

## Novel Concepts for Novel Entities: Updating Ecotoxicology for a Sustainable Anthropocene

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E cotoxicology assumes that pollution impacts start at lower (molecular) levels of biological hierarchy and later cascade to ecologically more relevant levels. Another major assumption is of monotonic toxicity (i.e., equal or greater effects as contaminant exposure increases). These dogmas fostered an analytical reductionism that tackled traditional chemical pollution. Contemporary society requires a broader sense of sustainability, however. In this context, planetary boundaries<sup>2</sup> are of direct concern to ecotoxicology as the boundary "novel entities" refer to the new forms of chemical, particulate, energy, or microbiological contaminants. Reductionist ecotoxicology may fail to protect ecosystems whenever the effects of novel entities interact with the complexity of the biosphere.<sup>3</sup> Incremental improvements in current ecotoxicology are unlikely to provide timely solutions for the many pressing sustainability challenges. Thus, there are four vital updates required to prepare ecotoxicology for the Anthropocene.

Update 1: Single vs Mixture. Toxicity risk assessments are based on single compounds, whereas the environmental exposure occurs as complex contaminant mixtures. This deep-rooted problem has particularly acute consequences now. There are ~8 000 000 commercial chemicals, but ecotoxicological data are available for less than ~100 000.4 Testing individual contaminants is a challenge and testing all relevant mixtures and environmental conditions is virtually impossible. Despite achievements made on nontarget screening for environmental contaminants and toxicity, such piecemeal advances might provide only obsolete solutions. A new way to monitor homeostasis in multistressed biological systems focusing on biological resilience is required.<sup>3</sup>

Update 2: Lethal vs Sublethal. The increasing diversity of contaminants is accompanied by a decrease of the lethal toxicity of new contaminants. Meant to be safer, novel entities entail individually lower lethality than their predecessors. Nevertheless, the perspective of a progressively diverse sublethal mixture of stressors threatens the central assumption of monotonicity. Acute mortality is a drastic outcome and it may be mostly monotonic to single chemicals. However, the sustainability of life forms (e.g., nourishing, reproduction, behavior) requires machinery that may be adversely affected in multiple nonmonotonic ways. From gene expression to endocrine systems, or from proper display of phenological traits in trees to the mating songs of animals, successful survival of populations is replete with responses highly dependent on physiological modulation (referred as mediation in statistics). Mediated processes often exhibit nonlinearity (i.e., one endpoint influences the dose-response of other endpoints), and hence lack of monotonicity. Low doses of pollutants could interact with vital processes other than lethal toxicity targets, thus modulating significant sublethal effects. Numerous critical environmental transitions are attributed to the interaction of sublethal stressors.<sup>6</sup> Sublethal contaminants, albeit individually accounting for negligible lethality, in combination may trigger more severe effects at population levels indirectly by adverse effects on reproduction (behavior, gamete production, etc.) or on the immune system as shown for endocrine disruptors and light pollution. Ecotoxicology should go beyond lethality and focus on the resilience of biological systems.

Update 3: Chemical vs Novel Entity. Contaminants are chemicals, materials, particles, or energy. Current ecotoxicological principles apply predominantly to chemicals, however. Moreover, the combination of chemical and nonchemical stressors frequently yields more-than-additive effects.<sup>3</sup> Novel entities with potential to impact the biosphere such as microbiological contaminants, nanoparticles, polymer-based materials, and light pollution interact with biota differently from chemicals. Traditional assumptions might simply not hold true because these stressors differ in their inherent energetic, temporal, and spatial patterns. We reported clear nonmonotonicity for a microbial-based biopesticide used

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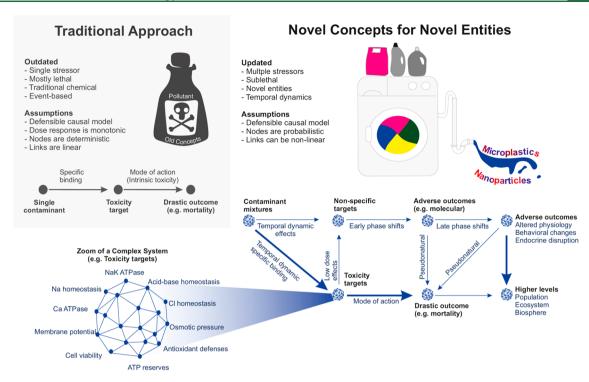


Figure 1. Ecotoxicology of the Anthropocene includes (1) changing assumptions and (2) establishing a causal homeostasis network in which biological systems facing pollution are complex systems where novel entities initiate adaptation, feedback loops, phase transitions, modulation, and evolution. This considers traditional toxicity targets and effects influencing higher levels of biological organization.

worldwide, <sup>1</sup> a contaminant that adds further complexity as it may reproduce and mutate. <sup>7</sup> Another example is artificial light at night (ALAN). Organisms evolved distinct strategies to cope with sunlight, which is several orders of magnitude more intense than urban night light. Nevertheless, ALAN disturbs the morpho-physio-phenological traits of plants, <sup>8</sup> animals, <sup>9</sup> and microbes. <sup>10</sup> It is important that the shapes of dose—responses are characterized for typical novel entities independently of their lethality at high exposure.

Update 4: Event vs Continuous Exposure. Ecotoxicological models often involve abrupt constant exposure to contaminants for a fairly short period, during which effects are evaluated. Yet environmental exposures dynamically change over time and space. The paucity of comparisons of eventbased and continuous exposure hinders evaluation of which is more relevant for risk assessment. The predominance of lowdose exposures discussed above suggests that gradual and continuous (or sequential) exposures may well be the most relevant for sublethal effects and long-term sustainability. Event-based exposures also neglect the importance of biology in the toxicity, for example. the adaptive (e.g., acclimation) and nonadaptive (e.g., sensitization) properties of biological receptors such as molecular networks, individuals, populations, or ecological communities.<sup>3</sup> Studies on the adverse outcomes under various temporal dynamics are essential for future ecotoxicology. In this sense, causal models from epidemiology and time-varying sequential exposures offer a starting point.

An updated ecotoxicology would switch focus from individual contaminants to the resilience of biological systems.<sup>3</sup> This is achieved with concepts of complexity theory and causal inference<sup>2,11,12</sup> and investigation of emergent properties that cannot be predicted alone by the individual parts of the system. For instance, consider the traditional linear causal model in which a single contaminant (e.g., copper) acts on a toxicity

target (e.g., enzyme activity) to cause a deterministic severe outcome (e.g., mortality) (Figure 1). Anthropocene ecotoxicology should ponder the diversity of stressors (e.g., metals, organic pollutants, particles, energy, etc.) in their temporal dynamic interaction with specific toxicity targets (e.g., biomolecules) and nonspecific targets (e.g., epigenetics, or any response modulator) that trigger probabilistic effects (e.g., mortality, endocrine disruption, behavioral change). In such novel models, a network of nodes (contaminants, enzymes, biological responses) are connected by nonlinear structured causal equations that allow the whole system to respond when stressed. Complexity theory shows that nearly all rules applicable to individual nodes are not relevant to a network, and complex systems often have an underlying simplicity. Thus, the connectivity of nodes affected is more important than the particular properties of individual contaminants (i.e., effects on more central parts are more likely to trigger systemic responses). This novel approach to ecotoxicology is a complex system where novel entities affect biological systems initiating responses at various and interacting levels.

The microplastics debate encapsulates the necessity for updates. Society wants action because microplastics contain a complex cocktail of compounds (update 1) that cause sublethal effects (update 2) with undefined intrinsic toxicity (update 3), and that gradually accumulate in the environment (update 4). But scientists have divided opinions. <sup>13,14</sup> We need to acknowledge that the reductionist approach cannot tackle this kind of complexity and may also marginalize the contribution of ecotoxicology to the solutions of global issues. <sup>3,5</sup> It is time to face the problem and adopt novel concepts for the novel entities threatening the biosphere in the Anthropocene.

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Notes

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