Guibin Jiang · Xiangdong Li *Editors*

A New Paradigm for Environmental Chemistry and Toxicology

From Concepts to Insights

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Foreword

Researchers from every academic discipline strive to understand the world around them and to solve the big problems facing humanity. When they have made new discoveries, they share them with their peers. With respect to these objectives, environmental chemists and toxicologists are unexceptional. Sometimes, we advance the field by publishing journal articles reporting the unexpected occurrence of a new family of contaminants, a previously unrecognized response to chemical exposure or a new way of understanding toxicokinetics. At other times, our contributions involve peer-reviewed critical reviews or perspective articles that use existing data to propose new ways of categorizing and explaining environmental phenomena. And sometimes progress comes in the form of a research monograph.

Unlike scientific journals, which sometimes sacrifice pedagogy for brevity and rapid publication, a research monograph provides authors with the opportunity to fully describe the relevant background and motivation for their work along with its importance and the future research opportunities that their research creates. A monograph also provides its editors with a chance to advance the field in a manner that may not be evident to the individual teams of authors. The editors of a research monograph carefully choose the authors and topics of individual chapters in much the same way as an artist creates a mosaic. Every individual chapter of the monograph describes the most recent developments in a specific field, but it is the holistic, overall view of the field that the reader gets by considering all of the chapters *in toto* that advances the discipline. For the newcomer to the field, a research monograph can be a point of entry that connects what might otherwise seem like a disconnected set of topics. For the experienced professional, a research monograph can open up opportunities to build connections and to tailor the next set of research studies to topics that can advance the overall objectives of the community.

A New Paradigm for Environmental Chemistry and Toxicology challenges our community to embrace a paradigm shift in the way that it operates. In the book's final chapter, Jin, Jiang and Li advocate for systems-level thinking to address the seemingly daunting challenge of responsibly managing chemicals in the Anthropocene. Their call for change could not have come from more qualified editors and it could not have come at a more opportune time. After a period of rapid development in the 1980s, the fields of environmental chemistry and toxicology have made incremental progress through the application of new analytical and bioanalytical tools, the extension of conceptual models to new families of contaminants and the analysis of data from long-term monitoring programs. Over the past 40 years, the number of peer-reviewed papers in the field has increased by over an order of magnitude as more countries join in the quest to protect the environment. But in light of civilization's exceedance of planetary boundaries, this is not enough.

As we learn more about the subtle impacts of chemical fate, transport and effects and as the industry continues to produce new families of chemicals in consumer products, crop protection products, medicines and fuels, it is becoming evident that a new approach is needed. Simply saying that we need to transcend disciplinary boundaries is not going to achieve this goal. No single investigator, no matter how brilliant and hardworking they may be, can master every aspect of this complex problem. We will always need researchers who can advance an

individual discipline by applying cutting-edge tools to advance understanding. However, if we want to be part of the solution to the world's problems, we have to find more effective ways to collaborate and to apply these tools simultaneously.

This research monograph brings together some of the leading environmental researchers interested in chemical fate, effects and treatment to create a mosaic that provides the reader with an understanding of where the field has been and where it is going. Considered individually, every chapter provides the reader with a thorough understanding of some of the key issues where progress is being made in specific sub-disciplines. Considered in its entirety, *A New Paradigm for Environmental Chemistry and Toxicology* lives up to its name by providing the reader with the knowledge needed to engage in this exciting and challenging next stage of progress in the discipline.

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Acknowledgements

With the tremendous developments in environmental chemistry and toxicology in the past 50 years, new theories have emerged, innovative methods have been proposed, and fresh applications have been conducted for various environmental problems. However, we are facing more complicated ecosystems both locally and globally. To address a series of global environmental issues and the future health of our planet, current research has migrated from assessments of past segregated phenomenological exposure and its effects based upon case chemicals towards a more predictive and scientific system with generalized principles and translational evidence that are applicable for policymakers and managers alike.

To reflect the state-of-the-art research fronts on environmental chemistry and toxicology, we have edited a reference book to illustrate the new paradigm shift from concepts to insights. With Springer Nature expressing interest in publishing the book, our work started in August 2018 with an initial plan of major chapter contents and potential contributors. It took several months before we had written confirmation from most of the selected authors. As we would like to have the book launch ceremony in August 2019 during one of the largest environmental chemistry conferences (The 10th National Conference on Environmental Chemistry in China), we had to set a strict deadline (31st May 2019) for the full chapter submission. Even though several authors could not meet the deadline, we are still very pleased to have 16 chapters on cutting-edge progress in environmental chemistry and toxicology. We are most grateful for the authors' dedication and contributions. It has been a great experience working with them on these important and interesting book chapters.

There are many people we would like to acknowledge in preparing the book for publication. Dr. Ling Jin (Research Assistant Professor of The Hong Kong Polytechnic University) provided great help in planning the book chapters and recommending leading authors. He also helped in drafting the last chapter to summarize the recent developments in environmental chemistry and toxicology since the publication of *Silent Spring* in 1962. Miss Anisha Tsang (Research Institute for Sustainable Urban Development, The Hong Kong Polytechnic University) provided excellent secretarial support in liaising with chapter authors, copyright clearance, and final document submissions. Miss Cherry Ma, our Coordinating Editor at Springer Nature China Office, offered excellent help at every stage of the book development. We are very grateful for her patience and cooperation. We are also grateful for Mr. Leon Lee (our summer intern from the University of East Anglia) for his careful proof read of the whole book.

We are most thankful for Prof. David Sedlak's remarkable and inspiring "Foreword" to the book. We hope the readers find the collections of theoretical developments and technological breakthroughs in environmental chemistry and toxicology useful and valuable.

July 2019

Guibin Jiang
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Contents

The Exposome: Pursuing the Totality of Exposure

The Exposome: Pursuing the Totality of Exposure

Vrinda Kalia, Robert Barouki, and Gary W. Miller

Abstract

Environmental determinants of health need to be measured and analyzed using system approaches that account for interactions between different agents that can elicit a biological response. The exposome offers a useful framework to examine the totality of exposures and their contribution to health and disease. Advances in exposure science, analytical chemistry, molecular biology, and toxicology have primed us to investigate the health effects of exposure to mixtures and concomitant exposures.

1 Introduction

The role of the environment in disease etiology has received increased attention over the past several years. The genome and genetic variations account for far less of the disease burden in the population than was previously thought and the variation in population burden of disease is now largely attributed to nongenetic factors. A meta-analysis of 2,748 twin studies reported that the environmental contribution to thousands of complex human phenotypes was nearly equal to that of genetics (Polderman et al. 2015). A study in monozygotic twins found that the average genetic risk attributed to 28 chronic diseases was just 19% (range: 3–49%) (Rappaport 2016).

The environment encompasses a broad range of factors in the physical world. It includes but is not limited to dietary factors, exposure to infectious and synergistic organisms, toxicant exposures through various media and routes, the built environment, and neighborhood-level characteristics such as access to healthy food and parks. Furthermore, it includes structural policies that control access to healthcare and influence other health-related behaviours and choices. Given how diverse the environmental health umbrella is, it is not surprising that there are several definitions of what the environment constitutes. For the purpose of this chapter, we define the environment as all nongenetic factors that can be measured in the human body which may contribute to variability in disease risk and burden in an individual and the population.

2 Historical Perspective

The effect of the environment on human health has been suggested for millennia. In 400 BC, Hippocrates penned "On Airs, Waters, and Places" discussing the possible role of air and water quality, and climate on human health (Hippocrates 1881). The ancient Romans were aware of the adverse effects from exposure to lead from pipes that conducted water. Vitruvius, a Roman architect and civil engineer, noted that using earthen pipes to transport water would be safer for health than using pipes that contained lead (Hodge 1981). In the nineteenth century, public health efforts were focused on preventing exposure to infectious agents in the environment. Using epidemiological approaches, John Snow discovered a point of water contamination as the cause of a cholera epidemic in London in 1854 (Ruths 2009). These findings and others led to changes in water distribution systems, sewage treatment, and food handling in London. Water and sanitation remain important environmental determinants of health in many developing countries.

Most modern environmental epidemiology studies begin with observations of regional differences in disease rates. Adverse health effects associated with exposure to air pollution were discovered through atmospheric inversion phenomena that led to greater exposure for an extended period over specific geographic regions like Donora in the USA

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(1948), London in the UK (1952), and the Meuse Valley in Belgium (1930) (Nemery et al. 2001; Bell et al. 2004; Jacobs et al. 2018). Several other ecological studies were seminal in establishing relationships between air pollution exposure and adverse health outcomes (Dockery 1753). In the 1960s–70s, research focus shifted toward chemical and physical agents in the environment that can affect human health. Several researchers and public health agencies studied the effect of exposure to volatile organic compounds, metals, particulate matter, pesticides, and radiation on health. Books like *Silent Spring* (1962) and *Our Stolen Future* (1996) were critical in raising public awareness in the US on the societal cost of exposure to persistent organic pollutants and endocrine-disrupting chemicals. Recently, the effects of natural disasters, the built environment and global climate change on health have also been investigated.

Increased research efforts in precision medicine have also benefited environmental health research. Advances in molecular techniques have made it possible to study gene x environment interactions that can alter disease risk. The human genome project provided tools to make environmental determinants of health personalized, offering the opportunity to discern how certain genotypes may be more susceptible to effects of an environmental exposure (Collins et al. 2003). Apart from the geographical and genotypic context, the life stage during exposure can also alter disease risk and susceptibility to exposure. The developmental origins of health and disease (DoHAD) hypothesis has led to the discovery of epigenetic transfer of information from parent to offspring and unveiled the vulnerability of the fetus to environmental toxicants and their effect on development and health in later life (Barker 2007).

Advances in environmental chemistry and toxicology have been critical in understanding environmental contributors of human disease. Environmental epidemiology uses both to assign exposure and to determine the biological plausibility of observed association between exposure and outcome.

3 The Exposome

In order to understand the mechanisms by which environmental exposures can affect human health, researchers and regulators have studied exposures in great detail and described the effect of exposure in isolation to a number of chemicals on various health outcomes. However, real-world exposures do not occur in isolation and are accompanied with other exposures and context-specific factors. Besides, human interaction with the environment is lifelong, constant, and spatiotemporally dynamic. Most epidemiological and toxicological studies do not account for this chronic, low-dose exposure to environmental chemicals. To account for this reality, Christopher Wild formally introduced the concept of the exposome in 2005. He defined it as the "life-course environmental exposures (including lifestyle factors), from the prenatal period onwards" (Wild 2005). The formal definition has undergone several revisions but most versions agree that the exposome comprises the entire set of lifelong environmental exposures and the biological response associated with these exposures (Wild 2012; Rappaport 2011; Miller and Jones 2014; Miller 2014). Investigating the biological response to an exposure accounts for toxicity mechanisms and interindividual variability in response. It also allows for the measurement of transient exposures that would be invisible through traditional approaches of exposure assessment. Since the environment is dynamic across the life course, assessing all exposures appears a daunting task. However, recent advances in methods bring optimism and avenues for creativity in the field.

3.1 Tools to Monitor the Exogenous Exposures at the Population Level

Remote sensing is the science of gaining information on objects from a distance and has been used to identify exposures related to the urban environment. Specifically, they can be used to estimate population-level exposure to air pollution, changes in temperature, amount of green space assessed using a normalized difference vegetation index, and provide information on outdoor light-at-night exposure (Larkin and Hystad 2018; Markevych et al. 2017; Turner et al. 2017; Kloog et al. 2008; Rybnikova et al. 2016). Further, remote sensing data from a number of satellites has been integrated to determine global fine particulate matter concentrations (van Donkelaar et al. 2010).

Mobile and stationary sensing monitors are usually used to make exposure measurements in specific locations. They can be a part of national networks of measurement or be related to study-specific measurement campaigns. National networks tend to have limited coverage but can be used as part of a distributed sensor network, which uses low-cost sensors to fill in spatial gaps that national networks are unable to meet. These have been implemented in West Oakland, California (West Oakland Air Quality Study), and in Eindhoven, The Netherlands (AERIAS Project). However, low-cost sensors still require rigorous validation, limiting their widespread application (Curto et al. 2018). Mobile measurement campaigns have been implemented more recently in a few places, like Karlsruhe, Germany, and Zurich, Switzerland (Hagemann et al. 2014; Hasenfratz et al. 2015).

Modeling approaches find utility in distilling GIS and satellite data or spatial resolution. Models such as land use regression, kriging, and maximum entropy models have

been considered by researchers and will need to be elaborated (Jerrett et al. 2010). Data generated from population-level exposure assessments provides opportunity to create ecological studies that can provide links between exposure and population health. Most of these data sources, however, are ineffective at determining individual exposure levels. They will need to be integrated with individual-level measures for validation.

3.2 Tools to Monitor the Exogenous Exposures at the Individual Level

External sensors can be used to track a myriad of personal information. Personal location data obtained through GPS devices enable integration of exposure maps with individual location markers to get personal exposure estimates (Asimina et al. 2018). Accelerometers and other activity tracking personal devices like Jawbone, FitBit, Apple Watch, and Polar (Loh 2017) can be used to ascertain both external exposures and certain lifestyle factors related to exercise and diet. Personal sensing technologies can also be used to assess air pollution exposure, changes in ambient temperature, and presence of green space (Nieuwenhuijsen et al. 2014). Passive dosimeters like silicone wristbands can also be used for personal exposure assessment and provide valuable semi-quantitative information on several chemicals (O'Connell et al. 2014).

Smartphone-based sensors and assessments can integrate data from personal sensors like accelerometers, GPS, barometers, thermometers, and ambient light sensors to record personal exposures. Their high penetrance worldwide provides a unique opportunity to obtain large amounts of personal data from diverse individuals (Murphy and King 2016; van Wel et al. 2017).

Personal sensors to monitor heart rate, glucose levels, blood pressure, muscle activity, body temperature, and sweat production are being developed and will require validation before their implementation in large population studies. Compared to measurements of external exposure, individual-level data is more actionable, can be used for personalized advice, and can be related to internal dose and associated biological responses.

3.3 Tools to Measure Endogenous Response and the Exposome

Techniques in molecular biology have shown exponential advancement in the past three decades. These advances have increased the resolution at which biological response to perturbations from environmental exposures is measured. Exposures to environmental factors can induce local and global changes in gene expression, enzyme activity, metabolite pathway alterations, and protein synthesis/folding. Deep molecular phenotyping can provide information on acute biological responses and also provide measures of long-term changes in physiology which can be viewed as markers of exposure memory (Go and Jones 2016; Weinhold 2006; Jeanneret et al. 2014).

Metabolomics. The metabolome is comprised of small molecules in a biological matrix that is <2000 Daltons in molecular mass. It is thought of as the functional output of genes and proteins, and their interaction with the environment. Recent advances in mass spectrometric techniques have made it possible to capture previously undetected small molecules, with estimates suggesting the metabolome may comprise of more than 1 million chemical features (Uppal et al. 2016). Chemical signals derived from a biological sample can arise from an endogenous metabolism, environmental chemical exposures, diet, the microbiome, personal care products, and drugs (Petrick et al. 2017; Liu et al. 2016; Jones 2016; Walker et al. 2019; Walker et al. 2016). Using an untargeted approach, metabolomics can expand surveillance of environmental chemicals, detect new xenobiotic chemicals, and identify unknown pollutants (Bonvallot et al. 2013; Roca et al. 2014; Jamin et al. 2014). Historically, metabolomics has not focused on those exogenous chemicals, but recent efforts are increasing the identity of environmental chemicals through these untargeted approaches. By simultaneously measuring exposure and biological response, metabolomics offers the opportunity to link exposure to molecules associated with exposure. While the identity of most chemical features that are measured using untargeted high-resolution metabolomics remain unknown, the technique offers a powerful opportunity for hypothesis generation and identification of unknown chemicals of interest related to a health outcome.

Transcriptomics. Gene expression is the process by which genetic data encoded by DNA is transcribed to RNA, which then initiates and directs protein synthesis in a cell. Cellular function regulation involves a complex series of steps that control the amount of RNA, and in turn, protein that is synthesized. Thus, exposures that alter functional regulation in the cell can be detected using transcriptomic and metabolomic analyses. Chemical exposures have been linked with distinct gene expression profiles that have been seen in humans and model organisms (Hamadeh et al. 2002). Transcriptomic analyses in human samples involve DNA microarray hybridization, which uses 40,000–50,000 molecular probes to seek RNA transcripts (McHale et al. 2009; Spira et al. 2004; Fry et al. 2007). Next-generation sequencing has made it possible to measure the effect of exposures on different types of RNA in a sample, including mRNA, microRNA, small interfering RNA, and long non-coding RNA. Databases that curate gene expression

profiles across different exposures and model organisms provide opportunities to compare experimental data with previously generated gene expression profiles (Grondin et al. 2018).

Proteomics. Protein measurement can elucidate signaling, inflammation, oxidative stress, and tissue damage in a biological sample. Levels of proteins and their posttranslational modifications are closer to function than gene expression data. Measuring proteins can be targeted using enzyme-linked immunosorbent assays (ELISA), or newer multiplexed bead-based assays that are capable of measuring more than 50 proteins in a small amount of biological material (Elshal and McCoy 2006; Tighe et al. 2015). While the use of high-resolution mass spectrometers in untargeted proteomics is insightful, it is also challenging due to difficulties in detecting low-abundance proteins. Chemical exposure to reactive electrophiles has been achieved through protein adductomics platforms, which can measure more than 100 human serum albumin adducts at the Cys34 site. Protein adductomics has been used to assess exposure to lifestyle factors, indoor air pollution, and ambient air pollution (Rappaport et al. 2012; Grigoryan et al. 2016; Liu et al. 2018).

Epigenomics. Epigenetic changes on DNA can alter gene expression. These changes can occur through the addition or removal of methyl groups on CpG dinucleotides, or through histone modifications. These modifications can be long term and have the potential to be transferred to the next generation if they occur in germ cells. Different stressors including chemical exposures can lead to specific epigenetic signatures that persist even after the stressor has been removed (Fernandez et al. 2012). Thus, epigenetic profiles can be used to monitor exposure history and to assess acute or chronic stress (Go and Jones 2016; Go and Jones 2014). High-throughput assays based on parallel sequencing of DNA with bisulfite conversions can measure up to 850,000 CpG sites within the human genome. Epigenome-wide association studies have revealed distinct methylation patterns associated with chemical exposures, providing insight into the mechanisms underlying the biological responses (Bollati et al. 2007; Seow et al. 2014; Hou et al. 2012).

Multi-omics assessment of the exposome. Information from different layers of the biochemical dogma can be integrated to paint a holistic picture of biological response to an environmental perturbation (Fig. 1). Using approaches from systems biology, we can gain a deeper understanding of environmental influences on human health by integrating across epigenomic, transcriptomic, proteomic, and metabolomic changes associated with exposures. The integration of high-dimensional data has benefited from the development of statistical approaches that identify interactions among biological response networks (Uppal et al. 2018; Kalia et al. 2019). The continued use of deep molecular phenotyping of cohort studies will generate data needed to spur new discoveries and methods (Vineis 2017; Vrijheid 2014; Li et al. 2017; Barouki et al. 2018; Carvaillo et al. 2019).

3.4 Considerations in Measuring Exposure and Biological Response

We have learned several lessons from environmental epidemiology about associations between exposure and disease. Investigators have recognized the importance of accuracy and precision while measuring exposure. Accurate exposure assessment is essential to detect and quantify a dose–response relationship. Inaccuracy can lead to mis-measurement of a continuous exposure measure or can lead to misclassification of a dichotomous exposure status, which can severely bias results toward the null. Using biomarkers of exposure has several advantages: 1. Detection of the biomarker proves absorption of the compound, 2. It accounts for bioavailability of the compound, and 3. It integrates measures over all routes of exposure. However, it remains hard to tell where in the environment the compound came from, positing the need to compare internal dose data with data collected from external monitors and measurements. Further, since biomarker collection is expensive and relies on access to biological matrix availability, we can also validate other less expensive measurement methods by validation against biomarkers measured in a subset of the population. Epidemiological studies that provide causal interpretation of observations have good study designs. These study designs account for all variables that can confound relationships between exposure and response, and provide the means to uncover temporal relationships.

4 An International Perspective

Chris Wild's article (Wild 2005) describing the exposome concept raised a huge interest in the scientific community, which did not translate immediately into identified projects in Europe until the European commission launched research calls on the exposome within the seventh framework (FP7). In 2012 and 2013, three projects were launched, HELIX, Exposomics, and then HEALS. The concept was not to develop facilities, but rather to form integrated projects that would encompass the complexity of the exposome. Each project had its own perspective. HELIX, for example, focused on the pregnancy exposome by studying several EU birth cohorts (Maitre et al. 2018), Exposomics focused on the short and long-term effects of exposure to water and air pollutants (Turner et al. 2018), and HEAL focused on modeling and multidisciplinarity to develop a new "exposome" cohort (Steckling et al. 2018). More recently, the

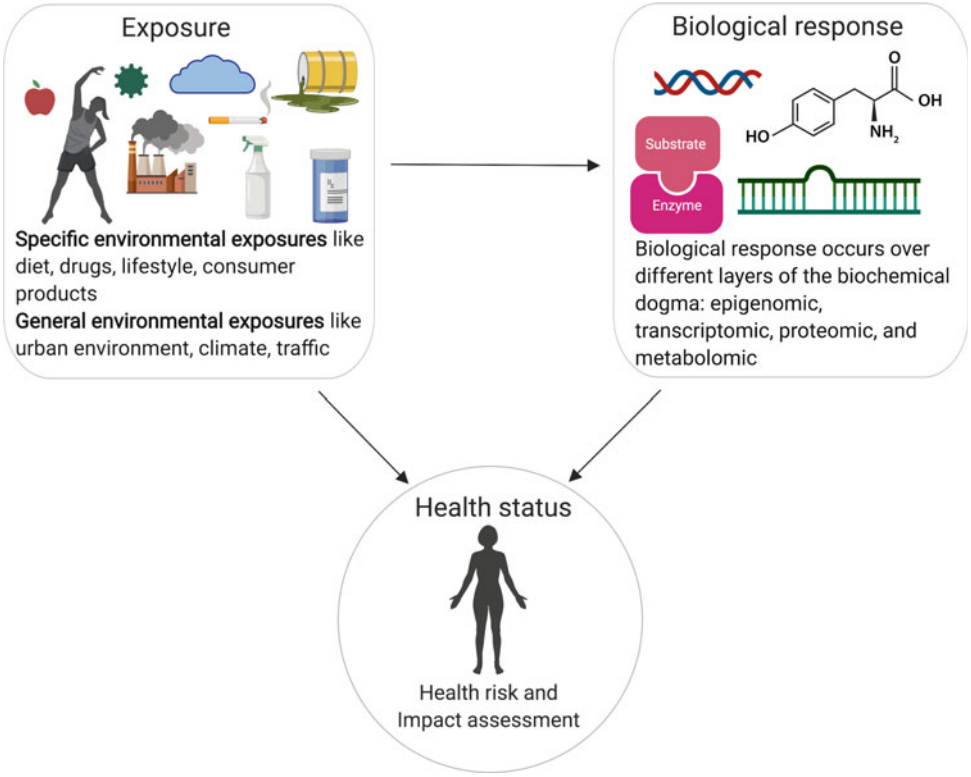

Fig. 1 The exposome concept Environmental exposures can derive from individual factors (like diet) and from general sources (like air pollution). Exposures that affect health leave a biological fingerprint that can be measured through changes in biological response in different biochemical layers. Integrating measures of external exposure and internal biological response create the exposomic framework to assess health status through risk and impact assessment. (Created with BioRender)

European Commission launched a new call within the H2020 framework, which will support 4–5 projects with a clear focus on the development of an exposome toolbox that should be coordinated by a cluster gathering of those projects. It is fair to say that several other projects within the EU are inspired by or address one of the exposures that constitute the exposome (Karjalainen et al. 2017). As an example, the EU biomonitoring program, HBM4EU, focuses on chemical exposures, while the project Lifepath addresses primarily socioeconomic aspects. There are other projects addressing urban exposures or the eco-exposome. While all these projects do not focus per se on technology developments, they do allow significant technological progress, most notably in analytical methodologies, sensor technology, biostatistics, and bioinformatics. Clearly, the upcoming exposome toolbox cluster will highlight and further develop these methodologies with the aim to support public health and regulatory decisions as well as informed individual prevention.

5 Environmental Chemistry and the Exposome

Chemicals released into the environment usually undergo transformations under different environmental conditions to produce intermediate chemicals. Several tools have been developed (Ruttkies 2016; Djoumbou-Feunang et al. 2019) which can help predict and identify unknown chemical signals measured in human and environmental samples. Efforts are underway to use high-resolution mass spectrometers to characterize all chemicals present in an environmental sample. Methods have been developed to identify "known unknown" chemicals using spectral fragmentation patterns that can help deduce chemical structure and identity (Schymanski et al. 2015; Gago-Ferrero et al. 2015).

In an epidemiological setting, Liang and colleagues used high-resolution metabolomics to characterize plasma and saliva samples from participants of a traffic-related air pollution exposure study. They measured a number of traffic-related air pollutants using external monitors and measured the association between exposure and metabolic profiles of the participants. Chemical features of interest that were significantly associated with exposure belonged to metabolic pathways related to inflammation and oxidative stress, including leukotriene and vitamin E metabolism (Liang et al. 2018).

6 The Exposome and Toxicology

More than 85,000 chemicals are registered with the EPA for manufacture, import, and use in commercial products. Approximately, 112,000 chemicals and compounds are registered with the US Food and Drug Administration as drugs or food additives (Niedzwiecki et al. 2019).

A majority of these chemicals have little information on their health effects at low concentrations and their influence as complex mixtures seen in real-world scenarios. This poses a significant challenge that requires expertise across several disciplines. Toxicologists have been systematically working through this list of chemicals that contribute to the chemical exposome. High-throughput screening assays have gained popularity for their efficiency and the high resolution of data they produce. They both conserve time and provide valuable insight for researchers toward the affected organ system or pathway that may be perturbed due to an exposure. The National Toxicology Program in the US has been leading a shift in current toxicological research, moving away from in vivo testing and incorporating high-throughput in vitro assays, model organisms, and computational models to study the adverse effects of exposure to chemical mixtures (Council 2007). Some of these methods are discussed below.

Structure–activity relationship (SAR). This method uses physical and chemical characteristics to predict toxicity based on the similar-property principle, i.e., similar structure = similar biological activity (Tong et al. 2003). These methods can be quantitative (mathematical modeling) or qualitative (recognize substructures that afford toxic properties). They have found utility in predicting toxicokinetics, half-lives, and the ability of chemicals to cross the blood brain barrier.

In vitro testing. Human cell lines and animal cell lines transfected to express human genes can be used to create assays to measure molecular changes due to different exposures. Modifying assay parameters and changing culture conditions can alter the context of exposures to answer specific biological questions. As an example, in vitro cell lines have been used to study the effect of exposure to mixtures on receptor ligand binding and activation. A group of researchers found that at low concentrations, a combination of two known pregnane X receptor (PXR) ligands resulted in a synergistic effect on activation of the receptor, which was not observed with each chemical alone. The researchers suggested that the two ligands together form a "supermolecular ligand" within the ligand-binding pocket of the nuclear receptor (Delfosse 2015). Findings such as these support the exposome concept in toxicological studies.

Cell-based in vitro assays can be used for high-throughput screens, which offer an economical way to screen a large number of chemicals in a short period. These screens are widely accepted in the pharmaceutical industry to predict therapeutic action, pharmacokinetics, interactions with enzymes, biotransformation, metabolic products, and have been used to rapidly detect interactions of drugs with genetic polymorphisms. Further, all methods described to measure biological response (Sect. 3.3.) can be applied on a cellular level to ascertain changes in gene expression, protein expression, metabolism, and epigenetic modifications due to an exposure.

Model organisms. While cell-based assays serve as excellent screening tools, single cells don't represent complex tissue interactions of a whole organism. To this end, model organisms like *Caenorhabditis elegans* (worms) and *Danio rerio* (zebrafish) have been gaining popularity as toxicological models. The short generation times of *C. elegans* make them excellent models to study aging and life course specific changes in response to exposure. Several molecular pathways have been conserved across evolution-making discoveries and observations in these models relevant for the human context. In a metabolomic study, Jones and colleagues described changes in metabolism in *C. elegans* as a result of exposure to a mixture of the heavy metal nickel and the pesticide chlorpyrifos. The authors noted changes in metabolism of the branched-chain amino acids and tricarboxylic acid cycle intermediates. They also found changes in reproduction (brood size) due to exposure to this mixture of toxicants (Jones et al. 2012).

7 Conclusion and Future Directions

Understanding the relationship between the totality of environmental exposures and health poses many challenges. Many exposures are largely involuntary and dynamic, and not all environmental exposures have been fully characterized. Studying the exposome thus relies on cutting-edge technologies that can detect and identify chemicals we are exposed to, moving beyond a targeted list of known chemicals of interest. Analysis and interpretation of this data requires various data analytical techniques: dimension reduction techniques, data integration, network analysis, and longitudinal analysis to name a few. Apart from novel data analytical applications, the field will also need to think about confounders and effect modifiers when measuring associations between exposure and disease. For example, how should social class or socioeconomic status be treated in a model—as a confounder, effect modifier, or a determinant of exposure? Uncovering the exposome will need input from scientists working in the fields of environmental chemistry, toxicology, exposure science, epidemiology, molecular biology, analytic chemistry, bioinformatics, and engineering. Thus, a multifaceted problem will be best tackled with multidisciplinary research teams.

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Insights into Exposure Sources, Processes, and Impacts

In Situ Passive Sampling Techniques for Monitoring Environmental Mixture Exposure

Lian-Jun Bao, Rainer Lohmann, Derek Muir, and Eddy Y. Zeng

Abstract

A large number of passive sampler devices have been developed for in situ sensing of polar and nonpolar organic chemicals in the environment. This chapter compiles and analyzes available information on the current progress in quantitation theories and technological improvements. The results show that it is critical to determine sorbent phase-water partition coefficients and sampling rates of target analytes for quantitation with the equilibrium and kinetic sampling strategies. Compared to passive sampling of organic contaminants in air, overlying water and sediment porewater, which has been extensively documented, measurements of organic contaminants in soil and at the air–soil interface have been largely unsuccessful with passive samplers. In addition, the combination of in situ passive sampling devices and bioassays could be a promising tool for directly assessing air and water quality with biological effects.

Keywords

Passive sampling • Organic contaminants • Field application • Biological effects

1 Introduction

A large number of organic chemicals are synthesized and registered, with the total number registered by government agencies reaching almost 394,000 worldwide (http://support.cas.org/). Most organic chemicals can be released into the environment through a variety of pathways, such as direct atmospheric emissions and domestic, industrial, and agricultural wastewater discharge, etc., which poses potential health hazards to organisms and humans. Monitoring of organic contaminants in the environment is necessary for examining their occurrence and ecological risk though a mixture of exposures. Of particular note is that gaseous or freely dissolved organic contaminants are considered bioavailable for organisms. Conventional active sampling methods involve relatively complex and time-consuming procedures only provide instantaneous concentrations of target analytes. Comparatively, passive sampling techniques, on the principle of "like dissolves like" with sorbent phases, are easy to operate and often yield time-weighted average concentrations. Due to a great enrichment in the sorbent phase, the detection limits of a mixture of organic contaminants for passive sampling techniques can be lower than those using active sampling methods if the sampling costs are similar.

Because passive sampling techniques are simple to operate and cost-effective, they have opened up a new opportunity for in situ tracking dissolved organic chemicals including polar and nonpolar in air, water, and sediment. For instance, the Global Atmospheric Passive Sampling (GAPS) Network initiated in December 2004 has conducted measurements of persistent organic pollutants (POPs) and priority chemicals in the atmosphere with passive air samplers (Pozo et al. 2009). The GAPS monitoring program has covered more than 55 sites on 7 continents in urban, rural, and remote regions (Koblizkova et al. 2012). In 2010, Lohmann and Muir (2010) called for the establishment of a monitoring network of POPs in global aquatic environments using passive sampling devices, especially with polyethylene (PE) as a sorption phase. In

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2016, two workshops, initiated by the co-authors of this chapter and with the participation of more than a dozen experts, were held in Guangzhou, China to discuss the key steps for establishing the Aquatic Global Passive Sampling network and launch the first round of global sampling activities (Lohmann et al. 2017).

Over the decades, an increasing number of in situ passive sampler devices have been developed with different sorbent phases. The corresponding quantitation methods have also been established and tested in under field conditions. Some in situ passive sampler devices, such as semipermeable membrane device (SPMD) and PE diffusion bag, have gradually been adopted as routine monitoring tools by local and national government agencies (Interstate Technology and Regulatory Council 2004; Huckins and Alvarez 2019). To date, new materials have been synthesized and used as novel sorbent phases (Ren et al. 2018; Zheng et al. 2018). A recent innovation is the development of samplers using multi-material 3D printing to produce low-cost passive sampler devices with porous membranes, which were initially used for evaluating the uptake of atrazine in water (Kalsoom et al. 2018).

This chapter reviews the latest developments in typical passive samplers for sensing polar and nonpolar organic chemicals in environments in an attempt to comprehend the current progress in quantitation theories and technological improvements of in situ passive sampling devices.

2 Quantitation Theory

The essential and principal objective of in situ passive samplers is to quantify the gaseous or freely dissolved organic contaminants in air, water, or sediment. Generally, the quantitation methods have been developed based on the partition process of a target analyte between the sorbent phase and environmental matrix within a passive sampler (Fig. 1). Here, two quantitation methods for in situ sampling on equilibrium partitioning and kinetically controlled diffusion respectively are introduced.

2.1 Equilibrium Sampling

When a target analyte in an environmental matrix (air or water) equilibrates with that in the sorbent phase of a passive sampler, its gaseous or freely dissolved concentration (defined as C_f) can be derived by

$$C_f = C_s/K_f \quad (1)$$

where C_s is the analyte concentration in the sorbent phase at equilibrium and K_f is the equilibrium partition coefficient of

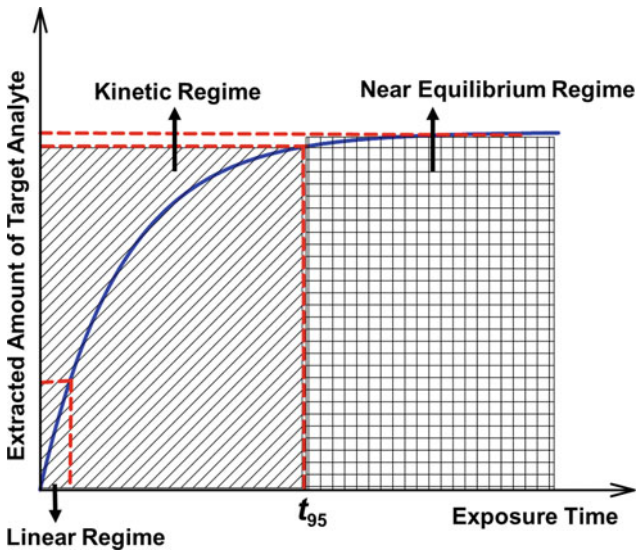

Fig. 1 Typical extraction profile of a target analyte in a passive sampler's sorbent phase (Ouyang and Pawliszyn 2008)

the analyte between the sorbent phase and environmental matrix. The determination of K_f is the key step for both quantitation methods.

Over the decades, the K_f values for a large number of organic contaminants in different sorbent phases have been determined and summarized in some review articles. For example, Difilippo and Eganhouse (2010) compiled 55 references to evaluate the experimentally determined polydimethylsiloxane (PDMS)-water K_f for polycyclic aromatic hydrocarbons (PAHs), polychlorinated biphenyls (PCBs), chlorinated benzenes, DDT compounds, hexachlorocyclohexanes, chlorinated cyclodienes, organophosphorus insecticides, pyrethroids, carbamates, triazines, polybrominated diphenyl ethers (PBDEs), and BTEX at different temperatures and with different coating thicknesses of PDMS coating in freshwater or seawater. Lohmann (2012) also summarized a list of K_f for PAHs, PCBs, PBDEs, organochlorine pesticide, triclosan, etc. between low-density polyethylene (LDPE) and water. Recently, Lao et al. (2017) experimentally determined K_f values of 112 moderately hydrophobic organic compounds including PAHs, PBDEs, PCBs, and pesticides between poly (methyl methacrylate) and water. Smedes (2018) also measured silicone–water K_f values of 80 organic compounds, such as phthalates, musks, organophosphorus flame retardants, chlorobenzenes, pesticides, selected PCBs, and a number of miscellaneous compounds using a cosolvent method. Collectively, it is interesting to note that the relationships between log K_f and log K_{ow} (octanol–water partition coefficients) were established for unknown compounds in these four aforementioned and other references (Bao et al. 2011; Yang et al. 2006). It has been debated for years whether the relationship between log K_f and log K_{ow} should continue to be linear or

become nonlinear as log K_{ow} reaches 7–7.5 and beyond. Several factors, such as poor mass balance, low solubility for very hydrophobic organic chemicals (VHOCs), loss of VHOCs to container surfaces by sorption, nonequilibrium state, chemical molecular volume, and energy barrier for chemical diffusion into polymer structure have been implicated as the causes for the aforementioned relationships (Lao et al. 2017; Bao et al. 2011). Apparently, further investigations into the correlative relationship between log K_f and log K_{ow} are necessary and beneficial for extending the application of passive samplers to nontarget VHOCs. In addition, the effects of temperature, ionic strength, and pressure on the K_f have been reported and should also be taken into account in developing passive sampling methods.

2.2 Kinetic Sampling

Compared to equilibrium sampling, the advantage of kinetic sampling is the relatively shorter sampling time required, which would somewhat reduce the likelihood for loss or damage of passive samplers in field deployment. On the other hand, the detection limits with the same amount of sorbent phase is greater for kinetic sampling than for equilibrium sampling for obvious reasons. Generally, the kinetically controlled diffusion process for HOCs is divided into two regimes, i.e., linear and curvilinear (Fig. 1). Within the linear uptake regime, C_f can be calculated by

$$C_f = N/R_s t \tag{2}$$

where N is the analyte mass in the sorbent phase at sampling time t and R_s is the sampling rate. Within the curvilinear uptake regime, C_f can be determined by

$$C_f = \frac{C_s^t}{K_f(1 - \exp(-\frac{R_s t}{K_f m_s}))} \tag{3}$$

where C_s^t is the analyte concentration in the sorbent phase at sampling time t and m_s is the mass of the sorbent phase. Obviously, it is critical to determine R_s for estimating C_f.

To in situ calibrate R_s of target analytes, the best approach is to spike performance reference compounds (PRCs) into the sorbent phase before deployment, assuming that the isotropic exchange kinetics between the uptake of the target analytes to the sorbent phase and the dissipation of PRCs from the sorbent phase to ambient environment are the same. Under this assumption, C_f can be expressed as

$$C_f = \frac{C_s^t}{K_f(1 - \frac{q}{q_0})} \tag{4}$$

where q and q_0 are the amounts of a PRC at time t and 0 on the sorbent phase. Equation (4) indicates that C_f can be directly determined from the initial and remaining amounts of the PRC in the sorbent phase and the equilibrium partition coefficient K_f. For the best calibration, the PRCs should be the isotopically labeled analogues of the target analytes. If isotopically labeled PRCs are not available, unlabeled and homologous chemicals which have similar physiochemical properties with the target analytes but are seldom detected in the environment can be used as PRCs. Several calibration methods, such as non-linear least squares regression (Booij and Smedes 2010), molar volume adjustment (Tomaszewsky and Luthy 2008), correlation between and log R_s and log K_{ow} (Yao et al. 2016), one-dimensional model (Fernandez et al. 2009), and exposure adjustment factors (Huckins et al. 2002), have been developed to estimate the R_s of a suite of analytes without isotopically labeled PRCs. However, the limitations of PRCs calibration methods (Liu et al. 2013a), such as high cost and retained fraction, have been recognized. Hysteretic desorption of PRCs from PE and PDMS occurred with in situ passive sampling HOCs in sediment porewater under stagnant conditions, resulting in anisotropic exchange kinetics of PRCs and target analytes (Bao et al. 2016; Choi et al. 2016). Such anisotropic exchange kinetics in sediment requires more complicated use of PRC-based calibration methods; several of these have been detailed in the literature (Fernandez et al. 2009; Sanders et al. 2018; Thompson et al. 2015). To deal with this issue pragmatically, periodic agitation was introduced for in situ passive sampling of VHOCs in sediment porewater (Jalalizadeh and Ghosh 2017).

Besides dynamic conditions, complex environmental matrices also exhibit some effects on kinetic sampling. Lin et al. (2018) found that the dissipation rates of HOCs from PDMS fiber in water were enhanced by a factor of 70 and 34 with addition of humic acid and 2-hydroxypropl-β-cyclodextrin, respectively. They also developed a quantitative structure–activity relationship model to associate the experimental dissipation rates of the target HOCs with their physical–chemical properties and dissolved organic matter contents (Lin et al. 2018), which may be applied in estimating dissipation rates of HOCs in natural environments.

Kinetic sampling is often adopted for polar organic chemicals. Similar to HOCs, the quantitation methods for most polar passive samplers, such as Chemcatcher™ and polar organic chemical integrative sampler (POCIS), are also based on the uptake profiles of target analytes in the sorbent phase (Gong et al. 2018). As a result, Eq. (3) has been used to calculate the concentrations of polar organic chemicals in water with the aforementioned passive samplers. However, it should be noted that the PRC calibration method is not suitable for in situ calibration of the sampling rates of polar organic chemicals because of the anisotropic kinetics (Guibal et al. 2015; Fauvelle et al. 2012). Given the common structures of polar passive samplers, such as POCIS and

diffusive gradients in thin film technology (DGT), diffusive layer is usually designed to ensure that the uptake of target analytes into the samplers is a linear process. Under this circumstance, Eq. (2) can be used to quantify concentrations of polar organic compounds in water or sediment porewater. Alternatively, the concentration of a target analyte can be obtained by (Davison and Zhang 1994)

$$C_{\mathrm{f}} = \frac{M\Delta g}{DAt} \tag{5}$$

where M is the analyte mass in the receiving or sorbent phase; Δg is the thickness of diffusive layer; D is the diffusion coefficient of the analyte through the diffusive layer; and A and t are the exposed area and sampling time, respectively. In addition, a series of environmental factors, such as hydrodynamic conditions, temperature, pH, ionic strength, and dissolved organic matter, have some impacts on passive sampling of polar organic chemicals. These issues were recently reviewed by Gong et al. (2018). Also, standardization of the sampler layout has been recommended to better calculate the sampling rates of polar organic compounds with passive samplers (Booij and Chen 2018).

3 Method Development

3.1 Polar Organic Chemicals

Chemcatcher™ and POCIS are the common passive samplers for measuring polar organic chemicals in water. Their configurations with different receiving phases or sorbent phases have been described in previous studies (Bernard et al. 2019; Kingston et al. 2000; Ahrens et al. 2018). Here, a newly developed promising sampler is introduced as an example of recent progress in method development.

The emerging sampler is organic-DGT, named as o-DGT. In fact, DGT has been widely used to measure free elements in aquatic environments since 1994 (Davison and Zhang 1994). Recently, it was modified for polar organic chemicals by replacing inorganic diffusive gel and receiving phase with organic gels. The superiority of o-DGT over Chemcatcher™ and POCIS is the independence of sampling rates with hydrodynamic conditions (Challis et al. 2016). Collectively, the main configurations of all o-DGT samplers are similar, with a protected filter, diffusive phase, and binding agent (receiving phase), which looks like a sandwich. The materials for diffusive phases and binding agents of o-DGT samplers vary with different applications. For example, Challis et al. (2018) used o-DGT sampler with a 0.75 mm Waters OASIS HLB binding gel and outer diffusive gel of same thickness, both of which were made of 1.5% agarose, to determine 27 pharmaceuticals and 7 pesticides along the Red River from the United States–Canada border. Two novel o-DGT samplers were developed, which consist of XAD18 and HLB, respectively, as binding phases to measure perfluoroalkyl substances and organophosphorus flame retardants in aquatic system (Zou et al. 2018; Guan et al. 2018). Chen et al. (2015) used o-DGT samplers with a 0.5 mm XAD18 resin gel as a binding phase, 0.8 mm agarose diffusive gel, and polyethersulfone filter membrane to in situ measure the concentrations and fluxes of four antibiotics in soils. XDA-1 resin was used as binding phase of o-DGT sampler for measuring endocrine disrupting chemicals in seawaters (Xie et al. 2018). Of particular note is that a porous carbon material from metal–organic framework was used as novel binding gel to in situ measure antibiotics in water (Ren et al. 2018). The cyclodextrin polymer membrane was also adopted as the novel binding phase of DGT sampler to determine the concentrations of triclosan, triclocarbon, and methyl triclosan in rivers (Wei et al. 2019). In summary, o-DGT samplers are an important and emerging passive technique for in situ sampling of polar organic chemicals and moderate HOCs in water and soil.

3.2 Nonpolar Organic Chemicals

3.2.1 Polyurethane Foam Disk

Polyurethane foam (PUF) has been used to collect gaseous HOCs with an active high-volume air sampler. It is also employed as a sorbent phase (PUF disk) in passive air sampling—this is one of a few passive samplers that actually also collects HOCs on particles (Rauert et al. 2018; Francisco et al. 2017). Generally, a PUF disk consists of two stainless steel domes or bowls with external diameters of 30 and 20 cm, respectively. Polyurethane foam as the sorbent phase PUF is housed inside the lower dome, and target compounds in the air are allowed to freely pass through the gap between the domes and holes in the bottom surface of the lower dome and sorbed into the PUF (Pozo et al. 2004). The domes are designed to protect the PUF from potential damage by precipitation, particle deposition, sunlight (for degradation of the target chemicals), and wind. Another type of passive air sampler, i.e., polymer-coated glass, contains the same shelter as the PUF disk, but has a thin layer of ethylene vinyl acetate as the sorbent phase. Apparently, this PUF is supposed to sense HOCs in the gaseous phase. Abdallah and Harrad (2010) modified the PUF disk for monitoring brominated flame retardants in the vapor and particulate phases in indoor air. In their design, the PUF was mounted from the middle of the lower dome to the top of the upper dome and a glass fiber filter (GFF) was suspended in the middle of the lower dome for collection of depositing particulates. Similarly, Tao et al. (2007) used PUF and GFF to construct a passive air sampler capable of collecting

gaseous and particle-affiliated PAHs. The shelter is a stainless steel cylinder with an upper cover and a porous bottom plate, and air can easily flow over the cylinder through the holes in the bottom plate. Particulates are trapped by the GFF suspended in the cylinder at the height of 10 mm, while gaseous PAHs are sorbed by the PUF attached to the top cover. The GFF and PUF are supported by backup plates fastened over a certain screw stem with nuts.

Passive air samplers with PUF as the sorbent phase are the most widely used devices in field monitoring of HOCs. The impregnation of ground XAD resins into PUF also greatly improves the sensitivity of detecting HOCs in field application (Koblizkova et al. 2012). The PUF disk has been used to measure PAHs, PCBs, PBDEs, OCPs, and polychlorinated naphthalenes (PCNs) in the atmosphere of Europe, Chile, and other countries (Pozo et al. 2004; Jaward et al. 2004a, b; Wilford et al. 2004). The sampling time of PUF disk for chemicals with log K_{OA} greater than 8.5 can be several weeks or even months (e.g., 100 and 450 days) (Wilford et al. 2004; Shoeib and Harner 2002). Because sampling rates are strongly dependent on wind speed, prolonged sampling time can lead to large uncertainties for quantitative measurements (Wilford et al. 2004; Shoeib and Harner 2002; Tuduri et al. 2006). Additionally, small amounts of particulates enriched with low volatile HOCs may be accumulated by the PUF disk during outdoor exposure (Wilford et al. 2004; Jaward et al. 2004), undermining the measurement accuracy for gaseous HOCs. This was probably the main reason for adjusting the position of PUF and adding GFF for collecting particles in modified PUF disks (Wilford et al. 2004; Jaward et al. 2004). While this can undermine the measurement accuracy for gaseous HOCs, it has major benefits for determining total airborne concentrations of semi-volatile compounds. Further studies with dome-enclosed PUF disk samplers has demonstrated that they accumulate particles, ranging in size from 250 to 4140 nm, with no discrimination compared to conventional PS-1-type active air samplers (Markovic et al. 2015).

3.2.2 XAD

XAD-2 (styrene-divinylbenzene copolymer) resins have long been used for high-volume active air sampling. A novel passive sampler using the same resin was first reported by Wania et al. (2003). The sampler consists of a narrow resin-filled cylinder made of a fine stainless steel mesh placed in a protective sampling shelter with an opening at the bottom and under the cap at the top. Comparison of XAD and PUF-passives, as well as active XAD-PUF sandwich (high volume and low volume) sampling for pesticides in air, showed that all four yielded similar concentrations with no systematic bias among them Hayward et al. (2010). However, the XAD-passive had slower update rates than PUF-passives and thus appears to be best for long-term deployments while PUF-PAS deployed for 3-month periods are able to reveal seasonal patterns quite clearly (Gouin et al. 2008). XAD-2 is more dense (bulk density = 640 kg m^{-3} vs. 20–40 kg m^{-3} for PUF) and less porous (porosity = 0.41 for XAD-2 vs. 0.97 for PUF) than PUFs. XAD-based passives are also less likely to accumulate airborne particles than PUF-passives due to sampler design and the very small pore diameter of XAD-2 (90Å) (Armitage et al. 2013). Sampling rates for XAD-passives have been shown to be sensitive to temperature and thus results are often reported in terms of nanograms per sampler rather than converted to concentrations. XAD-passives have been used for numerous studies of global air concentrations of relatively volatile organics such as volatile methyl siloxanes (Xu and Wania 2013) and perfluoroalkyl substances (Gawor et al. 2014), as well as for current use pesticides (Shunthirasingham et al. 2010).

3.2.3 Polyethylene

Because of its cost-effectiveness and ease to handle, polyethylene (PE), especially low-density polyethylene (LDPE), has emerged as the widest applied sorbent phase for in situ passive samplers. Under field conditions, the structure of PE-based devices is often quite simple. In earlier applications, bare PE films with different thicknesses ranging from 25 to 100 μm (Fig. 2a) were used to sense HOCs in air, overlying water, and sediment porewater (Cornelissen et al. 2008; Ruge et al. 2018; Apell and Gschwend 2016). Over the years, certain external supporting frames have gradually been designed to handle LDPE films more easily or to determine concentration profiles of HOCs in porewater and/or at the sediment–water interface. For example, Lohmann et al. (2017) designed a stainless steel cage to hold a total of 24 LDPE or silicone rubber sheets, each sized in 4 cm (width) × 8 cm (length), for measuring HOCs in freshwater and seawater across the globe. Oen et al. (2011) fixed LDPE films to a stainless steel sediment-penetrating rod and deployed it in San Francisco Bay, California, USA for determining vertical pore water profiles of PCBs. Lin et al. (2015) designed a central probe (Fig. 2c) with a tripod frame for landing on sediment bed to sense concentration profiles of HOCs from 30 cm above to 30 below the sediment–water interface. The probe is a hollow stainless steel tube attached with 24 depressions wrapped by PE films at 2.5 cm intervals. In addition, a sampling box for collecting PAHs and PCBs in soil air was designed to contain LDPE strips strung on a carrier, which were deployed on a grate above the soil (Donald and Anderson 2017).

Our group has also developed a series of in situ passive samplers (Fig. 2b, d, e, and f) with PE as the sorbent phase, including open water passive sampler, multi-section passive sampler, sediment–water interface passive sampler, and air–water passive sampler, which can be used to determine

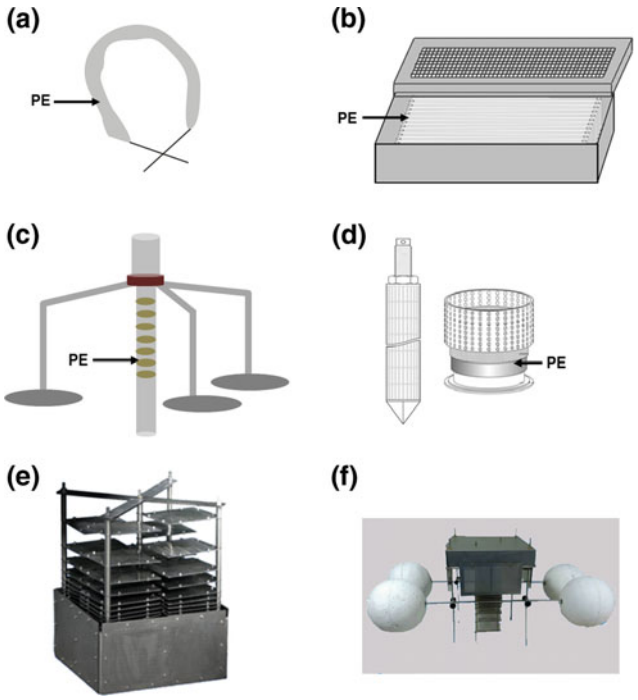

Fig. 2 Typical passive samplers based on polyethylene (PE) or polyoxymethlyene (POM) film: **a** PE membrane (Adams et al. 2007); **b** Passive water sampler (Bao et al. 2012); **c** A probe for measuring concentration profiles of HOCs at the sediment–water interface (Lin et al. 2015); **d** multi-section passive sampler (Liu et al. 2013b); **e** passive sampling device for measuring sediment-water diffusion fluxes of hydrophobic organic chemicals (Liu et al. 2013c); **f** air–water passive sampler for measuring concentration profiles of HOCs at the air–water interface (Wu et al. 2016)

concentrations, depth profiles, and exchange fluxes of HOCs in overlying water, sediment porewater, and sediment–water/air–water interfaces, respectively. All samplers were so designed to prevent large particles from adhesion onto LDPE film by adding GFF and porous shield. With this protective mechanism, target chemicals are allowed to freely penetrate through the porous shield and GFF and diffuse into LDPE phase. Specifically, the open water sampler (Fig. 2b) is composed of a rectangular copper box with two open frames, which are filled with two stainless steel porous plates, and GFF (Bao et al. 2012). Strips of LDPE in the copper box are fastened in a bracket of comb-like structures (Bao et al. 2012). The sediment porewater sampler (Fig. 2d) consists of a series of sampling cells isolated from each other with seclusion rings (Liu et al. 2013b). The sediment porewater sampler is able to measure concentration profiles of sediment porewater HOCs at 2 cm intervals (Liu et al. 2013b). The sediment–water interface sampler (Fig. 2e) is comprised of one upper and one lower section, intended for collecting HOCs in overlying water and sediment porewater, respectively (Liu et al. 2013c). In the upper section, the sampling cells are in a horizontal spiral arrangement and isolated by stainless steel spacers of different thicknesses. In the lower section, the sampling cells, like sandwiched LDPE strips, are arranged vertically and isolated by stainless steel grating panels at an identical interval of 0.2 cm. Similarly, the air–water sampler (Fig. 2f) consists of two parts, intending for sensing gaseous and freely dissolved HOCs in air and water, respectively (Wu et al. 2016). For the upper part, an external setup was designed to protect the sampler from rainfall and photolysis of target analytes from sunlight. Four floats are fastened in two parallel support rods to ensure the sampler floating in water. The consecutive sampling units are placed horizontally and separated by stainless steel spacers of different thicknesses.

3.2.4 Silicone Rubber

Silicone rubber is a silicon–oxygen polymer with high content of PDMS, the commonly used sorbent phase for solid-phase microextraction. As a polymer sorbent phase, silicone rubber has been used as different bare shapes, such as rods, sheets, and tubes, for in situ passive sampling of HOCs in surface water (Emelogu et al. 2013a; Silva-Barni et al. 2019; van Pinxteren et al. 2010). It can be cut into trips similar to PE film and acts as the sorbent phase for the aforementioned sampling devices. It should be noted that silicone rubber membrane is softer and sticker than PE film at the same thickness, thereby relatively thicker silicone rubber (often 0.5 mm) can be adopted. Compared to PE, silicone rubber exhibits greater accumulation of moderate and light HOCs and is allowed to sense HOCs with a wider range of log K_{ow} in water (Pintado-Herrera et al. 2016; Allan et al. 2013).

Besides field measurement of organic contaminants, silicone rubber has been widely used in toxicological tests with in vitro and in vivo bioassays by exposing test organisms, genes, and cells to extracts of in situ passive samplers (Emelogu et al. 2013b; De Baat et al. 2019). For example, Liscio et al. (2014) observed anti-androgenic effects in extracts from silicone strips, which were deployed for 14 days in a river contaminated by wastewater effluent. Novak et al. (2018) also observed quantifiable endocrine disruption effects in extracts of silicone rubber samplers with 5-d deployment in the Danube River. Obviously, the combination of passive sampling techniques, not limited to silicone rubber, and bioassays may be a promising tool for directly assessing water quality and identifying new and emerging nontarget analytes with biological effects.

4 Conclusions

Passive sampling techniques have been widely used to in situ measure the concentrations of organic contaminants in the environment, determine their exchange fluxes between