Unraveling contaminant effects on biodiversity across scales: the macroecotoxicology perspective

Gabriel M. Moulatlet[1*], Mariana V. Capparelli[2,], Daniela M. Truchet[3], Andreu Rico[4], Fabricio Villalobos[1]

[1]Red de Biologia Evolutiva, Instituto de Ecología, A.C. - INECOL, Xalapa, Veracruz, México

[2]IMDEA Water Institute, Alcalá de Henares, Madrid, 28805, Spain

[3]UMR CNRS 6553 ECOBIO, Ecosystems, Biodiversity, Evolution, Université de Rennes, 35000 Rennes, France

[4]Institut Cavanilles de Biodiversitat i Biologia Evolutiva, Universitat de València, C/ Catedràtic José Beltrán Martinez 2, Paterna (València), 46980, Spain

*Correspondence: mandaprogabriel@gmail.com (G.M. Moulatlet)

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Abstract

With the spread of contaminants across the globe, ecosystems are increasingly exposed to pollutants at varying levels of biological organization. The effects of a wide range of contaminants on individuals have been extensively studied within the discipline of ecotoxicology, but understanding the generality of species' responses across taxa and ecosystems remains a major challenge. This is because such responses are shaped by eco-physiological, geographic, and evolutionary factors, dimensions that ecotoxicology has not been able to fully capture on its own. While these dimensions are frequently explored in macroecological studies, such research rarely considers environmental contamination as a variable capable of influencing species occurrence and distribution patterns. Here, we explore the potential of macroecotoxicology as a sub-discipline capable of integrating the core principles of both ecotoxicology and macroecology. By benefiting from recent advances in these disciplines, macroecotoxicological research would allow us to scale responses from individual organisms' sensitivity up to broader patterns of species distribution and ecosystem response, contributing to the development of predictive frameworks for biodiversity change in a rapidly transforming world.

Introduction

"(...) the critical problem in ecotoxicology is one of scaling. How do effects on individuals become aggregated to populations and to species, and how much detail do we need to document species distributions? Until such issues can be addressed, the science of ecotoxicology will be unable to deal adequately with the preservation of our life-support systems." - Simon Levin [1]

Among the main anthropogenic impacts, contamination is a key driver of biodiversity loss, with effects that are ongoing and intensifying [2–4]. In fact, the high concentrations of some contaminants in ecosystems have already exceeded the planetary boundary for chemical pollution [5], and their toxicity affects species' biology from single cell to ecosystem levels [6]. Understanding the effect of contaminants on ecosystems is the holy grain of ecotoxicology (Box 1). However, so far, ecotoxicology has focused on assessing chemical effects on individuals, primarily under laboratory conditions, and extrapolating these findings to (semi-)field conditions to estimate population-level effects with the help of models [7]. For many years, scaling up laboratory results to the landscape scale has been the main challenge of integrating ecotoxicology with other disciplines. Particularly, connecting ecotoxicology with macroecology, the discipline dedicated to understanding emerging biodiversity patterns across scales, is still hampered by technical and theoretical issues on how to associate species-level responses to contaminants with large-scale biological drivers. Fourteen years ago, acknowledging the need for scaling up contamination effects on species [8] called for the integration of both disciplines into a new subdiscipline called macroecotoxicology. While the idea was well received, the extent to which this subdiscipline has advanced remains limited. Here, we discuss the recent theoretical and methodological advances in both disciplines that will support the surge of macroecotoxicology and propose a framework and research directions to assess changes in global biodiversity patterns to contamination in a changing world.

Since the proposal of macroecotoxicology as a new subdiscipline, ecotoxicology has advanced in methods to extrapolate the sensitivity of untested species to different contaminants, to improve the link between exposure and effects on individuals and population endpoints, and in experimental knowledge and modelling tools that help extrapolate chemical effects to community and ecosystem levels, including impacts on biodiversity and ecosystem functions and services. These advances now enable the identification of species and biological traits most vulnerable to toxic pressure [9], as well as associated changes in biodiversity [10]. In turn, macroecology has seen advances in management and analysis of larger amounts of data, allowing it to test long-standing ecological questions across spatial and temporal scales [11]. Given these advances, we believe the time is ripe for macroecotoxicology to help identify emergent, large-scale patterns in ecological systems, particularly concerning species diversity, abundance, and geographic distribution [12]. We also advocate for the inclusion of contaminants in macroecological studies, as their ubiquitous presence in all ecosystems may change our view of biodiversity patterns [13]. Many efforts to bridge the gap between the impact of contaminants and their widespread effects on biodiversity exist [14–19]. Yet, to increase our predictive power for detecting changes in species distributions caused by exposure to contaminants and for how contaminants can lead to biodiversity changes [20], we propose a framework for asking relevant questions and obtaining data to understand the effect of contaminants over species distributions and global biodiversity.

Advances in Ecotoxicology

During the last few years, new approaches based on artificial intelligence algorithms [21,22] (Box 2) along with increased knowledge on taxonomic relatedness, biological traits, and novel chemical predictors have been capable of determining sensitivity endpoints (LC50, EC50 or NOECs) of a wide number of species and chemical combinations with limited biases [23–25]. These advances have opened the possibility of evaluating the impact of complex contaminant mixtures in regions where theoretical ecosystem sensitivity is unknown. In this direction, current research aims to develop similar extrapolation models to calculate toxicokinetic parameters, enabling the assessment of chemical bioconcentration and individual effects under varying exposure conditions [26]. This would provide a refined link between dynamic exposure concentration profiles and biological responses across large-scale areas. Further, agent-based models are increasingly used in prospective ecological risk assessments to evaluate how populations respond to chemicals in heterogenous environmental scenarios. These models integrate species' life-history traits and individual movement patterns to assess population dynamics under realistic, spatio-temporally dynamic exposure [26,27]. Advancements in computing power, coupled with large-scale models of contaminant fate and exposure, also allow quantifying the potential long-term impacts of pollutants on population and species dynamics at wider scales that those used traditionally by agent-based models [28], while generalized models can identify trait combinations that render species more vulnerable to chemical exposure across different environmental contexts [29].

Additionally, there has been a sharp increase in both field monitoring, encompassing biological responses and chemical stressors, and in micro- and mesocosm experiments that assess the impact of chemical exposure gradients on populations and communities [30]. Novel experimental methods allow organisms to move through heterogeneous, multicompartment environments, moving beyond the forced chemical exposure to which they are subjected in standard toxicity tests [31,32]. This enables the direct quantification of avoidance, escaping, and movement behaviors under realistic exposure scenarios. Such data is essential for understanding how chemical barriers, such as polluted river stretches or point-source contamination hotspots (e.g., wastewater effluent discharges), influence the spatial distribution of species, and can be integrated into landscape-scale evaluations [33,34].

Finally, omics studies have advanced ecotoxicology by using functional genomics to reveal novel molecular mechanisms, developing dose-dependent transcriptomics pipelines for high-throughput pathway-level testing, and applying eDNA metabarcoding to assess chemical effects on communities in mesocosms and the field [35,36]. These approaches not only improve laboratory relevance but also link ecological models to systems biology, offering a new paradigm for ecotoxicology that can consider chemical effects in heterogeneous exposure and ecological landscapes, which would allow an effective integration of macroecological principles.

Advances in Macroecology

From a methodological perspective, macroecology has improved its modeling toolkit for better understanding the effects and dynamics of both ecological and evolutionary processes on biodiversity patterns [11]. For instance, explicit consideration of spatial autocorrelation and phylogenetic effects as an intrinsic source of data structure has led to more appropriate statistical models, avoiding confounding factors. Moreover, thanks to the increasing computational capacities and data availability (e.g., geographic distributions and phylogenetic relationships for tens of thousands of species), it is now possible to apply null models that control the effect of different factors such as climatic gradients at large taxonomic and spatial scales and compare them to observed patterns (McGill 2019). Importantly, more recent modelling approaches now allow the direct evaluation of hypothesized processes (e.g., selection, dispersal, diversification) on biodiversity patterns through mechanistic computer simulations [37,38]. These mechanistic simulation models provide a deeper understanding of the role of ecological and evolutionary drivers on macroecological patterns that can be applied to different taxa and across different spatial and temporal scales.

From a theoretical point of view, macroecology has broadened its focus from taxonomic diversity, namely species richness, to other dimensions of biodiversity such as phylogenetic and functional diversities representing the evolutionary history and trait variety, respectively, of species assemblages [39,40]. Additional dimensions such as ecological interactions [41] and behavior [42] are also being investigated under a macroecological perspective. All these diversity dimensions are considered complementary and thus important to robustly study and understand biodiversity patterns across scales. Along with the recognition of different dimensions of biodiversity, macroecology is now more explicitly "evolutionary" by considering phylogenetic data and methods and being fully integrated with macroevolution to comprehensively "answer fundamental questions about biodiversity" [43,44].

Notwithstanding the advances in macroecology, including the description and evaluation of biodiversity patterns for taxa beyond charismatic groups such as tetrapods [45], several knowledge shortfalls remain that hinder our understanding of both large scale patterns and underlying processes (Hortal et al. 2015). These shortfalls are mainly related to the lack of data on several aspects of species' biology, ecology and evolution, with many recent efforts aiming at filling them [46]. However, other species' aspects remain unknown and naming them can help not only to identify them but also to foster biodiversity monitoring and conservation in a rapidly changing world [47,48]. In this vein, here we propose a new biodiversity knowledge shortfall regarding the lack of data on species responses to contamination, which we label the Carlsonian shortfall in honor of Rachel Carlson (Box 3).

How can macroecotoxicology help reveal global diversity patterns?

We define macroecotoxicology as a new subdiscipline that integrates macroecology and ecotoxicology. Macroecotoxicology aims to investigate species' responses to chemicals across broad geographic and taxonomic scales, trying to explain changes in species distribution and biodiversity patterns caused by widespread contaminants. Thus, identifying critical, unresolved questions concerning the effects of chemical contaminants on biodiversity patterns and providing powerful tools to address these questions.

Despite the growing availability of global data on chemical contamination, ecotoxicology and macroecology are unlikely to establish a comprehensive understanding of contaminant impacts if pursued independently [49,50]. True integration between these disciplines requires research questions to be formulated with an explicit acknowledgment of both ecological/evolutionary mechanisms and large-scale environmental patterns. Some of these questions may be built upon established hypotheses and theoretical frameworks from either discipline, while others should adopt a more exploratory approach, initially focusing on pattern description. From a broader perspective, macroecotoxicological research should address issues of regional to global significance, with a clear emphasis on conservation relevance. For example, global exposure data for contaminants such as PFAS, pesticides, and metals can reveal patterns that govern bioaccumulation and effects across latitudinal gradients and diverse ecological contexts [51]. Such questions must also consider how chemical contaminants can reshape biodiversity, potentially altering existing patterns and processes.

Those questions should be elaborated centering on the responses of individual species to chemical contaminants (Figure 1a), thereby establishing the species—analogous to its role in macroecology—as the fundamental analytical unit [52]. Focusing on species-level attributes enables integrating ecotoxicological responses (e.g., bioaccumulation, biomarker activity) with biological characteristics (e.g., functional traits) that are inherently species-specific. This perspective is grounded in the understanding that each species exhibits a unique combination of ecological, geographical, and evolutionary attributes [53], which collectively determine its susceptibility to chemical contamination.

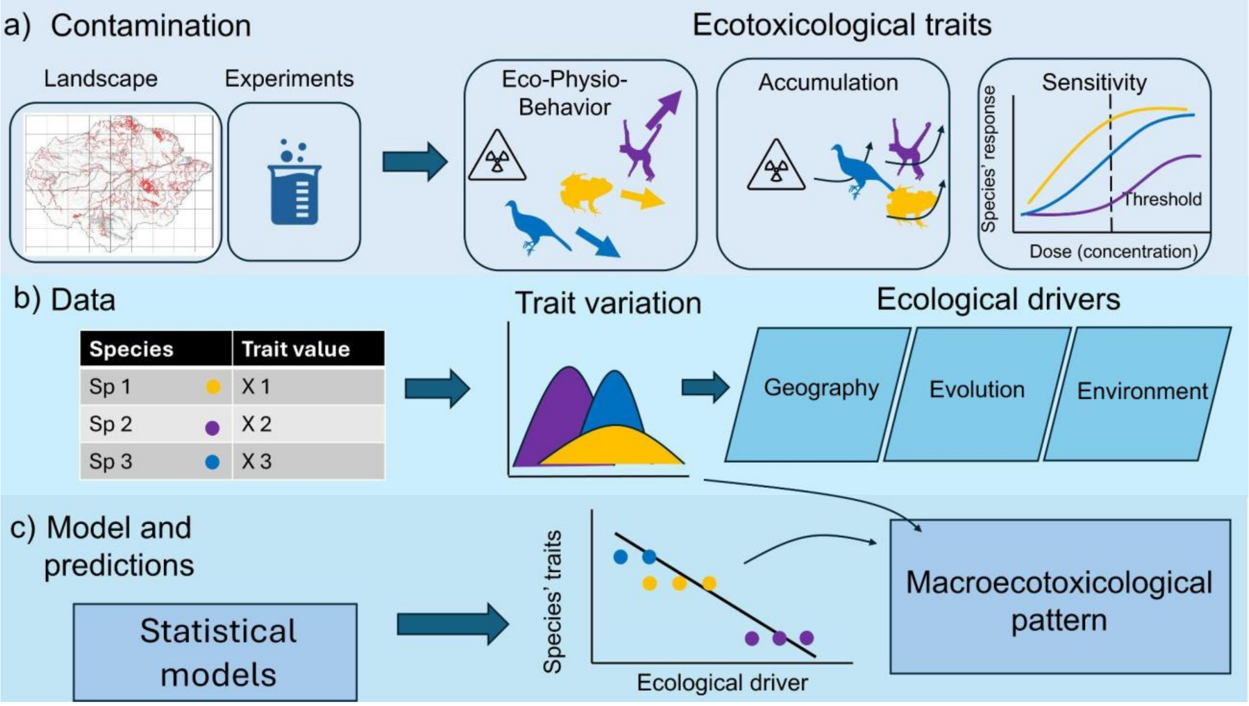

Figure 1. Integrating ecotoxicological responses into a macroecological perspective. a) Contamination can be mapped from the landscape or from laboratory experiments, from which individual species' ecotoxicological responses (e.g. sensitivity) will be obtained. Those responses are gathered into databases (b) and assigned to species-specific ecological drivers, whose variation can already be used to map macroecotoxicological patterns. Prediction can be done using statistical models (c) that control for sources of heterogeneity when modelling macroecotoxicological patterns by using ecological drivers as predictors.

Macroecotoxicology should emphasize the use of ecotoxicological traits (e.g., bioaccumulation capacity), while life-history traits can be incorporated to assess the likelihood of contaminants affecting species from similar functional or phylogenetic groups, or to assess long-term vulnerability (i.e., capacity to avoid exposure and to recover from pulsed exposures) [51,54]. Ecotoxicological traits should then be linked to species-specific biological traits (Figure 1b), creating new predictive opportunities for evaluating the geographical, evolutionary and ecological dimension of contaminant impacts on biodiversity patterns [13].

Which are the ecotoxicological traits that can be used in macroecotoxicology?

The presence of chemical contaminants in organism tissues and their surrounding environments serves as a clear indicator of exposure and potential ecological impact [55]. In contrast, species sensitivity to contaminants represents measurable biological responses to chemical stressors and we therefore proposed them as the primary response variables in macroecotoxicology (Figure 1a). Other ecotoxicological endpoints—such as mortality, growth inhibition, or behavioral alterations—also provide valuable information on contaminant effects, although they are not considered biomarkers *sensu stricto* [56]. Within the macroecotoxicological framework, individual-level responses are aggregated at the species level, mirroring macroecology, where traits measured in individuals capture within-species variation but are ultimately summarized (e.g., averaged) to the species level for large-scale assessments [40,57].

Chemical pollution affects growth, reproduction, behavior, and fitness, ultimately contributing to biodiversity shifts. Organisms respond through conserved molecular pathways collectively termed the “chemical defensome”, including efflux transporters, antioxidant systems, transcription factors, and biotransformation enzymes [34]. Although many components of the defensome are evolutionarily conserved, their expression and effectiveness vary across taxa and environmental contexts. Behavioral responses, particularly spatial avoidance, can be viewed as an extension of these defense mechanisms at the organismal level. Therefore, macroecotoxicological approaches should explicitly acknowledge that toxicity thresholds and exposure regimes are context-dependent and shaped by spatiotemporal heterogeneity, movement behavior, and multilevel biological responses. Incorporating these dynamics will strengthen the ecological realism and predictive credibility of the proposed framework.

Sources of heterogeneity and predictions

Ecotoxicological traits are not fixed in space and time, but quite variable depending on the environmental conditions, fate of the contaminants, and the media where they are found. Moreover, intraspecific variation is expected due to the environmental conditions, level of contamination (and the interaction between both) on which populations of the same species are exposed. Macroecology deals with such variation by using statistical and quantitative methods to account for population or other sources of variation, thus we proposed that similar methods be used in macroecotoxicology (Figure 1c). For instance, intraspecific population variability can be controlled in the random term of mixed models [58,59].

Many ecotoxicological assessments implicitly assume homogeneous and static exposure. In reality, both contaminants and organisms are distributed nonrandomly across heterogeneous environments. Most toxicity evidence derives from laboratory tests that restrict organism movement and impose uniform exposure conditions. While foundational, such approaches may underestimate the dynamic spatiotemporal interactions that shape real-world wildlife–pollution relationships. [33] propose a three-pronged framework integrating *in silico* spatial modeling of exposure and effects by using toxicokinetic and toxicodynamic models, laboratory experiments allowing movement, and field-based tracking of free-ranging organisms to better capture these dynamics. Advances in telemetry, remote sensing, and computational modeling now make such integration feasible.

Importantly, ecotoxicological data, ranging from environmental concentrations of chemicals across different matrices to laboratory exposure levels and associated toxicological responses, is not standardized (e.g., concentration units, endpoints), and integration into macroecotoxicology requires making use of statistics that help achieve generality, but on the risk of losing ecological specificity.

Emergent biodiversity patterns that can be detected by macroecotoxicology

The synthesis of individual responses to contaminants—as obtained from ecotoxicology—with their intrinsic relationship to geographical, evolutionary, and ecological drivers—as obtained from macroecology—allows for the mapping of biodiversity patterns under the lens of macroecotoxicology. Here, we present three examples of classic biodiversity gradients and frame them within a macroecotoxicological approach to explore how chemical pollution may reinforce or disrupt these established patterns (Figure 1c):

1. Variation in species sensitivity or vulnerability to contamination along latitudinal gradients. The Latitudinal Diversity Gradient (LDG) refers to the well-established pattern of increasing species richness from temperate (higher-latitude) to tropical (lower-latitude) regions, a trend consistently observed across most taxa [60]. This global biodiversity pattern may be influenced by the uneven spatial distribution of chemical contaminants, as they may cause direct mortality or impair the ecophysiological functions of exposed organisms, leading to local biodiversity loss and potentially altering the LDG itself [61,62]. Understanding how species sensitivity to contamination intersects with the LDG, or any geographic pattern for that matter, is therefore critical for anticipating biodiversity responses under intensifying global pollution [51].

2. Variation in functional traits across space is often described by ecogeographical rules, such as Bergmann's rule, the tendency of species to exhibit larger body sizes in colder (typically higher latitude) environments, and Rapoport's rule, the tendency of species' geographic range sizes to increase towards higher latitudes [63]. These spatial patterns reflect adaptations to broad-scale environmental gradients. However, environmental chemical contamination has the potential to disrupt these patterns by altering the expression of functional traits. For instance, recent studies have shown that exposure to metals can influence organismal size, with smaller body sizes commonly observed in taxa inhabiting highly contaminated environments [64,65]. On the other hand, size is also one of the most important traits to classify invertebrates' sensitivity to insecticides [66]. These findings suggest that contaminants may act as additional selective pressures, modifying established ecogeographical trends and potentially reshaping trait geographical variation at regional and global scales.

3. Variation in species interactions within and across ecological networks (e.g., food webs) is fundamental to maintaining ecosystem structure and functionality [67,68]. When contaminants are incorporated into these networks, they can disrupt ecological interactions, alter trophic dynamics, and ultimately compromise the integrity of the network's structure [69–71]. The hypothesis is that more complex food webs (in the tropics) will be more stable to chemical pollution, although the percentage of species extinctions may be larger [72]. This has been demonstrated empirically, and macroecotoxicology could test for such hypotheses at regional to global scales using experiments and models. The varying persistence of certain chemical contaminants in the environment further exacerbates these disruptions by driving shifts in community composition [73]. These changes can reduce ecological complexity and destabilize ecosystem functioning, all of which can be documented at large spatial and taxonomic scales by considering different ecological networks across geographic/environmental gradients.

Concluding remarks

A central challenge in ecotoxicology has been understanding the effects of diverse chemical contaminants while scaling information obtained at the individual species level to broader ecosystem-level responses [74]. Macroecotoxicology embraces this issue as an initiative seeking an interdisciplinary synthesis between ecotoxicology and macroecology, encouraging collaboration across these fields. Macroecotoxicology warrants further development to address critical knowledge gaps in how chemical contamination influences biodiversity, enabling the scaling of (sub)organismal effects to regional and global levels.

The general macroecotoxicology framework begins by formulating research questions that explicitly address the effects of contaminants on emergent biodiversity patterns. One or more contaminants of interest and their potential impacts on biodiversity can then be selected, ideally encompassing multiple species across broad geographic scales. The knowledge gained from field monitoring and ecosystem modeling is poised to elevate macroecotoxicology to the next level, where species interactions and shifts in abiotic parameters will feed back into species distributions across complex landscapes. The subsequent step involves quantifying species' responses using known and novel toxicity endpoints, bioaccumulation data, and biomarkers, either from existing ecotoxicological datasets, through targeted literature reviews or by using taxonomy or trait-based extrapolation models. Finally, the framework can be applied to evaluate how contamination may influence biodiversity patterns, thereby linking species-level ecotoxicological responses to large-scale ecological and evolutionary processes (Figure 1).

It is important to acknowledge that macroecotoxicology is not a panacea for contamination crisis, as contamination is spreading faster than our research and our ability to understand its consequences and how it is reshaping biodiversity patterns [75]. Nevertheless, considering that contamination may represent an underrecognized driver of species distribution shifts and given the extensive datasets already available on contaminants and biodiversity, there is a timely opportunity to advance macroscale analyses that integrate ecotoxicological and macroecological perspectives. We contend that the time is ripe to formally establish macroecotoxicology as a subdiscipline capable of tackling some of the most urgent ecological challenges of the Anthropocene.

BOX 1: A brief history of ecotoxicology development and current approaches

The term ecotoxicology was introduced and studies began in the 1960s, initially inspired by Rachel Carson's influential book *Silent Spring* and later formalized by René Truhaut in 1969 [75]. From its inception, ecotoxicology has been a multidisciplinary science, combining elements of ecology and toxicology, and integrating a wide array of fields, including biochemistry, physiology, bioinformatics, biostatistics, and, more recently, the omics sciences. It has focused on the study of the exposure, accumulation, and effects of environmental stressors across multiple levels of biological organization, from molecules, cells, and organs to whole organisms, populations, communities, and ultimately ecosystems and the biosphere [50].

The primary objective of ecotoxicology remains to understand and predict the effects of contaminant-induced stress on ecological systems. Although more complex approaches involving multiple species are increasingly used in ecotoxicology, single-species and single-contaminant test batteries remain the primary tool for ecotoxicological assessments and continue to underpin the development of environmental regulations [76]. These tests encompass a broad range of toxicant modes of action, making them valuable for predictive effect evaluations [77]. Current ecotoxicological approaches still rely largely on the assessment of biochemical biomarkers, particularly those related to oxidative stress. These biomarkers quantify the measurable effects of contaminants primarily at the individual and population levels, both in field and laboratory settings [56]. However, this bottom-up approach, which extrapolates individual-level responses to predict ecosystem-level outcomes, has long been a challenge in ecotoxicology [1], as it may fail to capture consistent patterns across spatial and temporal scales.

Ecotoxicological methods have traditionally relied on standardized toxicity testing to quantify organismal tolerance thresholds, commonly expressed as LC_{50} or EC_{50} values, or as no-observed-effect concentrations (NOEC) derived from biological responses and biomarkers under controlled laboratory conditions. These approaches have been instrumental in establishing regulatory benchmarks and enabling cross-study comparability. However, because standardized protocols are typically developed for a limited number of model organisms and well-characterized contaminants, the resulting datasets are unevenly distributed across taxa and chemical classes. As a consequence, extrapolating toxicological knowledge to untested species and emerging contaminants remains one of the central challenges in ecotoxicology.

In recent decades, the field has expanded to include contaminants of emerging concern, such as nanoparticles, newly synthesized pesticides, antibiotics, complex pharmaceuticals, and micro- and nanoplastics [50]. At the same time, it has increasingly been recognized that chemical pollution does not act in isolation. Major global stressors—including climate change, habitat modification, eutrophication, and overexploitation—interact with contaminant exposure in complex and often non-linear ways. Addressing the combined and potentially synergistic effects of chemical and climate-related stressors represents a critical frontier for contemporary ecotoxicology.

Importantly, ecotoxicology is not limited to laboratory-based threshold testing. Long-standing field-integrated frameworks, such as the Sediment Quality Triad (SQT), explicitly combine chemical analyses, toxicity bioassays, and benthic community assessments to evaluate the ecological consequences of contaminated sediments [78]. By integrating chemistry, organism-level toxicity, and in situ community structure, the SQT captures mixture effects and the influence of natural environmental variables (e.g., sediment grain size, salinity, organic matter) in ways that single-species endpoints alone cannot. Since its development, the SQT approach has been refined and adapted across ecosystems and stressor types [79,80], demonstrating the field’s capacity to incorporate ecological realism into risk assessment.

Building on these foundations, an important opportunity lies in connecting ecotoxicological datasets with large functional trait databases—encompassing ecological, morphological, life-history, dietary, and habitat-related characteristics across taxa (e.g., TRY, FishBase, AmphiBIO, PanTHERIA, AVONET, MarLIN). Integrating trait-based ecological information with toxicological endpoints would not replace existing risk assessment frameworks but would expand their analytical scope. Such integration could improve cross-taxon comparability, help identify trait-mediated sensitivity patterns, and enable broader-scale analyses of vulnerability across environmental gradients. Ultimately, this combined approach could strengthen our capacity to detect macroecotoxicological patterns while remaining grounded in empirically validated field and laboratory methods.

Where to find the available ecotoxicological data?

As concern about contaminant-driven biodiversity change grows, several authors have called for the integration of ecotoxicological data into large, publicly accessible repositories such as the ECOTOXicology Knowledgebase (ECOTOX) [81] and the Curated Aquatic Toxicology Database (EnviroTox) [82]. These initiatives represent important steps toward harmonizing information generated by individual studies into unified datasets. Given that data sharing is still not a universal practice in ecotoxicology [83], such databases are essential foundations for advancing comparative and large-scale analyses.

The current structure of these repositories reveals important limitations. Most entries prioritize taxonomic descriptors (e.g., species name, genus, class) and standardized toxicological endpoints, while ecological metadata remains sparse. Functional traits, trophic position, life-history strategy, body size, and physiological characteristics are rarely incorporated in a systematic way. The absence of this contextual information constrains cross-species comparability and limits the integration of ecotoxicology with macroecological theory. Expanding database architectures to include trait-based and ecological descriptors would substantially enhance their utility for macroecotoxicological analyses.

Beyond harmonized databases, valuable cross-taxonomic information can be retrieved from bibliographic repositories such as Google Scholar and Web of Science, particularly for endpoints such as bioaccumulation [51]. Nevertheless, reliance on literature mining introduces additional heterogeneity in methodologies, reporting standards, and exposure conditions. Broader adoption of open science principles and standardized data reporting in ecotoxicology [84] would significantly increase the availability and comparability of primary datasets, facilitating regional and continental-scale syntheses. Incentivizing the publication of raw experimental data, rather than summary statistics alone, is particularly important given that species-level contamination response data remains unavailable for the vast majority of taxa.

Despite these advances, current ecotoxicological datasets exhibit substantial structural biases that constrain the immediate feasibility of large-scale macroecotoxicological forecasting. Strong taxonomic bias persists, with disproportionate representation of model organisms such as *Daphnia magna*, *Danio rerio*, and a limited set of standardized laboratory species. In contrast, marine invertebrates, wild plant species (including macrophytes), tropical taxa, and threatened species remain markedly underrepresented. Geographic bias constitutes an additional constraint. A large proportion of available data originates from Europe, North America (Global North), and, more recently, China, while Africa, South America, and many tropical and biodiversity-rich regions remain sparsely represented. Such spatial imbalance reduces the capacity to generalize findings across climatic gradients and socio-environmental contexts, and it complicates the development of globally applicable predictive frameworks.

Chemical bias further restricts potential extrapolation. Toxicological assessments are heavily concentrated on metals, legacy pesticides, hydrocarbons, and a relatively small subset of pharmaceuticals and modern pesticides. Thousands of emerging contaminants lack standardized ecotoxicological profiles, creating significant uncertainty in any attempt to construct global-scale predictive models. Taken together, these structural constraints indicate that the current database infrastructure is not yet sufficient to fully support robust global macroecotoxicological forecasting for a wide array of daily-use chemicals. Rather than providing an immediate operational predictive framework, macroecotoxicology should be viewed as a long-term research agenda that requires coordinated data harmonization, expansion of taxonomic and geographic coverage, incorporation of ecological metadata, and rigorous uncertainty quantification. Nonetheless, existing databases constitute an essential starting point. When used critically acknowledging methodological limitations, structural data inequalities, and technical barriers, they offer a foundation upon which more integrative and predictive macroecotoxicological approaches can gradually be developed.

BOX 2. The role of artificial intelligence (AI) and machine learning (ML) in macroecotoxicology

The predictive potential of macroecotoxicology could be substantially strengthened by integrating emerging AI and ML approaches. In ecotoxicology, recent studies have demonstrated that ML models trained on individual toxic responses can successfully predict mixture toxicity under environmentally realistic conditions, outperforming classical concentration addition and independent action models when the mode of action is unknown [85]. Rather than relying exclusively on mechanistic assumptions, these approaches learn empirical relationships between individual and combined responses. However, their predictive reliability remains contingent upon the representativeness and breadth of training datasets, and their transferability across chemical domains and ecological contexts requires further evaluation [85].

Extending this logic to macroecotoxicology would involve moving beyond the description of spatial patterns toward explicitly validated predictive frameworks [46]. For example, spatially explicit ML models could integrate land-use data, agricultural intensity, livestock density, climatic variables, estimated contaminant loads, and species functional traits to forecast regional vulnerability, biodiversity loss, or functional homogenization. Crucially, such models would need independent validation datasets, cross-regional testing, and explicit uncertainty propagation to ensure robustness and avoid overfitting to geographically biased data.

Similarly, predictive models could integrate species traits (e.g., body mass, metabolic rate, life-history strategy), environmental parameters (temperature, soil/sediment properties, water chemistry), and contaminant exposure metrics to estimate expected sensitivity at broader ecological scales. This approach would reconnect functional macroecology with ecotoxicology and analytical chemistry, allowing trait-mediated vulnerability to be tested rather than merely inferred.

In the context of species responses under chemical pressure, macroecotoxicology could integrate species distribution models with contaminant exposure layers to evaluate niche contraction, range shifts, or altered suitability under combined climate and chemical stressors. Importantly, predictive performance should be assessed through out-of-sample forecasting, temporal validation, and quantification of model uncertainty. Addressing uncertainty propagation, data imbalance, and limits to transferability across taxa and regions is essential before claims of forecasting biodiversity change can be fully supported.

Therefore, while macroecotoxicology currently provides a conceptual framework that links biodiversity patterns with contaminant pressures, its predictive capacity will depend on rigorous model validation, transparent uncertainty analysis, and the development of transferable, multiscale datasets.

BOX 3: A new knowledge shortfall?

We identify a novel type of biodiversity knowledge shortfall [86]: the lack of information on species' responses to chemical contaminants across spatial and taxonomic scales. As knowledge on the fate and distribution of chemical contaminants is advancing rapidly [74,87,88], the understanding of the impacts of these contaminants on biodiversity, including humans [89], is still largely unknown [90,91]. This is partly due to the rapid production and release of new chemicals into the environment [20], but also to the fact that the impact of contaminants has been re-addressed over time, so chemical contaminants that were supposedly harmless to the biota and have been applied in industrial products for years, are now known as extremely toxic [92].

Altogether, the listed ecotoxicology databases in this opinion paper comprise ~17,000 species of 590 orders and ~18,000 chemicals. It represents a huge effort but still contains information for a relatively minor number of existing species. We do not intend to report an exhaustive search for ecotoxicological responses, but to explicitly acknowledge our ignorance of the effect of chemical contaminants on the biodiversity of ecosystems, the known unknown. Therefore, we propose the *Carlsonian* shortfall as a new knowledge shortfall to be added to the existing ones, named after Rachel Carlson, the pioneer in addressing contaminant bioaccumulation and endocrine disruptions in birds and in the fight for a responsible development of new chemicals [93]. Importantly, this is the first shortfall named after a woman, acknowledging gender inequality in STEM.

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