as interspecific competition or predation, can be included as separate factors in single-species population models, i.e. avoiding the need to explicitly model several species, but this is still not a common practice.