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Review Article

Environmental Toxicology: Modern Approaches for Assessing Ecological and Human Health Risks

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ABSTRACT

Environmental toxicology has advanced significantly to address the increasing complexity of pollutants that affect both ecosystems and human health. The emerging contaminants such as microplastics and endocrine disrupting chemicals present significant risks due to their potential for bioaccumulation and biomagnification within food chains. These pollutants can induce significant physiological disturbances including oxidative stress, hormonal imbalance and other cellular alterations. Furthermore, climate driven changes such as temperature fluctuations and extreme weather events influence the distribution, persistence and toxicity of environmental contaminants. These factors often interact with biological stressors, intensifying ecological impacts and emphasising the need for adaptive environmental management strategies. Environmental toxicology is witnessing a paradigm shift from conventional animal-based testing to innovative methodological approaches. High-throughput in vitro screening, organ-on-a-chip technology that mimic tissue level interactions and computational toxicology are transforming toxicological research. Artificial Intelligence and Machine Learning are increasingly used to predict toxicant fate, identify exposure pathways, and evaluate long-term ecological consequences. These technologies help prioritise chemicals for testing, while reducing research costs, and ethical concerns associated with animal experimentation. Modern risk assessment frameworks now integrate genomics, proteomics and metabolomics with agent-based ecological modelling to enable the identification of system level biological responses, including epigenetic modifications associated with pollution related diseases. Such integrative approaches support evidence-based regulatory decisions, guiding emission control policies and promoting sustainable bioremediation strategies for safeguarding ecosystems and public health. The integration of data-driven technologies, non-animal experimental models, and multi-scale ecological modelling is redefining environmental toxicology. These advances enhance the ability to anticipate and mitigate emerging environmental threats, ultimately contributing to the protection of ecosystem integrity and public health in a rapidly changing global environment.

1. Introduction

Environmental toxicology examines the effects of chemical pollutants on living organisms, ecosystems, and human health, with increasing attention being given to the complex and cumulative impacts of emerging contaminants in modern environments (Walker et al., 2012; Landrigan et al., 2018). As industrialization and anthropogenic activities continue to introduce diverse pollutants into air, water, and soil, understanding their toxicological consequences has become essential for safeguarding ecological integrity and public health

(Newman, 2015). Traditionally, environmental toxicology has relied heavily on whole-animal testing to assess the safety and hazards of chemical substances. However, these conventional methods are often limited by high costs, low throughput, lengthy experimental timelines, and growing ethical concerns regarding animal welfare (Ankley *et al.*, 2010).

To overcome these limitations, the field is increasingly shifting toward New Approach Methodologies (NAMs), which include advanced in vitro systems, in silico computational models, organ-on-chip technologies, and high-throughput

screening platforms (ECHA, 2020; Hartung, 2009). These innovative tools offer faster, cost-effective, and ethically sustainable alternatives for toxicity assessment while improving mechanistic understanding of toxic responses. Simultaneously, environmental toxicologists are confronting a new generation of emerging threats, including microplastics, endocrine-disrupting chemicals (EDCs), pharmaceuticals, nanoparticles, and persistent organic pollutants, all of which pose significant risks even at low environmental concentrations (Galloway *et al.*, 2017; Gore *et al.*, 2015).

Moreover, the interactions between chemical pollutants and climate-related stressors such as rising temperatures, ocean acidification, drought, and habitat alteration are increasingly recognized as important determinants of toxicity outcomes (Noyes *et al.*, 2009). These synergistic effects can amplify pollutant bioavailability, toxicity, and ecological vulnerability, complicating traditional risk prediction models. Therefore, integrated and systems-based frameworks are being developed to enhance environmental risk assessment by combining multi-omics technologies, adverse outcome pathways (AOPs), computational toxicology, and ecological modelling (Ankley *et al.*, 2010).

2. Emerging Contaminants and Associated Risks

Emerging contaminants, particularly microplastics and endocrine-disrupting chemicals (EDCs), have become major concerns in environmental toxicology due to their persistence, widespread distribution, and potential to affect both ecological and human health (Galloway *et al.*, 2017; Gore *et al.*, 2015). Microplastics, tiny plastic particles less than 5 mm in size, originate from the breakdown of larger plastic debris or from manufactured products such as cosmetics and synthetic textiles. Because of their small size and large surface area, microplastics readily adsorb toxic substances including heavy metals, pesticides, and persistent organic pollutants, thereby acting as carriers that transport hazardous chemicals through environmental systems (Rochman *et al.*, 2013). Similarly, EDCs such as bisphenol A (BPA), phthalates, and certain pesticides interfere with hormonal signaling pathways even at low concentrations, posing chronic health risks to exposed organisms (Diamanti-Kandarakis *et al.*, 2009).

Once introduced into aquatic and terrestrial ecosystems, these contaminants can accumulate in organisms and progressively biomagnify across food chains (Walker *et al.*, 2012). Their presence has been linked to the generation of reactive oxygen species (ROS), which induce oxidative stress, cellular damage, inflammation, and DNA disruption in exposed organisms (Lushchak, 2011). In addition, EDCs can interfere with endocrine regulation by disrupting thyroid, reproductive, and developmental hormone pathways, leading to abnormalities such as reduced fertility, altered growth, developmental deformities, and behavioral changes in wildlife (Gore *et al.*, 2015).

Climate change further intensifies the risks associated with these contaminants by altering their environmental behaviour and toxicity (Noyes *et al.*, 2009). Rising global temperatures can enhance microbial degradation and weathering processes, increasing the breakdown of plastics and releasing sorbed toxins into surrounding environments. Warmer conditions may also elevate metabolic rates in organisms, potentially increasing contaminant uptake and sensitivity (Noyes *et al.*, 2009). Extreme weather events such as floods and storms contribute to

the redistribution of sediments contaminated with legacy pollutants, spreading toxic substances into previously unaffected habitats and increasing ecological exposure.

The ecological consequences of emerging contaminants extend across multiple trophic levels. Primary producers such as algae may experience altered growth and productivity, potentially contributing to harmful algal blooms and ecosystem imbalance. Aquatic invertebrates and fish can suffer physiological and reproductive impairments, while long-term accumulation in predators may result in population declines among birds, marine mammals, and other apex species (Rochman *et al.*, 2013). For humans, exposure occurs primarily through contaminated seafood, drinking water, and food products, with studies linking chronic exposure to metabolic disorders, endocrine dysfunction, infertility, immune suppression, and increased risk of developmental abnormalities (Landrigan *et al.*, 2018).

Collectively, the growing prevalence of emerging contaminants, coupled with climate-related environmental changes, underscores the urgent need for improved monitoring, regulatory policies, and integrated toxicological assessment strategies to mitigate their long-term ecological and public health impacts.

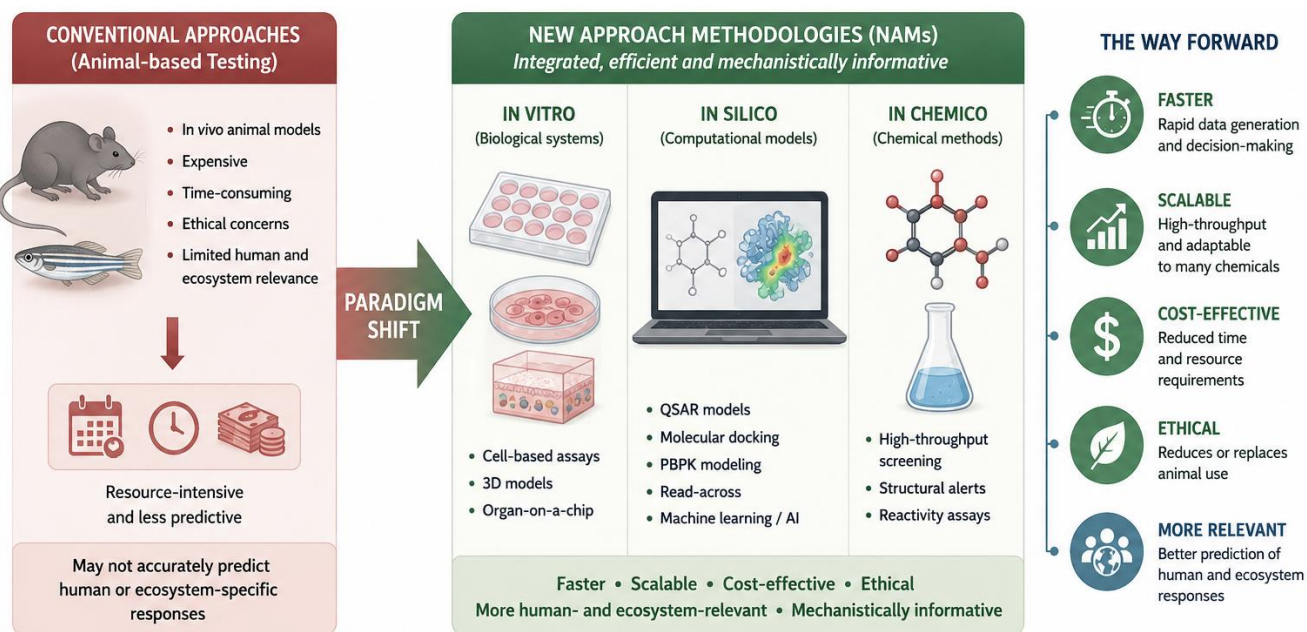
3. Paradigm Shift in Methodologies

Environmental toxicology is undergoing a significant methodological transformation with the adoption of New Approach Methodologies (NAMs), which are gradually replacing traditional animal-based testing with more efficient, ethical, and mechanistically informative alternatives (Hartung, 2009) (Figure-1). Conventional toxicological assessments have long depended on *in vivo* animal models to evaluate chemical hazards; however, these methods are often expensive, time-consuming, ethically contentious, and may not always accurately predict human or ecosystem-specific responses. In response, modern toxicology is embracing NAMs, which incorporate *in vitro*, *in silico*, and *in chemico* approaches to provide faster, scalable, and biologically relevant toxicity assessments (ECHA, 2020).

One of the most impactful innovations within this shift is high-throughput screening, which enables the rapid testing of thousands of chemicals across numerous biological endpoints simultaneously. Programs such as Tox21 utilize automated robotic platforms and cell-based assays to evaluate chemical bioactivity profiles, helping researchers identify toxicity pathways and prioritize hazardous compounds for further investigation (Kavlock *et al.*, 2012). HTS significantly accelerates hazard identification compared to traditional one-chemical-at-a-time animal studies and supports large-scale screening of environmental pollutants.

Another transformative advancement is organ-on-a-chip technology, which recreates miniature, physiologically relevant tissue environments on microfluidic chips (Bhatia & Ingber, 2014; Swapna *et al.*, 2024). These systems mimic the structural and functional complexity of living organs by integrating flowing fluids, multiple cell types, and dynamic biochemical conditions. Unlike conventional static cell cultures, organ-on-a-chip platforms better simulate *in vivo* interactions, making them valuable for studying chemical toxicity, metabolism, and tissue-specific responses under realistic biological conditions. Such systems are increasingly used to model organs like the

Figure-1. Paradigm Shift in Methodologies in Environmental biology



liver, lung, kidney, and gut for environmental and pharmaceutical toxicology studies.

Complementing experimental NAMs, computational toxicology has emerged as a powerful predictive discipline that uses computer-based modelling to estimate toxicological outcomes. Techniques such as Quantitative Structure-Activity Relationship modelling, molecular docking, and pharmacokinetic simulations allow scientists to predict absorption, distribution, metabolism, and excretion properties, receptor binding affinity, and toxicodynamic interactions of chemicals without laboratory testing (Raies & Bajic, 2016). These approaches also contribute to the development of Adverse Outcome Pathways, which map the sequence of molecular and cellular events leading from chemical exposure to adverse biological outcomes.

Furthermore, the integration of artificial intelligence (AI) and machine learning (ML) is revolutionizing toxicological data analysis by enabling advanced pattern recognition and predictive modelling from large, complex datasets such as genomics, proteomics, and metabolomics (Luechtefeld et al., 2018). AI-driven models can detect subtle toxicity signatures, forecast chronic and long-term biological effects, and predict phenomena such as epigenetic modifications, transgenerational impacts, and disease susceptibility arising from environmental exposures. These technologies enhance the precision and predictive capability of toxicological assessments, particularly for low-dose and mixture exposures.

Collectively, these methodological advancements are dramatically reducing reliance on animal testing by as much as 80–90% in certain screening pipelines while improving throughput, cost-efficiency, and relevance to human biology. This paradigm shift represents a move toward a more predictive, mechanism-based, and ethically sustainable framework in environmental toxicology, aligning scientific innovation with regulatory modernization and global efforts to promote humane research practices.

4. Modern Risk Assessment Frameworks

Modern environmental risk assessment is increasingly shifting toward integrative and mechanistic frameworks that combine advanced experimental, computational, and systems-level approaches to better predict the impacts of contaminants on organisms, ecosystems, and human health (Ankley et al., 2010). Traditional risk assessment models, which often relied on single-endpoint toxicity data and generalized exposure estimates, are now being replaced by more dynamic frameworks capable of addressing the complexity of modern environmental pollutants and multiple interacting stressors. Central to this transformation is the integration of New Approach Methodologies (NAMs) with predictive biological models to create comprehensive and evidence-based toxicity evaluation systems.

A key component of these frameworks is the application of Adverse Outcome Pathways which provide a structured model linking molecular-level chemical interactions to broader biological and ecological consequences. AOPs trace toxicity from the molecular initiating event such as a chemical binding to a receptor or enzyme inhibition through successive key events at the cellular, tissue, and organ levels, ultimately culminating in adverse outcomes at the organism, population, or ecosystem scale. By organizing mechanistic toxicological data into a biologically meaningful sequence, AOPs improve hazard prediction, facilitate regulatory decision-making, and support the interpretation of NAM-generated datasets.

The incorporation of omics technologies, including genomics, proteomics, and metabolomics, has further enhanced modern risk assessment by enabling the identification of sensitive molecular biomarkers associated with pollutant exposure and early toxic effects (Hasin et al., 2017). These high-resolution analytical tools allow researchers to detect alterations in gene expression, protein synthesis, and metabolic pathways before overt toxicity becomes visible. For instance, endocrine-disrupting chemicals have been shown to induce DNA methylation changes, histone modifications, and other epigenetic alterations, which may affect gene regulation, developmental programming, and disease susceptibility across generations (Diamanti-Kandarakis et al., 2009). Such

biomarkers provide valuable early-warning indicators of sublethal stress and chronic exposure.

To better understand ecological implications, agent-based models and ecological simulation platforms are increasingly used to predict how pollutants interact with environmental and climate-related variables across ecosystems (Grimm & Railsback, 2005; Namthabhad et al., 2014). These models simulate the behavior and interactions of individual organisms or populations within complex environments, enabling researchers to assess pollutant effects under varying scenarios such as habitat change, temperature rise, altered food webs, or combined chemical stressors. By incorporating both biological and environmental variability, ABMs improve forecasting of long-term ecological consequences, including species decline, altered trophic interactions, and ecosystem instability under pollutant-climate synergy conditions.

Regulatory agencies worldwide are actively incorporating these modern tools into chemical safety assessment frameworks. Organizations such as the United States Environmental Protection Agency and the European Chemicals Agency under REACH increasingly prioritize NAM-based evidence for chemical screening, hazard prioritization, and regulatory decision-making (ECHA, 2020; Gujjeti et al., 2014). One widely used strategy is read-across, in which toxicity data from structurally or mechanistically similar chemicals are used to predict the properties of data-deficient compounds, thereby reducing redundant testing and filling critical information gaps efficiently. This approach supports regulatory efficiency while minimizing animal use and resource expenditure.

5. Case Studies

Several recent case studies illustrate how modern environmental toxicology is increasingly applying innovative technologies and interdisciplinary approaches to better understand contaminant effects and improve environmental management.

One important example involves microplastics, which have emerged as a major global contaminant of concern. Laboratory-based *in vitro* assays using human and animal cell lines have demonstrated that exposure to microplastics can induce significant toxic effects, including oxidative stress, inflammation, and reproductive damage. In particular, studies on gonadal and reproductive cell lines have revealed that microplastic exposure may impair hormone regulation, damage gamete-producing tissues, and alter fertility-related cellular pathways (Galloway et al., 2017; Gurrupu et al., 2017). To expand the relevance of these findings beyond laboratory systems, artificial intelligence (AI)-based predictive models are increasingly being used to extrapolate toxicity data across species. These models integrate mechanistic toxicology and comparative physiology data to estimate how similar reproductive and developmental effects may occur in aquatic and terrestrial wildlife, thereby improving ecological risk forecasting.

Another compelling case concerns the interaction between climate stressors and chemical toxicity, often referred to as climate - toxin synergy. Computational and ecological modelling studies have shown that rising environmental temperatures can amplify the toxic effects of pollutants, particularly in aquatic organisms. For instance, predictive models indicate that heat-stressed fish exposed to pesticides

may experience a 20-50% increase in toxicity compared to exposure under normal thermal conditions (Noyes et al., 2009). Elevated temperatures can enhance metabolic activity, increase contaminant uptake, weaken detoxification pathways, and exacerbate oxidative stress, making organisms more vulnerable to chemical insults. These findings highlight the importance of considering climate change as a co-stressor in future toxicological risk assessments.

A third emerging application involves bioremediation strategies, such as vermicomposting, in which earthworms are used to degrade and detoxify environmental contaminants in waste materials and soils. Modern toxicological tools are now being integrated with such remediation approaches to evaluate effectiveness and ecological safety. For example, NAM-based assays have been employed to assess the ability of earthworms to reduce concentrations of endocrine-disrupting chemicals (EDCs) during composting processes, while simultaneously monitoring biomarkers of stress, enzyme activity, and contaminant degradation pathways. This integration helps optimize sustainable remediation strategies and ensures that remediation organisms themselves are not adversely affected during pollutant breakdown (Edwards & Arancon, 2004).

6. Discussion and Future Directions

The integration of New Approach Methodologies (NAMs) into environmental toxicology has significantly enhanced the ability to move from reactive hazard identification toward proactive environmental management and prevention (ECHA, 2020). These approaches provide regulators and scientists with faster, more mechanistic, and ethically sustainable tools for detecting hazards before large-scale ecological damage occurs. Consequently, NAMs are increasingly supporting progressive environmental policies, including the European Union Chemicals Strategy for Sustainability, which aims to improve chemical safety, reduce hazardous exposures, and promote sustainable innovation across industries.

Despite these advancements, several challenges remain before widespread implementation can be fully achieved. One of the major limitations is the need for validation and standardization of NAM platforms to ensure reproducibility, reliability, and regulatory acceptance across laboratories and jurisdictions. Additionally, the vast amount of toxicological data generated through omics, HTS, and computational modelling requires improved data harmonization and interoperability to facilitate integration across databases and analytical systems (Hasin et al., 2017; Al-Masri et al., 2024). Another challenge lies in scaling current methods to effectively assess complex chemical mixtures, which more accurately reflect real-world environmental exposures but remain difficult to model and test comprehensively.

Looking forward, the future of environmental toxicology is expected to involve the development of hybrid AI-NAM platforms that combine artificial intelligence, biosensors, automated toxicity screening, and predictive ecological modelling into unified systems for real-time environmental monitoring. These next-generation platforms could allow continuous surveillance of pollutants, rapid prediction of toxicity outcomes, and immediate identification of ecological threats, thereby transforming environmental risk management into a more dynamic and responsive process.

7. Conclusion

Modern environmental toxicology is rapidly evolving into a predictive, integrative, and technology-driven discipline that addresses increasingly complex environmental challenges through innovative scientific approaches. By incorporating New Approach Methodologies (NAMs), computational modelling, omics technologies, and AI-based analytics, the field has significantly improved its capacity to detect, predict, and mitigate the effects of emerging contaminants and multiple environmental stressors. These advancements not only reduce dependence on traditional animal testing but also provide more precise and human-relevant insights into toxicological mechanisms. As environmental threats become increasingly multifaceted due to pollution, climate change, and chemical complexity, the continued integration of advanced methodologies will play a critical role in strengthening global defenses against ecological degradation and human health risks, ultimately promoting long-term environmental sustainability and resilience

Competing interests:

The authors declare that they have no competing interests

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