REVIEW

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Emerging contaminants: A One Health perspective

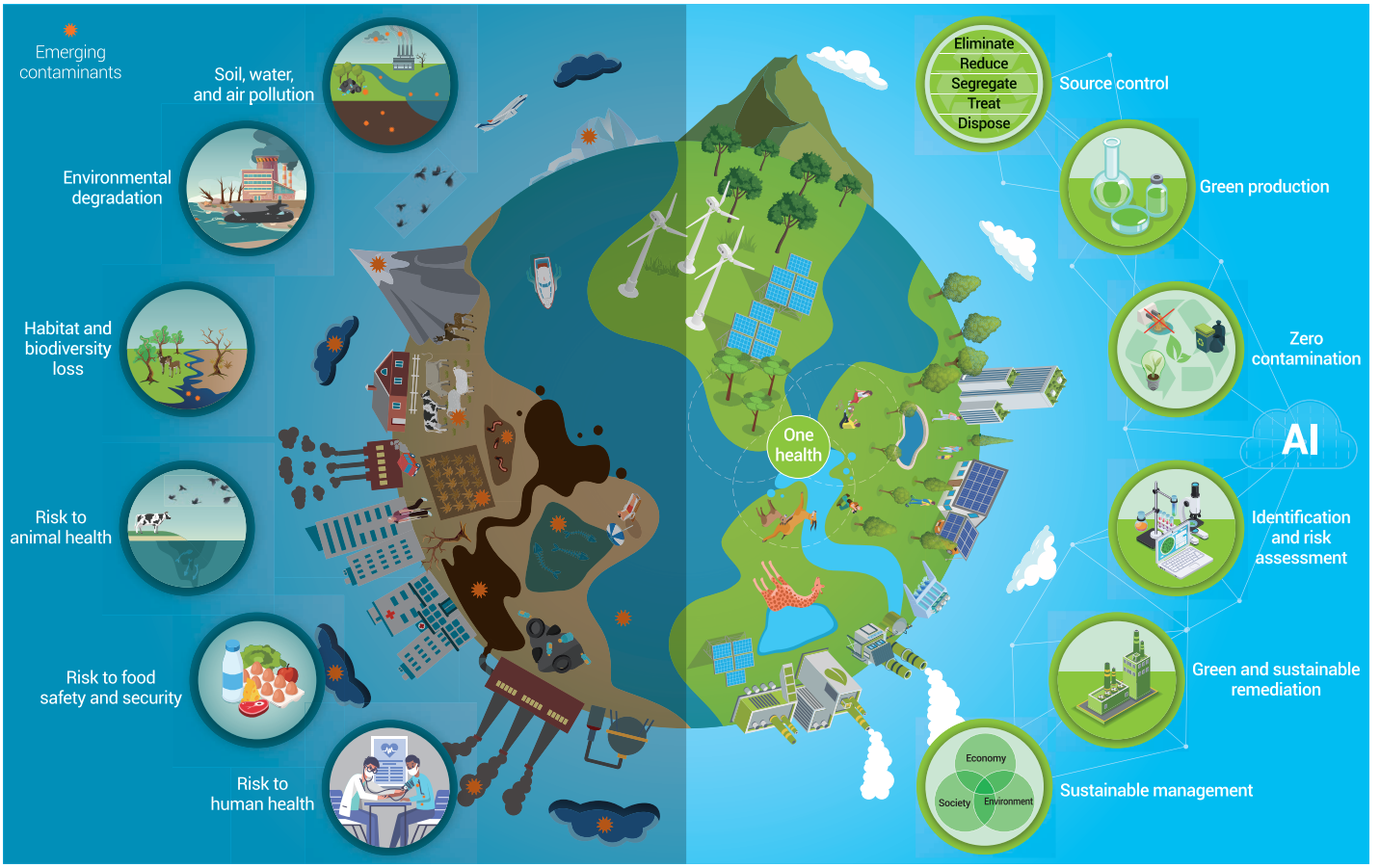
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GRAPHICAL ABSTRACT



PUBLIC SUMMARY

- The global economy stimulates the continuous production and release of new chemical and biological agents that challenge global health and sustainability.
- Integrating green and benign-by-design principles into production processes is crucial for eliminating hazardous materials from global supply chains.
- Emerging environmental management practices are essential for environmental restoration and promoting global health and sustainability.
- This review explores the sources of emerging contaminants and their impact on planetary health, with an emphasis on source control and remediation strategies.
- Adopting a One Health approach through interdisciplinary collaboration is essential for addressing emerging contaminants and their complex impacts.

REVIEW

Emerging contaminants: A One Health perspective

Fang Wang,[1,2,*] Leilei Xiang,[1,2] Kelvin Sze-Yin Leung,[3,4] Martin Elsner,[5] Ying Zhang,[6] Yuming Guo,[7] Bo Pan,[8] Hongwen Sun,[9] Taicheng An,[10] Guangguo Ying,[11] Bryan W. Brooks,[12,13] Deyi Hou,[14] Damian E. Helbling,[15] Jianqiang Sun,[16] Hao Qiu,[17] Timothy M. Vogel,[18] Wei Zhang,[19] Yanzheng Gao,[20] Myrna J. Simpson,[21] Yi Luo,[9,22] Scott X. Chang,[23] Guanyong Su,[24] Bryan M. Wong,[25] Tzung-May Fu,[26] Dong Zhu,[27] Karl J. Jobst,[28] Chengjun Ge,[29] Frederic Coulon,[30] Jean Damascene Harindintwali,[1,2] Xiankui Zeng,[31] Haijun Wang,[32] Yuhao Fu,[1,2] Zhong Wei,[33] Rainer Lohmann,[34] Changer Chen,[11] Yang Song,[1,2] Concepcion Sanchez-Cid,[35] Yu Wang,[1,2] Ali El-Naggar,[36,23] Yiming Yao,[9] Yanran Huang,[37] Japhet Cheuk-Fung Law,[3] Chenggang Gu,[1,2] Huizhong Shen,[26] Yanpeng Gao,[10] Chao Qin,[20] Hao Li,[8] Tong Zhang,[38] Natàlia Corcoll,[39] Min Liu,[40] Daniel S. Alessi,[41] Hui Li,[19] Kristian K. Brandt,[42,43]

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Environmental pollution is escalating due to rapid global development that often prioritizes human needs over planetary health. Despite global efforts to mitigate legacy pollutants, the continuous introduction of new substances remains a major threat to both people and the planet. In response, global initiatives are focusing on risk assessment and regulation of emerging contaminants, as demonstrated by the ongoing efforts to establish the UN's Intergovernmental Science-Policy Panel on Chemicals, Waste, and Pollution Prevention. This review identifies the sources and impacts of emerging contaminants on planetary health, emphasizing the importance of adopting a One Health approach. Strategies for monitoring and addressing these pollutants are discussed, underscoring the need for robust and socially equitable environmental policies at both regional and international levels. Urgent actions are needed to transition toward sustainable pollution management practices to safeguard our planet for future generations.

INTRODUCTION

Before the Industrial Revolution, naturally occurring pathogens, including bacteria, fungi, and viruses, were the primary contaminants of concern, presenting threats to both human and ecosystem health.[1] However, industrialization brought about significant changes in pollution patterns, introducing new contaminants into the environment such as heavy metals, industrial chemicals, and particulate matter. With the onset of the Anthropocene, humans have increasingly depleted natural resources and developed new chemical molecules, or novel entities, in pursuit of global development, resulting in waste streams transgressing planetary boundaries, disrupting natural ecosystems,[2,3] and inducing changes in agricultural practices, which led to the evolution of wild-type pathogens.[4] Various geogenic chemicals, encompassing metal(loid)s and other hazardous substances, are consistently discharged into the environment through diverse anthropogenic activities such as mining, mineral processing, energy production, construction, and agriculture.[5]

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Beyond geogenic chemicals, the production of synthetic chemicals has surged since the mid-twentieth century, marking what is often referred to as the second chemical revolution (i.e., unprecedented development and use of novel synthetic chemicals).[6] This surge is shown by the rapid growth of the Chemical Abstract Service Registry, which grew from 20 million in 2002 to over 204 million by 2023, suggesting an addition of nearly 15,000 new chemicals daily.[7] Moreover, there has been a significant rise in efforts to genetically modify microorganisms.[8,9] While synthetic chemicals and genetically engineered microorganisms have contributed positively to human well-being by facilitating the development of new drugs and advanced materials and enhancing agricultural productivity,

concerns have been raised over their risks to public health and the environment. Persson et al.[10] recently highlighted that humanity has exceeded the planetary boundary, or safe operating space, for anthropogenic chemicals, as the rate of chemical production outpaces the rate of hazard assessments and the establishment of regulatory measures. Similarly, Bernhardt et al.[11] argued that synthetic chemicals are agents of global change.

Emerging contaminants (ECs), also referred to as contaminants of emerging concern (CECs), are newly identified synthetic or naturally occurring chemicals or biological agents that are detected in the environment and potentially hazardous or recently determined to be hazardous to humans and ecosystems. The risks associated with these contaminants are not fully understood. They may include pharmaceuticals and personal care products (PPCPs), per- and poly-fluoroalkyl substances (PFAS), emerging pathogens, cyanotoxins and other natural toxins, pesticides, industrial chemicals, micro/nano plastics, nanomaterials, antibiotic resistance genes (ARGs), and other exogenous substances that are found in the environment but are not yet well understood in terms of their impacts on humans and natural ecosystems.[12–14] These contaminants can enter the environment through various pathways, such as industrial discharge, agricultural runoff, and improper waste disposal, leading to air, water, soil, and food contamination. They can become part of complex mixtures of chemical pollutants and biological hazards.[7] Furthermore, these ECs have the potential to undergo additional transformation and long-range transport, creating unforeseen and uncharacterized chemicals and causing chemical pollution in areas distant from the source.[15]

Pollution continues to pose a significant global threat, resulting in millions of premature deaths annually[16,17] and widespread environmental degradation.[5] Concurrently, thousands of species are facing extinction. These alarming challenges underscore the pressing need for comprehensive strategies to address the interconnected environmental and human health issues.[18] Adopting a One Health perspective recognizes the interconnectedness of human health, animal health, and the environment, emphasizing the need for collaborative efforts to address EC issues. By leveraging expertise from various fields such as medicine, veterinary science, environmental science, and public health, integrated approaches will reduce risks linked to ECs and enhance the well-being of all organisms. In addition, it is timely to integrate an Indigenous world-view as the One Health concept is deeply embedded in their wider relationships with the environment. Indigenous people consider that all animate and inanimate, physical and metaphysical phenomena are connected through elaborate and complex webs of relationships.[19] While focusing on ECs is crucial, dealing with existing legacy pollutants is equally important. Innovative approaches such as green chemistry, machine learning, and interdisciplinary cooperation are essential to overcome these challenges. Moreover, educational reforms are crucial to preparing future generations to effectively address environmental and health crises.[20]

In this review, we provide a holistic perspective on ECs, which are recognized as significant threats to human health and the sustainability of ecosystems. Through the One Health approach lens, we acknowledge the intricate connections among the health of people, animals, plants, and our shared environment. Our focus encompasses the production, utilization, and dissemination of ECs in everyday life, emphasizing their potential adverse effects, whether encountered individually or with other pollutants. These effects span various environments, affecting human health and the well-being of animals, plants, and microorganisms. We investigate methods for detecting and analyzing ECs, critically assess regulatory frameworks and policies, and propose innovative solutions to reduce their detrimental impacts on human and environmental health. By adopting the One Health approach, we underscore the necessity for a collaborative, multisectoral, and transdisciplinary response to effectively address challenges posed by ECs and to promote a sustainable and healthy future for all forms of life.

HISTORICAL PERSPECTIVE OF ECs

Since the mid-twentieth century, the global socio-economic landscape has undergone a profound transformation, marked by a surge in industrial activity and technological advancement. This period has seen a dramatic rise in the extraction and utilization of natural resources, particularly critical minerals and petrochemicals, which are indispensable for expanding industrial sectors and the broader modernization process. The repercussions of this intensified resource exploitation have been far reaching, leading to modifications in geochemical cycles and the distribution of metals.[21] Moreover, this era has been characterized by the synthesis, use, and release of novel chemical compounds, many of which persist in the environment and have the potential to accumulate biologically, thus emerging as new environmental contaminants.[22]

The toxicity of metal(loid)s, such as lead, mercury, cadmium, arsenic, cobalt, and chromium, as well as organic pollutants such as dichlorodiphenyltrichloroethane (DDT) and polychlorinated biphenyls (PCBs), has long been recognized.[5] Some of these pollutants have been banned or had limits imposed on their use due to their adverse environmental and health effects, prompting efforts to regulate their concentrations in water, soils, and other environmental media.[23] Although much is understood about legacy contaminants, ongoing advances in analytical technology and toxicology continue to reveal new risks to human health and the environment posed by ECs, enabling a better understanding of the sources, persistence, bioaccumulation potential, mobility, and toxicity of such contaminants.

The increasing focus on environmental pollution has led to the identification of substances that have transitioned from being celebrated as beneficial chemicals to contaminants of significant concern. Examples of such evolving contaminants include plastics and their by-products, atrazine, triphenyl phosphate, tungsten, PFAS, chlorofluorocarbons, neonicotinoids, glyphosate, and many others (Table 1). This evolution is attributed to improved detection capabilities for inorganic and organic contaminants at trace levels and a better understanding of their wider ecosystem and health effects (Figure 1).

Nowadays, significant attention has been devoted to addressing a wide array of ECs, which nowadays extends beyond newly introduced substances to include CECs, which have been present for some time but have recently garnered attention due to their potential impacts. As of February 2024, the US Environmental Protection Agency (EPA) Toxic Substances Control Act (TSCA) Chemical Substance Inventory contains 86,741 potentially hazardous chemicals, with 42,293 currently commercially active.[24] Additionally, as a network of reference laboratories, research centres and related organisations for monitoring of emerging environmental substances, the NORMAN has identified over 700 of the most discussed ECs.[25] Further, Wang et al.[1] identified that over 350,000 chemicals and chemical mixtures have been registered for commercial use around the world. The continuous expansion of these inventories is expected due to the ongoing discovery of new substances and increased scrutiny of existing ones. Herein, a One Health approach is particularly relevant to the assessment and management of ECs.[26–28] In the subsequent sections, we will focus on prominent emerging contaminants categorized based on their current attention and potential concern (Table 1).

PRODUCTION, USE, AND ENVIRONMENTAL RELEASE OF ECs

Production and use of ECs

Over the last century, global population growth, fueled by industrialization and urbanization, has spurred increased demand for consumer goods. Consequently, industries producing these goods, such as pharmaceuticals, household products, and plastics, have expanded significantly.[50] The extensive use and improper disposal of these products have led to their omnipresence in the natural environment, causing continuous contamination with potentially harmful chemicals from diverse sources.[51] Taking plastics as an example, their global production has surged to 460 million tons (Mt) in 2019 from 234 Mt in 2000, resulting in a doubling of plastic waste generation over the past two decades.[52] This increase in plastic production and consumption has contributed to the proliferation of micro/nano-plastics in various ecosystems. While microplastics (MPs) only account for 12% of plastic waste in the natural environment, they are of significant concern because of their potential long-term impacts on ecosystems and organisms.[52,53] Over time, larger plastic particles can break down into micro/nanoplastics through mechanical action and biological fragmentation (including microbial degradation and grind by metazoa during ingestion), leading to the continuous accumulation of these particles.[54–56] This pollution is considered irreversible due to the lasting environmental impact long after the elimination of plastic emission sources.[56]

PPCPs represent one of the largest groups of ECs, encompassing a wide array of compounds with diverse chemical and physical properties. These substances are commonly used in daily life for various purposes, including human and animal healthcare. With over 50,000 different types of PPCPs currently produced

Table 1. List of prominent ECs categorized based on their current attention and potential concern

Categories	Secondary categories	Examples of emerging contaminants
Organic emerging contaminants	Endocrine-disrupting compounds (EDCs)	17-Alpha-ethinylestradiol (EE2) [29], 17-Beta-estradiol (E2) [29], Estrone (E1) [29] Steroid hormones [30], Phthalate acid esters (PAEs), Bisphenols [31]
	Food and feed additives	2,6-Ditert-butyl-4-methylphenol [29]
	Persistent organic pollutants (POPs)	Brominated flame retardants [32], Polychlorinated biphenyls (PCBs) [31], Polycyclic aromatic hydrocarbons (PAHs) [33], Dichlorodiphenyltrichloroethane (DDT) [34], Perfluorinated chemicals [34], Polybrominated diphenyl ethers (PBDEs) [35,36] Per- and Polyfluoroalkyl Substances (PFAS) [37]
	Pharmaceuticals and personal care products (PPCPs)	Disinfectants: Disinfection (Byproducts, Chlorate, Formaldehyde) [37], Pentachlorophenol and its salts and esters [32], Diclofenac [29]; Cosmetics: 2-Ethylhexyl 4-methoxycinnamate [29]; Analgesics and anti-inflammatories [38]: Flumequine, Trimethoprim, Ketorolac, Pain reliever, Illicit drugs [39], Antibiotics [32], Macrolide antibiotics [29]
	Surfactants [40]	
	Organic solvents/plastic additives	Hexachlorobutadiene [32], Dechlorane plus (both cis and trans isomers), Dichloromethane [32], Chloroform [32], Nonylphenols [32]
	Pesticides [30] and Herbicides	Methiocarb [29], Neonicotinoids [29], Oxadiazon [29], Tri-allate [29], Perchlorate [37], Dicofol [32]
	Cyanotoxins [37]	Microcystin(s) [37], Cylindrospermopsin [37], Anatoxin(s) [37], Saxitoxin(s) [37]
Inorganic emerging contaminants	Metals	Strontium, Manganese, Tungsten, Lithium [37]
	Nanoparticles [30]	
	Radionuclides and nuclear waste [41]	H-3, Sr-90, Cs-137, Tc-99, I-129, Pu-239, Pu-240, (233, 234, 235, 238) U, Am-241
Biological emerging contaminants	Pathogenic bacteria [37]	
	Antibiotic-resistant microorganisms[42]	
	Antibiotic resistance genes (ARGs)[42]	
	Virus [43]	
	Protein contaminants [44-47]	
	Genetically Modified Organisms (GMOs)	
	Inoculations with novel strains	
	Different types of RNA (e.g., RNAi and other Biologicals)	
	Certain peptide complexes	
Other emerging contaminants	Micro- and nanoplastics [48]	
	Liquid crystal monomers [49]	
	Environmentally persistent free radicals	
	Substances of unknown or variable composition, complex reaction products, or biological materials	

The table categorizes ECs into three groups: those currently in the spotlight (highlighted in blue), those with potential concern but less current attention (highlighted in purple), and contaminants of the past that are now emerging with renewed concern. Some ECs have been identified for control by various environmental regulatory agencies, including the Ministry of Ecology and Environment of the People's Republic of China,[32] the European Union,[29] and the US EPA.[37] It is important to note that this table provides only a selection of examples for each category, and there are many more ECs within each group.[29–49]

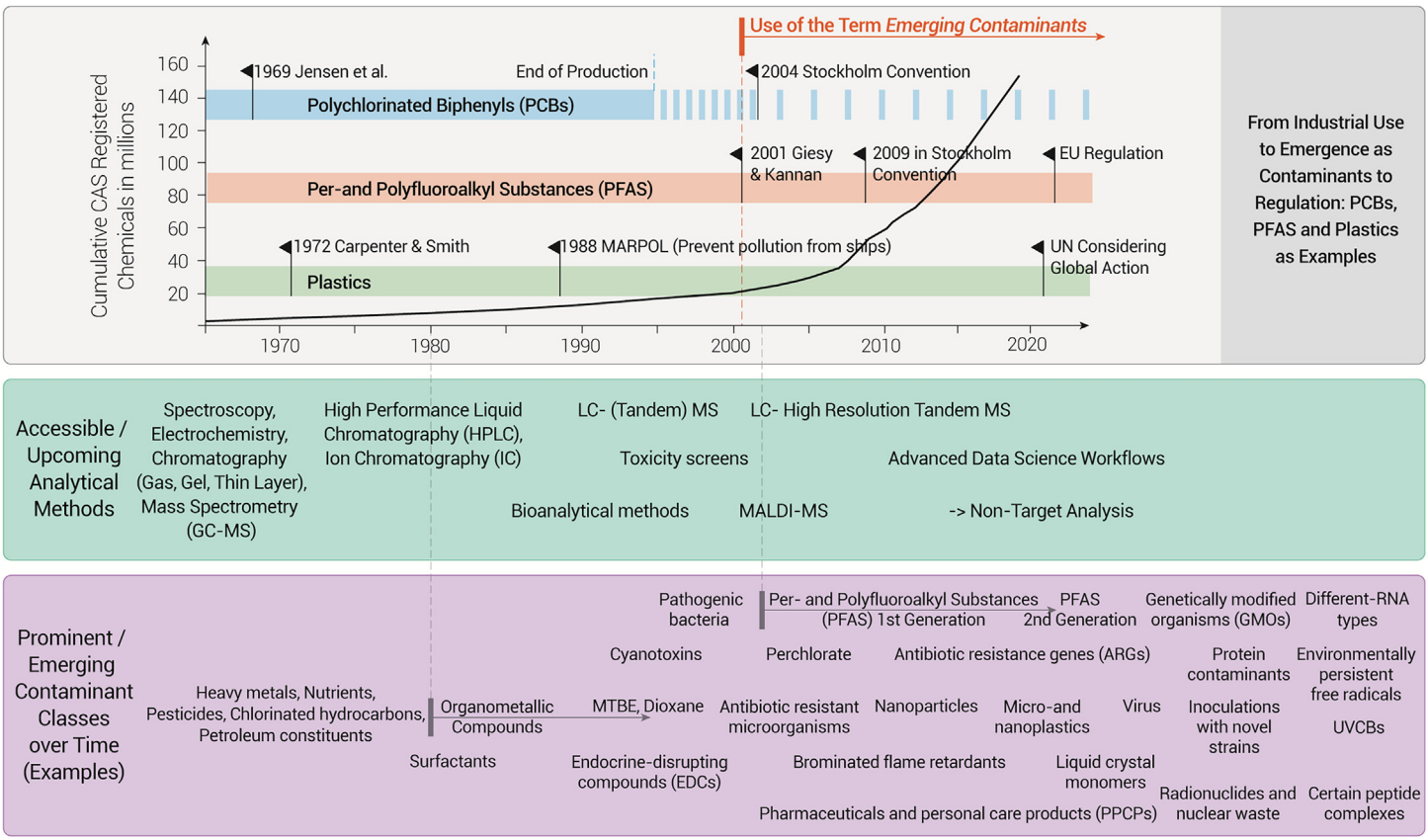


Figure 1. The evolution of ECs in relation to the advances in the detection and tracking of potentially toxic chemicals in the environment or biological systems, even at trace levels
Since the early 2000s, the term ECs has been used to describe the discovery of new pollutant classes. Polychlorinated biphenyls (PCBs), per- and polyfluoroalkyl substances (PFAS), and plastics exemplify problematic substances that were in use for decades (gray bars) but emerged as contaminants (pins) and were regulated and discontinued (faded-out shadow) with different lag times. Arrows in the lower panel indicate ECs that originated as replacements for other pollutants.

and approximately 30 million metric tons used globally, the prevalence of these compounds may be increasing annually.[57] Pharmaceuticals as the main components of PPCPs include numerous types of drugs and their metabolites, such as antibiotics (for both humans and livestock), hormones, non-steroidal anti-inflammatory drugs, anticancer drugs, antiepileptics, antidepressants, and β-blockers.[58] Among these biologically active substances, antibiotics have emerged as the most commonly reported PPCPs over the past few decades,[59,60] with the global consumption rate increasing from 9.8 to 14.3 defined daily doses per 1,000 population per day between 2000 and 2018.[61] The increasing prevalence of associated ARGs is a well-documented health concern and is now recognized as a prominent global threat to public health.[62] Besides pharmaceuticals, PPCPs also encompass various chemicals in body lotions, disinfectants, eye care, hair care, handwash, insect repellent, lipsticks, moisturizers, fragrances, shampoo, soaps, sunscreen creams, and plasticizers used in product packaging and lining[63] and PFAS compounds added to cosmetics.[64]

Over time, advancements in knowledge and analytical methods have led to the detection of risks associated with various chemicals. During the recent COVID-19 pandemic, 64.7% of respondents never disinfected their hands using sanitizers before the COVID-19 outbreak, but 91.0% disinfect their hands at least twice per day after the COVID-19 outbreak.[65] Therefore, particular attention has been paid to biocides found in disinfectants.[66] With the implementation of advanced analytical instruments such as high-resolution mass spectrometry (HRMS) and artificial intelligence (AI) techniques, the potential risks posed by a broader range of PPCPs are expected to be uncovered PPCPs in the future. After production and application, PPCPs are primarily introduced to the environment directly or indirectly through the discharge of raw sewage or treated effluents of various quality from wastewater treatment, animal husbandry, animal manure, or municipal treatment plant sludge as fertilizer, and landfill leachate.[67–69] In fact, the presence of PPCPs in surface water has become an indicator of an urbanizing water cycle.[70]

Engineered nanoparticles (ENPs), one of the most typical ECs, were included in the list of ECs by EPA in 2010.[71] ENPs such as carbon nanoparticles (NPs),[72] TiO_2 NPs,[73] and hydroxyapatite[74] are widely incorporated in a diverse range of consumable goods, including commercial cosmetics, sporting goods, sunscreen, and toothpaste. In terms of global production, SiO_2 NPs and TiO_2 NPs were the largest, followed by AlOx NPs, CeO_2 NPs, FeOx NPs, and ZnO NPs, carbon nanotubes (CNTs) (100–1,000 tons per year [t $year^{-1}$] in 2010) and AgO NPs (55 t $year^{-1}$ in 2010).[75] The increasing application of ENPs in consumer products has caused their increased occurrence in the natural ecosystems.[76]

Pathways for environmental release of ECs

To better understand and address ECs and their harmful impacts, it is crucial to thoroughly analyze the characteristics of these substances, how they are released into the environment, and how they can affect living organisms. For example, a number of big research questions were identified by Boxall et al. to understand the risks of PPCPs in the environment, and, more recently, a synthesis of progress toward answering most of these questions was provided, within which a number of timely research needs remain unanswered.[77] We can work toward a more sustainable approach by using innovative technologies to identify these contaminants, eliminate their sources, and apply green chemistry principles for designing safer chemicals.[78] This comprehensive understanding of problematic substances and their pathways of exposure is essential for developing effective strategies.[79,80] Figure 2 illustrates the release processes and potential pathways of emerging pollutants in different environmental compartments.

In both urban and rural areas, sources of ECs can be categorized as point source discharges from wastewater treatment plants (WWTPs), which include effluents from domestic, industrial, and hospital sectors and non-point sources such as stormwater runoff from agriculture (including livestock and aquaculture) and urban areas.[81–84] Additionally, ECs may originate from household products and leachates from landfills, among other sources. Conventional WWTPs were not explicitly designed to remove ECs effectively. As a result, many contaminants have been reported in treated effluents at concentrations typically ranging from ng/L to μg/L.[80,85,86] The continuous discharge of ECs in these effluents challenges existing global chemical management approaches that identify chemicals



Figure 2. Schematic illustration of the multifaceted pathways of EC production, utilization, and environmental release Sectors such as industries, agriculture, households, hospitals, and wastewater treatment plants all contribute to the distribution of these contaminants. From industrial processes to agricultural practices and everyday household activities to medical and treatment facilities to effluent discharges, these sources collectively disseminate ECs into the environment.

as persistent using cutoff values[87] because effective exposure duration increases when introduction rates from sewage or effluent discharge exceed the rate of degradation.[88] Efficient treatment of wastewater containing various chemical contaminants and pathogenic microorganisms remains a significant challenge in environmental engineering,[89] particularly in low- and middle-income countries.

Food production has significantly increased in recent years to meet the growing global demand. As a result, agricultural activities have become common contributors to releasing emerging pollutants into the environment.[53,90,91] This is often linked to the discharge of agrochemicals,[83] antibiotic residue from livestock wastes,[91] microplastic debris resulting from the extensive use of plastic mulching film,[53] and pathogens introduced through the application of livestock manure or WWTP biosolids as fertilizer.[92] Without significant alterations to existing practices, new pollutants produced by intensive farming are expected to continue accumulating in soils, potentially polluting nearby water bodies through surface runoff and infiltration.[83] Additionally, there is a risk for these pollutants to enter the atmosphere through agricultural spray drift or volatilization following pesticide application.[93]

Beyond the discharge of effluents from WWTPs and agricultural activities, leachate from landfills, where household wastes are deposited, constitutes a significant source of emerging pollutants in terrestrial ecosystems (Figure 2).[79,94–97] PPCPs, endocrine-disrupting chemicals, and ARGs have been detected in untreated landfill leachate at concentrations ranging from ng/L to μg/L,[95,98] with some concentrations surpassing proposed safe thresholds for the emergence of antibiotic resistance.[99,100] When these potentially toxic leachates seep out or overflow into water bodies, they can adversely affect aquatic organisms.[97] The construction industry is a significant environmental concern as it generates various contaminants, including construction and demolition waste, fly ash, plastic waste, and dust, during construction.[101,102] These pollutants can potentially affect the living conditions of nearby residents and construction workers.[103] However, the environmental fate of emerging pollutants associated with building sites remains largely unknown, and the application of new building materials that are being developed, such as engineered living materials,[104] could also exacerbate this problem.

Particulate contaminants, such as ultrafine particles, micro(nano)plastics, and ENPs, may be released into the atmosphere through processes including volatilization, aerosol formation, and diffusive exchange.[105,106] These airborne pollutants could further be transported to surrounding or remote areas through dry or wet deposition or wind events.[105,107] These particles could also carry other PPCPs and move to a remote area. Fernandez et al.[108] found that polycyclic aromatic hydrocarbons (PAHs), PCBs, and polybrominated diphenyl ethers are present in remote high-mountain European lakes, indicating a long-range atmospheric movement of such pollutants from urban to remote areas with the help of aerosol particles. Meteorological factors, including temperature, precipitation, wind speed, and boundary-layer mixing, play vital roles in affecting the migration behavior of airborne pollutants.[109] Atmospheric compartments, mainly consisting of outdoor and ambient air, atmospheric fallout, and suspended or street/road dust, have become the transport medium of airborne contaminants and a point source of emerging pollutants in terrestrial and aquatic ecosystems.[107,110]

NPs can be formed by anthropogenic activities such as combustion in cooking, vehicles, thermal power plants, aircraft engines, chemical manufacturing, ore refining, smelting, and welding.[111] There are three potential entry points for NPs into the environment over their lifespan: (1) during the manufacture of raw materials and nano-enabled goods, (2) during use, and (3) after disposal of items containing NPs (waste treatment).[112] Life-cycle estimates indicate that the majority of NP emissions occur during the use stage and after disposal in landfills.[113] However, emissions during manufacture account for less than 2% of the total output.[114] ENPs may be released directly or indirectly into the environment via a built environmental system such as WWTPs or waste disposal facilities. As for direct ENP emission, ENPs can act as fertilizers to remediate soil, control the release of plant growth-regulating substances, detect pathogenic bacteria, and control plant diseases and pests. Potential secondary emissions may occur through various pathways, including the discharge from WWTPs, the utilization of biosolids as soil amendments, or leachates from landfill sites. These engineered systems play a pivotal role in dictating the destiny of ENPs, influencing whether they are discharged as effluent or incorporated into biosolids, and determining their state (whether they remain bare, coated, or undergo chemical or physical transformations).[115] Sun et al.[116] reported that, in the European Union in 2014, the sinks of TiO_2 NPs, ZnO NPs, AgO NPs, and CNTs were mainly landfills (7,000 t $year^{-1}$), sediments (7,600 t $year^{-1}$), and soils (8,400 t $year^{-1}$). The predominant emission pathway of TiO_2 NPs and ZnO occurs via wastewater and

ultimately accumulates in sewage. CNTs and AgO NPs are primarily discharged into the environment during their manufacturing and application processes, where they are subsequently deposited in landfill sites.

Additionally, concerns have been raised about the environmental and human health risks of emerging protein contaminants such as proteinaceous infectious particles (prions).[117,118] Prions are misfolded forms (PrP^{Sc}) of normal cellular prion proteins (PrP^{C}) that are capable of self-templating (thus their infectivity), and various prion strains can cause fatal neurodegenerative diseases in various hosts, such as Creutzfeldt-Jakob disease in humans, bovine spongiform encephalopathy in cattle, and chronic wasting disease (CWD) in cervids. Take CWD prions as an example: once released into the environment, they can attach to soil particles, remaining as long-term sources of contamination.[119] Subsequently, these prions may be absorbed by plants from the soil and then transferred to animals through the food chain. Consequently, the presence and spread of these prions in the environment are frequently linked to the movement patterns and breeding practices of infected animals.

In summary, ECs could, directly and indirectly, enter the environment from various sources, such as industrial and agricultural operations; mining and construction activities; oil and chemical leaks; diffuse sources such as stormwater drains, roads, and parking areas, and wastewater treatment systems (Figure 2)[51,120]; and the use of a wide range of consumer products. ECs in soil or landfills can also seep into adjacent groundwater.[121,122] River networks and wind can transport these pollutants from residential, industrial, and agricultural areas to remote regions and eventually into marine environments.[51] Understanding the environmental release processes and transformation pathways of ECs is pivotal for evaluating their potential ecological impacts and for developing efficient mitigation and remediation strategies.

ADVANCES IN THE DETECTION AND ANALYSIS OF ECs

The development of new analytical techniques and technologies has significantly enhanced the detection and analysis of ECs. This progress has bolstered our capability to extract, quantify, and detect ECs in environmental samples. Mass spectrometry (MS) and bioanalytical techniques have been particularly effective in analyzing emerging organic contaminants.[123] Furthermore, electrochemical detection methods, with a focus on green technology, have emerged to measure ECs, especially pharmaceuticals.[124] These innovations have played a crucial role in elucidating the sources, classification, fate, and transport of ECs and in the development of treatment technologies for their removal.[125]

Sampling and analytical methods

Advanced sampling and separation. Recent global initiatives are reshaping the future of analytical chemistry, focusing on sustainable technologies. This impact is particularly evident in methodologies for sampling and sample preparation to detect and characterize ECs. Among these advancements is the solid-phase microextraction (SPME) chemical biopsy approach, which offers a flexible format for high-throughput quantification of ECs.[126] Enhanced by matrix-compatible thin film coatings and balanced coverage phenomena, SPME effectively eliminates matrix effects and extracts a wide range of compounds with diverse physicochemical properties. It is effective not only with gas chromatography (GC)-MS and liquid chromatography (LC)-MS but also with direct MS coupling, showing versatility and effectiveness in analysis.[127–129] Extraction techniques for ECs have evolved to enable on-site sampling using thin films, either through spot[130] or time-weighted average sampling methods.[131] *In vivo* sampling, employing a small-needle format, allows for the direct assessment of exposome effects in response to environmental pollution at the sampling site.[132] These designed probes conduct non-exhaustive sampling over longer periods, accumulating sufficient analytes for sensitive detection via chromatography or MS. Additionally, a filter-incorporated needle-trap device facilitates the simultaneous determination of free and particle-bound pollutants in a single step when combined with SPME and measured directly with GC-MS. Portable GC-MS instruments enable gas sampling for on-site analysis.[133] These advancements promise to enhance environmental protection efforts by generating large volumes of scientific data using simple, cost-effective, and sustainable analytical instrumentation. Moreover, these tools facilitate the untargeted characterization of samples, thereby aiding in the discovery of new compounds, including ECs.

Apart from mass spectrometric detection, chromatographic separation is also crucial in analyzing ECs. LC or GC is typically coupled to MS for analysis. However, very polar fractions are a problem for both. Being nonvolatile, they cannot be analyzed by GC or retained by the stationary phase of LC. Alternative chromatographic separation methods are being explored to close this gap. For example, a recent study combined supercritical fluid chromatography (SFC) with HRMS to identify unknown disinfection by-products in drinking water.[134] Hydrophilic interaction chromatography (HILIC) is also commonly employed in orthogonal analysis to analyze polar compounds. For example, HILIC-HRMS was applied in disinfected water analysis, leading to the identification of a new class of polar disinfection by-products (DBPs)—halomethanesulfonic acids.[135,136] An alternative that has emerged in recent years is an extra separation dimension (i.e., ion mobility spectrometry [IMS]) hyphenated to the conventional GC- or LC-MS systems. IMS is a rapid gas-phase separation technique that separates ions based on their size, shape, and charge. IMS is particularly useful for the separation of isomeric analytes or coeluting matrix components. The collision cross section (CCS) values provided by IMS analysis supplement the common identification parameters such as retention time (RT) and mass-to-charge ratio (m/z) for the screening and structural elucidation of ECs. The inclusion of IMS in non-targeted analysis significantly improves confidence in the elucidation of unknown chemical structures. For instance, ion mobility-MS (IM-MS) has been used to analyze ECs in human urine samples.[137] In another example, a non-targeted LC-IM-MS analysis of emerging PFAS in aqueous film-forming foams used CCS to enhance confidence in identifying unknown chemical structures and improve specificity in suspect screening.[138]

Advanced MS. MS is among the most applied techniques for the analysis of ECs. HRMS instruments, such as time-of-flight (TOF) and Orbitrap mass spectrometers, offer high mass accuracy and resolution that are critical for identifying ECs through structural elucidation (see Table S1). More recently, HRMS has been applied in identifying transformation products and metabolites of ECs[139] and in the non-targeted analysis/suspect screening of ECs.[140] HRMS has revealed many new ECs in the environment and elucidated their transformation products and metabolites. Compared with other analytical techniques, the capability to conduct non-targeted analysis is an invaluable advantage of HRMS in ECs' analysis. HRMS enables the integration of non-targeted analysis with bioassays and in chemico methods to identify bioactive and toxic chemicals in a sample. This combined approach enables the precise identification and broad capture of bioactive/toxic chemicals.[141] For instance, an estrogen receptor α (Erα) protein affinity assay combined with HRMS has been applied to identify Erα-active compounds in source and drinking water samples from major rivers in China.[142] In combination with effect-directed analyses, ultrahigh-resolution MS (i.e., Fourier transform ion cyclotron resonance MS) was adopted to identify the toxicity drivers of unknown disinfection by-products in chlorinated and chloraminated drinking waters.[143] In addition to *in vitro* bioassays, *in chemico* methods based on key chemical reactions (i.e., molecular initiating events) have also been applied to identify and measure the toxicities of environmental samples.[144] The combination of *in vitro* and *in chemico* assays with non-targeted chemical analysis represents a novel, more effective approach to identifying the bioactive/toxic contaminants in our environment.[145,146]

Other advanced analytical chemistry techniques. Nuclear magnetic resonance (NMR) spectroscopy is an advanced method for characterizing the chemistry of environmental samples.[147] NMR has several advantages for the discovery of contaminants, potential transformation products, and characterizing the reactivity of contaminants over other techniques. The primary advantage is that structural elucidation can be performed without an authentic standard because the molecular profile from different NMR experiments can be used for complete structural elucidation. Another advantage is that NMR can leverage different nuclei to explore the structure of different metals and organic contaminants and their interactions with environmental and biological media. However, NMR is less sensitive than the previously described MS techniques, which can result in higher sample needs for characterization. NMR is also less accessible than other instruments, which has created a barrier in the broader application of this powerful and versatile technique for characterizing metals and contaminants and their impacts on both environmental and human health.

Electron paramagnetic resonance (EPR) can be used to detect environmentally persistent free radical (EPFR) signals without the need to capture reagents, unlike common short-lived free radicals. However, the presence of particles or colloids associated with EPFRs, along with the co-existence of

paramagnetic components such as transition metals in the matrices and varying environmental conditions such as humidity and temperature, can significantly interfere with EPR detection.[147,148] The interference of components makes it impractical to separate them, as they likely contribute to the formation of EPFRs. Additionally, the diverse chemical structures of EPFRs pose a challenge to their identification. Researchers have categorized EPFR types based on *g* values and bandwidth, referring to them as oxygen centered and/or carbon centered. However, studies have shown that both parent chemicals and their degradation by-products contribute to EPFR formation, potentially playing simultaneous roles.[149] The reactivity of EPFRs varies with their structures, yet attributing signals to specific structures or quantifying the contributions of different structures remains elusive.

Suspected-target and non-target screening approaches

The number of anthropogenic chemicals has grown beyond our capacity to study them using traditional environmental monitoring approaches that rely upon the development of targeted analytical methods tailor-made to individual chemicals.[150] This challenge drives the need to develop suspect and non-targeted screening (NTS) methodologies to identify ECs in complex environmental and biological media.[141] The past three decades have witnessed the development of a wide range of HRMS instruments that are capable of resolving hundreds or even thousands of chemical compounds (M) by measuring the *m/z* of their corresponding (quasi)molecular ions (e.g., $M^{\cdot+}$, $[M + H]^+$, and $[M - H]^-$) with sub-part-per-million (<1 ppm) accuracy. The following sections provide a brief primer on the methodologies employed in the NTS of ECs.

Suspect screening. Modern HRMS can gather both *m/z* and CCS data for numerous compounds within a sample. However, sorting through these data and differentiating between ECs and the matrix is akin to finding a needle in a haystack. Comparison of experimentally obtained mass spectra with those compiled in spectral libraries (e.g., the National Institute of Standards and Technology [NIST] Mass Spectral Library) has been a time-honored approach to identifying an unknown.[151,152] One drawback of spectral library searching is the finite size of the library, which may not contain (bio)transformation products, by-products, or proprietary compounds whose authentic standards may not be readily available.[153] Another challenge is the reproducibility of collision-induced dissociation spectra, which vary between laboratories depending on the instrument and experimental conditions. Suspected screening practitioners increasingly rely on structure databases (e.g., PubChem, CompTox Chemicals Dashboard),[154] which are orders of magnitude larger than spectral libraries. Current suspect screening methods involve the creation of a list of structures whose computed/predicted properties are then compared with those obtained by experiment. However, the database's structural form does not always match the chemical structure observed by HRMS.[155] The experimental measurements are compiled using a peak-picking algorithm, the choice of which may influence the reliability and reproducibility of results.[156] The analyst is also cautioned that no single instrumental method is capable of detecting all chemical compounds and that each step of the analysis could remove compounds present in the sample.[157,158] This is particularly relevant when a large suspect list consists of compounds with a wide range of properties. For example, an instrumental method suitable for the analysis of anionic PFAS may not be appropriate for emerging brominated flame retardants. Black et al.[157] have highlighted the urgent need to develop predictive methods to assess which compounds will be detectable using a given set of experimental and instrumental conditions. The identity of a compound cannot be confirmed by its mass alone. This is why *in silico* (i.e., computer modeling) methods are essential to predicting the dissociation of compounds on the suspect list, their chromatographic RT, and CCS to assist in differentiating similar compounds. The application of harmonized values, such as the unified retention time index (RTI), is also utilized in several wide screening workflows in Europe.[159,160] With the help of RTIs, the number of false positives can be reduced in the first screening step from suspect screening and non-target screening workflows. Quantum chemical[161] and machine-learning-based methods[162] are capable of predicting ion ratios but at greater computational cost. Chromatographic RT[163] and CCS[164] can also be predicted using machine learning models.

Nontargeted screening. A disadvantage of suspect screening is the fact that it requires prior knowledge of the occurrence of impurities and transformation products that are often unknown. Consequently, these compounds are absent from structure libraries, leaving the analyst with the unenviable task of answering the question, "What organic compounds are present in the environment that should not be there?" without knowing their structure(s) beforehand. Consequently, the analyst must identify the structures of the compounds detected in an NTS experiment using first-principles interpretation of their mass spectra. However, this is currently impractical for all compounds detected, which number in the thousands. Therefore, practitioners of NTS have developed a range of experimental and computational strategies to prioritize mass spectra for structure elucidation. Environmental risk assessment efforts have shown that >60% of compounds with the potential to persist in the environment and bioaccumulate contain the elements chlorine, bromine, or fluorine.[165] Their mass spectra also display characteristics unique to the presence of halogens, and NTS strategies to identify ECs have largely focused on halogenated compounds.[166–171] Emerging PFAS are more challenging to recognize since ^{19}F is a single stable isotope. However, a previous study has shown that isotopic ratios (i.e., $^{13}C/^{12}C$) can still be used to discover PFAS, which are characterized by having fewer carbon atoms than other non-fluorinated compounds with the same molecular weight.[170] Recently, Zweigle et al.[172] have exploited this characteristic to develop a novel approach to PFAS discovery that involves plotting the mass defect normalized to the number of carbons (MD/C) vs. mass normalized to the number of carbon atoms (m/C). Cl-, Br-, and F-containing compounds can also be revealed using ion mobility because halogenated compounds are characterized by relatively small CCS compared to their molecular weight.[173,174] However, the most common approach to the discovery of unknown pollutants involves monitoring a fragment ion that is common to an entire class of pollutants. Machine learning is increasingly being used to guide NTS. Methods that predict a spectrum from a structure, such as competitive fragmentation modeling identification (CFM-ID)[162] are becoming more mature. However, the reverse problem of predicting a structure from a spectrum has yet to be solved. Boiko et al.[175] have recently reported on an automated tool that can assign elemental compositions in an unbiased, unconstrained way. It is anticipated that further growth in the areas of machine learning and AI will eventually enable true, unsupervised NTS.[176]

Advanced bioanalysis

Bioanalytical techniques. While chemical analysis-based methodologies offer significant advantages, such as low detection limits, excellent accuracy, and good selectivity for monitoring ECs, the steady growth in the development of biosensors, also known as bioanalytical tools,[177] for environmental analysis cannot be overlooked. This growth is largely attributable to their superior capabilities in rapid, specific analysis and real-time monitoring. Biosensors, which are analytical devices that combine a biological recognition element with a transducer,[178] have been developed to detect various ECs. Detectable ECs include antibiotics,[179] pesticides,[180] bisphenol A,[181,182] and microplastics.[183] Biosensors effectively detect ECs in environmental samples[184] as well as in foodstuffs and biological samples,[185–188] particularly within an effects-directed analysis framework.[189]

Recent advancements in biosensor technology have seen the introduction of novel biological recognition elements, such as aptamers, in sensor development. Aptamer-based biosensors, or aptasensors, have emerged as robust and powerful analytical tools for the detection of ECs. This is largely because of their high specificity for small molecules, low fabrication cost, design flexibility, and high stability. For example, specific aptamers have been developed to detect chloramphenicol in honey and enrofloxacin in sewage water.[190,191] The possibility of incorporating advanced engineered nanomaterials, such as carbon-based nanomaterials, metal-organic frameworks, and noble metal NPs, into biosensor systems is being explored.[192] With their good electrical conductivity, nanoscale size, and compatibility with biological molecules, these nanomaterials could significantly enhance biosensor performance. Indeed, nanomaterials have been found to increase biosensor sensitivities and lower the limit of detection by several orders of magnitude.[193]

Advanced analytical techniques for biological contaminants. Recent advancements in the detection of biological ECs, such as pathogens, ARGs, and functional genes associated with the biosynthesis of cyanobacterial toxins, have been facilitated by high-throughput quantitative polymerase chain reaction (qPCR) and next-generation sequencing-based methods.[194–196] A comprehensive study recently outlined the advantages and disadvantages of these methods, including classical cultivation-based techniques, for ARG detection.[197] One of the significant benefits of sequencing methods is their ability to identify a



Figure 3. Pathways through which ECs enter the environment and their subsequent fate ECs can originate from various sources, such as industrial discharges, agricultural runoff, and wastewater effluents. Once released, ECs can undergo transformation processes such as degradation, volatilization, and bioaccumulation, influencing their distribution across different environmental compartments, including water bodies, soils, and the atmosphere.

wide range of pathogens or ARGs across diverse microorganisms present in samples.[198] Despite their high-throughput nature, the sensitivity of these methods relies heavily on the effectiveness of the analysis pipelines.[199] In recent years, computational tools have played a pivotal role in enhancing pathogen surveillance. Notably, the development of a comprehensive pathogen database has empowered the multiple bacterial pathogen detection (MBPD) pipeline to achieve holistic habitat surveillance and coinfections of pathogenic bacteria.[200] Moreover, advancements in understanding the genomic signatures of pathogens through deep-learning approaches, such as DCiPatho, have enabled highly accurate identification of pathogens on a genomic scale.[201] Despite the strides made in pathogen detection through sequencing methods, monitoring the environmental dissemination of high-risk ARGs, particularly originating from pathogen hosts, remains challenging and requires novel tools.

The analytical methods for cyanobacterial toxins include biological (mouse bioassay), biochemical (enzyme-linked immunosorbent assay, protein phosphatase inhibition assay), chemical (high-pressure liquid chromatography [HPLC];, LC-MS, high-performance capillary electrophoresis, thin-layer chromatography, and GC), and molecular biological (conventional PCR, qPCR, biosensor method).[202] The chemical method is the most researched and well established and is by far the most commonly used.

DISTRIBUTION AND FATE OF ECs

Emerging organic contaminants

Terrestrial ecosystems face numerous challenges arising from introducing and accumulating a range of potentially toxic organic substances (Figure 3). Synthetic and naturally occurring emerging organic contaminants (EOCs) are widespread across diverse environmental settings. Despite often existing in low concentrations, these EOCs can exert significant and enduring effects, prompting extensive research into their distribution and fate in recent years. EOCs originate from various sources, including industrial waste, agricultural runoff, and household products. They can be categorized based on their chemical properties and sources, with subsequent subsections discussing some of the most prevalent types.

Pharmaceuticals and personal care products. PPCPs represent substances utilized for personal health or cosmetic purposes that can find their way into the environment through multiple pathways, including excretion post consumption.[203] Among PPCPs, pharmaceuticals, especially antibiotics, raise significant concerns due to their widespread use and potential environmental impact. Antibiotics, primarily administered orally for bacterial infection treatment in humans and animals, undergo enzyme-mediated metabolism before excretion, involving phase I and II processes.[204] Phase I metabolism involves oxidation, reduction, and hydrolysis, transforming parent compounds into various metabolites, while phase II metabolism entails conjugation with molecules such as glucuronic acid or sulfate, further altering their chemical structure. Consequently, resulting metabolites may enter the environment at higher concentrations than their parent compounds due to these metabolic processes.[205] Some pharmaceuticals resist biochemical transformation during metabolism and are excreted unchanged, entering the environment in multiple forms.[206] Understanding these metabolic pathways is pivotal for identifying the diverse forms of pharmaceuticals in the environment and assessing their potential ecological and human health impacts.

Pharmaceuticals and other PPCPs enter the environment through various pathways, such as wastewater discharge from sewage treatment plants and

animal farms, excretion from humans and animals, and improper disposal practices.[206] Despite efforts in wastewater treatment, PPCPs are not effectively targeted for removal, often persisting due to treatment conditions.[207] National surveys, such as one conducted in the United States, have shown that final effluents from WWTPs receiving discharges from PPCP manufacturers may contain concentrations of PPCPs 10–1,000 times higher than those typically found in WWTPs without such inputs.[208] This trend was also observed globally, particularly for commonly used PPCPs such as antibiotics.[206] Advanced analytical techniques have enabled the detection of PPCPs in sewage, groundwater, surface waters, drinking water, soil, and aquatic organisms across numerous countries, even at low concentrations.[209–211] For instance, a comprehensive survey conducted in 2015 identified over 600 different pharmaceutical substances and their transformation products across more than 70 countries on all continents.[212]

Once in the environment, PPCPs undergo various processes determining their fate. Some PPCPs can degrade over time through microbial action, although the rate of biodegradation varies based on the compound's chemical structure. PPCPs can also adsorb onto soil particles or sediment in water bodies, influencing their mobility and bioavailability. Aquatic organisms, such as fish, mollusks, and algae, can take up PPCPs from water through direct exposure or diet. It was evident that log Dow, rather than log K_{OW} (n-octanol-water partition coefficient), is a better indicator of their bioaccumulation and trophic magnification for a marine food web.[213] However, the apparent volume of distribution represents a promising proportionality constant to understanding the bioaccumulation of ionizable chemicals.[214] Once in the water bodies, most PPCPs remain in the water phase because of their hydrophilic nature, such as sulfonamide antibiotics, whereas some hydrophobic ones (e.g., estrogens) might sorb to sediments or be accumulated by organisms.[215] The presence of antibiotic residues in the environment might increase the risk of antibiotic resistance dissemination in environmental settings and consequently transfer to the human microbiome. Terrestrial organisms, including plants and insects, can also be exposed to PPCPs through the contaminated soil. Antibiotics are usually the most abundant PPCPs in plants originating from soils that were amended with biosolids and animal manure applications. For plants, hydrophobic compounds may partition into lipids and will be predominantly retained by roots, while most hydrophilic compounds will move to the xylem (in equilibrium with the water).[216] Further studies are needed to understand the bioaccumulation of ionizable PPCPs in aquatic and terrestrial organisms.[217]

Cyanotoxins and other algae toxins. Risks of toxins produced during harmful blooms of algae, cyanobacteria, and other organisms represent a classic One Health topic (www.cdc.gov/habs/ohhabs.html). Cyanobacterial blooms stimulated by multiple factors, such as global warming and eutrophication of water bodies, have led to a significant increase in the frequency, distribution range, intensity, and duration of cyanobacterial blooms, thus further exacerbating the risk of algal toxin poisoning.[218,219] Cyanotoxins can be classified into three groups based on their chemical structure: cyclic peptide, alkaloid, and lipopolysaccharide (LPS). Depending on the mode of toxicity to animals, toxins can be classified as hepatotoxic cyclic peptide toxins (represented as microcystin and nodularin), neurotoxic alkaloidal toxins (anatoxin, saxitoxin), cytotoxic alkaloidal toxins (cylindrospermopsin), dermatologic toxicity of alkaloidal toxins (aplysiatoxin; lyngbyatoxin), irritant toxins (LPS), and some other biologically active substances.[220] Globally, microcystin-LR is the most common cyanotoxin in freshwater, brackish water, and marine habitats.[221] Lakes and reservoirs differ in morphology and trophic status, which can affect the dispersal and distribution of cyanotoxins.[222] At the same time, cyanotoxins are subject to transport and diffusion at the sediment-water interface, with different types of sediments exhibiting different adsorption capacities.[223] Notably, algae, cyanotoxins, and toxins present in a variety of freshwater, marine, soil, and terrestrial species can be wind driven to float in the air and transported over greater distances.[224] Moreover, cyanotoxins in the atmosphere may, under certain conditions, settle on the ground or in water bodies and affect the surrounding environments.[225] The accumulation of cyanotoxins involves a complex process of gradual accumulation and transfer in ecosystems. The process can be manifested primarily through the cascading of cyanotoxins through the food chain and their progressive enrichment in organisms. For example, fish and shellfish, organisms that consume food rich in cyanobacterial toxins, accumulate the toxin in their tissues, resulting in a gradual buildup of cyanotoxins in the upper levels of the food chain.[226]

Emerging inorganic contaminants

Engineered nanoparticles. ENPs that accumulate in the environment will undergo a series of physical, chemical, and biological processes such as chemical transformation, aggregation, and dissolution. The interplay between these processes and the ENP transport ultimately determines the potential fate of ENPs.[227] The chemical transformation process mainly includes the dissolution and sulfidation of ENPs. In a series of studies, it has been found that the dissolution of NPs is triggered by particle-inherent factors (e.g., surface coating, particle size, shape, and aggregation state) and environmental parameters such as solution pH, dissolved organic carbon, and temperature.[228] Thereinto, the most commonly occurring passivation process, that is, the sulfidation of NPs, makes their surface appear to be almost inert, thus affecting the reactivity.

The colloidal stability of ENPs is a crucial factor that influences their fate and environmental effects.[229] The homo-aggregation (interactions between the same ENPs) of NPs is positively correlated with the NP concentrations. The aggregation characteristics are often explained by the classical Derjaguin-Landau-Verwey-Overbeek theory. Owing to the low predicted ambient concentrations of ENPs (e.g., in the range of pg/L to low μg/L for surface water), homo-aggregation is less likely to happen and is affected by ionic strength. The aggregation rate of NPs increases with the surrounding medium's ionic strength, and multivalent cations are more efficient than monovalent cations.[230,231] However, heteroaggregation of ENPs with mineral particles is more common in natural environments,[232] which ultimately affects the environmental fate of ENPs and their risk to ecosystems and organisms.[233] The majority of the studies on ENP transport in porous media used water-saturated artificial columns often packed with quartz sand, while only a few involved natural soils.[234] Key environmental factors controlling ENP transport processes are solution ionic composition, pH, and natural organic matter (NOM) chemistry, while the degree of water saturation in porous media such as soils is an additional physical factor. The impact of ionic composition, NOM, and solution pH on the NP fate is similar in aquatic systems and saturated and unsaturated porous media. For plants, an increasing number of studies related these factors to plant uptake. For instance, size-exclusion limits that range from <10 nm to the uptake of cells exceeding 20 nm for the uptake of leaves and can reach 100 nm in exceptional cases.[235–237] Assimilation of elements from larger particles is possible if they dissolve, while low zeta potentials usually favor direct particle uptake.

Radionuclides and nuclear wastes. Whether released from nuclear power plants, medical facilities, or sites where radioactive material was improperly disposed of, radionuclides pose considerable challenges to environmental quality and human well-being.[238] Radionuclides undergo radioactive decay, emitting radiation over time.[238] Nuclear wastes threaten ecosystem health. Strict regulations govern the handling and disposal of nuclear waste to prevent environmental contamination.[239,240] Consideration should extend beyond physical and chemical interactions to encompass biological uptake and long-term ecological consequences of radionuclides and nuclear waste.

Biological contaminants

Pathogenic bacteria. The intricate interplay between pathogenic bacteria and various environmental sources, particularly in agricultural settings, underscores the complexity of this challenge.[241,242] Agricultural soils are often underestimated as reservoirs of human and animal pathogens and can give rise to a spectrum of diseases affecting air, water, and food.[243] For example, bacterial species such as *Bacillus anthracis*, *Vibrio cholera*, and *Burkholderia pseudomallei* have the potential to cause severe infection and, in some cases, death through direct contact.[244,245] Foodborne pathogens such as *Escherichia coli* O157:H7 and *Salmonella enterica* can also enter the food chain, triggering epidemics with severe health consequences.[246,247]

Antibiotic-resistant bacteria and resistance genes. Antibiotics and antibiotic-resistant bacteria (ARBs) carrying ARGs have existed for hundreds of thousands of years before the discovery of antibiotics by humans.[248,249] However, the industrialization and widespread use of antibiotics in both human and animal populations have exerted unprecedented selective pressure on bacteria across various interconnected niches, including human, animal, and environmental microbiomes. This has led to the accelerated development of antibiotic resistance traits within these communities on a global scale.[250,251] Thus, anthropogenic activities could increase the emergence of ARBs, their resistance genes, and

their dissemination between the human, animal, and environmental compartments, aggravating the existing antibiotic resistance crisis.[252] For example, the extensive use of antibiotics and the intensive agricultural practices prevalent in modern farming have transformed soil ecosystems into potential reservoirs of pathogens and ARGs.[253] Within this soil environment, the biopollutome emerges as a complex network of pathogens and ARGs, creating a prevalent threat to ecosystems.[254] Although multiple barriers restrict the flow of both bacteria and genes, pathogens recurrently acquire new resistance factors from other species, thereby reducing our ability to prevent and treat bacterial infections,[62] which demands urgent and effective measures to control the formation and dissemination of ARB.

Antibiotic resistance has been referred to as a silent pandemic and has emerged as a significant concern in the realm of biological ECs.[255] Hence, the increasing number of antibiotic-resistant microbes poses threats to human health. Over the last decade, ARGs have been detected in all habitats, including the natural environment and human industrial habitats.[256] Anthropogenic activities play a key role in selecting genes from environmental and cellular sources, facilitating their subsequent co-option to confer antibiotic resistance. With increasing human activities, microorganisms and their genetic material move more often between humans, animals, and the environment, which collectively increases opportunities for the transmission and evolution of ARGs.[256–258] Once these drug-resistant genes are transferred to human-associated pathogenic bacteria, such as *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* species (ESKAPE) pathogens and plant pathogens, it may further exacerbate the clinical pathogenic risks.[259] These pathogens are not only present in the bodies of humans and animals but can also enter the water through excretions such as feces, urine, and saliva and spread through respiratory secretions into the air. The threat posed by pathogenic bacteria also presents a significant challenge within the One Health framework.[252] Over the past two decades, infectious diseases have been accountable for approximately 15 million global deaths annually.[260] Meanwhile, plant diseases contribute to the loss of up to 30% of global food production each year.[261]

ARB and ARGs originating from human activities are recognized as emerging biological contaminants that can potentially affect environmental ecosystems.[262,263] Apart from antibiotics, a range of non-antibiotic pollutants such as heavy metals, disinfectants, biocides, and non-antibiotic drugs can alter bacterial behavior and contribute to the development of antibiotic resistance.[264–268] Furthermore, ARB and ARGs can disseminate back to the human and animal microbiomes[269] through food ingestion, drinking water, and direct contact while swimming in contaminated water and while in contact with contaminated crops, thus creating a loop between the human, animal, and environmental microbiomes. Nevertheless, future research should provide quantitative information about the dissemination routes of ARB and ARGs from the environment to the human microbiome by considering human exposure and the probability of successful colonization of the human microbiome by these biological pollutants. There is an urgent need to move from descriptive, qualitative, or semi-quantitative research to quantitative risk assessments of the drivers of antibiotic resistance proliferation in the environment and its dissemination to the human microbiome.[270]

Viruses. Among microorganisms, viruses are most prone to becoming emerging pathogens because they can infect their hosts and adapt to new environments through mutation, genetic recombination, and reassortment.[271] The pathogenicity of many bacteria is due to the virulence factors they carry encoded by lysogenic phages.[272] Soil plays a significant role in the distribution and transmission of viruses in natural environments.[273] Research indicates that viruses can survive in soil for varying durations depending on factors such as temperature, moisture content, pH, and the presence of an envelope. Enveloped viruses such as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can survive for up to 90 days in soils with 10% moisture content.[274] Additionally, enteric viruses can persist on surfaces such as door handles, banisters, and food, contributing to their transmission.[244] The abundance of viruses in soil is higher in environments with high organic matter and moisture content.[274] Changes in soil moisture levels can affect the composition and activity of soil DNA and RNA viruses, potentially affecting soil ecology.[275] Understanding how viruses interact with soil is crucial for assessing their environmental impact and potential transmission pathways. Because the size of the host is tens to thousands of times larger than the size of the virus, viruses are more flexible than bacteria in terms of transport and dispersal by animals, wind, or rain.[276] Influenza viruses,[277] hepatitis A viruses, coronaviruses,[251,278] and others, can survive in the soil for a long time, leading to human exposure.

Protein contaminants. Prions and Bt proteins are considered two important classes of emerging protein contaminants. Prion proteins can bind to soils and suspend in water, thus persisting in the environment for years and serving as a significant environmental reservoir for disease propagation.[44–47] Our understanding of the fate and transport of prion proteins in the environment is very limited. Using sand or soil columns, previous studies found that recPrP and purified PrP^{Sc} had limited mobility, where the migration of recPrP was smaller than 1 cm in the quartz sand column and purified recPrP was primarily retained near the point of contamination in soil columns.[279,280] Bt proteins were found to persist in soils for 2 months, 180 days, and up to 234 days, respectively, and were found to have the potential to be transported through the landscape by sediments and crop residue debris in surface runoff.[281–283] Nonetheless, significant knowledge gaps remain in understanding the fate, transport, and environmental risks of protein contaminants (e.g., prions and Bt proteins).

Microplastics and nanoplastics

As one of the world's most prominent emerging pollutants, microplastics are ubiquitously distributed across the atmosphere, pedosphere, hydrosphere, and biosphere. Micro- and nanoplastics (MNPs) could be widely detected in the terrestrial ecosystem and human body.[284] Microplastic fragmentation by rotifers in aquatic ecosystems has been reported to contribute to global nanoplastic pollution.[55] Plastic particles enter the environment from ubiquitous sources, posing a potential threat to aquatic organisms, soil, the atmosphere, and human health.[285,286] Atmospheric microplastics are found in both indoor and outdoor air. Indoors, concentrations in residential homes can be as high as 1.96×10^4 particles m^{-2} day^{-1}), while in schools, they can be as low as 6.20×10^3 particles m^{-2} day^{-1}), and in dormitories (9.9×10^3 particles m^{-2} day^{-1})) they are 5.5 times higher than in offices (1.8×10^3 particles m^{-2} day^{-1})). The abundance of MPs in outdoor air showed regional differences, with higher abundance of MPs in urban air than in rural air, and higher levels of MPs in cities in northern China than in southern cities.[287] Some studies have shown that atmospheric deposition of MPs ranges from 0.5 to 1,357 MP m^{-2} day^{-1} (outdoors) and 475 to 19,600 MP m^{-2} day^{-1} (indoors). During deposition, microplastics can utilize plant stomata (20–40 μm long and 5–10 μm wide), with 20–200 nm of microplastics accumulating in the stomatal lumen and passing through the stomata into leaf tissue. Research has validated the capability of polystyrene (PS) nanoplastics to infiltrate leaves and migrate to plant roots, demonstrating their ability to penetrate plant leaves through foliar exposure.[288] Within the phloem, nanoplastics can travel alongside bulk water or sap, a process influenced by sap's composition and flow rate within the stem. Furthermore, the downward movement of nanoplastics within vascular tissues requires traversal through various physiological barriers, including intercellular plasmodesmata, vesicles, and conductive cells.[289] Consequently, the continuous aggregation of nanoplastics could potentially obstruct the vascular system, impeding the downward translocation of smaller nanoplastics.[289] The average abundance of microplastics in fish in the oceans was 3.5 ± 0.8 particles/stripe, but, in highly polluted waters, in contrast, oysters had the highest abundance of 99.9 particles/individual.[290]

MNPs accumulate in many organisms in the environment, which leads to food chain pollution affecting the life and health of all organisms in the food chain. MNPs are not easy to degrade after being ingested by animals so they accumulate continuously in the body. For example, research demonstrated that mice administered 0.2- to ~0.3-μm PS particles at a concentration of 250 μg.μL−1 via gavage exhibited absorption of plastic particles into various organs including the blood, liver, brain, spleen, testis, bladder, and others through the intestinal tract, leading to multi-organ toxicity.[291] MNPs can be detected in human feces, which indicates that the intake of MNPs is high.[292] After MNPs enter the gastrointestinal tract through food, the undigested MNPs are excreted with feces, but smaller MNPs will enter the systemic circulation. Some studies have found that there are MNPs in human blood, so MNPs may be transported to various organs through blood, but the mechanism of MNPs entering the blood circulation is still unclear and needs further study.[293] The maximum particle diameter of MNPs taken up by organisms is determined by the morphology of species'

feeding and digestive organs.[294] MNPs mainly enter the respiratory and gastrointestinal tracts and can then be transferred to other secondary organs according to their size and shape.

Liquid crystal monomers. Liquid crystal monomers (LCMs) are a class of synthesized organic chemicals that are key materials for liquid crystal displays (LCDs), which can undergo phase transitions between liquid and solid states at specific temperatures. LCMs are typically diphenyl-based compounds that contain functional groups such as cyano, fluorine, chlorine, or bromine.[295] The production output of LCMs for LCD panels is approximately 500 t $year^{-1}$.[296] However, the environmental release of LCMs during the use and dismantling of waste LCDs is a concern, and global estimates range from 1.07 to 107 kg/year.[297] Numerous studies have indicated the widespread presence of LCMs in the environment, and projections suggest a significant increase in their prevalence in the near future.[49] These LCMs exhibit environmental persistence, long-range migratory capabilities, and potentially harmful impacts on various species.[298] Consequently, LCMs have gained attention as ECs because of their distinctive properties, including persistence, bioaccumulation, toxicity, and extensive environmental distribution.[297]

LCMs have been found in various environmental matrices, indicating their widespread distribution and potential exposure risk to organisms. Air is considered a significant transport medium for LCMs, allowing their migration from e-waste recycling sites to the surrounding environment. Investigations into waste LCD panel dismantling revealed atmospheric concentrations of LCMs at 68,800–385,000 pg/m^3.[299] LCMs have also been observed in indoor and outdoor dust, sediment, landfill leachate, sewage sludge, and soil samples. LCMs median levels in dust collected across China ranged from 41.6 to 171 ng/g,[300] depending on the sampling region. LCM concentrations in urban soils from different functional zones ranged from 0.774 to 12.9 ng/g dry weight (dw).[301] In biota samples, LCMs were found in wild aquatic invertebrates and fishes.[302] LCMs were also detected in the hands, forehead skin wipes, and serum of e-waste dismantling workers.[303] The LCM concentrations in the serum samples of the occupational workers were significantly higher than those in the reference serum samples, indicating a high exposure risk in the occupational population.[175] These studies have provided direct evidence of LCMs in the environment, indicating their widespread pollution and highlighting the importance of understanding their distribution and fate.

Environmentally persistent free radical signals. Unlike traditional free radicals with lifetimes spanning milliseconds and microseconds, EPFRs are stabilized on or in specific particles, with lifetimes extending beyond days and even months. EPFRs exhibit stability and ubiquity in various environmental matrices such as atmospheric particulates, soil, biochar, and microplastics.[304,305] Their presence is potentially implicated in diverse environmental and biological processes. Notably, EPFRs have been observed to mediate the generation of a significant amount of reactive oxygen species (ROS),[306] recognized for their involvement in chemical degradation[307] and the induction of oxidative stress, which can adversely affect organisms, leading to DNA damage and diseases such as lung and cardiovascular diseases.[308] Ongoing research is addressing various aspects of EPFRs, each presenting substantial challenges.

RISKS OF ECs TO PLANETARY HEALTH

Environmental quality implications

ECs present substantial risks to planetary health by disrupting ecosystems, endangering wildlife, and posing threats to human well-being.[309] These contaminants exhibit characteristics such as persistence, bioaccumulation, and mobility, potentially forming enduring environmental footprints that jeopardize ecosystems.[310] They can persist in the environment for extended periods without degradation, leading to bioaccumulation in organisms and the subsequent risk of reaching harmful concentrations. Many ECs demonstrate ecotoxicity, posing threats to aquatic life, plants, and other organisms; for instance, pharmaceuticals such as antibiotics and hormones can disrupt the endocrine systems of terrestrial and aquatic species, causing reproductive and developmental impairments.[311] In natural settings, ecosystems often face mixtures of ECs rather than isolated substances, with interactions between these compounds potentially resulting in synergistic or antagonistic effects that amplify ecological risks.[7] Moreover, some ECs, such as plastics and microplastics, can serve as carriers for other contaminants, facilitating their accumulation in aquatic organisms and potential entry into the food chain.[312,313] Understanding the movement of ECs through the environment is vital for assessing their risks; factors such as volatility, solubility, and adsorption to soil particles influence contaminant transport through air, water, and soil, affecting their distribution and exposure pathways. Investigating the effects of ECs on soil, water, and air ecosystems is crucial for comprehensively evaluating their environmental implications. Here we consider some environmental quality implications of ECs in atmospheric, terrestrial, and aquatic systems.

Soil ecosystems. ECs, such as PPCPs, pesticides, and industrial chemicals, have been increasingly detected in soil environments worldwide.[314] These contaminants threaten soil organisms, including bacteria, fungi, earthworms, insects, and plants. Exposure to ECs can adversely affect soil organisms, disrupting their physiological functions, reproductive capabilities, behavior, and overall health (Figure 4). Among these, PFAS and MPs have garnered much attention for their potential to alter the composition and functionality of soil bacteria and fungi.[315–318] Studies indicate that exposure to such ECs can lead to shifts in microbial community structures,[319,320] affecting the abundance and diversity of key microorganisms involved in nutrient cycling and organic matter decomposition.[321–323] On the other hand, exposure to ECs can lead to the selection of bacteria and fungi that can catabolize these pollutants.[324] Cyanotoxins can enter the soil through runoff and rainfall leaching. Accumulation of cyanotoxins in the soils can adversely affect plant health, animal health, microorganisms, and consequently soil health.[325] Furthermore, cyanotoxins affect aerobic microbial communities at the sediment-water column interface, which may affect nitrogen transformation.[326] The repercussions of these disruptions extend beyond the immediate microbial community, with potential consequences for soil health and ecosystem functioning. The metabolic activities of soil microorganisms, essential for maintaining soil fertility, are particularly vulnerable to ECs.[327,328] The interference with microbial functions can hinder nutrient cycling processes, leading to imbalances in the availability of essential elements for retaining soil productivity.[329,330] Additionally, the disruption of microbial communities may compromise the soil's ability to resist pathogens and maintain resilience in the face of environmental stressors and climate change.[331,332] The relationships between soil microorganisms and ECs necessitate further research to unravel the mechanisms underlying these effects and develop strategies for mitigating their impact on soil health.

The effects of ECs on plants reverberate through the entire ecosystem, influencing the structure and dynamics of plant communities.[333–335] While the contaminants encompass a broad range, their overarching impact on plant health remains a common theme. ECs in soils can impede plant growth and development, posing challenges to individual species and the overall biodiversity of plant communities. One notable consequence is the alteration of nutrient uptake mechanisms in plants. ECs such as ENPs, PFAS, and MPs have been shown to interfere with the physiological processes that govern nutrient absorption.[335–337] This disruption can lead to nutrient deficiencies, compromising the health and vigor of plant populations. Furthermore, contaminants may accumulate in plant tissues, potentially entering the food chain and posing risks to organisms feeding on contaminated plants (including human beings).[338,339] Water transport mechanisms within plants are also vulnerable to the presence of ECs in soils. Certain contaminants can impede the movement of water through plant tissues. This disruption can cause reduced growth, altered reproductive patterns, and overall compromised resilience in plant communities.[340–342] As we strive to understand the broader implications of ECs on soil plants, exploring the connections between soil, plants, and the myriad ECs that shape their interactions becomes imperative.

The impact of ECs on soil animals encompasses a wide range of organisms such as protozoa, earthworms, nematodes, and arthropods. The broad category of ECs, including but not limited to PFAS, persistent organic pollutants (POPs), and microplastics, have been reported to influence the ecological dynamics of soil animals, with cascading effects on the entire soil food web.[343–345] Bioaccumulation is a common phenomenon observed in soil-dwelling organisms exposed to ECs. Contaminants accumulate in the tissues of these organisms, leading to elevated concentrations that can disrupt physiological functions and compromise overall health. This bioaccumulation introduces complexities to soil food webs, potentially affecting higher trophic levels that rely on soil animals for sustenance.[346,347] Furthermore, soil animals can also act as carriers, leading to the migration of ECs.[348,349] Nevertheless, the toxicity mechanisms of ECs in soil animals remain poorly understood. Ongoing

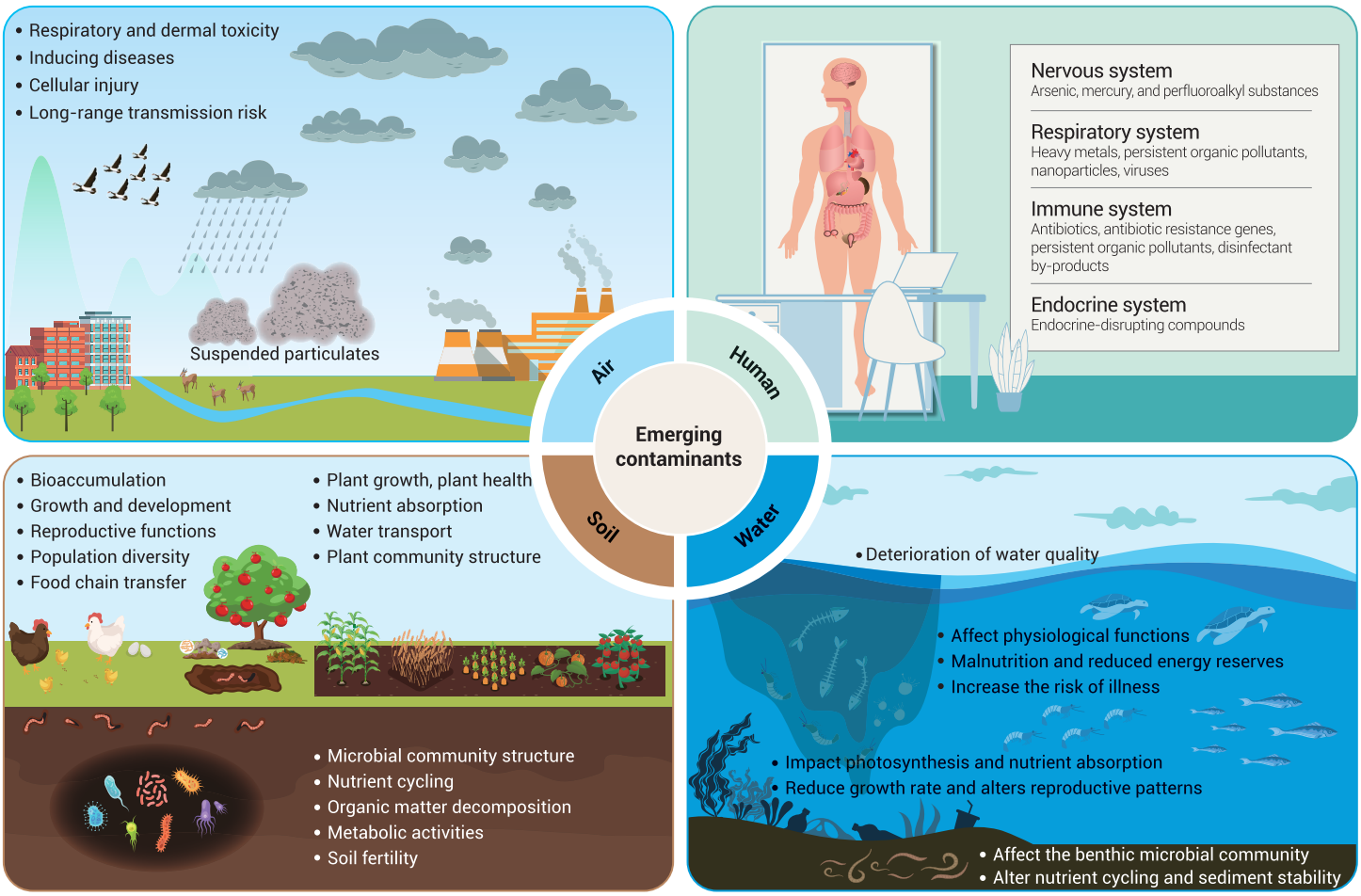


Figure 4. Interconnected negative impacts of ECs on human health, air quality, water systems, and soil ecosystems

research efforts should aim to elucidate how ECs affect soil animal populations, paving the way for informed conservation and management strategies to safeguard soil biodiversity.

In summary, the effects and impacts of ECs on soil ecosystems are complex and multifaceted. The overarching influence of these contaminants on soil microorganisms, plants, and animals underscores the need for comprehensive research to unravel the complex web of interactions within soil ecosystems. By examining the broader category of ECs without fixating on specific types, scientists can better comprehend the interconnected challenges posed by these pollutants. Continued investigation is essential to inform sustainable soil management practices that mitigate the adverse effects of ECs and preserve the health and functionality of soil ecosystems.

Aquatic systems. As a vital component of various ecosystems, the aquatic environment faces increasing challenges due to the presence of diverse ECs. For example, endocrine-disrupting compounds (EDCs) in water bodies can affect aquatic ecosystems.[350] These compounds interfere with the endocrine systems of aquatic organisms, leading to disruptions in reproductive, developmental, and physiological processes.[350,351] Recent studies highlighted the widespread occurrence of EDCs in water bodies, emphasizing their potential to disrupt the health of fish and amphibians.[350–353] The bioaccumulation of EDCs in aquatic organisms underscores the need for continuous monitoring and regulatory measures to mitigate their impact. POPs, including PCBs, PFAS, and organochlorine pesticides, have long-lasting effects on water and sediment quality.[354,355] Bioaccumulation of POPs in fatty tissues of aquatic organisms poses ecological risks.[355] As noted above, PPCPs also enter water bodies through various pathways, raising concerns about their potential impact on aquatic organisms.[215,356,357] Cyanotoxins provide a competitive advantage for cyanobacteria and drastically reduce the populations of certain species in aquatic ecosystems, upsetting the ecological balance.[358,359] At the same time, cyanotoxins can cause water pollution problems and directly threaten drinking water quality.[360] Cyanotoxins may drastically reduce the populations of some species in water bodies, upsetting the original ecological balance. Secondly, the toxic effects of cyanotoxins may also affect the variety and abundance of microorganisms in water bodies, thereby interfering with aquatic ecological processes. In some locations at some times, cyanotoxins and other toxins produced by harmful algae blooms can represent the greatest EC water quality threat to public health and ecosystems.[361,362]

To allow for ENP-tailored risk assessment, the developers and regulators must know the most important parameters governing the behavior and toxicity of ENPs. Engineering nanomaterial wastes in the environment are not easy to degrade and will accumulate and remain in the soil and higher plants through transport, which is bound to have a significant impact on the growth of higher plants.[363] The biological effects of ENPs on higher plants can directly affect ecosystems' health, stability, and sustainable development.[363] On the one hand, the presence of ENPs (such as TiO_2 NPs, ZnO NPs, Fe_3O_4 NPs, and CNTs) can have a catalytic interaction on plant growth by increasing root activity, increasing water absorption, enhancing photosynthesis, or improving rhizosphere soil microbial communities and increasing metabolic enzyme activity. Several recent reviews have discussed ENP accumulation in terrestrial plants, which can induce physiological and biochemical responses in plants.[364–366] Cao et al.[367] documented impacts on carbon fixation and water use efficiency during photosynthesis in response to CeO_2 NP exposure, which may indirectly influence soil organisms via the effect on soil moisture. On the other hand, ENPs (such as ZnO NPs, AgO NPs, CuO NPs, and CeO_2 NPs) may be potentially harmful to biota via reducing seed germination, generating ROS, enhancing membrane permeability, inhibiting antioxidant enzyme activity, or damaging root hairs through physical friction. Mechanism and mode of toxicity vary among ENPs.[368] Oxidative stress is a frequently reported phenomenon.[369] At present, research on the biological effects of ENPs mainly includes the mechanism of toxicity of ENPs to plants under different conditions and the role of ENPs in environmental systems from the perspective of organisms. Although the research has enhanced the theoretical value of nanobiology effects and toxicity research to a certain extent, there are

often many contradictions in related research results. This is due to differences in the physical and chemical properties of ENPs themselves (such as composition, shape, surface coating, and charge), or differences in culture substrates, treatment methods, and plant species, resulting in different stability and biocompatibility in the environment. This then affects the interaction between ENPs and plants.[370] ENPs accumulated in plants may also spread through the food chain to higher trophic organisms, causing certain ecological risks.

In recent years, several independent studies have shown that AgNPs exhibit certain cellular or systemic toxicity to cells and body systems under both *in vitro* and *in vivo* conditions.[371,372] Ag^+ mainly exerts cellular/bacterial toxicity through the following toxicological mechanisms: (1) interfere with the normal Na^+ and K^+ ion channels on the cell membrane, resulting in the imbalance of the membrane potential inside and outside the cell,[373] or bind to the sulfhydryl-containing (-SH) proteins on the cell membrane to inactivate them, destroy the barrier function and material exchange function of the cell membrane, and directly lead to cell necrosis[373]; (2) enter the cytoplasm of cells, interact with sulfhydryl-containing proteins, and destroy the protein structure, resulting in the inactivation of biologically active enzymes, the imbalance of intracellular REDOX reaction, and the generation of a large number of ROS leading to cell damage.[374] Nano-copper, a prominent metal nanomaterial, finds widespread use across various domains.[375,376] However, concerns have been raised regarding the significant harm nano-coppers can pose to human health and environmental safety. The liver is the main organ that is influenced by nanomaterials because it is the main organ involved in the metabolism of CuNPs.[377] Tang et al.[378] also found that the liver was the target organ for the accumulation of copper NPs through gavage. Lei et al.[379] found that CuNPs could significantly increase triglyceride and phospholipid levels in the body through NMR technology and pattern recognition methods. Oral administration of CuNPs can cause hepatomegaly, hepatocyte necrosis, and hepatic insufficiency in rats and mice.[380] In addition, Cu exposure can also produce significant toxic effects on the kidney, spleen, nerve, and gastrointestinal tract.[379,381–383]

Biological contaminants influence the microbial composition of sediments. The introduction of ARGs and drug-resistant bacteria into sediments can alter the balance of microbial communities, potentially affecting nutrient cycling, sediment stability, and other crucial ecological processes.[384] Viruses and pathogenic bacteria contribute to microbial contamination, affecting water quality in aquatic environments.[385,386] Elevated microbial loads can compromise the safety of water for both aquatic life and human consumption, leading to the spread of waterborne diseases and affecting overall ecosystem health.[387,388] Biological contaminants can also be toxic to aquatic plants. Viruses, pathogenic bacteria, and other biological agents may induce stress on plants, affecting their uptake of nutrients, growth rates, and overall health.[388,389] These effects can lead to changes in the abundance and distribution of aquatic vegetation. Aquatic plants can serve as vectors for transmitting pathogenic bacteria and viruses.[390,391] The presence of drug-resistant bacteria in plant tissues may contribute to the dissemination of antibiotic resistance in aquatic environments.[391,392] This transmission pathway can have cascading effects on the health of associated aquatic fauna. Aquatic fauna are susceptible to infections caused by biological contaminants. Viruses, pathogenic bacteria, and antibiotic-resistant organisms can compromise the immune systems of aquatic organisms, increasing their vulnerability to diseases.[393] This heightened disease susceptibility may lead to declines in the population of aquatic organisms and disruptions in the ecological balance of aquatic ecosystems.[394–396] Emerging biological contaminants can affect the reproduction and development of aquatic animals.[394–396] Genetically modified organisms (GMOs) and RNA-based technologies, such as RNAi, can introduce novel genetic material into aquatic ecosystems. RNAi and other biological contaminants may interfere with the normal reproductive processes of aquatic organisms, potentially leading to reduced reproductive success, developmental abnormalities, and altered population dynamics.[395,397]

Microplastics act as carriers of various pollutants, such as PCBs, PAHs, and heavy metal(loid)s.[398] These contaminants can leach from the surface of microplastics, leading to chemical contamination of water and sediments.[399] This process introduces a new dimension of pollution to aquatic environments, affecting the overall quality of these habitats.[400] Microplastics can also negatively affect the physiology of aquatic plants, affecting processes such as photosynthesis and nutrient uptake.[401,402] This can lead to reduced growth rates, altered reproductive patterns, and diminished aquatic plant health.[401,402] Moreover, microplastics are often mistaken for food by aquatic organisms, leading to ingestion at various trophic levels.[403] This ingestion can cause physical harm, including internal injuries, blockages, and interference with digestive processes. The presence of microplastics in the digestive tracts of aquatic animals can also lead to malnutrition and reduced energy reserves.[404–406] The toxicological consequences of microplastic-associated contaminants include disruption of endocrine systems, suppression of the immune system, and increased susceptibility to diseases. These effects can have profound implications for the health and survival of aquatic fauna.[407,408]

Other ECs, such as liquid crystals, oil spills, prions, and a class of ECs called unknown or variable composition, complex reaction products, or biological materials (UVCBs), can also introduce hazardous substances into aquatic environments. The discharge of liquid crystal contaminants can disrupt water quality and affect the health of aquatic organisms.[409] The presence of these compounds may alter nutrient cycling and cause ecological imbalances.[409] Organometals, such as organomercury and organotin compounds, exhibit high toxicity to aquatic organisms. These contaminants can interfere with cellular functions, impair reproduction, and cause behavioral changes in fish and invertebrates.[410,411] Accumulation of organometals in sediments may have long-term implications for benthic communities. Oil spills and organic solvents, including methyl *tert*-butyl ether (MTBE), can contaminate habitats.[411,412] These contaminants can form slicks on the water surface, affect light penetration, and reduce oxygen exchange. The effects include the smothering of aquatic vegetation and disruption of feeding behaviors in aquatic animals.[411,412] Prions associated with neurodegenerative diseases can enter aquatic environments through various pathways.[413] The presence of prions may pose a risk to the health of aquatic animals, potentially leading to neurological disorders. The effects on fish and other aquatic organisms are not fully understood but warrant further investigation.[413,414] The UVCBs may also have unpredictable impacts on water and sediment quality and the health of aquatic plants and animals.[415] Therefore, much research is needed to understand the specific effects of individual UVCBs.

Air quality. While the Industrial Revolution was a great success in technology, society, and services, it also introduced a significant quantity of harmful pollutants into the atmosphere.[416] These air pollutants can penetrate the respiratory system through inhalation. Meanwhile, for certain compounds, direct air-to-skin dermal uptake is comparable to the inhalation intake, imposing a significant burden on human health.[417–424]

Numerous animal and human studies have shown that exposure to air pollutants, including ECs (e.g., PAHs, perfluoroalkyl sulfonate, organophosphorus ester, polybrominated diphenyl ethers [PBDEs], and paraben), can contribute to respiratory,[425] dermal,[426] cardiovascular,[427] and immune disease[428] and mortality.[429] Early exposure to these pollutants in humans tends to trigger and exacerbate multiple diseases in their later life.[428,430] It is confirmed that these air pollutants contribute to the production of ROS in mitochondria, cell membranes, and endoplasmic reticulum, ultimately leading to cell injury and adverse outcomes.[431,432] Furthermore, these airborne pollutants can greatly affect ecology and human health because of their long-range transport, persistence, and toxicity.[105] Importantly, complex airborne ECs can cause unpredictable toxic effects and health risks by interfering with transport, metabolism, and bioavailability after entering the human body.[433] For example, triphenyl phosphate levels on the skin surface of e-waste dismantlers were negatively correlated with the levels of three thyroid hormones used to evaluate thyroid function.[434] Human exposure to pollutants from coking contamination, including aromatic compounds mixture, metabolites of PAHs and their derivatives, chlorophenols, and nitrophenols, could increase DNA damage and lipid peroxidation, which is associated with increased disease risks.[200,201] Unexpectedly, residents near coking plants faced a 1.4-times higher risk due to coking contamination.[201] In addition, concentrations of ECs in the atmosphere reached thousands of picograms per cubic meter in emission sources or urban air.[105] The presence of ECs also appeared in remote areas, such as the Arctic region, because of their persistence and long-range atmospheric transport.[435,436]

Notably, bioaerosol is another air pollutant of concern, which is a subset of atmospheric particles composed of bacteria, fungi, viruses, and their products, ranging in size from 0.001 nm to 100 μm. Cyanotoxins may enter the atmosphere in the form of aerosols and spread further afield, posing a potential threat to atmospheric safety and contributing to the ecological risk of "air eutrophication."[437,438] Bioaerosol is commonly released into the atmosphere from soil,

water, vegetation, animals (including humans), composting, sewage treatment plants, landfills, farms, and healthcare sites.[439–442] Due to the diffusion of plant pollen, spores, and reproductive units of microorganisms, bioaerosols can be transported over long distances across geographical barriers,[443] posing a high public health risk. The occasional epidemiological spread of bioaerosol components can be highly disruptive to societies and economies, as demonstrated by the COVID-19 global pandemic.[444] A previous study summarized the size-dependent particle deposition law of bioaerosols in different areas of the respiratory tract, showing that particles with a particle size larger than 0.5 μm mainly deposit in the head airway through natural sedimentation and impact, while particles with a particle size smaller than 0.5 μm can reach the lower respiratory tract through further diffusion.[445] It further leads to health complications, such as allergic reactions, infectious diseases, acute toxic effects, respiratory diseases, neurological effects, and toxic reactions to cancer and non-specific symptoms.[446]

Risks to human health

Various ECs stemming from sources such as industrial discharges, agricultural runoff, and improper waste disposal can permeate the soil, water bodies, and the air, establishing intricate exposure pathways for wildlife and humans.[447] These substances may enter the human body through various exposure routes, including ingesting contaminated water or food, inhaling air pollutants, and dermal contact with contaminated surfaces.[448–450] Their persistent nature, mobility, and potential to accumulate in the environment heighten the risks of exposure, intensifying their impact on health.[449,451] We recognize the diverse literature that has examined the public health effects of ECs, and, instead of providing a comprehensive critical review, here we aim to highlight some of the related efforts in this fast-moving area of basic and translational research.

The onset of various omic approaches, including genomics, proteomics, transcriptomics, and metabolomics, has enabled the detection of molecular-level perturbations due to environmental exposure and become increasingly used to investigate how environmental contaminants alter the biological function of organisms.[452,453] Often, these findings are integrated within the development and application of adverse outcome pathways, which are chemically agnostic conceptual models that link molecular initiation events to higher levels of biological responses of relevance to chemical risk assessment.[454]

Because the experimental design of metabolomic approaches is highly versatile, it can be applied to study multiple scenarios with various environmental conditions and different organisms, as well as complex contaminant mixtures and wastewater effluents.[452,455,456] Many studies have demonstrated the high utility of metabolomic approaches to rapidly detect fundamental shifts in organism function for a host of environmental model organisms and demonstrated how these approaches can complement traditional toxicity indicators.[107,181,457–459] Despite widespread concern, understanding the human health risks and toxic mechanisms remains challenging because of their dynamic nature, complex compositions, and interactions of contaminants and their mixtures, which present difficulties for conventional monitoring and modeling frameworks.[449] Nonetheless, evidence, although generally not well established, has suggested that exposures to ECs are associated with the following diseases.

Antibiotic resistance and infectious diseases. One of the pressing and increasing health threats posed by ECs is the rise of antibiotic resistance. PPCPs (e.g., antibacterial creams and ointments), when improperly used, disposed of, or inadequately treated, could contribute to the development of ARBs.[242,460,461] This outcome poses a significant threat to public health as conventional treatments become less effective, leading to an increased prevalence of infectious diseases.[461] For example, symptoms of infectious diseases, particularly those related to airway infections (e.g., lung infections), were much more common among individuals with compromised health or chronic conditions who used antibacterial medications.[462] It has also been suggested that antibiotic resistance could amplify the mortality risks during pandemics of bacterial diseases, including tuberculosis and cholera, and even viral diseases, particularly in the case of influenza, where a significant proportion of deaths often is caused by bacterial pneumonia coinfections.[463]

Endocrine disruption and reproductive disorders. Endocrine-disrupting chemicals, such as bisphenol A (BPA) and phthalates in plastics, represent a class of ECs that mimic or interfere with the endocrine hormones, often acting as agonists or antagonists. Endocrine-disrupting chemicals primarily target the female reproductive system. They can increase the risk of various reproductive disorders, including fertility issues, developmental abnormalities, and hormone-sensitive cancers (e.g., breast cancer).[464–466] For instance, individuals with polycystic ovarian syndrome (PCOS), a condition affecting nearly 10% of women of childbearing age with unclear etiology, have been found to have higher BPA in their serum, urine, and follicular fluid compared to those without PCOS, suggesting that BPA exposure is an important contributor to the pathogenesis of PCOS.[464]

Cardiopulmonary diseases. Airborne particulates can carry various ECs, including heavy metals (metalloids), POPs, NPs, and even viruses.[467] The respiratory and cardiovascular systems become the primary targets, with potential consequences ranging from irritations (e.g., coughing) to chronic cardiopulmonary diseases (e.g., hypertension and chronic obstructive pulmonary diseases).[468,469] A recent meta-analysis comprising 13 studies showed that higher exposure levels of PFAS, especially for perfluorooctane sulfonic acid (PFOS), perfluorooctanoic acid (PFOA), and perfluorononanoic acid, were significantly associated with a higher risk of hypertension.[470] Notably, particulates with smaller sizes are much more harmful than larger particles because of the longer residence time and greater capacity for deeper penetration in the respiratory tract.[106,471] Therefore, the airborne fine particulates could further amplify the health risks of the ECs contained. For instance, the interaction between airborne fine particles and viruses, such as H1N1, has been shown to extend viral distribution and aggravate respiratory tract infection.[467]

Neurotoxicity. Substantial evidence suggests that certain ECs, such as heavy metal(loid)s (e.g., arsenic and mercury), cyanotoxins,[472] and POPs (e.g., perfluoroalkyl compounds), possess neurotoxic properties.[473,474] Chronic exposure to these substances is associated with an increased risk of neurological disorders, including cognitive impairments, developmental delays, and neurodegenerative diseases.[475,476] Even at low concentrations, these substances could exhibit great and long-lasting neurotoxicity.[477] Early-life exposures are identified as a critical causal factor for the later development of Alzheimer's and Parkinson's diseases.[478] Regions contaminated with PFAS in the drinking water exhibited a 33% higher mortality from Alzheimer's disease compared with uncontaminated areas.[479]

Immune system impacts and allergic reactions. ECs may influence the immune system, potentially leading to compromised immunity or triggering allergic reactions. Studies have reported that these substances can affect the activation and survival of immune cells, potentially contributing to allergic rhinitis and other allergic responses.[480] For example, epidemiological studies have demonstrated the immunosuppressive effects of PFAS on pediatric vaccination and other immune-related responses for both children and adults (e.g., diminished antibodies after vaccinations, increased risk of asthma).[477,481,482] A most recent study showed that prenatal exposure to PFOS and PFOA increased the risk of non-atopic asthma at the age of 6 years by up to 2-fold.[483]

The description of EPFR reactivity and risks. Recent research has focused on understanding the properties and potential hazards of EPFR-containing particles. These particles have been found to display significant reactivity and toxicity, which is a cause for concern.[484,485] As a result, it is crucial to establish parameters to describe their reactivities to better understand their potential impact on human health and the environment. One potential parameter to describe the reactivity of EPFR-containing particles is the intensity of EPFR signals. However, this approach has limitations, as the detected EPFR signals are associated with various structures with different reactivities.[486] Additionally, the captured ROS may not fully explain the reactivity of EPFRs, as their reactivity may occur through direct contact with target reactants without the generation of ROS, and the instantly captured ROS signals may not represent the reactivity of long-lasting EPFRs.[487] Further research is necessary to develop a proper parameter that correlates with the reactivity of EPFRs, which differs from the detected EPR signals, to evaluate their environmental implications accurately. Additionally, researchers should consider that EPFRs coexist with other chemical components, such as the parent chemicals, their degradation by-products, and reactive inorganic particles. The impacts of these coexisting components should be considered when identifying the reactivities or risks of EPFRs.

The reactivities of EPFRs can lead to both adverse and beneficial effects, making their manipulation highly context dependent. When EPFRs have detrimental environmental impacts, efforts should be made to mitigate or eliminate them. Conversely, if EPFRs play a positive role in pollution control, their influence should be enhanced and utilized, as seen in applications such as biochar for organic contaminant degradation.[488] Although EPFR formation has been studied in

various processes,[489,490] understanding the preferred or unpreferred conditions for EPFR formation and quantitative descriptions of their generation and decay kinetics remains limited. EPFRs differ from common contaminants, being highly dynamic and composed of various structures, necessitating studies on their environmental behavior and risks and the development of standardized experimental protocols and standard reference samples.

In summary, the health risks associated with ECs will continue to be a major public health concern. More high-quality evidence and comprehensive strategies are urgently needed to better understand and mitigate their health effects. This requires interdisciplinary efforts, from establishing standardized contamination and public health surveillance systems to employing advanced epidemiological and molecular modeling and implementing evidence-based strategies. As we navigate this complex terrain, prioritizing research, regulatory measures, and public awareness will be paramount to curbing the adverse health effects of ECs and ensuring a healthier future for all.

MODEL-BASED ASSESSMENT OF FATE AND TOXICOLOGICAL RISKS OF ECs

Modeling migration and environmental impacts of ECs

The development of mathematical models to understand the migration and impacts of ECs in water, soil, and air ecosystems is a current focal point in environmental pollution research.[491] These models serve as valuable complements to monitoring networks, enriching our comprehension of EC sources, distributions, and life cycles. They also offer insights into the influencing mechanisms and environmental factors shaping EC dynamics. By facilitating comprehensive risk assessments for both human health and ecosystems, EC models play a pivotal role in providing early warnings, projecting outcomes under future climate scenarios, and evaluating the efficacy of remediation technologies.

Quantitative structure-activity relationships (QSARs), one class of numerically analytical models that are developed highlighting the intrinsic correlations with or dependency on a pool of topologically, spectrally, and physicochemically interpretable structural information, can be used as an alternative approach to unravel the toxicologically relevant or environmental influencing mechanism and the structural requirements for transfer, migration, and toxicity of ECs. Furthermore, QSARs developed using advanced statistical methods, such as machine-learning techniques, along with comprehensive datasets encompassing not only structural descriptors but also environmental factors, can effectively predict the environmental fate of ECs, including volatilization, photodegradation, and bioaccumulation..[492,493] Although QSARs were classically applied to the virtue screening of novel effective drugs for human health, the application of QSARs in environmental research arouses new vitality and greatly facilitates understanding the cause for the variance of toxicology and behavior of pollutants and even provides basic data guiding risk management and remediation administration. Nevertheless, the development of QSAR models is typically hindered by several limitations. These include a scarcity of experimental training data, issues related to over-fitting and noise in statistical techniques, and a lack of consideration for environmental factors. These environmental factors play a crucial role in influencing the transport, precipitation, adsorption, and desorption processes in environmental matrices. On the contrary, the stability, reliability, and predictability of QSARs would be enhanced if meta-learning big data were involved in development.[494] The integration of environmental and structural factors of ECs is likely to aggravate the uncertainty of QSARs because they are hardly accommodated with the significant correlation in one model, whereas it is of particular interest for augmentation of the QSAR applicability domain. Given the numerous limitations of QSARs, high uncertainty or application factors are applied to QSAR modeling outputs during early tiers of risk assessment.

Various modeling approaches have been developed to study the transport and impacts of ECs, including fate and transport models, multimedia models, and pharmacokinetic models. Fate and transport models simulate the movement and transformation of pollutants in different environmental compartments, such as air, water, soil, and biota.[495] Multimedia models integrate the fate and transport processes across multiple compartments to assess the overall environmental behavior of pollutants on regional to global scales.[490] Pharmacokinetic models focus on the uptake, distribution, metabolism, and elimination of pollutants within organisms. These models draw from the findings of laboratory and field experiments to represent the physicochemical, mineralogical, and hydraulic properties of ECs, adsorption-desorption, chemical/biological transformation, and their retention in and exchange across environmental compartments.

Numerical models that integrate multiple components, multiphase flow, and multiple reaction mechanisms have become the mainstream for simulating ECs in soil-groundwater systems. Notable examples include TMVOC,[496] TOUGHREACT,[497] RT3D,[498] PFLOTRAN,[499] and PHT3D.[500] For ECs in ecosystems, bioaccumulation models have been developed to integrate ecological principles, dynamic processes, and complex environmental conditions to describe and predict contaminants accumulation and migration processes within ecosystems, such as CalTOX[501] and KABAM.[502] However, due to the complex toxic mechanisms and biological effects involved in the transport processes of ECs in organisms,[150] there is currently a lack of universal, process-based models for the migration of ECs in ecosystems.

Research efforts have increasingly focused on exploring the potential of atmospheric transport as a significant mechanism for redistributing ECs across various environmental compartments on both regional and global scales. To study this phenomenon, scientists have developed trajectory models as well as regional and global three-dimensional chemical transport models. These models aim to simulate the transport and evolution of a wide array of ECs, including microplastics, POPs, PFOS, and PAHs. For instance, certain POPs undergo long-range atmospheric transport, leading to their subsequent deposition onto the Earth's surface and potential re-emission.[503] This process, commonly referred to as "hopping," facilitates the rapid transport of POPs to northern high latitudes at rates approximately 10 times faster than in tropical regions.[495] Studies also reveal that, despite global reductions in PAH emissions in recent decades, the concentrations of airborne PAHs in the Arctic region have not shown a significant decline because of the offset from increased volatilization from surfaces (e.g., ocean, snow, ice, permafrost, and soil) because of climate warming.[504]

Despite recent progress, important challenges remain in modeling ECs to understand their fates and impacts. The scarcity of observations is a key limiting factor in evaluating the models of most ECs, which calls for the design of multi-scale observation networks guided by models. Additionally, in the case of many ECs, there is still a lack of comprehensive understanding of transport and fate processes and toxicology within and across environmental compartments. In particular, researchers have increasingly highlighted the complex impacts of multi-pollutant interactions. Finally, the framework to represent ECs through different environment compartments may see a revolution catalyzed by the rapid development of Earth-system models.

Advancing evaluation and management of ECs through AI

In recent years, there has been a significant increase in the use of machine learning to understand and predict the chemical reactivity, toxicity, transport, and remediation of environmental contaminants.[505] Among the various environmental contaminants being explored by these computational methods, PFAS have garnered particular scientific attention.[506,507] The majority of machine-learning studies on PFAS have focused on supervised learning techniques, with only a handful of studies using unsupervised learning approaches. Within the former, the Wong group carried out the first machine-learning study on PFAS to predict and rationalize carbon-fluorine (C–F) bond dissociation energies to aid in their efficient treatment/removal.[508] Using random forest, least absolute shrinkage and selection operator regression, and feedforward neural networks, accurate predictions for C–F bond dissociation energies within chemical accuracy of the PFAS reference data were obtained (deviations less than 0.70 kcal/mol). In addition, this pioneering study demonstrated the efficiency of the machine-learning approach, which required less than 10 min to train the data and less than a second to predict a new compound's C–F bond dissociation energy.

Within the area of unsupervised machine learning, new unsupervised/semi-supervised machine-learning models have been created to automatically predict the bioactivities of PFAS in various human biological targets, including enzymes, genes, proteins, and cell lines.[509] The semi-supervised metric learning models were used to predict the bioactivity of PFAS found in the recent Organisation of Economic Co-operation and Development (OECD) report list, which contains 4730 PFAS used in a broad range of industries and consumers. Other studies have also used machine learning to predict the bioconcentration of organic contaminants by plants, the ecotoxicity of chemicals, and the dissipation of organic contaminants in plants.[510,511] Together, these studies highlight



Figure 5. Strategies for controlling ECs encompass various measures, including pollution control at the source, sustainable remediation to clean up contaminated sites, and sustainable management practices to prevent contamination

the capabilities of machine learning to understand the reactivity of PFAS, which other researchers can leverage to predict and screen other environmental contaminants.

AI is poised to revolutionize pollution control at the source, sustainable remediation of contaminated sites, and the implementation of sustainable management practices to prevent contamination (Figure 5). Through the utilization of AI technologies, such as machine learning and deep learning, significant progress can be achieved in addressing environmental challenges.[176] AI can improve the efficiency and effectiveness of pollution-control measures by analyzing intricate datasets, forecasting contaminant behavior, and refining remediation strategies.[512] Furthermore, AI can play a pivotal role in monitoring air and water quality, pinpointing pollution sources, and predicting the dispersion of pollutants to enable prompt and targeted remediation actions. In addition, AI-driven digital simulations and digital twins can replicate environmental scenarios, assess remediation approaches, and monitor the success of mitigation efforts to enhance decision making and resource allocation in pollution management.[513] Overall, AI serves as a potent tool for enhancing environmental sustainability by offering data-driven insights, optimizing remediation endeavors, and advocating proactive measures to safeguard the environment.

GLOBAL EFFORTS TO CONTROL ECs

Pollution prevention

The increasing recognition of ECs has led to global efforts to devise efficient strategies for their prevention, detection, and remediation (Figure 5). Governments worldwide have initiated policies to encourage industries and economic sectors to reduce source pollution by changing their production processes, operations, and material usage. For instance, the European Union has implemented a series of policies and regulations to ensure the protection of the environment and reduce pollution. One of the key components of this environmental framework is the Integrated Pollution Prevention and Control (IPPC) directive, which came into effect in 2008 to prevent and reduce pollution from industrial operations.[514] This directive applies to various sectors, including energy, mining, and manufacturing, and requires industries to adopt best available techniques (BATs) to reduce emissions and waste generation.[515] The IPPC directive complements other regulations such as the Registration, Evaluation, Authorisation, and Restriction of Chemicals (REACH), the Zero Pollution Action Plan, and the "polluter-pays" principle.[516] These regulations hold industries and businesses accountable for their environmental impact, promote sustainable practices, and ensure the long-term health and well-being of people and ecosystems. Similarly, the United States Congress enacted the Pollution Prevention Act (PPA) to promote industry pollution prevention and reduction efforts. The act aimed to encourage businesses to adopt practices that would minimize or eliminate pollution at the source through changes in production processes, operation methods, and the use of raw materials.

To balance economic development and environmental stewardship, the Chinese government has implemented diverse laws and regulations to address pollution and enhance the country's environmental conditions.[517] The Environmental Protection Law (EPL), initially enacted in 1989 and revised in 2014, stands as a cornerstone of legislation governing environmental protection in China.[518] Beyond the EPL, the country has introduced specific laws and regulations focusing on distinct facets of environmental protection, encompassing the Water Pollution Prevention and Control Law, Air Pollution Prevention and Control Law, Soil Pollution Prevention and Control Law, and recently the Action Plan for Controlling Emerging Contaminants in 2022 issued by the state council. Several other countries have also enacted numerous regulations to prevent pollution and minimize environmental contamination across different industries. The United Nations Environment Programme has reported a 38-fold surge in environmental legislation implemented from 1972 to 2019.[519] As of 2017, 176 countries possess legislative frameworks for the environment, and 150 countries have incorporated environmental protection or the entitlement to a healthy environment in their constitutions.[520] Additionally, 164 countries have instituted government-level entities tasked with overseeing environmental protection.

Despite these advancements, enforcing these laws faces challenges, as weak enforcement is a global trend exacerbating environmental threats. The difficulties in enforcing global environmental law stem from the reluctance of

individual states and the lack of effective enforcement mechanisms on the international level.[521] While there has been a rise in cooperative international efforts to protect the environment, the enforcement of these laws remains a common issue. The disparity in environmental protection legislation among high-, middle-, and low-income countries may result in outsourcing production-linked emissions to low-income countries. In some developing nations, the execution and enforcement of pollution control policies are hindered by underfunded and politically weak government bodies responsible for implementation, which hampers effective enforcement.[522] The focus on economic growth over environmental protection during the transition phase has resulted in inconsistent and incoherent environmental laws and regulations.[523] Additionally, weak property rights, poor access to credit, and limited technology choices distort the costs of improvements to environmental quality, further hindering effective pollution control.[524] The inadequacy of current pollution-prevention measures necessitates more concrete actions to address pollution on a global scale. Several strategies can be implemented to achieve this, including enforcing regulatory frameworks, adopting sustainable practices, promoting technological innovation, and engaging the public actively. These multifaceted approaches are essential for reducing pollution levels and ensuring the preservation of the environment for future generations. Herein, green chemistry presents particularly important opportunities for innovation and pollution prevention as we strive to achieve the UN's Sustainable Development Goals.[525] However, as identified by Erythropel et al.,[78] two green chemistry principles of particular relevance to ECs, design benign chemicals (principle 4) and design for degradation (principle 10), have received relatively little attention, and thus represent timely research opportunities for pollution prevention.

Pollution remediation technologies

Many remediation technologies have been developed to tackle the urgent global problem of the environmental accumulation of anthropogenic pollutants.[526] These technologies are vital in cleaning up contaminated sites and restoring them to environmentally acceptable conditions. Remediation methods span a spectrum of approaches, including physical techniques such as excavation, soil vapor extraction, and chemical and biological treatments designed to degrade or immobilize contaminants in both soil and water.[527] The choice of a specific environmental remediation method is contingent on the type and extent of contamination, with each method having its own set of advantages and disadvantages.

Physical remediation techniques employ various processes and technologies to extract pollutants from the soil, restoring its usability. These encompass physical engineering measures, soil heat-treatment technology, and adsorption technology.[528] Soil heat technology, conventionally used for pollutant removal via soil-heating-induced volatilization, also emerges as an alternative for enhancing soil conditions.[529,530] Additionally, adsorption, a conventional physical remediation method, relies significantly on the robust adsorptive capacities of activated carbon and biochar materials.[531,532] The large specific surface area, porous structure, and various forms of activated carbon enable efficient absorption of a broad spectrum of pollutants.[533] Biochar, recognized as an environmentally friendly material, not only plays a pivotal role in alleviating soil contamination but also enhances the properties of degraded soil, serving as an ideal habitat for beneficial microbes.[534,535] Ultrasonic waves are effective in destroying the structure of algae cells through the mechanical vibration effect.[536] Additionally, physical methods such as manual salvage or mechanical algae removal equipment can be used to prevent the accumulation of cyanobacteria. Furthermore, the photocatalytic degradation of cyanotoxins can be achieved through the use of ultraviolet or visible-light irradiation.[537]

The handling of environmental pollutants such as agricultural film and other plastic waste could be effectively addressed through physical recycling methods followed by the reuse of processed materials.[538,539] Physical recycling involves systematically sorting, cleaning, shredding, and melting of plastic waste to create new raw materials. These materials find application in producing diverse items such as fertilizer bags, garbage bags, and agricultural recycling water pipes.[540] This approach not only mitigates the environmental repercussions of plastic pollution by diverting waste from landfills but also contributes to diminishing the need to produce new plastic. However, it is essential to acknowledge that mechanical recycling processes, including sorting, grinding, washing, drying, and regranulation, may introduce pollution, such as volatile organic compounds and microplastic emissions.[541] The economic viability of the recycling technology is also a major consideration.

In the field of chemical remediation, emphasis is placed on altering and diminishing the mobility and harmfulness of environmental contaminants through a range of chemical methods. Such techniques encompass photolysis, Fenton reactions, photocatalytic processes, and electrochemical remediation strategies.[542] Photolysis leverages light radiation to decompose contaminants in soil, water, or air.[543] When contaminants are exposed to light radiation, the energy from the light can initiate chemical reactions that break down the contaminants into less harmful substances. Photolysis is particularly effective for degrading organic compounds, such as industrial chemicals, that are difficult to remove using other methods.[544]

Fenton technology is a chemical remediation method that uses the oxidation of iron ions (Fe^{2+}) in the presence of hydrogen peroxide to generate hydroxyl radicals.[545] These hydroxyl radicals are highly reactive and effectively oxidize pollutants, transforming them into less toxic substances. This process has been widely studied and applied to treat various types of contaminated water and soil.[546] Photocatalysis is another commonly used chemical remediation method that involves using catalysts to produce hydroxyl radicals, which then facilitate the rapid oxidation and decomposition of pollutants.[547] This method has shown promise in treating organic pollutants and has been extensively researched for its potential applications in environmental remediation.[548,549] Electric remediation, also known as electrokinetic remediation, uses direct electric current to remove organic and inorganic contaminants from contaminated soils[550] by enriching contaminants to either the cathode or anode zone through electroosmosis, electromigration, and electrophoresis under an electric field.[551] This technology is considered environmentally friendly and can be used to migrate and remove pollutants from the soil and sediment matrix.

While physical and chemical remediation methods have played crucial roles in combatting environmental contamination, they come with inherent limitations, including the necessity for advanced infrastructure, skilled personnel, high processing costs, increased reagent requirements, and the potential generation of secondary pollutants. For instance, *in situ* chemical oxidation is considered a rapid and effective means of eliminating organic pollutants from contaminated areas.[552,553] However, it is expensive and can yield undesirable harmful oxidation by-products, further harming the environment. Additionally, potent oxidizing agents pose substantial health risks to those handling them, underscoring the ongoing need for research and innovation in developing more sustainable and efficient remediation strategies.[554]

Bioremediation is a remediation approach that uses a biological system, such as bacteria, fungi, microalgae, or plants, to eliminate or neutralize pollutants from a contaminated site.[555] This method is considered cost-effective because of the relatively low cost of implementing and maintaining bioremediation systems compared with other remediation techniques.[556,557] Additionally, bioremediation is viewed as an eco-friendly approach because it relies on natural processes and does not involve the use of harsh chemicals that may further harm the environment. Furthermore, bioremediation is socially acceptable as it aligns with the growing emphasis on sustainable and environmentally conscious practices.[554] While bioremediation is a promising approach for managing pollutants in the environment, its full potential has yet to be realized because of several challenges associated with its implementation in natural environments.[558] One of the primary challenges is the poor colonization and performance of inoculated microbes in natural environments. When introduced into contaminated sites, these microbes may struggle to survive and effectively degrade pollutants due to competition with native microorganisms, limited availability of nutrients (including trace concentration of micropollutants well below KM),[559,560] and adverse environmental conditions.[561] Additionally, the use of plants in bioremediation can be time consuming, as they require sufficient time to grow and establish themselves before they can effectively remove pollutants from the environment. Furthermore, high concentrations of mixed pollutants in contaminated sites can inhibit the growth of both plants and microbes, limiting their ability to remediate the environment.[562] The environmental heterogeneity of contaminated sites also poses a challenge, as different areas within a site may have varying levels and types of contamination, requiring a tailored approach for effective remediation. To address these challenges, researchers have proposed integrating plants, adsorbents (such as biochar), and microbes into a single system for remediating contaminated sites.[554,563] This integrated approach aims to

leverage the complementary abilities of plants, adsorbents, and microbes to enhance the overall remediation process. By combining these elements, researchers seek to create a synergistic system that can more effectively mitigate the challenges associated with bioremediation and improve its overall performance in diverse environmental settings. Microbiome management is also an interesting development perspective in bioremediation.[564]

Sustainable management strategies

In addressing the challenges of ECs, sustainable management plays a pivotal role in their control and governance. Emphasis should be directed to advancing technologies for the management of ECs and undertaking critical research on environmental risk assessment and management of toxic and hazardous chemicals. Further research on the ecological and environmental harm mechanisms of ECs should be accelerated, and investments should be made in research on new theories and technologies for sustainable management strategies related to ECs. An environmental risk management information system for chemical substances should be established, and a platform for calculating toxicology and exposure prediction of chemical substances should be built. The early assessment and identification of key pollutants are essential for efficient control. Besides, innovation and education in green and sustainable chemistry, technology, and engineering can promote the generation of greener and more sustainable products and processes.[565,566]

Enterprises associated with emerging pollutants should actively implement their primary responsibility; increasing national and corporate investment in scientific research is imperative for effective governance of emerging pollutants. In recognizing that scientific research is fundamental to decision making in pollution control, sustained efforts are needed to enhance technological input. This effort involves understanding potential emerging pollutants' origins, trends, hazards, and control technologies. Scientific decision making facilitates precise and effective pollution-control measures.

Actively engaging in international cooperation is crucial, especially in cases where comprehensive research information is lacking. Utilizing global expertise and experiences in scientific research and management accelerates the screening and environmental risk control of emerging pollutants. Simultaneously, mechanisms for fund allocation are established, drawing insights from international conventions to support pollution-control initiatives at international, national, regional, and corporate levels.

Rigorous adherence to national and local requirements for the governance and sustainable control of ECs is required. Administrative departments should strengthen the supervision of the production, processing, use, import, and export of prohibited or restricted toxic and harmful chemical substances and their related products and scientifically and sustainably manage new pollutants from the source. Those comprehensive sustainable management strategies encompassing technological innovation, ecological understanding, and corporate responsibility aim to address the multifaceted challenges posed by ECs in a sustainable manner.

MANAGEMENT AND EDUCATION

Regulatory measures and policies

The increasing global production and use of chemicals in a widening range of applications and products requires a strict hazard assessment and management to protect public health and the environment. Regulatory measures and policies, therefore, play a key role in managing the production, use, and disposal of chemicals to minimize potential harm. These measures aim to strike a balance between industrial innovation and the search for environmentally safe chemicals to protect the health of organisms at all biological scales.[451,567]

A cornerstone of chemicals management is national regulation such as the European REACH and the assessment schemes of, for instance, the US EPA or the Chinese Ministry of Ecology and Environment that require manufacturers of chemicals to carry out comprehensive safety studies before placing their products on the market. However, regulatory efforts are not effective or equitable without effective implementation and enforcement of such policies. On an international scale, corresponding frameworks, in which scientific experts assess data on chemicals for potential hazards, exposure levels, bioaccumulation, and toxicity, include the Basel (on hazardous waste), Rotterdam (on information on exported hazardous substances), Stockholm on POPs, and Minamata (on mercury) conventions. The Globally Harmonized System of Classification and Labelling of Chemicals is a prime example of an international effort at the UN level to standardize management and assessment practices. Internationally accepted tools for testing, evaluating, and managing chemicals have been developed by the OECD and its members. Outside the OECD, the Inter-Organization Programme for the Sound Management of Chemicals provides comprehensive support to emerging economies and developing countries, where new chemical industries and consumer markets rapidly develop, but often with limited infrastructure and capacity for proper management of chemicals and waste.

One of the 17 Sustainable Development Goals (SDGs), launched by the UN General Assembly in 2015, addresses the sound management of chemicals and all wastes throughout their life cycles and decreasing their release into air, water, and land. However, more effort is needed to achieve the goal of preventing significant adverse effects of chemical pollution on human health and the environment, as stated in the United Nations Environment Programme's Global Chemicals Outlook II.[568] It is well documented that chemical pollution causes a wide range of damages to human and ecosystem health at local, regional, and global scales.[5] Among other factors, pollution is responsible for global biodiversity loss,[165,569] human diseases,[17,570] soil and water degradation,[571–573] stratospheric ozone depletion,[574] and climate change.[575]

Policymakers need to balance economic, social, and environmental arguments when deciding on measures for the sound management of chemicals. Where there is evidence of environmental impact and harm from exposure to, e.g., endocrine-disrupting chemicals, PFAS, and many other chemicals, regulators may impose restrictions, bans, or set limits on emissions and discharges into the environment. These measures are often based on scientific evidence and aim to protect vulnerable populations and ecosystems. Here, the precautionary principle is an important strategy that requires taking preventive action in the face of uncertainty about potential harm. Where scientific evidence is inconclusive, regulators should opt for a cautious approach and impose restrictions until further research clarifies potential risks.

Efforts to improve the handling of chemicals go beyond their production and application stages to include properly disposing of waste and recycling products containing dangerous substances. While progress has been made in many areas, there is an urgent need for a more consistent alignment of all actors on this common goal of chemical safety. International cooperation is therefore essential to address the global nature of pollution by chemicals and waste. Recently, scientists asked for the establishment of an overarching international body to facilitate and foster broad bidirectional science-policy interactions on chemicals and waste.[576] Such a science-policy panel (SPP) must address chemical pollution's multifaceted and heterogeneous impacts that often show dynamic development. The scope of this new SPP goes beyond the remit of the above-mentioned existing bodies because their scopes and mandates are limited to certain chemicals, geographical areas, or jurisdictions. Rather, the SPP needs to work on the large array of "chemicals of emerging concern" and novel waste streams, besides the well-described legacy pollutants, trying to avoid "analysis paralysis" (the inability of decision making by overanalysis or overthinking).[577] The SPP must establish and enforce a strict conflict-of-interest policy.[578] In particular, experts with a conflict of interest connected to a financial or material gain would pose a high risk of conflicting and/or incompatible outcomes or delayed implementation of solutions in the decision-making process and should not be allowed to participate in the core work of the SPP, but they may still participate and contribute as observers. Independent audits should be established to verify compliance with conflict-of-interest provisions to recommend corrective action if necessary and ensure that the outputs of SPPs are transparent, impartial, credible, and scientifically robust.

The new SPP, currently prepared by the United Nations Environment Programme (UNEP) Open-ended Working Group, is expected to strengthen these efforts by recognizing the interconnectedness of global chemical trade and pollution. Through regulatory measures, society can harness the benefits of chemicals while minimizing the adverse effects of hazardous chemicals.

Public awareness and education

Public awareness and education initiatives are instrumental in engaging individuals and communities in the efforts to address emerging pollutants. By increasing public knowledge and understanding of emerging pollutants, their

sources, and potential impacts, we can promote responsible behavior and encourage individuals to make informed choices that contribute to pollution prevention. There is a need to conduct public education through educational campaigns, workshops, and outreach programs on the scientific aspects of ECs, guiding the public in developing a scientific awareness of the environmental risks associated with ECs and fostering a commitment to green consumption principles. Those can empower individuals to adopt environmentally friendly practices and support sustainable behaviors. For example, drug take back events for unused medicines (i.e. www.dea.gov/takebackday), which can build up residences even after expiration dates, represent effective education and outreach strategies that empower people to contribute to pollution prevention by reducing the common practice of disposing unused pharmaceuticals in sewage systems, and thereby decreasing environmental introduction concentrations of these ECs.[598–601] Meanwhile, drawing inspiration from existing international conventions, the control of emerging pollutants is executed in accordance with international law. Besides, leveraging international conventions becomes pivotal as it refines its regulatory framework and establishes a robust governance system for emerging pollutants. Collaboratively with the global community, environmental risk identification, assessment, and control of chemicals are conducted. This not only realizes commitment to controlling emerging pollutants but also fosters global initiatives for pollution control, propelling the green development of the global chemical industry and contributing to worldwide environmental governance. To actively engage in international environmental agreements concerning ECs and participate in global initiatives for managing these contaminants is essential. By actively contributing to international conventions and actions related to ECs, a positive impact can be made on global environmental governance.

SOME LESSONS LEARNED

The systematic discovery of new contaminants has traditionally been a common pursuit in Environmental Sciences. Compound classes that were initially considered safe and inert (e.g., chlorinated hydrocarbons in the old times, PFAS at present) turned out to be prominent contaminants as more comprehensive evidence emerged.[579] At the same time, the number of chemicals registered by the Chemical Abstract Service is increasing exponentially (Figure 1), augmenting the likelihood of adverse effects and reinforcing efforts to recognize potential pollutants of tomorrow early on.[150] As illustrated in Figure 1, over the years, many relevant chemicals, pathogens, and (nano)particles have been discovered. They subsequently became the subject of in-depth fate and remediation studies before being the equivalent of "usual suspects" and making their way into regulation and routine monitoring efforts. While the term ECs is an ephemeral classification, a review of the last decades can highlight the drivers that make chemicals emerge and illustrate the time span between emergence and further action.

One important driver of discoveries is analytical innovation, as illustrated in Figure 1. Biannual reviews on water analysis and ECs in the journal Analytical Chemistry are a telling record of how access to new methodologies has been instrumental in bringing new contaminants to the radar. As exemplified in Fishman and Erdmann,[580] water analysis in the early 1970s was dominated by spectroscopy, electrochemistry, MS, thin layer, and GC and focused on inorganic species, petroleum hydrocarbons, and persistent organochlorides. Twenty years later, a broader suite of organic compounds had become accessible by dedicated sample extraction, HPLC, GC-MS, and the advent of biochemical methods.[581,582] In the early 2000s, the introduction of matrix-assisted laser desorption-ionization (MALDI)-MS made fingerprinting of bacteria possible, and the introduction of LC-MS revolutionized routine monitoring of organic compounds such as PPCPs. At that time, the term ECs came up.[583] Today, 20 years later, high-resolution mass spectrometers and advanced data processing have catalyzed non-target screening for organic compounds, bringing to our attention a broad contaminant range, including PFAS and inadvertent transformation products.[209]

Another driver of emerging concern is situations in which chemicals are not necessarily new but occur in such quantities that they can no longer be overlooked. Hence, the general public feels urged to address them according to the precautionary principle, even though analytical methods are yet to be established for some of them. Examples are engineered microparticles and NPs, microplastics,[584] or hydraulic-fracturing chemicals in unconventional gas exploration.[585] Well-known chemicals may also become of emerging concern at the moment that they are subject to stricter drinking water standards, such as perchlorate[586] or PFAS.[587] The emergence of new diseases, such as during the SARS-CoV-2 pandemic, can finally drive the installation of entirely new monitoring efforts, such as screening wastewater for COVID variants.[588]

Environmental science can make particularly important contributions if it succeeds in discovering problematic transformation products as ECs that would otherwise remain overlooked. Examples are disinfection by-products such as bromate during water treatment.[589] A particularly visible case is N-(1,3-dimethylbutyl)-N′-phenyl-p-phenylenediamine (6PPD)-quinone, a highly toxic ozonation product of the tire additive 6PPD, which has led to an enigmatic acute mortality of coho salmon in the US Pacific Northwest.[139,590]

In particularly notorious cases, chemicals emerge as contaminants after they were introduced to replace other, regulated ones. Examples are MTBE, or 1,4-dioxane, which were introduced in lieu of tetraethyl lead to boost octane numbers in gasoline,[591] or the second generation of PFAS, which have replaced the first one of PFAS or PFOA only to be recognized to be equally problematic.[592]

FUTURE DIRECTIONS AND CHALLENGES

Achieving sustainable development remains a lofty goal rather than a concrete reality without unified global endeavors to mitigate and prevent environmental pollution. While regulations have been implemented to address legacy contaminants, many unregulated chemicals and biological entities continue to be released into the environment. Moreover, enforcement and implementation of regulations for existing pollutants are inconsistent or lacking in many regions globally, posing significant threats to public health, biodiversity, and ecosystem services. The escalating presence of ECs in the environment raises apprehensions regarding their enduring and unforeseen impacts on ecosystems, water quality, and human welfare. This comprehensive review thoroughly examined the sources, behavior, pathways, and fate of ECs in the environment from various perspectives. Additionally, we explored the impacts of these contaminants on planetary health, encompassing humans, animals, and their interconnected environments, all within the framework of One Health. Notwithstanding the extensive insights into ECs presented in this review, substantial challenges persist within the current global development systems, hindering effective efforts to mitigate the impact of environmental pollution on planetary health.

(1) Chemicals are crucial in modern society, and their production is increasing. However, regulating their production and use is challenging because of the global development framework. When a regulated chemical is phased out, it is often replaced with another, potentially causing new or different types of environmental or human health impacts. This process requires a balance between the benefits of synthetic chemicals and the potential risks. With thousands of new synthetic chemicals entering the environment, many not thoroughly tested, there is a need to intensify research on ECs and create a comprehensive public database detailing their sources and environmental behavior. We must advance adverse outcome pathways[454] and cross-species extrapolation approaches[593,594] to understand chemical attributes that target particularly susceptible species and advance the precision of environmental assessments for ECs.[595] Doing so promises to inform chemical substitutions in commerce without regrets[596] and the sustainable molecular design of less hazardous substances.[597]

(2) Each year, households and workplaces contribute significantly to environmental contamination by releasing harmful chemicals through various everyday products, including toothpaste, shampoo, body creams, cleaning agents, and plastic bags. The lack of transparency from companies regarding the ingredients and quantities used in their products complicates the identification of the contaminants people may be exposed to and the potential health risks associated with them. PFAS serve as a prime example of such chemicals. Despite being in commercial use since the 1940s, their toxicity was not widely recognized until the late 1990s. Some companies were aware of the potential toxicity of PFAS but continued to incorporate them into their products. This scenario highlights the importance of transparency in chemical manufacturing processes and underscores the necessity

for comprehensive testing of chemicals before their incorporation into consumer goods.

(3) Efforts to combat environmental pollution face persistent challenges, including the complexity of pollutants, inadequate technological solutions, and difficulties in implementing comprehensive environmental policies. Chemical remediation techniques, often preferred, paradoxically result in greater environmental impacts than the pollution they aim to remediate. While biological methods such as bioremediation and phytoremediation offer eco-friendly alternatives, they are less efficient and more time consuming. The introduction of lab-grown or engineered microorganisms during bioremediation also carries the risk of disrupting natural ecosystems and causing unforeseen impacts. Addressing these challenges requires intensified research on innovative remediation options to effectively control pollution, enhance environmental health, and maximize ecological sustainability. Tailored remediation strategies, considering specific site conditions and contaminant characteristics, need to be developed to navigate these complex challenges. Simply stated, we need to advance green and sustainable chemistry and green engineering to realize more sustainable pollution prevention in the future.

(4) The intricate interplay between environmental pollution and climate change and other factors of global environmental change presents a formidable challenge that cannot be tackled in isolation. These environmental issues are interconnected and can amplify each other, resulting in profound consequences for ecosystems, human health, and the planet at large. Recognizing the interlinked nature of these challenges is imperative for formulating sustainable solutions that safeguard ecosystems, human well-being, and the prospects of future generations. Hence, there is a pressing need for integrated approaches that concurrently tackle global environmental change, underpinned by science-based policies and collaborative endeavors. This holistic strategy is imperative for steering the world toward a more resilient and sustainable future.

In summary, the continuous generation and utilization of new products contribute to the introduction of ECs into the environment. To confront this challenge effectively, comprehensive research is imperative to understand the sources and potential repercussions of these pollutants on human health, ecosystems, and animals in agriculture, embracing the One Health. Furthermore, evaluating how these contaminants interact with various environmental factors, both living and non-living, is crucial within our ever-changing environments. Leveraging advancements in analytical techniques and AI is indispensable for monitoring these emerging environmental pollutants and predicting their behavior within intricate environmental systems. Additionally, careful consideration of the potential risks stemming from advancements in material production across diverse domains, including biotechnology and nanotechnology, is vital for fostering the responsible development of materials for environmental purposes. Addressing environmental pollution demands a paradigm shift in our lifestyles, advocating for policies geared toward minimizing contaminants and implementing coordinated efforts to tackle existing pollutants through global cooperation. This collective endeavor is vital for safeguarding the health and sustainability of our planet for the benefit of both current and future generations, aligning with the principles of One Health.

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AUTHOR CONTRIBUTIONS

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DECLARATION OF INTERESTS

The authors declare no competing interests.

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