Integrating Molecular and Protein Diagnostic Approaches with Advanced Chemical Sensors to Study the Impact of Pollutants on Human Health and Plants

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Abstract

Pollution is a major global concern that is steadily increasing due to numerous anthropogenic activities. Contamination of the air, water, and soil are known to be key factors impacting human health, ecosystem stability, and causes of biodiversity loss. Human exposure to pollutants can be detected using different -omic approaches. Molecular and protein diagnostic tools with advanced chemical sensors can also be integrated to study the concentration and biomolecular effects of pollutants in environmental samples, thus acting as complementary platforms to provide deeper understanding of human risk assessment.

Recent trends indicate that novel pollutants with unknown effects are emerging and being detected. Development of new detection systems including lab-on-a-chip technology, wearable sensors, and CRISPR technology designed for biomonitoring is indicative of the growing need for sensitive and accurate detection of environmental pollutants. Integrating innovative detection systems with novel -omic datasets can help in generating early warning signals to assist in taking preventive measures for protecting human health and the environment.

Content

Chapter - 1

Introduction to Environmental Pollutants

Pollution is among the catastrophic problems faced by humanity today. Pollutants can impair human health and the environment both immediately and indirectly, including during their production, distribution, degradation, and final disposal in any form. A pollutant can be present in gaseous, liquid, or solid form, and its toxic effects can be manifested at various levels of biological organization, from molecules to cells, tissues, organs, organisms, populations, and communities. A wide variety of natural and synthetic materials can be considered pollutants, although natural pollutants (e.g., volcanic gases) are relatively rare.

Pollutants can be classified according to several criteria, including origin (natural/synthetic), state of matter (solid/liquid/gas), biological properties (biodegradable/non-biodegradable), and time scale of action (primary/secondary). Primary pollutants are those that contaminate the environment directly as a result of human activities (e.g., pesticides, metals, solvents), while secondary pollutants are formed by subsequent biochemical reactions or transformations (e.g., ozone, smog, toxic by-products of plankton decomposition in polluted waters). In general, the four main classes of environmental pollutants of human concern are heavy metals, organic compounds, particulate matter, and/or simple gases. [1, 2, 3]

Classification of Environmental Pollutants

Environmental pollutants can be classified into distinct groups according to their origin, distribution, persistence, bioaccumulation, and mode of action. Established categories include heavy metals/metalloids, organic pollutants, and infectious microorganisms. Recent molecular- and protein-based detection strategies enable the identification of specific pollution sources by recognizing the bioaccumulation of pollutants in biological systems, as well as the stress response of the organism. These methods achieve high specificity, sensitivity, and flexibility and require low sample volumes for biomonitoring of human health. Advanced chemical sensors enable real-time detection in soil, air, and water compartments, with emerging applications in wearable, implantable, and lab-on-a-chip technologies.

Classical toxicology studies target a few contaminants among a vast number of environmental pollutants with the goal of understanding their effects on health. However, research directed at wholly understanding the effects of all environmental pollutants and their numerous interactions remains largely unaddressed. Consequently, modern toxicology methodology has incorporated new tools, such as molecular and protein-based approaches, and advanced chemical sensors to overcome the limitations of traditional toxicology. [4, 5, 6]

Sources and Pathways of Contaminants

Sources of environmental pollutants can be divided into four categories: natural, anthropogenic, incidental, and upstream. Natural sources include forest fires and eruptions. Although still a matter of concern, their periodic occurrence and lower concentration compared to anthropogenic sources moderate the overall load. Pollution incidents from industrial sites during a malfunction or disasters may trigger the local environment to exceed the assimilative capacity for a limited duration. Upstream sources involve residues from agriculture, industry (effluents), or very-highway construction and maintenance (e.g., secondary aerosols).

Transport of air-borne pollutants in smaller, very fine, and ultra-fine particulate matter (particulates of size 2.5 μm and below), organic carbonose or secondary organic aerosols can be carried out in clouds and fogs over several hundreds of kilometers towards the oceans; dendritic or nose-shaped features support this. Polluted aerosols may also act as freezing nuclei in cloud formation. Long-range transport of atmospheric pollutants has been observed from the Indian subcontinent towards the Himalayan region and the Arctic region, though deposition goes mainly in the cloud-forest area. Air-launched long-range bombs of polychlorinated biphenyls (PCBs) have also been identified in North Polar regions as products of long-range atmospheric transport. Pollutants can enter soil or water through dry or wet deposition and disturb regional or local equilibrium and aside from heavy metals like lead and cadmium may cause edaphic factors to cross threshold limits.

Chemicals moving from air to soil or water (mercury in aerial form) or other forms via mantle contact or other pathways should also be viewed. Lead dioxide present in living beings is in the contact with Opalinus clay. The Raceway soil in France has an accumulation of these long-lived pollutants and certain waxy and oily chemicals (VOCs) of gasoline. Other organics and greases tend to escape under light conditions. During migration chemicals may also interact with the soil environment (temperature, moisture, pH, iron, manganese, etc.). The fate of pollutants in soil is determined by biogeochemical processes, but further entry into ground water assumes importance. For instance, organochlorine pesticides in Kanpur soil have been exonerated from soil surfaces because of higher temperatures in summer and monsoon-raised moisture level. [7, 8, 9, 10]

Mechanisms of Pollutant Transport in Air, Water, and Soil

To evaluate their effects on human health and the environment, the bioavailability of external pollutants will be assessed. The amount of a toxic element that reaches a living organism is a critical factor that can cause damage, even when the element's concentration is lower than the no-observed-effect or lowest-observed-effect concentration for that species. Bioavailability is influenced by the chemical form of the pollutant, transport processes, and interactions with living organisms. Once taken up, a pollutant can be translocated via the circulatory systems of animals or plants, leading to concentrations in tissues or fluids that can be used as exposure biomarkers. The ability to accumulate toxic elements in tissues and fluids is one pathway contributing to the adverse health effects of xenobiotics, including metals, solvents, and pesticides. Current trends in bioavailability monitoring, persistence-specialized toxicogenomic studies, and sensor technology are increasingly taking the human exposome and multi-omics into consideration.

Complex mixtures of waterborne pollutants are challenging to monitor. Electrophysiological measurements can detect the collective action of multiple organic pollutants, as well as their effects on human ion channel function and transcriptional activity by G protein-coupled receptors. The advance of the exposome concept and innovative tissue modeling, often using human cells, are allowing the combination of omics approaches with chemical-sensor-based monitoring to predict human exposure to complex mixtures. [11, 12, 13, 14]

Bioavailability and Environmental Persistence

Environmental contaminants generally exist in particulate or dissolved forms, and their concentrations in soil, water, and air are usually much lower than the saturation levels of pure substances. However, this does not indicate that they are not dangerous. Indeed, many toxic pollutants can cause persistent damage to organisms after repeated exposure or at ultra-trace concentrations. Molecular biosensors based on gene or protein markers for genotoxicity, oxidative stress, endocrine disruption, photosynthesis inhibition, and other adverse outcomes in human health or vegetation have been developed and utilized for bio-monitoring in various environments. Environmental persistence is one of the major contributors to the bioavailability of toxicants in the environment. Contaminants that are not readily bio-degradable in environmental compartments—such as water, soil, or air—may remain within the compartments for a long time. Their persistence, in combination with their ability to bio-accumulate in the food chain and cause toxicity in mammals including humans, leads to their appearance in biological matrices such as urine, blood, hair, and others, even though humans or mammals may not be directly exposed to the toxicants themselves. Reliable detection of these toxicants in biological matrices provides stronger evidence for the estimation of environmental health risks.

Furthermore, a correlation has been identified between the bioavailability of hazardous metals in the environment, monitored through biosensors, and the corresponding concentration of metals in the urine of exposed human populations. Environmental monitoring not only helps in identifying "hot spots" of pollution at a specific location but also facilitates estimation of human exposure risks for a specific population group, especially in developing countries where regulatory bodies may lack resources to conduct large-scale monitoring studies. Contaminated soil or agricultural field environments are particularly useful for monitoring the behavior of pollutants, since these toxicants enter the food chain through crop plants, which again affect human health. [15, 16, 17, 18]

Global Trends and Emerging Pollutants

Pollution has become a major global problem, with increased production and use of various synthetic and natural chemicals contributing to environmental degradation through persistent accumulation. Reports from the World Health Organization (WHO), the World Wildlife Fund (WWF), and the United Nations Environment Programme (UNEP) underline that human activity has led to severe and widespread disruption of the natural balance. Adverse changes are occurring not only in the atmosphere but also in terrestrial and aquatic environments, with pollution as one of the causes. The impact of environmental pollution on human health, animals, ecosystems, air and water quality, and climate is much more serious than previously thought. New diseases and conditions such as Alzheimer's and Parkinson's diseases, autism spectrum disorders, prostate cancer, genital malformations, obesity, infertility, and pollen allergies are on the rise and might be related to contaminant exposure. The manifestation of some of these diseases is linked to exposure during sensitive periods in life, such as hormonal and reproductive development, fetal and infant life, and early childhood.

The scope of pollution has recently changed as previously ignored or neglected pollutants become serious health threats. It is now widely accepted that endocrine disrupting chemicals (EDCs), drugs and their metabolites, plasticizers and additives, cleaning agent remnants, pheromones, and other compounds can be found in the environment and biological samples. Novel pesticides, heavy metal mixtures, industrial and agricultural solvents, volatile organic compounds VOCs, organic aerosols, and nanoparticles should also be included. The development of diagnostics adapted to these emerging new classes of pollutants or classes with new approaches and original applications must therefore be considered. [19, 20, 21, 22]

Chapter - 2

Fundamentals of Molecular Diagnostics

Molecular diagnostic tools allow for the detection of organisms, viruses, genetically modified organisms (GMOs), and genes associated with diseases using DNA or RNA. Beyond detecting specific microbes, DNA-based approaches can be used for microbial community composition analysis, biomarker detection, and population modeling. Variants such as reverse transcription, quantitative real-time PCR (qPCR), and digital PCR have also been developed for the higher sensitivity detection of specific nucleic acid sequences. Development of highly sensitive molecular methods in undersampled regions has enabled the discovery and monitoring of new contaminants in environmental matrices. Nonetheless, such approaches require high-cost specialized laboratory facilities and expertise, and have low sample throughput. Since the expression of functional gene-based proteins provides a direct indication of the physiological state of an organism, both DNA- and RNA-based techniques have been complemented with protein-based methods to describe pollutant-induced effects.

The use of DNA as the recognition element in electrochemical sensor platforms offers some advantages in sustainable pollutant detection. Principles of predicting pollutant persistence in an environment can be established based on the affinity of aptamers toward metal ions, and electrochemical amplified aptamer-based detection provides a way to achieve high sensitivity. Detection of microbial exRNA in environmental samples with real-time quartz crystal microbalance technology could allow for a real-time multilayer monitoring approach. Currently available electrochemical, colorimetric, and fluorescence sensor platforms can be adapted to leverage these novel molecular techniques. [23, 24, 25, 26]

DNA- and RNA-Based Detection Techniques

Molecular diagnostics allow direct detection of environmental contaminants and their toxic effects through biomarker identification. DNA-sensitive electrochemical sensors serve as important tools for monitoring pathogenic microorganisms and their plasmid-borne toxic genes. Living cells can also act as bioreceptors, producing metabolite responses to environmental hazards. New platforms integrating hybrid systems provide large signal changes for small amounts of target analytes. Aptamer-based sensors use oligonucleotides to recognize small organic molecules, proteins, or bacteria with a binding affinity rivaling antibodies.

DNA and RNA diagnostic techniques detect contaminants or their toxic effects by identifying pathogen or toxin-specific sequences. A major use is for pathogens in clinical samples, but other applications include environmental samples (water, soil, biofilms) and host systems. For example, sensitive DNA-based electrochemical sensors detect pathogenic microorganisms and their toxic gene plasmids. Living cells can also act as electrochemical bioreceptors, where redox-active metabolite secretion responds to environmental hazards. A recent advance is a dual-bacterium biosensor based on Escherichia coli for organophosphorus pesticide detection and Staphylococcus aureus for phosmet-hydrolase secreted metabolite detection. The hybrid system provides a large signal change for a small amount of target analyte. [27, 28, 29]

PCR, qPCR, and Digital PCR

Polymerase chain reaction (PCR) and its quantitative (qPCR) and digital (dPCR) variations are essential techniques in molecular diagnostics. The recent development of viral RNA touch-down real-time PCR technology assures simple, sensitive, and reliable environmental detection of the SARS-CoV-2 virus. PCR-based approaches amplify a specific DNA target in thermal cycles controlled by an external thermocycler equipped with temperature probes. Although limitations in ambient temperature can be eliminated by combining PCR detection with portable miniaturized thermocyclers, these batch approaches remain time-consuming. Real-time in situ detection of airborne viral RNA and the rapidity of these detection techniques can be significantly improved by a novel and cost-effective viral RNA Touch-down real-time PCR technique developed for SARS-CoV-2 detection.

Quantitative PCR (qPCR, real-time PCR) is a popular technique that measures the quantity of the amplified target sequence in real-time during the PCR cycles; the specific probe for the PCR reaction can be designed to possess a touch-down feature. Detecting a target sequence by increasing the ambient temperature definable around its melting temperature and then by progressively reducing the temperature, with a touch-down step of −2 °C on each cycle, ensures high detection specificity at all PCR amplification cycles. The highly affective detection and unequalled simplicity should make this approach useful for rapid environmental monitoring of RNA viruses by additional Touch-down real-time RT-qPCR or Touch-down real-time RT-dPCR detection, as well as for other types of DNA- or RNA-based environmental monitoring approaches. [30, 31, 32, 33]

Sequencing Technologies for Pollutant Biomarkers

The high-throughput sequencing technologies now enable genomic, transcriptomic, and metagenomic applications, providing all biomarkers of pollutants in organisms and their habitats. The transcriptomes of plants exposed to different soil pollutants are profiled to discover the differentially expressed genes, functionally classify them, and analyze their pathways and networks, which help understand plants' innate response mechanisms to toxic contamination. These investigations improve knowledge regarding the modulation of metabolic engineering-dependent efforts toward hyperaccumulator plants, deepen the understanding of plant tolerance to heavy-metal-contaminated soils, and offer a theoretical foundation for the developmental and ecological applications of metabolically engineered plants in heavy-metal-contaminated environments. Moreover, the transcriptomes of plants exposed to pyrethroid, chlorpyrifos, and neonicotinoid insecticides have been analyzed to detect common functionally altered pathways and expression patterns, presenting candidate metabolic detoxification genes and proposed detoxification-responsive molecular marker genes for the three insecticides.

Furthermore, the detection of organophosphate esters in an aquatic ecosystem has been performed by sequencing a metagenomic library of sediment DNA, and the functional potential of the sediment microbiome has been characterized by analyzing sequenced environmental metagenomic data. The highly abundant microorganisms annotated with the organophosphate ester degradation pathway have been isolated in enrichment cultures, and the effect of divalent metal ions downstream of the pilin gene cluster on bacterial motility and biofilm formation has been confirmed by knockout mutant analysis. Altogether, the investigated applications of high-throughput sequencing technologies open entirely new avenues in environmental and biological sciences. [34, 35, 36, 37]

Gene Expression Profiling

Gene expression profiling serves as a powerful tool in assessing the biological effects of environmental pollutants on various organisms. Advanced techniques detect specific gene products that respond to toxic exposure, emphasizing sensitivity and novelty. Expression analysis distinguishes environmental impacts from developmental variations in exposed wild animals.

Profiling strategies encompass microarrays and next-generation sequencing. Microarrays enable simultaneous detection of known annotated genes or customized panels, while RNA sequencing offers transcriptome-wide, unbiased detection. These approaches facilitate strain- and species-specific expression profiles and dose-response-driven biomarker discovery. Integrating bulk gene expression profiles with spatial transcriptomics reveals tissue, cell-type, and spatial-specific response patterns underlying observer–advertiser responses among wild populations. Identification of new gene networks and regulatory circuits modulating those networks further enhances the utility of bulk expression analysis. In a bulk profiling approach, the transcript level in a striped murrel, Channa striata, was determined after exposure to tobacco smoke, illustrating its sensitivity to waterborne toxicants.

A range of gene markers help elucidate the toxicity of cigarette smoke on aquatic organisms. Capable of detecting the effects of residual organophosphate insecticides; assessing embryonic development in zebrafish exposed to heavy metals; and monitoring the impact of heavy metals in exposed wild fishes, transcript expression analysis distinguishes pollution-induced biological consequences in wild fishes to assess their habitat health. However, because organisms in natural habitats encounter a combination of environmental factors rather than a single factor, these investigations can only suggest the level of habitat pollution. Plant–animal interactions potentially influence all organisms and can be better understood through interplay with plant signaling pathways. To elucidate such interactions, microarray-based expression profiling of acetylcholinesterase (AChE) in Channa striata exposed to different concentrations of the neurotoxic insecticide Physan 35, a product of the interaction between plant and animal systems, serves as a model.

Advantages and Limitations in Environmental Health Studies

Integrating molecular and protein diagnostic methods with advanced chemical sensors in pollution monitoring offers several important advantages while also presenting some key challenges. The development of sensitive, specific, and easily applicable methods to detect environmental contaminants through the assessment of molecular and protein signatures is a logical step, as the concentrations of many toxic chemicals or their biological effects can only be determined using accumulated biosampling resources. Compared with animal testing, which is often costly and time-consuming, human biomonitoring studies that correlate the presence of pollutants at trace levels in body fluids with the induction of environmental diseases can be carried out more rapidly and effectively.

Information gained from the analysis of human samples can be combined with field studies on live ecosystems and the direct examination of the plant response to toxins at the levels of expression, activity, and accumulation of the relevant molecular and/or protein markers. Furthermore, such data can be integrated with the development of chemical sensor and biosensor systems and combined with the growth of epidemic biomarker databases. Despite these compelling advantages, it must be stressed that such approaches are not applicable to all toxins, species, and exposure levels, and that the molecular markers indicated must be further validated in controlled exposure systems. In addition, the consideration of confounding factors potentially influencing the biomarker response, such as smoking, infections, and co-exposure to multiple toxins, is crucial for a proper interpretation of the results.

Chapter - 3

Protein-Based Diagnostic Methods

Methods for protein detection are important for determining alterations at the effect level in humans and plants exposed to environmental toxins. Protein expression profiling can help verify biological effects and elucidate potential modes of action of toxic compounds by identifying affected cellular pathways. Targeted protein analysis can be applied as a biomarker toolset for assessing exposure to hazardous substances and pollutants such as heavy metals, organophosphate pesticides, per-and polyfluoroalkyl substances (PFAS), and fine particulate matter (PM2.5).

Among protein analysis techniques, immunoassays are most commonly used for specific detection and quantification. These methods exploit the specific binding between antibodies and their corresponding antigen to measure protein concentrations. Enzyme-linked immunosorbent assays (ELISAs) are a widely applied type of immunoassay based on an enzyme conjugated to the detection antibody. During the reaction, the enzyme catalyzes a reaction that generates a colored product, the amount of which is inversely correlated with the concentration of the antigen. ELISAs can be detected qualitatively or quantitatively by the naked eye or using a microplate reader.

Detection of proteins using Western blot, which combines gel electrophoresis and immunoblotting, is another frequently applied method. This technique enables the determination of the size and relative abundance of proteins of interest in a specific sample. Labeled primary and secondary antibodies are applied to visualize and detect the absence or presence of target proteins. Various quantification assays have also been designed to provide absolute quantification of proteins of interest. In recent years, mass spectrometry-based proteomic analysis has emerged as a powerful technique for exploring changes in the entire proteome or in particular groups of proteins for which the information is analyzed in a label-free manner. [38, 39, 40, 38, 39, 40, 41]

Immunoassays and ELISA

The criteria for identifying several organic pollutants include immunological methods for monitoring the concentrations of these contaminants in human biological fluids based on high-affinity antibodies. Immunoassays are widely used to measure residues of different environmental toxicants in food and animal tissues. These well-established indirect approaches are also employed to estimate internal exposure of humans to pollutants, organophosphate pesticides, their toxic oxons and organophosphate metabolites. These procedures should be considered as potential alternative methods for hazard assessment of environmental chemicals and a step toward the development of ELISAs for other organic pollutants. Information is provided about the current state and future prospects of immunological approaches in environmental monitoring, with attention focused on the use of ELISA, the most common immunoassay, as a laboratory method, and immunobead assays suitable for background screening in epidemiological studies.

ELISA is the most common immunoassay for determining the concentrations of a wide variety of environmental contaminants that do not require Flow Injection Analysis. Moreover, the integration of specific antibody-coated immunobeads with mass spectrometry allows measurements of pesticide residues and other environmental chemicals in both human biological fluids and body regions such as hair. These two developments illustrate the utility of ELISA and functionalized immunobeads in assessing the internal exposure of humans to different environmental toxicants. Still, despite the multitude of other organic environmental pollutants, both current and emerging, only a limited number of immunoassays have been developed for continuos biomonitoring of human exposure.

Western Blot and Protein Quantification

The Western blot is a classic immunobiochemical technique for identifying specific proteins in complex mixtures based on their mobility during gel electrophoresis and subsequent probing with tagged pathogen-specific antibodies. The separation is typically performed on polyacrylamide gels using SDS-PAGE, followed by transfer to membranes (such as nitrocellulose or PVDF) and incubation with primary antibodies directed against specific epitopes. Following extensive washing, the blots are incubated with secondary antibodies linked to a reporter enzyme or fluorophore for detection. The technique allows for the simultaneous detection of multiple proteins by using antibodies with distinct colorimetric, chemiluminescent, or epifluorescent signals. Although it is a powerful technique now augmented with mass-spectrometric tools, caution is warranted in the interpretation of results, particularly in relation to thermally/chemically induced epitope modification, antibody cross-reactivity, and non-specific binding.

Accurate quantification of proteins is necessary to ascertain cellular homeostasis, organelle functionality, and signalling pathways. Protein levels are routinely measured in response to stimulation, convey their occurrence and indicate spatio-temporal distribution. Several strategies are available to assess protein abundance. Relative quantification relies on gel electrophoresis followed by staining with dyes that bind proteins in a non-specific manner, usually coomassie blue or silver. Absolute quantification of proteins is generally achieved by purification and use of standard curves together with mass spectrometry. For many applications, including the validation of proteomics data and the study of specific pathways or networks under biological or environmental stress conditions, the use of dedicated commercial antibodies enables simple and sensitive relative quantification in large sample cohorts with no requirement for protein pre-fractionation. [42, 43, 44]

Mass Spectrometry Proteomics

Mass spectrometry provides diverse options and protocols for protein detection, and sample preparation may include gel or solution-based fractionation, as well as no fractionation. Protein identification and quantification follow from database searching or label-free analysis of spectra together with intensity-based or spectral-counting approaches. Multiple reaction monitoring enables sensitive analyses of targeted proteins, while isobaric tagging with quantitation by mass spectrometry permits label-based quantitation. The sensitive and specific characteristics of mass spectrometry enable simultaneous analysis of a large number of proteins, including low-abundance proteins, in various environmental samples, such as those affected by heavy metals, organic pollutants, or particulate matter.

Mass spectrometry has become a leading analytical tool for the qualitative and quantitative analyses of proteins, as well as for the characterization of proteomes from various biological sources in different localities. It measures ion relative abundance as a function of mass-to-charge ratio (m/z) and is composed of components for analyte volatilization, ionization, mass separation, detection, and data analysis. Phase-transition-surface-adsorption and sublimation electrospray ionization allow sampling under ambient conditions, while intermediate coupling yields greater sensitivity and ultra-high-resolution results than traditional coupling methods. Sophisticated ion-cluster and laser-spray mass-extraction imaging techniques, along with selectivity of the stable-isotope perturbation effect for protein quantitation, apply to tissue environments.

Metabolomics has gained wide recognition as a rapidly evolving field of inquiry because a relatively small number of metabolites represent a snapshot of metabolic perturbation at the time of sampling. Metabolite concentrations are also a direct reflection of the activity of the underlying pathways leading to their production. By contrast, the information content of proteomics is far greater than that contained within the protein concentrations of a particular state. However, with some exceptions, such as heat shock and hypoxia-induced proteins, most proteins are present at concentrations within an order of magnitude of their detection limits. Thus, protein level changes, their identity, and the changes in protein interaction networks incorporate dynamic changes in function. [45, 46, 47, 48]

Protein Biomarkers of Toxic Exposure

Protein modifications serve not only as dynamic signals of stress responses in various organisms and ecophysiological conditions, but also as potential early warnings of ecosystem health and metabolic conditions. Additionally, they provide valuable information on the cellular and molecular effects of high levels of heavy metals such as mercury, lead, cadmium, and arsenic; their mixtures; and compounds that share similar modes of action. Particular attention has been devoted to the response of heat-shock and metallothionein-like proteins, oxidative stress markers, and protein patterns that result from the interaction of toxic agents with the proteome.

Immunological techniques, labelled fluorescent probes, and chemical sensor systems based on enzyme activity or protein expression alterations have all been used for the quantification of these indicators in environmental matrices. Protein-based early-warning biosensor systems for studying damage patterns, cellular responses, and compensatory mechanisms in plants and animals under stress conditions are also becoming increasingly attractive. At the same time, the search for protein patterns associated with the effect of low pollutant concentrations in natural ecosystems promises to enhance the predictive power of ecosystem modelling. [49, 50, 51, 52]

Sensitivity and Specificity Considerations

Sensitive and specific detection of environmental toxicants and their biological effects is essential for understanding their impact. Protein-level effects are pertinent to real-time monitoring, while biomarker-based methodologies permit integrated exposure analysis.

Detection of toxicants within human biological materials is an optimal approach, as it provides knowledge on the actual exposure dose while considering the interactions occurring at different biological levels. National Health and Nutrition Examination Survey and European biomonitoring studies have assessed the population's exposure load to multiple environmental pollutants. Molecular and protein-based biomarkers of chronic toxicity indicate the activation of metabolic cascades, including oxidative stress, genotoxicity, and cellular distress. The assessment of exposure dose in conjunction with the biomarker response level enables the development of PBK models for a better understanding of the pollutant mechanisms and their impacts. [53, 54, 55, 56]

Chapter - 4

Chemical Sensors and Biosensors

Chemical sensors are analytical devices capable of detecting chemical substances in the environment via a biological or biomimetic receptor, sensing element, transducer, and signal processor. They provide real-time information on analyte concentration and allow a faster response and greater flexibility than other techniques like spectrophotometry. Recent developments show promising results, expanding beyond the classroom to industrial applications. The integrated use of nanotechnology is opening new possibilities by enhancing the performance of traditional chemical sensors based on electrochemical, optical, mass, acoustic, or piezoelectric methods, as well as by creating nanostructured sensors. These sensors, capable of measuring pollutants at ultratrace concentration, are among the most sensitive detection systems.

Biosensors are analytical devices incorporating a biological sensing element in intimate contact with a transducer, allowing quantitative or semi-quantitative determination of specific analytes. They exploit natural biology to assess the presence of, or exposure to, various toxic compounds. Biosensors can include antibodies, enzymes, DNA, RNA, or living cells as the recognition element, enabling detection through various mechanisms, including electrochemical, mass, optical, surface plasmon resonance, thermal, and piezoelectric. Sensors fashioned from recognition elements that interact with a transduction platform downstream can be adapted to detect a broad spectrum of toxic compounds. The use of electrochemical sensors with antibodies-functionalized surfaces enables the detection of toxic compounds at concentrations lower than permissible limits. [57, 58, 59, 60]

Electrochemical Sensor Fundamentals

An electrochemical sensor generates an electrical signal in response to the chemical analyte concentration. Depending on signal characteristics, the sensor type may be classified as amperometric, potentiometric, or conductometric. Unique interactions at the electrode-solution interface produce current density (amperometric), potential distribution (potentiometric), or overall electrolyte conductivity signal (conductometric) changes whose magnitude is proportional to the target concentration. Amperometric sensors have found greatest application and commercial sensor development.

Electrochemical sensors often consist of two electrodes: a working (sensing) electrode, where the electrochemical reaction occurs, and a reference electrode (RE) with stable potential. A potentiostat maintains potential across the electrodes, and the resulting displacement current is recorded. In a flow-through system, an auxiliary electrode may be included for current-carrying purposes. The signal is influenced by bulk concentration, reaction reversibility, ion transfer kinetics, and the supporting solution. Linear response is usually achieved at low concentration in a sufficiently large supporting electrolyte concentration compared to the analyte. Amperometric detection methods using an enzyme label are an attractive alternative to classical ELISA. [23, 61, 62, 25]

Optical and Fluorescent Sensors

Optical and fluorescent sensors provide a diverse range of chemical analysis techniques, capitalizing on unique molecular properties for chemical, biological, and environmental pollutant detection. Chemical and biochemical species can be probed via their characteristic photophysical features—absorption, emission, or fluorescence properties—within the ultraviolet (UV), near-UV, visible, or near-infrared regions. A primary photophysical process consists of the absorption of radiation, which promotes an electron from its ground state to an excited state. The phenomenon of fluorescence involves the subsequent re-emission of energy, with the time period between excitation and emission expressed as lifetime (or average lifetime). Lifetime based detection is particularly effective, allowing for the separation of signal from scattered light.

Fluorescent sensors often employ molecular probes that change their fluorescent properties (fluorescence intensity, emission spectrum, excited-state lifetime or formation of new fluorescent species) upon complexing or interaction with the analyte or environmental perturbations. Suitable references or inert substrates are necessary to obtain reliable and repeatable results. In addition, fluorophores with different emission wavelengths may be used together as ratiometric sensors, with detection limited only by the sampling system itself, rather than the sensors. [63, 64, 65, 66]

Nanomaterial-Enhanced Chemical Sensors

The use of nanomaterials to enhance the performance of chemical sensors has been demonstrated in many applications in the field of environmental detection. Due to their unique physical and chemical properties —higher porosity and surface area, increased reactivity, easier detection and separation—nanomaterials speed up and amplify both the detection processes and sensor responses. Metal nanoparticles, metal oxide nanoparticles, carbon nanotubes, semiconducting quantum dots, silica and polymer nanofibres have all been used to modify and improve chemical sensors by using them as identification elements or as signal amplifiers.

Nanoparticles can be used for surface-enhanced Raman scattering (SERS) and surface-enhanced fluorescence (SEF) detection due to the strong enhancement of electrical and optical signals, or they can be applied in catalytic reactions with their large surface area and specific structural features. The nanostructured sensing membranes were found to be of great promise for toxic and harmful gas detection. Assemblies of short carbon nanotubes and silver nanoparticles embedded in an insulating polymer were used as transducers, leading to sensitive sensor devices with fast response time. Sensors based on silica nanofibres and metal oxide semiconductor nanofibres have been proposed for humidity detection, and silica nanofilms have been fabricated for detecting Thiopurine drugs. [67, 68, 69, 70]

Bio-recognition Elements (Antibodies, Aptamers, Enzymes)

Electrochemical and optical sensors may use an enzyme, antibody, or aptamer as bio-recognition elements. Enzyme-based sensors leverage enzyme reactivity and inhibition, or enzymatic reactions. In immunosensors, the analyte interacts with an immobilized antibody, enabling selective identification and quantification. Aptasensors utilize single-stranded DNA or RNA oligonucleotides with specific affinities toward target analytes.

The sensitivity of an enzymatic biosensor stems from the unique catalytic characteristics of the enzyme, and its selectivity depends on the specificity of the substrate. Enzymatic inhibition in biosensors can be either competitive or non-competitive. Competitive inhibition occurs when the analyte chemically resembles the substrate and competes for the active site, while non-competitive inhibition arises when the analyte binds to an allosteric site, altering the conformation of the enzyme or enzyme-substrate complex. In these studies, the enzyme label function merely to generate the detectable product, allowing easy control of the electroactive product concentration during sensor signal generation.

Immunosensors are separative, label-free, and biomolecule-interaction-based. The interfacial signal change occurs due to the formation of the specific antigen–antibody complex. The sensitivity and dynamic range of immunosensors depend on the antibody immobilization density on the surface of the transducer and the antibody–antigen mass transport effect. An increase in local biolayer thickness raises the current response, although high concentration may result in mass transport effect dependence.

Aptasensors operate via preferential binding of a single-stranded DNA or RNA oligonucleotide toward ubiquitous analytes like metal ions, small molecules, or proteins. Aptamers serve as biorecognition elements for various metal ions, organophosphorus compounds, narcotic drugs, and amino acids. The measurement principle relies on the structure-switching property of aptamer. Response enhancement is obtained through coupling with DNA polymerase or label-free electrochemical detection strategy. [71, 72, 73, 74]

Sensor Calibration and Validation

Chemical sensor performance is influenced by a variety of factors such as temperature, humidity, and possible matrix effects, meaning that prior to analysis the sensor's simple calibration should be done. Calibration provides the conversion function of the signal generated by a sensor into an analyte concentration and it can be achieved by using test analytes in standard solutions at known analyte concentrations progressively applied to the sensor elements. Those solutions should have analyte concentrations above and below the concentration levels expected in the sample and an appropriate fit should adjust the data, either linear or non-linear like polynomial, exponential, logarithmic or power. When this type of calibration is performed it is also possible to calculate the limits of detection (LOD) and quantification (LOQ). In order to make quantitative analysis in more complex samples, it is necessary to validate the proposed method, which consists of the check of parameters like repeatability, reproducibility, stability, response time, temperature dependance, robustness, selectivity and response range. Validated methods are usually applied in real samples.

The validation of sensors employing bacterial biosensors can be made by evaluating the effect of growth substrate composition, the presence or absence of a quenching agent and the sensor Fresnel reflectance. Other approaches for sensor validation employ chemometric data treatment strategies like Partial Least Square Regression (PLSR). Such advances allow investigation of sensor array responses located in fingerprinted regions without any prior calibration or validation by using pixel-based regression maps based on PLSR. [75, 76, 77, 78]

Chapter - 5

Integration of Molecular Tools with Chemical Sensors

A combinatorial approach integrating safe molecular indicators in tissues of human beings and plants with highly sensitive advanced chemical sensors offers great potential for early warning of pollutant effects. Mental and physical health risks, along with compromised food quality and safety, have caused increasing concern in recent years. These threats are often due to environmental pollution by metals and organics. Diagnostic assessments of molecular indicators of exposure and effects facilitate investigation of these risks. Detection of endogenous molecular biomarkers in biological samples is increasingly applied for early human risk identification. In parallel, there is a compelling need for smart sensing devices for real-time monitoring of contamination levels to protect human and ecosystem health and avert costly remediation.

Tissue deposition of various toxicants is known to cause responses and protective mechanisms in plants and humans. The potent toxic effects of environmental pollutants, including heavy metals, pesticides, endocrine-disrupting chemicals, urban and biomass-burning soot, and their mixtures, generate organismic stress responses such as gene deregulation, protein over- or under-expression, and distinctive profiles of biosynthetic metabolites in plants. Molecular indicators of these responses at the level of genes, proteins, and metabolites have been proposed for sensitive human and plant risk assessments. Integrating these tools with advanced chemical sensing technologies for detection of the toxicants in air, water, and soil is a logical next step to facilitate predictive pollution impact evaluations. Combining information on pollutant concentrations and bioindicators in a single smart device supports environmentally relevant human safety and food quality management. [79, 80, 81, 82]

Hybrid DNA-Based Sensor Systems

Hybrid DNA-based sensors integrate the advantages of molecular diagnostics for versatile detection of specific targets and signal transduction technologies for real-time pollutant systems engineering. DNA hybridization generally occurs in solution, which limits the response time and sensitivity. However, the structure of the detection assembly can be designed to enhance the detection sensitivity and shorten the time needed for hybridization. Optical and electrochemical biosensors have been developed for the target recognition of various pollutants based on DNA or RNA hybridization. The electrochemical sensors continuously monitor specific pathogens, viruses, and environmental chemicals by incorporating on-line sampling into the electrode configuration. DNA hybridization monitors chemical hazards and pathogens, signal amplification and transfer elements reduce the amount of complementary probes, and combine immobilized and solution hybridizations in one sensor assembly to achieve high sensitivity and shortened detection time.

Signal transduction or recognition elements of electrochemical and optical sensors are functionalized with DNA or RNA strands. They exploit the detection principle of sample concentrations, detection count rates, and registered counts of analytes in a batch-analytical mode. Optical DNA sensors directly observe microbe concentrations in environmental waters, while RNA molecules detect specific gene targets of pollutants. RNA interactions with Li+-modified Al/SiO2 layers are optically active and can be designed to assess the risk levels of such environmental pollutants. Reaction mixtures are embedded in sensor devices, which incorporate mixer elements, and chemical hazards are continuously traced in real-time. New-generation optical DNA chemical sensors equipped with oxidation-sensitive fluorescent tags allow for the determination of double-stranded DNA with a fixed detection zone in batch mode without electrode surface modification. [83, 84, 85, 86]

Protein-Antibody Functionalized Sensors

Lateral flow immunosensors functionalized with antibodies and monoclonal antibodies for the on-site detection of environmental toxins have been developed. Immunosensors based on nanomaterials and functional antibodies provide high sensitivity and low detection limits. These sensors can be used in the detection of phenolic compounds from industrial waste, aflatoxins, organophosphorus pesticides, dioxins, etc. Immunosensors with high stability and long shelf life have been developed through the use of recombinant proteins and nanomaterials. Various metal-labeled and enzyme-labeled immunosensors have been engineered to enable quantitative detection of a variety of environmental toxins. Detection limits of nanomaterial-labeled immunosensors can reach the low pM level.

Fluorescent immunoassays with a detection limit of 10 fg mL−1 have been employed for the on-site quantitative detection of polychlorinated biphenyls. An immunoassay based on a fluorescent carbon quantum dot–gold nanoparticle probe has been developed for visual detection of 2,4-dichlorophenoxyacetic acid with a detection limit of 200 pg mL−1. A fluorescence immunosensor with sensitivity at the low fM level for detecting 17β-estradiol has emerged. An immunochips prepared by the combination of molecular imprinting technique on a LSPR platform can detect 17β-estradiol at the femtomolar level. A magnetic lateral flow immunosensor for immunodetection and immunoquantification of 17β-estradiol has been proposed. [87, 88, 89, 90]

Aptasensors for Environmental Toxins

By virtue of its structure that can form multiple 3D shapes, DNA can be utilized as a nanomaterial in the development of highly selective biosensors, termed "aptasensors," which employ an aptamer as a recognition element. Aptamers, which are analogous to antibodies in function, can specifically bind to any target analytes with high affinity. Furthermore, selection is obtained by simple *in vitro* transcription and translation through a process termed SELEX (systematic evolution of ligands by exponential enrichment). High specificity is attributed to the unique structure of the aptamer that can bind to its target specifically, irrespective of the sequence.

Toxic and pathogenic pollutants can be directly detected using aptamers, which can also be utilized indirectly through the detection of nutrient depletion. These sensors can be either label-free or labeled with fluorescent molecules, nano-gold or horseradish peroxidase enzymes. An overview of aptasensors for heavy metals, dyes and pathogens is provided to demonstrate the versatility of aptamers. All available aptasensors to date have been developed in labs, and much more work is needed to make them user-friendly for on-site applications. [91, 92, 93, 94]

Real-Time Molecular Detection Platforms

The emergence of multi-signal biosensors capable of real-time detection and quantification of pollutants in human samples and environmental matrices is a pivotal advancement. These sensors enable continuous monitoring both internally and externally, acting as preventives against exposure to environmental contaminants. Integrating molecular biological techniques with advanced chemical sensors is particularly beneficial for detecting dangerous agents. Nucleic-acid-based sensors that provide sensitive and specific detection of foodborne and waterborne pathogens, viruses, bacterial toxins, and other environmental pollutants can be modified into real-time continuous monitoring systems. These sensors are immobilized on hard surfaces during detection steps but can be used as portable biosensors when placed in suspension. Molecular communication systems consisting of biosensor probes and chemical sensors as monitors have been developed for nucleic acid-based biosensor systems. The incorporation of DNA-repair-related sequences for signal amplification and detection enhancement has also been reported.

Detection platforms based on antibody- and aptamer-modified chemical sensors can be connected with molecular detection techniques to monitor specific targets in a time-saving manner. Biorecognition elements (antibodies, aptamers, enzymes, etc.) incorporated with advanced chemical sensors can also be integrated into real-time monitoring systems. Sensor devices using these biorecognition elements that allow direct determination of toxic compounds are valuable for accurate measurements of environmental contaminants. The combination of an aptamer-modified sensor and a chemical sensor configured to detect the products formed by the specific recognition reaction enables monitoring of pollutants without labeled signal reagents. Molecular detection approaches based on fluorescence technology have been combined with chemical sensors to realize real-time detection of foodborne pathogens. [95, 96, 97]

Signal Amplification and Detection Enhancement

Advancements in sensor sensitivity have been realized through the integration of a signal amplification strategy using unmodified gold nanoparticles (GNP) and PCR products containing the target sequences of the probe in the biosensor platform. The reaction mixture containing the PCR amplicon and the GNPs incubated at 70 °C for 40 min was used after cooling to room temperature for direct application on the sensor. Here, the GNPs participate in an avalanche-like amplification of the detection signals from the three-immobilized complementary probes on the chips, producing higher sensor responses. Furthermore, the rapid facile one-step synthesis of (6-amino-1,3-benzothiazol-2-yl) 3-(2-nitrobenzyl)-3-(substituted phenyl) thiazolidine-4-carboxylates have been successfully applied as an ecofriendly and low-cost sensor (within the limit of detection of 15 ng) for sensing niobium ions from contaminated water samples.The rapid signal enhancement strategy aids in electrochemical PCR detection of DNA by replication.

The devices for signaling transient state in (Gera *et al*. 2011), offer a robust, sensitive, and stable detection of target DNA by electropolymerization of an acrylamide-based hydrogel enclosing the context RNA on a glassy carbon electrode. Such devices are primarily used for signal amplification and sensor development.intigraphy of silica/polyaniline systems enriched by electrical polyaniline spray deposition on silicon wafer is expressed. Polyanilines in calculation of hydrogen peroxide by means of potentiometric systems are composed of galvanically deposited gold, in which bimetallic effect is responsible for their fast kinetic characteristic. The different ion selective sensors based on solid acrylic membrane are prepared and examined. Such an ecofriendly and cost-effective plant extract-mediated whitening property due to the presence of polysaccharides and of a low-cost and highly sensitive cholesterol biosensor based on modulation of reaction kinetics are also discussed in this work. [98, 99, 100, 101]

Chapter - 6

Pollutant Detection in Human Biological Samples

Chemical pollution is among the greatest environmental hazards for human health, with systemic, oncogenic, teratogenic, and endocrine-disrupting properties associated with contaminants, both known and suspected. Environmental monitoring is thus essential for investigating chemical exposure in human populations, supporting biomonitoring activities and exposure studies. Biofluids (blood, urine) provide convenient matrices for detecting a wide variety of compounds and associated biomarkers, enabling individual exposure assessment and possible correlation with health effects.

Heavy metals such as lead, cadmium, mercury, and arsenic accumulate in human tissues and can be quantified in blood and urine. Their distribution and the associated toxicological pathways are better understood, which has led to the identification of specific protein or metabolic markers of cellular and oxidative stress. In contrast, organic pollutants are more difficult to detect and non-invasive approaches are seldom used. Analysis of hair, nails, or amniotic fluid opens a window to other classes of organic pollutants (pesticides, plasticizers), while high-performance liquid chromatography (HPLC) and mass spectrometry offer particularly sensitive detection for the most toxic compounds. However, their presence and potential side effects are still frequently ignored when assessing human exposure, with the consequence that no specific early-warning signal system is available. Detecting such compounds in human samples is a valuable way to increase knowledge of potential toxicological effects related to organogenesis and growth. [102, 103, 104, 16]

Detection of Heavy Metals in Blood and Urine

Heavy metals are toxic elements that remain in the environment and food chain for decades. As a result, heavy metal accumulations can be detected in various human biological fluids, employing different detection methods. Analytical evaluations of blood and urine samples from individuals exposed to heavy metals have been employed as sensitive and effective techniques for human biomonitoring studies.

Heavy metals such as lead, arsenic, cadmium, mercury, and chromium have no biological role in living organisms, and their accumulations are either protoxic or toxic. When humans are exposed to high levels of toxic heavy metals, they become incorporated in blood or other tissues or excreted via available pathways. Consequently, some of them have considered these metals to be useful biological indicators. Because metals have longer half-lives, they are generally accumulated in blood or tissues; in contrast, the relationship of other metals with urine concentration is plausible because of their high turnover rate. As such, their detection in urine or blood is now being widely used to assess human exposure to these toxic agents. [105, 106, 107, 108]

Biomonitoring of Organic Pollutants

Biosampling and subsequent analysis utilizing various approaches remain important for assessing human exposure to organic pollutants. Blood, urine, amniotic fluid, breast milk, and, more recently, hair represent the most common biological samples used for biomonitoring. Concentrations in these fluids are usually presented in relation to the background levels of a reference population. The use of easily obtainable samples such as urine for exposure assessment monitoring is currently the most frequently utilized technique. Urinary metabolites present an expression of systemic exposure to organic pollutants over the previous few days or weeks, and biomonitoring studies have shown that concentrations in urine and blood OPEs, MEHP, HBCDD, and BPA are usually higher in pregnant than in non-pregnant women of reproductive age.

Measurable concentrations of organic pollutants and their metabolite or degradation products present in these samples are collected for biomonitoring purposes. These are typically considered environmental contaminants, even if they are ubiquitous in human exposure, given that they can be related to adverse effects in exposed humans or in wildlife. Although their concentrations are low—generally in the nano- to microgram range—they may reflect a significant toxic burden and risk for the exposed individual. These biomarkers may be related to neurodevelopmental, reproductive, and metabolic disorders; cancer; and risk of preterm delivery and low birth weight. [109, 110, 111]

Genotoxicity Assessment Using Molecular Biomarkers

Molecular biology techniques enable assessment of the genotoxic potential of pollutants by quantifying specific genes involved in the DNA repair response. Genotoxic exposure induces early activation of genes responsible for DNA damage repair, typically before the appearance of cytotoxic effects. Measurement of these genes in human biological fluids, such as blood or urine, may therefore indicate cellular exposure to DNA-damaging agents.

Damage caused by exposure of living organisms to different genotoxic agents may eventually lead to mutation or cancer. Alkylating agents lead to the formation of N-alkyl O6-alkyl-deoxyguanylic derivatives. These lesions are recognized and repaired by the base excision repair (BER) pathway, initiated through the activity of O6-alkylguanine transferase (AGT). Other bifunctional alkylating compounds, such as mitomycin C, can induce cross-links between the two strands of the DNA helix. Biological signaling in response to DNA cross-links is mediated primarily by the formation of single-stranded DNA (ssDNA) and is regulated by the Ataxia Telangiectasia and Rad3-Related (ATR) checkpoint pathway. The phosphorylated form of the Chk1 protein kinase is a downstream signaling component of the ATR pathway and functions as an essential regulator of cell-cycle progression in response to DNA damage.

Quantitative determination of the mRNA levels of genes involved in DNA repair, such as AGT or Chk1, in human peripheral blood mononuclear cells (PBMC) or urine sediment has been shown to serve as a biomarker for exposure to a wide variety of genotoxic agents. AGT expression can also be evaluated in buccal cells in response to genotoxic agent exposure. The expression of other genes has been monitored in response to cigarette smoking as a biological exposure index of tobacco smoke. [112, 113, 114]

Protein Markers of Oxidative and Cellular Stress

Controlled generation of reactive oxygen species (ROS) is essential for key physiological cellular processes such as cell signaling and control of cell proliferation. An imbalance between ROS production and removal results in oxidative stress, a deleterious condition that can cause biological molecules to undergo oxidation and is a proposed contributor to the normal aging process, neurodegeneration, cancer development, and premature birth.

Tissue levels of H2O2 and superoxide have been argued to control cellular proliferation, while high levels of oxidative modifications—such as protein carbonylation, lipid peroxidation, and DNA oxidation—have been associated with an increase in both permanent and reversible growth arrest. Neurons, because of their elevated metabolic activity and consequent greater production of ROS, may respond to increased H2O2 levels by selectively activating signal transduction pathways that promote long-term survival.

Besides hydrogen peroxide and superoxide, there are other molecules—e.g., REF-1, poly-ADP ribose polymerases, glutamyl carboxy-peptidase—that participate in the maintenance of redox homeostasis and can be quantified as biomarkers of oxidative stress. Furthermore, an imbalance in the ratio of the reduced and oxidized forms of glutathione contributes to redox-dependent pathological processes. Oxidative stress modifies levels of metabolites and proteins involved in respiration and carotenoid biosynthesis and affects chlorophyll a degradation during leaf senescence. [115, 116, 117, 118]

Multi-Omics Approaches in Human Exposure Studies

A multi-omics approach allows the simultaneous consideration of various omics levels (e.g., exposome, genome, transcriptome, proteome, and metabolome) in assessing the exposure of biological systems to potential toxins. First, such studies can elucidate the relationships between environmental contaminants and different health outcomes by integrating exposure data from multiple sources. Second, the availability of diverse molecular alteration data (i.e. genomics, transcriptomics, proteomics, metabolomics) enables the elucidation of biological response pathways at different biological levels. Finally, Systems Biology provides predictive and diagnostic knowledge through integrated network modeling. Integration of data from exposome studies and multi-omics analysis assists in the development of predictive biomarker signatures, improves hazard identification, and facilitates risk assessment at the population level.

Recent multi-omics studies that have integrated single exposures (such as those to ambient Particulate Matter (PM) or heavy metals) with molecular-, cellular-, and tissue-level responses at different biological levels have highlighted the strength of these approaches. Furthermore, multi-omics integration, allowing the combined assessment of various types of exposures (e.g., heavy metal mixture exposure) and health effects, strengthens the interpretation of underlying toxicity pathways. Multi-omics analyses have also linked aberrant baseline transcriptomes or metabolomics of different human tissues to COVID-19 or cancer incidence. [119, 120, 121, 122]

Chapter - 7

Pollutant Detection in Plant Tissues

Integrating protein- and molecularomic-based analyses with advanced chemical sensors permits effective evaluation of diverse chemicals that induce stress in plants. Research on different plant species has identified different omics responses to heavy metals, organic polluting agents and air pollutants. These responses provide evidence for the molecular mechanisms operating during phytotoxic stress and lead to the identification of highly sensitive genes and proteins that respond during early stages to low concentrations of stressors such as heavy metals or organic pollutants. Such results can ultimately be exploited to develop sensitive techniques capable of detecting environmental pollutants in plant tissues.

Emerging nanotechnology-based lab-on-a-chip platforms provide smart solutions for real-time monitoring of soil pollution at field sites. Sensor networks form part of an early-warning system for plant agriculture, while metabolomic-based approaches can identify organic pollutants in tested samples. The integration of these methodologies facilitates the proper regulation of agricultural practices and food safety by the efficient detection of environmental pollutants at both human and ecosystem levels. [123, 124, 125, 126]

Molecular Biomarkers in Plant Stress Response

Heavy metals, atmospheric pollutants, and pesticide residues exert deleterious effects on both human health and the environment. Plants carry out metabolic processes essential for their survival and are first to react to stress generated by external stimuli. Molecular mechanisms involved in the stress response can be simply classified into three different levels of complexity: changes at the level of genes (transcriptomics), proteins (proteomics), and metabolites and small compounds (metabolomics). Due to their crucial roles in plant metabolism, primary and secondary metabolites have proposed as reliable indicators of stress conditions in crops. Gene transcription and expression levels have confirmed their suitability as early and rapid diagnostic tools for assessing the exposure of plants to environmental factors.

In addition to transcriptomics, proteomics and metabolomics have gained popularity as advanced tools for studying plant responses to environmental agents. Protein quantification, followed by mass spectrometric identification and characterisation, is commonly used for the analysis of toxicant effects. Despite their advantages, the use of these techniques for routine analyses has mainly been confined to laboratory settings. Nevertheless, these analyses have greatly improved knowledge on plant responses to pollution and increased the possibility of detecting environmental contaminants. Early-warning systems able to predict the impact of polluted environments on crop health, heading for potential harvest losses, are an additional aspect to be considered in these investigations. [127, 44, 128, 129]

Protein Responses to Environmental Toxicants

Plants face various environmental stress factors, both biotic and abiotic. Among the abiotic stress factors, heavy metals, pesticides, excess salt concentration, and temperature extremes are the most prevalent and require immediate consideration. The adverse effects of super increase with the interaction of environmental components and may cause national-level disasters. Higher concentration of heavy metals, pesticides, high salt concentration by NaCl, RbCl, LiCl, KCl, and extreme temperatures (both low and high) decrease seed germination, seedling growth, and yield of different species of plants. These stressors cause oxidative stress, limit photosynthesis, and disturb the osmoregulatory mechanism of plants. Oxygen-free radicals such as superoxide radicals, hydroxyl ions, and hydrogen peroxide are produced and oxidize proteins, nucleic acids, and lipids, leading to membrane leakage and protein uncoiling. The content of MDA, an end product of lipid peroxidation, and the activity of enzymes such as superoxide dismutase (SOD), catalase (CAT), and peroxidase (POX) assist in the detection of oxidative stress in plants. The photosynthetic pigment and protein content act as stress indicators and provide information on the nature and extent of stress.

The pollution of soil with organic and inorganic contaminants has become a serious problem for the environment. Soil, as a medium of crop production, acts as a sink for contaminants released from anthropogenic activities. Protein biomarkers are useful tools for assessing the environmental quality of soil and the toxicological effects of contaminants. Specific changes in protein expression levels induced by stress in model plants have been observed with proteomic approaches. Detection of proteins associated with plant stress response in the soil provides evidence for the presence of contaminants at the sampling site. The use of soil protein expression patterns as molecular indicators of soil quality is considered a useful strategy for examining site-specific contamination and understanding the nature and level of contaminants in the soil environment. [130, 131, 132, 130, 131, 132, 133]

Uptake and Translocation Mechanisms in Plants

Pollutant transport mechanisms in plants are essential for understanding their negative effects on ecosystem health. These processes typically occur through the roots, with uptake directly from contaminated soil or indirectly from polluted water. After initial absorption, dissolved substances are translocated through plant tissues to leaves and other aerial parts where they reach toxic concentrations. Pollutant pathways leading to leaves include loading into the xylem for subsequent flow to the shoot, and movement via the phloem. The presence of transport proteins for specific contaminants has been confirmed in roots, but detailed studies on supranational transport are lacking.

Decreasing the concentration of hazardous chemicals in the edible tissues of plants is crucial for protecting human health. Two main strategies can be applied: degrading the harmful substance into a less harmful form or decreasing its concentration in a plant organ by altering its transport pathways. Phytoremediation, widely used to limit the accumulation of toxic metals in plant shoots, has been effectively combined with genetic engineering for increased efficacy in organic pollutant degradation.

In the last decade, several researchers have engineered genetically modified plants that can degrade toxic organic compounds. These plants can, hence, be used for phytoremediation as well as in precision agriculture, keeping the edible tissue safe from the chemical hazard. Asian rice adopts the lateral root system, an evolutionary characteristic of further optimizing the resource absorption ability and decreasing the detrimental biochemical signals. The essential role of the lateral system was evaluated via the oxygen isotope composition by Yang and colleagues.

Early-Warning Biosensor Systems for Agriculture

The interval between planting and harvesting crops can be adversely affected by disruptions stemming from the surrounding ecosystem. Organisms like viruses, bacteria, nematodes, etc., filter into agricultural systems from adjacent polluted environments resulting in severe stress that is manifested in the physiological, biochemical, molecular and protein levels of the endangered crops. Early-warning systems that can detect such hazards in the local environment before their penetration help ensure the safety of the food chain. Air or soil can be sufficiently polluted with environmental stress-inducing factors that can be detected using different multi-target bio-sensor systems.

These systems can detect heavy metals, organophosphorus pesticides or air pollutants, or a combination of these variables, during the short time from planting to first harvest. Transgenic Nicotiana using the heat-shock promoter driving a b-glucuronidase reporter gene is an approach that has been successfully used to prepare early warning biosensors to identify heat stress in the air around the crop. These plants ordinarily experience no-sign-to-very-low levels of expression, but their expression level quickly rises to measurable levels in air temperatures that exceed their heat-shock promoter threshold. Fields with such biosensors are thus able to indicate not only present levels of local heat stress but also offer advanced warning when thresholds that may be exceeded by stressed Succinyl-CoA and oxaloacetate levels in nearby crops are about to be exceeded. [134, 135, 136, 137]

Plant Metabolomics for Pollutant Identification

Integration of molecular diagnostics with state-of-the-art chemical sensors significantly improves pollutant monitoring in the environment and biosphere. A key aspect of this strategy relies on the parallel detection of molecular fingerprints that reveal chemical contamination and related cellular stress responses in plants. Accumulation of specific metabolites is recognized as a typical response of the plant system to environmental contamination and other stress conditions, as well as a detoxification mechanism under these conditions. Advanced metabolomic tools based on mass spectrometry and nuclear magnetic resonance methods can play a key role in the identification of molecular markers of exposure to a broad spectrum of environmental pollutants.

Metabolomic approaches assist in the identification of not only the nature of pollutants but also their physiological concentration levels, thereby fully characterizing the plant health status and environmental conditions. Such information is essential for providing warnings on agricultural produce safety and adequacy for human consumption. These developments enable the integration of metabolomic techniques with chemical sensors, increasing the reliability of signal responses for precision agriculture. [138, 139, 140, 141]

Chapter - 8

Toxicology of Heavy Metals

Heavy metals and metalloids are classified as priority toxicants because of their carcinogenic potency, mutagenicity, teratogenic properties, implication in several neurodegenerative diseases, and interference with the endocrine system. Lead and mercury exposure is associated with damage to the developing brain, resulting in reduced intelligence quotient (IQ) and memory impairments. Cadmium and arsenic are harmful to human health and development and can induce cancer in humans. Cadmium also mainly affects the kidney and bones. Accumulation of metals such as cadmium, lead, and mercury is linked with neurodegenerative diseases and prenatal neurodevelopmental toxicity. Moreover, arsenic exposure during pregnancy is related to fetal growth restriction, preterm birth, and stillbirth.

Heavy metals may be deposited in plants through the atmosphere, soil solution, or dust. The accumulation and translocation of heavy metals within plants depend on various factors, including the plant variety, the form of heavy metal, the plant growth stage, and the metal concentration in the growth medium. Molecular players such as heat-shock proteins (HSP), superoxide dismutase (SOD), and cytochrome P450 (CYP) have been evaluated as potential indicators of heavy metal stress in various plant species. In addition to these proteins, chemical sensors are emerging as an efficient tool for the first step detection of heavy metals in environmental samples. [142, 143, 144, 145]

Lead and Mercury Toxicodynamics

Lead (Pb) is a colorless, odorless, and tasteless metallic element widely distributed in the environment. Due to its chemical inertness, it has been widely used in industrial production; its main applications are in batteries and ammunition. Industrial emissions, vehicular emissions, use of gasoline with lead additive, cigarette smoke, smelting processes, and burning of lead acetate-having plants are also the common sources of lead. Soil- and water-borne lead can be translocated to plants. Industrial activities (e.g. automobile assembly factories, shipbuilding yards, and battery manufacturing plants); cement plants; mining; and the burning of leaded gasoline are possible sources of lead contamination. Lead's biological role remains unclear, but epidemiological studies have indicated its adverse effect on human health.

Major human exposure routes are from contaminated food, water, and air. Lead is not essential to cellular metabolism, but it can easily enter the human body and accumulate in tissues and organs, leading to toxicity. Pb is classed as a probable carcinogen in humans. Elucidating the mechanism of lead-induced toxicity is critical for understanding the underlying health impacts. Accumulated studies indicate that Pb can exert intrinsic and extrinsic toxicity to cells. Plausible lead-induced cellular toxicity mechanisms involve increased production of reactive oxygen species (ROS), inhibition of cellular DNA synthesis, alteration of cell membrane integrity, disruption of cytoskeletal integrity or dynamics, interference with cell cycle regulation, and induction of apoptosis. Studies have reported a number of lead-induced molecular and protein markers linked to accumulation, exposure, and toxicity in humans.

Mercury (Hg) is a well-documented neurotoxin, but little is known about the molecular mechanisms involved in Hg-induced neurotoxicity. Molecular damage caused by the toxic elements, especially in the nervous system, is not clear, although several experimental studies indicate that exposure to different oxidants may compromise neurogenesis in adults. In addition to expression pattern alterations, significant transcriptomic changes occurred in l-Hg-treated human neural precursor cells. Further analysis of the global gene expression signature and the enriched biological functions demonstrates the toxicopathy to be primarily associated with neurodevelopmental dysregulation processes. Mercury is widely distributed in the natural environment and is known to adversely affect a wide range of biological system functions. [146, 147, 148, 149]

Cadmium and Arsenic Effects on Human Health

Cadmium and arsenic are heavy metals of concern for human health because they cause several toxic effects. These metals are present in the human body in different quantities depending on geographic location, exposure route, attributes of the individual, and biological fluid analyzed (blood, urine, hair, etc.). The metal blood concentration is generally very low because cadmium and arsenic have a high affinity for sulfhydryl groups, which allows binding with plasma proteins and transferring to different organs and tissues. Two biological fluids typically analyzed in toxicology studies to monitor metal bioaccumulation are blood and urine. Additionally, blood and hair can be used to evaluate whether metals pass through the placental barrier and accumulate in the fetus during pregnancy.

High biomarker concentrations are correlated with increased mortality rates from cardiovascular and respiratory diseases, cancer, and other causes of death. Some studies also indicate that cadmium is associated with poor fetal development. Reproductive toxicity due to arsenic has also been described, as evidenced by adverse pregnancy outcomes and adverse effects on the fetus and newborn. Metal accumulation in the body can be determined by analyzing biological fluids that are easy to collect, such as blood and urine. These fluids serve as suitable matrices for exposure assessment, especially in population biomonitoring studies. Multi-omics studies provide a global picture of the effects of exposure to air pollution and environmental chemicals in vulnerable populations, thus extending the knowledge on cadmium and arsenic health implications and contributing to the establishment of preventive measures. [150, 151, 152, 153]

Heavy Metal Accumulation in Plants

Heavy metals are toxic elements that hinder metabolic function in plants and cause accumulation and translocation of metals in edible parts above the permissible limits, posing high health risks to humans. The physiological and biochemical responses of crops to metal stressors remain poorly understood, but they are crucial for elucidating the toxic mechanisms and aiding in plant detoxification and remediation strategies. The review of current literature aims to consolidate knowledge on the impact of Pb, Hg, Cd, and As on growth, reproductive fitness, photosynthetic machinery, antioxidant enzymes, and associated signalling molecules in plants.

Heavy metal pollution is extensively studied due to its growing association with ecosystem degradation and adverse effects on human health. Pollution created by heavy metals is unique compared to other contaminants because it influences all parts of the ecosystem, whereas other pollutants are either biological or chemical agents. Industrialization, urbanization, and anthropogenic activities have resulted in increasing concentrations of Pb, Hg, Cd, and As in soils, water, and air, which are toxic to all life forms. Heavy metals cannot be destroyed, and their accumulation in soil beyond threshold limits can have long-lasting negative effects on various living organisms, including plants. [154, 155, 156, 157]

Molecular and Protein-Level Toxicity Indicators

The adverse effects of heavy metals have been well-documented. They damage biomolecules such as proteins, lipids, and nucleic acids, leading to impaired cellular function and potentially cell death. Proteins are affected through the misfolding caused by metal ions binding to the amino acid side chains or by interactions with other cellular elements, like lipids. The ionization of cysteine side chain thiol groups—present in numerous enzymes—has proved particularly harmful due to the effect on the thiol groups' redox role in cells. Similarly, the formation of reactive oxygen species (ROS) catalyzed by copper, cadmium, and other metals has been widely studied. Excess ROS within cells can disrupt the oxidoreductive state, leading to oxidation of proteins, lipids, carbohydrates, and nucleic acids. Changes in the activities of antioxidant enzymes such as ascorbate peroxidase and superoxide dismutase, as well as metabolic products, may therefore serve as early indicators of toxicity.

Other molecular processes have been examined as markers of heavy-metal-related toxicity in both plants and mammals. RNA transcript levels of the heat-shock protein HSP70 have been correlated with heavy-metal exposure in several plant species. Changes in the LT50 (lethal time for 50% of the population) for seed germination have also been proposed as indicators of heavy-metal-accumulation stress in plants. Throughout, however, the time needed for markability in response to contamination has been neglected. In order to accurately indicate the time from first detection of stress to first detection of visible symptoms, a molecular marker that responds earlier and a second that responds later are required. [158, 159, 160]

Sensor-Based Heavy Metal Detection Techniques

Heavy metal accumulation in human tissues is associated with deleterious effects, and the detection of concentrations in biological fluids is commonly performed using atomic absorption spectroscopy (AAS). Despite its adequate reliability, this analytical technique requires sophisticated instrumentation and is influenced by high costs and time consumption, thus limiting the number of samples affordable for routine analysis. An alternative is the use of different classes of electrochemical sensors for determining lead (Pb), copper (Cu), manganese (Mn), zinc (Zn), cadmium (Cd), arsenic (As), mercury (Hg), iron (Fe), selenium (Se), and others. The corresponding detection limits are particularly useful for studying these toxic metals in the low concentrations frequently found in human samples. These devices are also suitable for point-of-care testing, since they can be miniaturized and integrated to smartphones in simple and inexpensive systems.

Heavy metals are known to exert damage in plant tissues through different modes of action. These injuries result in physiological imbalances that ultimately lead to soil degradation, decreased biomass production, and productivity loss. The characterization of metal concentrations in plant tissues is well established, with concentrations usually being determined by AAS. Nevertheless, direct determination by chemical sensors is also possible. Multiple commercially available sensors allow quantifying cadmium (Cd), lead (Pb), mercury (Hg), thallium (Tl), selenium (Se), zinc (Zn), copper (Cu), and other heavy metals. Copper oxide and gold nanoparticle-based chemiresistive sensors have also been developed for Cd detection. [161, 80, 142]

Chapter - 9

Organic Pollutants and Their Biological Impact

Numerous pesticides are available to safeguard crops from pests and diseases, encompassing organophosphates, carbamates, and organochlorines. Persistent exposure to these chemicals is linked to neurotoxicity through interactive mechanisms. Malathion, a widely used organophosphate, enters the bloodstream and poses risks to placental and fetal development. Its breakdown product malathion oxon and the carbamate carbofuran are also carcinogenic. Pesticides disrupt cellular homeostasis due to their higher affinity for cholinesterase than AchE. They inhibit the nicotinic receptor, leading to elevated catecholamines and catechol depletion, which may impede protein synthesis and energy production.

Among herbicides, 2,4-D is the most commonly employed Chlorinated hydrocarbon herbicides act as endocrine disruptors and impair immune function. Prolonged exposure to atrazine, a herbicide widely used in agriculture, has been associated with breast cancer. Endocrine Disrupting Chemicals (EDCs) are exogenous compounds that interfere with hormone signaling by inhibiting or activating hormonal synthesis and secretion. They disrupt homeostasis and modify hormonal responses in the target organ.IDs include diethylstilbestrol, phytoestrogens, phthalates, bisphenol A, heavy metals, pesticides, and certain polychlorinated biphenyls.

EDCs generate reactive oxygen species in target tissues, leading to oxidative stress. High-affinity estrogen or androgen receptors prevent ligand binding to low-affinity receptors. A disturbing ratio of free-to-finite high-affinity receptors has a deleterious impact on the organism. Many EDCs alter gene expression programming during embryonic development and are related to developmental disorders.

Leukemia is the most prevalent cancer among children and its incidence has increased during the past two decades. It has been related to exposure to certain industrial solvents, such as benzene, vinyl chloride, and alkyl-substituted chlorinated hydrocarbons and to exposure to chlorine, an industrial disinfectant commonly used in drinking-water. Exposure to chlorinated compounds has been linked to congenital malformations and altered neurodevelopment. In recent years, a potential association between major congenital malformations and maternal exposure to organic solvents has been established. [162, 163, 164, 165]

Pesticides and Herbicides Toxicity

Chronic pesticide exposure and the associated accumulation of their metabolic products have been shown to have a variety of biological effects, including neurotoxic, teratogenic, immunotoxic, reproductive, and potentially carcinogenic effects. Combined exposure to pesticides with other environmental pollutants raises the risk of their toxic effects on cancer, neurodegenerative diseases, and respiratory toxicity. In plants, the stress response to herbicides that inhibit the biosynthetic pathway of the amino acids valine, leucine, and isoleucine (such as herbicide BLEC—Boron Salt of Glyphosate) was studied using three different concentrations of the commercial herbicide, and with different periods of application. When exposed to the herbicide BLEC, plants experienced a reduction of chlorophyll and carotenoid pigments, and alterations in the activity of catalase, ascorbate peroxidase, and peroxidase. These distinctive physiological alterations can be used as markers to assess environmental stress for early detection of herbicide pollution in the environment.

In animals, toxyscybin, a cyanobacterial neurotoxin and a potential plant and animal mycotoxin, changed the expression of pro-inflammatory cytokines in the liver and brain of rats through the occurrence of oxidative stress and neuroinflammation, but did not induce damage to the post-implanted reproductive system. The intoxication derived from the consumption of artemisin (present in several species of the Artemisia spp. genus) used as alternative antimalarials can induce toxicity in fish by altering cell growth, vascularization, and ossiferous pattern formation in the developing embryo of Danio rerio. Artemisia cf. annua L. has artemisinin as its main active component and can be used to treat Plasmodium spp. infections. Exposure to commercial formulations of arsenic has also been implicated in thyroid-function alterations and hypothyroidism in experimental models. In natural and cultivated mushrooms, chemical contamination with heavy metals, pesticides, and mycotoxins has been detected. [166, 167, 168, 169]

Endocrine-Disrupting Chemicals (EDCs)

Numerous synthetic organic compounds produced by industrial processes can cause developmental and reproductive disorders. Hormones are such potent biological substances that abnormalities can occur even in cases of slight fluctuations in their concentrations. Environmental exposure to certain synthetic organic compounds may cause alterations, which are called endocrine disruptors. Some of the known endocrine disruptors are heavy metals, pesticides, polychlorinated biphenyls (PCBs), dioxins, and plasticizers that can be detected in human tissues.

Endocrine-disrupting chemicals (EDCs) or hormonally active agents are exogenous chemicals that interfere with the synthesis, secretion, transport, binding, action, or elimination of natural hormones of the body responsible for the maintenance of homeostasis, reproduction, development, and behavior. EDCs can be any natural or synthetic compound. The common classes of EDCs are polychlorinated biphenyls, organochlorine pesticides (dieldrin, oxalane, aldrin), organophosphate pesticides, natural estrogens (estrone, estradiol), synthetic estrogen (diethylstilbestrol), phthalates, parabens, alkylphenols, bisphenol-A, and cadmium. Some EDCs mimic the action of estrogens, some inhibit the action of estrogens, and some inhibit enzymes secreted by steroidogenic tissues.

Changes in hormone levels cause changes in metabolic processes. In addition to human health, EDCs can adversely affect wildlife, including both wildlife development and reproduction. EDCs can induce adverse reproduction and immune effects and tumors in wildlife. These effects can be attributed to exposure during sensitive windows and periods of development, expressing the same during puberty or sexual maturation. Studies have indicated that EDCs such as phthalates, dioxins, and alkylphenols can induce reproductive health effects in wildlife including mammals and birds. EDCs can induce reproductive tract malformations in animals; they can elicit abnormal sexual behavior, induce neurobehavioral deficits, decrease immune responses in species including but not limited to amphibians, fish, reptiles, birds, and mammals. [19, 170, 171, 172]

Industrial Solvents and VOCs

Human health can be affected by exposure, even at low concentrations. The acute effects occur when irritants or central nervous system agents produce symptoms after a single or short-term exposure. Chronic exposure leads to cancer, spontaneous abortion, reproductive problems, liver or kidney damage, neurological damage, or hypersensitization. Pollution usually results from exposure to a mixture of VOCs, which is why the effect of a mixture is determined whenever possible. Sweet-smelling VOCs exert an anesthetic effect when inhaled at a high concentration. Acetone, toluene, and benzene are used in paint thinners and nail polish removers; inhalation is potentially dangerous. Some VOCs can act like narcotic substances, causing headaches, dizziness, nausea, and loss of consciousness. The effect is called narcosis. Other VOCs form sensitization, producing symptoms similar to an allergy. In recent years, epidemiological studies have shown that the exposure of children to asbestos, dichlorophenyltrichloroethane (DDT), trichloroethylene, wood dust, and styrene is associated with an increased risk of brain tumors.

The exposure of children (in utero or after birth) to solvents (especially toluene and methylbenzene, xylene, and aliphatic solvents) has been associated with abnormal behavior; the fact that the groom and not the bride has been exposed appears to exclude intrauterine exposure. Children with febrile seizures in early childhood seem to be more susceptible to recurrent seizures when subsequently exposed to solvents. Several of these VOCs show mutagenic activity *in vitro* (i.e., in experiments in which the agent is applied to isolated cells or to a culture medium). The toxicity varies according to the species, sex, and strain of the experimental animal. [173, 174, 175, 176]

Plant and Human Biomarker Responses

Integrating molecular and protein diagnostic approaches with advanced chemical sensors to assess pollutant impacts on human health and plant systems

Pollutants generate specific biochemical responses in plant systems that can serve as sensitive indicators for monitoring environmental quality and the potential risk to food safety. Molecular and protein markers have been detected in food and feed crops exposed to heavy metal and organic pollution. Proteins involved in photosynthesis, defence response, ROS scavenging, and various other signal transduction pathways have emerged as important indicators of pollutant stress in plants. Detection of heavy metal accumulation and expression profiling of candidate genes in plants exposed to different pollutants can also indicate the nature of the underlying contaminant and its biological impact on food and feed crops. While these molecular and protein biomarkers have generally been applied in isolated cases of heavy metal or organic stress, their parallel application in different crops under multiple pollutant conditions will deliver early-warning signals for agricultural risk assessment. Such an approach will facilitate the interpretation of metabolomics results associated with multi-pollutant exposure.

Chemical sensor networks can be combined with a detection strategy involving the identification and quantification of molecular and protein stress-response biomarkers in plants. Plants constitute an immediate and highly sensitive bioreceptor for a variety of environmental pollutants. Sensor networks allowing simultaneous detection of heavy metals, organic pesticides, and endocrine disruptors in soil and water can be integrated within a risk-assessment system based on the identification and quantification of suitable molecular and protein biomarkers throughout the pollutant exposure range. Alterations in photosynthetic metabolites such as chlorophyll, carotenoid, and anthocyanin concentrations; antioxidant enzyme activity; malondialdehyde (MDA) content; levels of dissolved O2 and H2O2; and expression levels of candidate genes can indicate pollution threat to agricultural crops. [177, 178, 179, 180]

Chemical Sensor Platforms for Organic Pollutants

Coordination, metal-organic frameworks (MOFs), mesoporous carbon materials, monolithic supports, semiconductor metal oxides (SMOs), nanocrystals, and tuning of nanoparticle size and shape have been exploited for chemical sensors for the detection of polar organic compounds. MOFs such as Al-MOF, Co-MOF, Cu-MOF, and Zn-MOF have been developed for the detection of the following organic solvents: methanol, ethanol, acetone, dimethyl methyl phosphate (DMMP), and diethyl methylphosphonate. Mesoporous carbon materials were used in combination with ionic liquid for the detection of benzene, toluene, ethylbenzene, and xylene (BTEX).

Mesoporous carbon was used as a monolithic support for the determination of acetaldehyde, acetic acid, formaldehyde, and benzoic acid vapors. SMOs doped with Pt, Ti, Ag, and La, as well as Zn/SnO2 with a hierarchical flower-like structure, were employed as nanostructured sensors for the detection of isopropanol, acetone, DMMP, and tobacco smoke in the air. Au/CuO and Au/Al2O3 nanocrystals were also demonstrated to be sensitive for the detection of acetaldehyde and acetic acid, respectively. Tuning the metal nanoparticle size and shape was found to increase the sensitivity of acetaldehyde detection. [181, 182, 183, 184]

Chapter - 10

Air Pollution and Biomolecular Effects

PM2.5 and PM10 particulate matter have significant health impacts, including lung function impairment, cardiovascular disease, and morbidity in at-risk populations. Air pollution stimulates the generation of reactive oxygen species (ROS), and these species activate pro-inflammatory pathways, leading to toxic effects and associated health problems. Moreover, numerous studies have reported that air pollutants alter the expression of genes and proteins related to oxidative-stress and immune-modulatory response pathways. Monitoring of these genes and proteins has the potential to ensure good air quality in urban areas. Chemical sensors capable of detecting pollutants in urban air environments can contribute to reducing PM concentrations in urban air quality, thus avoiding PM-induced diseases.

Chemical sensor data can be exploited using pattern-recognition methods, as each pollutant produces a different signature. Pattern recognition methods can not only classify samples or predict concentrations but can also be applied predictively by feeding the model with new chemical data not yet analyzed. The integration of data from sensors able to monitor human biomarkers of environmental exposure with sensor networks can provide a broader picture of the air quality concerning human health, even considering multi-exposure not visible by monitoring a single pollutant. Further, both chemical sensor data and human biological data can be analyzed using artificial intelligence integrated with words extracted in multi-omic studies. Therefore, multi-omics data can support detection-monitoring-prediction-response systems that employ chemical sensors and send alerts to mobile devices when specific thresholds are reached. [185, 186, 187, 188]

PM2.5 and PM10 Health Impacts

High concentrations of airborne particulate matter (PM) with a diameter of <10 μm (PM10) and <2.5 μm (PM2.5) have been associated with an increase in respiratory and cardiovascular diseases, decreased lung function, and increased rates of hospital admissions and premature mortality. Respiratory and cardiovascular diseases make the greatest contribution, with the strength of the association relatively similar for these outcomes. Recent studies have shown that exposure to ambient PM10 is associated with an increase in respiratory and cardiovascular disease hospital admissions. PM2.5 and its constituents are linked to long-term and short-term cardiovascular mortality and morbidity. New potential links between PM2.5 components and diabetes, asthma, and diseases of the nervous and reproductive systems have emerged.

PM2.5, PM10, SPM, and TSP air pollution have intranasal and/or oral exposure development effects on various organs and tissues in mammals, resulting in various neurotheir expression levels being altered. Reactive oxygen species play a key role in PM2.5-related tissue and organ injury. PM2.5 and PM10 exposure induced ROS generation and dysregulated the expression of genes and proteins involved in the differentiation of neural progenitor cells. PM2.5 exposure during pregnancy is associated with abnormal fetal development, while childhood exposure has been linked to neurodevelopmental disease and altered brain morphology. Therefore, substantial evidence at the molecular, cellular, and organ levels points to the potential neurotoxic effects of PM2.5 in mammals, as do epidemiological studies. [189, 190, 191, 192]

Reactive Oxygen Species (ROS) Generation

Reactive oxygen species (ROS) are harmful oxidizing agents generated from oxygen metabolism during aerobic life. Their formation is a common response in all living organisms to different environmental stresses, such as exposure to heavy metals, organic pollutants, ionizing radiation, UV radiation, or pathogen attack. Generally, the levels of ROS are highly regulated by a network of antioxidant enzymes (singlet oxygen, hydrogen peroxide, hydroxyl radicals, and superoxide) and non-enzymatic antioxidants such as carotenoids, ascorbic acids, and tocopherols. In normal conditions, the production and detoxification rates of ROS are balanced; however, when the antioxidant defense system is compromised or overwhelmed under stress or disease conditions, ROS levels increase significantly.

Excessive levels of ROS can oxidize small molecules, lipids, proteins, carbohydrates, RNA, and DNA, thus disturbing the functionality and structure of biomolecules. This culminates in cell and tissue injury via lipid peroxidation, protein oxidation, and DNA conversion or single/DNA strand breaks, which is known as oxidative stress, a concept introduced in the 1980s. ROS generation can also induce cell apoptosis or necrosis through activation of the caspase pathway, phosphorylation/activation of c-Jun N-terminal kinase (JNK) or p38 mitogen-activated protein (MAP) kinase, dephosphorylation/inactivation of Akt, and/or release of cathepsin B, thereby contributing to diverse human diseases, such as cardiovascular diseases, metabolic diseases, cancers, neurodegeneration-associated diseases, fibrosis, and aging. [193, 194, 195, 193, 194, 195]

Air Pollutant-Induced Gene and Protein Expression

Airborne pollutants can induce various signaling mechanisms in mammals, and gene expression–based biological response studies are important for elucidating toxicity pathways. The major sources of air pollution, namely PM2.5 and PM10, produce different gene expression patterns in humans after exposure, with specific pathways such as cell toxicity taking place only for PM10 and enrichment of cardiac- and artery-related responses especially observed for PM2.5, indicating the need for paired analysis of hazard pathways. Exposure to other airborne toxic agents is also reflected by induction of a variety of genes and proteins, such as those belonging to the heat-shock protein family in rats after exposure to cigarette smoke, IL-6 and TNF-α in humans living in polluted environments, and those related to neurotoxicity and inflammation in human neuroblastoma cells after treatment with diesel exhaust particles. Analysis of chemicals and heavy metal content in PM2.5 samples by means of chemical sensors, combined with assessment of pathways activated on exposure of susceptible biological models, has potential for establishing comprehensive smart strategies for monitoring air quality. Integrating air-pollution databases with multiple sensor signals and molecular biomarker data also constitutes a powerful approach for unraveling the complexity of air pollution and providing further insights into the influence of the environment on human health.

The monitoring of gene expression signatures represents an efficient method for identifying biological responses to a variety of airborne pollutants, including PM2.5, PM10, polycyclic aromatic hydrocarbons, particulate material, particulate matter from wood combustion, and urban dust. Bortezomib, a proteasome inhibitor that irreversibly inhibits the 26S proteasome activity by binding to its catalytic sites, has been tested in a human neuroblastoma cell line exposed to ultrafine particulate matter, leading to the increased production of TNF-α and IL-6 following activation of NF-κB, STAT-1, and NF-κB (which is sequestered in the cytoplasm by IκB under basal conditions and further increases in response to TNF-α) and the pro-inflammatory signaling pathway downstream of the receptor for advanced glycation end products.

Biosensor Monitoring of Air Quality

Contaminated air is a crucial environmental health factor and a leading component of environmental degradation, impeding ecosystem functioning and human well-being. According to the World Health Organization (WHO), more than 90% of the global population breathes unclean air, with around 7 million annual deaths attributable to elevated PM in the air. The control of PM matter, particularly airborne particulate matter with a diameter of less than 2.5 μm (PM2.5) and less than 10 μm (PM10), is an urgent necessity. These particles can penetrate deep into the human respiratory system, reaching the lungs and subsequently entering the bloodstream, leading to extreme cardiovascular and pulmonary infections and diseases.

Air pollution generates a variety of chemical species, including reactive oxygen species (ROS) and interferents that provoke different toxic responses. PM exposure induces the expression of the CD74 and TNF-α genes involved in the inflammatory response, amongst many others. In addition to these genes, exposure of AF-5 cells to airborne particulates alters the expression of genes associated with stress response, glycolysis, and the cell cycle. Various chemical sensors and sensor networks are being developed for air quality monitoring, detection of specific substances, and long-range detection of priors. The increasing quantity of air quality monitoring data makes it possible to begin building automatic classification models in order to warn about certain air quality conditions. [197, 198, 199]

Smart Chemical Sensor Networks

Advances in Internet of Things (IoT) smart sensing technology permit integrating a variety of environmental data-gathering elements into a setup that can monitor a dataset of floods, earthquakes, speed of wind, rain, humidity, temperature, pollutants, smoke, and gas etc. A mobile application captures cancer blood test (complete blood count) results through an advertisement model along with details about trash cleaning through sensors and local government support. In a smartchemical network, sensor data from various pollutant sources can be combined through an artificial system. Sensor data can also be elaborately communicated with Intel Edison at a base station with Wi-Fi connectivity, enabling data processing and social media-accessible sharing of sensing evaluation-based data.

A smart network of sensors capable of monitoring air pollution, its impact on weather conditions, ghat traffic control, and control of accusing fire due to open burning can be developed. The project helps maintain the clean and green environment of Uttarakhand and aims to cover an area of 440 km2 in Garhwal. Nanomaterials have been used for monitoring air quality, with the area observing unique vehicular emission patterns, high concentrations of PM, gasses and noise pollution. The system can contribute to the tourism and overall growth of Uttarakhand with proper blanket initiation and guiding of tourists and pilgrims participating in the Char Dham Yatra. [200, 201, 202, 203]

Chapter - 11

Water and Soil Contamination Analysis

DNA and RNA markers are becoming increasingly useful in biomonitoring waterborne pollutants and their health effects in human populations. The risk of infection for various virus-causing diseases can be determined in the presence of coliforms in water samples. Emerging protein-based detection tools can also be employed to assess soil contamination. Soil proteins are subjected to disturbance or alteration and can serve as sensitive indicators of heavy metal stress in the soil environment. In addition, advanced modified chemical sensors have been developed to detect various water parameters. Implementable chemical sensors capable of monitoring bacterial contamination of natural water, as well as miniaturized devices incorporating electrochemical biosensors that can operate in the field for soil surveillance, have been fabricated.

The pathogenic effects of chemical, biological, and physical contaminants in soils, surface waters, and groundwater—including drugs and associated metabolites, bacteria, infused viruses, transport routes, and sources—continue to emerge as serious socio-ecological issues. Soil functions and parameters, such as microbial biomass carbon, dehydrogenase activity, and enzymatic activity, are primarily affected by heavy metals, causing disturbance of bacterial population and community structure. The analysis of biosensor data deployed in a Smart City Sensor Network, designed to detect the quality of environmental air and of water from lakes and rivers as well as the microbiological contamination of urban soil, also constitutes an integral approach for environmental surveillance. [204, 205, 206, 207, 208]

Molecular Markers of Waterborne Pollutants

The presence of high concentrations of waterborne pollutants has a significant impact on plant and animal health and subsequently on human health via food sources. In humans exposed to waterborne pollution, the molecules involved in the assessment of exposure and toxicity are DNA, RNA or proteins that usually participate in the biomarkers of toxicity or their regulation. Exposure can be determined from bodily fluids (blood/urine) or tissues and cells (skin or buccal mucosa) in which pollutants can be quantified directly.

DNA and RNA from a range of water pollutants have been tested in vertebrates and invertebrates. Avariety of heavy metals, pesticides, EDCs and hydrocarbons have been associated with DNA and RNA damage and induction of mutation and stress regimes in different human tissues. Bioindication of the exposure with these contaminants using human samples is more difficult; however, with high biomarker concentrations they can be used albeit their presence in several fresh and sea waters, as well as in human fluids/tissues, supports their use as toxicity markers. [209, 210, 211, 209, 210, 211, 212]

Protein Indicators of Soil Contamination

The contents of soils directly linked to agricultural practices and urban activities such as industry, transportation, and waste disposal-class waste discharges are prone to contamination. Toxic metals, pathogens, pesticides, organic fertilizers, and a wide variety of organic, inorganic, and synthetic materials now exist in these environments. The distribution and concentration of soil contaminants vary spatially and temporally, affecting soil quality and fertility. The use of biological indicators in soil quality assessment is growing, and common indicators include soil macrofauna, microorganisms, enzymes, and plant bioassays.

Surficial soil can be analyzed for the level of protein and gene expression response induced by soil deposition. Pollutants that can introduce such changes in gene and protein expression can be detected at an early stage and used to build detection systems for monitoring and prevention in situ. Such changes are important either because they can be used as sensitive indicators of contaminated environmental areas or because they have relevance to global warming.

Advanced Chemical Sensors for Water Quality

Detection of environmental pollutants in water and soil used by humans for drinking, bathing, irrigation, and other purposes is a necessity for ensuring public health and agriculture sustainability. Although chemical–physical sensor devices can allow for the detection of major water quality parameters, surveillance of contamination of the aquatic environment, including suitable sensors for heavy metals, pathogens, and other organic pollutants, is still to be fulfilled. For soil, sensitive and rapid devices tolerating the specificity of biological samples (especially at the pH level) and able to operate in field conditions are presently missing. Integration of molecular markers in soil and water is essential to monitor emerging pollutants and toxicity. Molecular sensor signals and their pattern matching with other sensor outputs need to be integrated in real-time networks capable of interpreting novel exposure pathways and health signals.

Advanced engineered chemical sensors are currently able to detect major pollutants at very low concentrations in different environmental compartments. However, new strategies exploiting nanotechnology concepts are required to facilitate their sensing ability, specifically for trace pollution detection. At the water level, developments in chip–mass spectrometry technologies and lab-on-a-chip devices will allow integrating sensor/fingerprinting and identification goals in a single effort, realizing the concept of smart sensors for water pollution monitoring. For soil, the combination of indigenous biological signals with chemical ones represents a major challenge, which is still to be addressed by research. These aspects highlight the need for integrative and multi-pollutant detection methods in order to guarantee ecosystem health. [213, 214, 215, 216]

Field-Deployable Soil Monitoring Devices

To prevent soil degradation and damage to terrestrial ecosystems and animal and human health, excessive soil contamination must be avoided. To this end, detection and monitoring systems are required for informing precautionary measures limiting the introduction of soil-borne toxicants. Recent advances in the field of soil analysis enable the integration of DNA- and protein-based diagnostic technologies with prototype label-free chemical sensors. These developments allow for direct detection of environmental pollutants in soils using Bio-DNA-DNA and Bio-protein probes.

Label-free sensors that have been successfully tested with actual soil samples include electrochemical chewing-gum-based DNA astrocytic probes for detection of mycotoxin-producing fungal species, such as Fusarium, meat-based monomer and dimer electrochemical sensors for the output of fragrance molecules by geosmin-, β-cyclocitral-, β-ionone-, β-carotene-, and β-jonone-producing soil bacteria, piezoelectric-sensor prototypes with bovine serum albumin and myoglobin for detection of crude-oil-degrading bacteria in soils and with chitinase for monitoring chitinase-producing bacteria. Overcoming drawbacks of standard microbiological analysis, such as long time of analysis and the limited number of microorganisms that can be detected with a single technique, the label-free sensors enable near real-time warning of undesirable microbial activities in the soil. [217, 218, 219]

Integrative Environmental Surveillance Methods

Integrating biological monitoring of contaminants in water and soil with traditional chemical analyses and advanced chemical sensors offers a comprehensive approach to examining pollutant impacts. Multi-omics technologies suffuse research into the interactions between environmental contaminants, their effects on human health, and toxic agent detection in biological samples and the surroundings. Integrated omic technologies allow simultaneous interactions between DNA, RNA, proteins, and metabolites to be investigated, enabling a more precise understanding of complex mechanisms and contributing to the development of early-warning systems.

Molecular and protein markers possess significant potential for detecting a wide range of potentially harmful contaminants in water and soil, as many toxic agents induce alterations in biological systems. Environmental monitoring is traditionally performed through chemical analysis, often not considering bioindicators that are increasingly proposed within regulatory frameworks. Continuous monitoring of biological responses in an organism or ecosystem can serve as an early-warning indication for advancing into disequilibrium. Integrative analytical methods combining chemical and biological analyses with advanced sensor networks provide comprehensive information. [220, 221, 220, 221, 222]

Chapter - 12

Nanotechnology in Pollutant Detection

Advancements in nanotechnology have led to the development of innovative tools to identify environmental pollutants and monitor their health effects. These tools enable rapid, sensitive, and highly specific detection of potentially toxic substances within biological fluids and living systems. In addition, nanoparticles can serve as contrast agents for diagnostic imaging methods like magnetic resonance imaging and computed tomography, assisting in the investigation of pollutant biodistribution and the molecular mechanisms underlying their toxicity. Despite these advantages, nanoparticles pose a potential risk to human health and ecosystems. Recent studies on the toxicity of the most common metal and metal oxide nanoparticles have highlighted their ability to cross membranes and enter cells, inducing toxic responses in various biological systems. Consequently, nanotoxicity research is crucial to clarify the potential hazards of using nanomaterials in environmental surveillance.

Nanoparticle-based biosensing devices offer a promising strategy for sensitive detection of hazardous substances, with several laboratories developing nanosensors with multifunctional capabilities. These flexible materials combine optical, electrical, electrochemical, magnetic, and surface-enhanced Raman scattering properties, which can be integrated into nanohybrid devices. Research over the past two decades has demonstrated the application of nanomaterials for highly sensitive and selective detection of environmental pollutants in air, soil, and water samples, including heavy metals, pesticides, dioxins, and polycyclic aromatic hydrocarbons. Furthermore, nanobiosensors are being constructed to monitor food quality and detect organic pollutants in food matrices, biological fluids, and plant tissues.

Nanoparticle-Based Diagnostic Tools

Nanoparticles (NPs) possess exceptional physicochemical features that increase the sensitivity and selectivity of standard analysis methods, rendering them useful in clinical diagnostics, advanced sensing systems, and environmental research. They provide both quality results for nanomolar or lower concentration detection and excellent repeatability for sample testing. Emerging and cutting-edge NP-based diagnostic tools with novel signals for detection of toxic substances at ultralow concentrations are of great importance to human beings. Advances in the establishment of ultra-sensitive NP-based detection systems with innovative detection signals open new paths in clinical diagnosis, toxicology, and environment monitoring.

Currently, nanomaterials are widely used in biological applications due to their high sensitivity, low detection limit, and ease of use when integrated into existing equipment. Their tunable size, simple synthesis, and inherent advantages as signal labels make NPs valuable in clinical diagnosis, toxicological test, and environmental monitoring. Among various analytical signals based on NPs, ternary coloring system signals, catalytic activity-based signals, enzyme mimetic activity, and surface enhance Raman scattering possess ultra-sensitive detection capability at picomolar or femtomolar levels. NPs with enzymatic activity can also be used to build biosensors based on colorimetric and electrochemical signals for detection of pesticide residues and other chemicals. [223, 224, 225, 226]

Nano-Biosensors for Trace Pollutants

The miniaturized sensors, using nanomaterials, enhance the sensitivity for detecting minimal amounts of infection; they are very small devices designed, for example, for detecting pollution or food contamination; they have all the biosensor characteristics, since they also have bio-recognition elements combined, and enable specific detection without contamination or interference from other substances. Various recent reports have shown that integrating biomolecular recognition elements into engineered surfaces whose dimensions are reduced into the nanoscale leads to enhanced sensitivity compared to the macromolecular equivalents in the bulk solution. Nano-biosensing devices are therefore tailored to detect invisibly small amounts of specific biomolecules or pathogens present at low concentrations.

In addition to the bio-recognition elements that enable specificity, the transducer also requires the aid of nanomaterials that confer detection at the pico- or femtomolar concentration levels. The progress in nanotechnology over the last two decades gives an additional opportunity for research at the nano-scale. The desired properties of nanomaterials become apparent when considering the importance of reduced dimensions in relevant physical processes. Nanomaterials with optical, electronic, or catalytic properties that differ from the bulk counterpart are already being used to enhance the sensitivity of all types of biosensors. [226, 227, 57, 228]

Nanomaterials in Protein and DNA Detection

Nanotechnology has ushered in an era of novel and advanced materials, including nanomaterials that possess a large surface-to-volume ratio and tunable surface properties. These significant characteristics make nanomaterials excellent candidates for enzyme immobilization, biomolecule labeling, and DNA and protein detection. Gold, silica, metal, and semiconductor nanoparticles (NPs) have been extensively employed in protein or enzyme assays based on fluorescence, mass spectrometry (MS), surface-enhanced Raman scattering (SERS), colorimetric detection, and electrochemical readout methods. Nanomaterials can also exhibit electrochemical catalytic activity for the redox reaction of biomolecules and are becoming an efficient tool in biosensing and detection applications.

Nanomaterials enhance protein detection through approaches that offer an improved signal-to-noise ratio, greater sensitivity, or more efficient separation. Gold nanoparticles (AuNPs) can efficiently accumulate chemiluminescence onto the surfaces of an enzyme-labeled antibody–antigen complex and thereby achieve an 800-fold increase in detection performance. Increasing the particle size of AuNPs effectively reduces the limits of detection. Such colorimetric immunoassays exploit the high reactivity, excellent catalytic activity toward H2O2 reduction, and strong surface plasmon resonance properties of AuNPs. In addition, AuNPs readily assemble with Escherichia coli, and the intrinsic peroxidase-like activity of the E. coli–AuNP composites can then be utilized for indirect colorimetric detection of pathogens.

Nanotoxicology and Environmental Safety

The rapid development of nanomaterials within electronics, optics, and medicine raises both safety and regulatory concerns. Thus, understanding the environmental impact of nanoscale compounds and ensuring that nanoparticle-based tools do not represent additional risks for the environment and human health are critical. Nanoscale structures inevitably enter the environment, including natural waters, soil, and the atmosphere. The presence of nanoparticles in soil and water, as well as their ability to penetrate tissues in plants and animals, have been shown to be potentially toxic. The toxic effects of nanoparticles are associated with their large specific surface area, and their toxicity mechanisms in living organisms differ significantly from those of transmicroscale bulk compounds.

Research on nanotoxicology is gaining momentum due to concerns about the environmental and health effects of commercialized nanomaterials. The investigation of the impact of nanomaterial-based diagnostic tools in the context of environmental safety is a challenging task. Toxicological safety testing is currently performed using traditional "high-throughput high-cost" wet-lab approaches that require a large number of experimental animals. Therefore, predictive toxicology that incorporates systems biology, integrative multi-omics analysis, and bioinformatics has emerged as a promising alternative for nanoagent safety assessment. Environmental safety evaluations of nanoparticle-based diagnostic nanoplatforms are irretrievable? Nevertheless, these assessments could be implemented in synergy with environmental surveillance and diagnostic monitoring efforts aimed at identifying nanomaterials in ecosystems. [229, 230, 231, 232]

Future Prospects in Nano-Integrated Platforms

The effects of engineered nanoparticles on both the environment and human health have been investigated in a variety of levels. Nanomaterial-based diagnostic approaches are being developed to identify different organic and inorganic pollutants, and the combination of nanotechnology with biosensors has led to the creation of nano-biosensors for the ultra-trace detection of heavy metals. Nanomaterials are also being synthesized and tested for their use as carriers for aptamer relays and amplifiers to facilitate protein and DNA detection, as well as being tested for their own untargeted toxicity and potential environmental impact. However, proteomics studies with nanoparticles have revealed the dangers of these technologies and how they may influence the ageing process of living organisms. Experimental setups at the nanoscale level are tested within a multiscale model for both the interaction of nanoparticles with cells and the interaction among the cells themselves.

The danger of nanotechnology lies not only in the functioning of the nanoparticles themselves but also in how its use in different products may affect nature. Future experimental studies are needed to address the safety of engineered nanomaterials and to carry out a transdisciplinary investigation into the interaction of nanoparticles across the environmental media and the living domains as a knowledge basis for predictive nano-safety models. The integrated application of many fresh−freshwater systems connected by monitoring, sensor, and communications networks is providing sound NBS solutions to current environmental pressures while helping develop new NBS for the future. These novel NBS may draw on mature research areas—such as water-safety, landslide, and forest-fire networks—as well as emerging strands, such as sanitisational solutions for growing metropolitan areas, pest prevention in urban forests, or monitoring and prevention of fresh−freshwater lens transfers. [233, 234, 235, 236]

Chapter - 13

Systems Biology Approaches

Integrating data from different omics-level biological responses can provide a complete landscape on environmental exposures and these biological discrimantors form the basis for adaptive, regulatory and pathway networks that respond to external perturbations. Building upon the Multi-Omics Biological Exposure Picture approach developed by Allorge and the Network Biology Toolbox scheme proposed by Acosta and Scelsi summarizes multi-omics Integrative and Predictive Platforms together with Predictive Toxicology Modeling and Gene-Protein Interaction Maps into one single framework supported with suitable experimental and computational tools.

Recent advances in sensor technology combined with the opportunities offered by Machine Learning expand the application of systems approaches for data analysis as a smart means to analyze complex signal patterns in chemical sensors and to investigate DNA and protein molecular signatures. Pattern recognition techniques can be employed to automate and optimize data treatment of chemical sensors used as pollution-like indicators for the recognition of bacterial contamination of drinking water. The application of Artificial Intelligence strategies focus on Predictive Exposure Modelings of responding biological biomarkers based on environmental contaminants, to reconstruct pollution environments with possible associations with health outcomes. [237, 238, 239, 240]

Integrative Multi-Omics Analysis

Integrative multi-omics analysis can bridge cellular and organism-level toxicological responses by combining nuclear molecular data with secretomic information from human or animal fluids like blood, mucus, urine, and saliva. Such integrative maps visualize the networks involved in cellular-to-organismal responses under exposure conditions. With the upcoming era of multi-omics data generation, one major challenge will be to develop the necessary algorithms and strategies to combine the multiple layers of omics data into cellular and organism-level responses to specific exposures or combinations of exposures, thereby supporting the identification of cellular- and organism-level response pathways.

Toxicogenomics aims to understand the effects of toxicants at the system level through the use of high-throughput technologies that measure gene, RNA, protein, and metabolome perturbations in cells or tissues and establish the underlying molecular networks. However, most studies consider only gene or protein responses. Moreover, Open-TG-GATEs, the first major long-term database of toxicogenomic studies using rats and various toxicants, focused solely on the transcriptome level. Recent efforts have visualized toxicology-related gene networks for individual chemicals. [241, 242, 243]

Network Modeling in Toxicity Pathways

In silico approaches have been established for the identification of the toxicity effect and a probable mechanism of toxicity directing towards toorganism. Network models play crucial roles in elucidating the underlying molecular mechanisms in various complex biological processes, including Ebstein–Barr virus (EBV) infection, acute stroke, cancer, diabetes, obesity, neuropathic pain, meningococcal disease, and Bacillus anthracis infection. For example, while predicting cellular hierarchies in development and cancer, Chen *et al*. constructed a gene-network model by integrating data from gene knockouts.

With the rapid development of systems biology, approaches built upon the combination of multiple gene expression data sets across different experimental conditions and species have become possible. These integrative approaches not only facilitate the exploration of gene–gene regulatory interactions, gene–protein interaction, and gene–metabolite relationship networks underlying different biological systems but also provide probabilistic foundations for elucidating complex phenotypes. A network-based approach has been also developed to infer cellular molecular indicators for predicting above-ground plant traits. Using such predictive interaction maps, it is expected that the marker of toxicity during toxic exposure can be successfully identified. [244, 245, 246, 244, 245, 246, 247]

Gene–Protein Interaction Maps

Gene–protein interaction maps can provide valuable information about toxicity mechanisms in humans or plants exposed to hazardous agents. Such data are limited and must be determined using an integrative systems biology approach combining transcriptomic, proteomic, and metabolomic data. Pathway enrichment analysis and gene-protein (GP) interaction networks for major toxicity-related pathways are identified, followed by experimental validation of critical genes and proteins.

Integrative genome-scale analysis of diverse transcriptomic, proteomic, and metabolomic data reveals a complex and diverse gene–protein interaction map for multiple toxicity-related pathways across different biological systems. The analysis prioritizes multiple genes and proteins in nearly all major pathways ranging from oxidative stress response to inflammation and DNA repair. Key GP interaction pairs for debris clearance, DNA damage response, inflammation response, and neuroiodine homeostasis are identified in environmental contamination studies, and the prediction capability of GP pairs for toxicity data is empirically validated. Integration of multi-omics data with GP interaction maps enables novel insights, high predictive power, selective gene–protein pair validation, and a more comprehensive understanding of toxicity mechanisms.

Computational Tools for Environmental Health

Computational techniques and tools are critical for analysing biological pathways underlying environmental health outcomes. Systems biology offers an integrative framework that connects multiple functional layers of living organisms (metabolome, proteome, transcriptome, genotype) into a coherent understanding of how the organisms react to endogenous and exogenous stimuli and function in an overall system mode. The integration of multi-omics data within reaction, interaction, and regulation networks is essential for analysing the interplay between pollutants and biological systems. To elucidate the effects of exposure to environmental pollutants, there are several methodologies and approaches that are frequently applied: (i) molecular responses to single and combined exposures, (ii) gene-based or transcript-based pathway lists and expression profiles, (iii) integrated multi-omics analyses, and (iv) biomarker-response signatures corresponding to organ-specific effects induced by a large number of chemicals.

Advances in predictive toxicology research can be achieved using computational models. Toxicological data from different biological levels (e.g., cells, tissues, organism) produced for chemicals of environmental and/or industrial interest can be integrated in a probabilistic framework for the identification of adverse effects and the elucidation of underlying toxicity pathways. Data-driven modelling can help in unveiling toxicity mechanisms by exposing the relationships between predictive biological signatures and toxic effects. Gene- or protein-based predictive signature patterns can be defined by multilabel classification techniques with overlapping labels in the response variable. [248, 249, 250, 251]

Predictive Toxicology Modeling

Machine learning and artificial intelligence (AI) have become crucial tools in predictive toxicology, allowing for the modeling of biological responses following exposure to a range of environmental chemicals. The combination of quantitative structure–activity relationship (QSAR) modeling in predictive toxicology, together with supervised and unsupervised machine-learning techniques, supports the generation of predictive ADMET (absorption, distribution, metabolism, excretion, toxicity) data for toxicants across all human-relevant chemical classes. Advances in high-throughput experimental techniques can create large and diverse data sets that are valuable for training prediction models. New deep-learning methods (e.g., deep neural networks and convolutional neural networks) can take advantage of these data sets to improve predictive performance. However, any training data set can never cover all substances that enter the food chain. New deep-learning approaches can exploit data from similar molecules to predict environmental toxicology. When sufficient toxicity data are available, they can be integrated with structural health effects to identify patterns across multiple toxicity pathways. Such advances allow for quantification of toxicity at virtually all relevant biological levels, whether omics data or toxicity *in vitro*, aquatics, mammals, or humans.

Predictive toxicology aims to integrate all available knowledge—from structural alerts to omics and multi-species population effects—to develop predictive models that quantify effects *in vivo* (animals, humans) and in ecotoxicology.

Environmental temperature or other predictors can be included in these predictions. Existing data on chronic toxicity in fishes, amphibians and mammals following long-term environmental exposure have already been collected and can be processed with predictive toxicology principles, thus establishing the first predictive model for long-term environmental exposure to these species. [252, 253, 254, 255]

Chapter - 14

Sensor Data Analysis and Machine Learning

Data acquisition from electrical, optical, and thermal sensors generates multidimensional datasets reflecting environmental exposure across multiple dimensions such as time, concentration, and temperature. Sensor information is processed using signal de-noising algorithms, compensated for drift and cross-interference, and subsequently analyzed by pattern recognition tools such as PCA, LDA, PLS-DA, ANN, and SVM methods to classify, quantify, and map the original entities or conditions in the real world. Molecular and protein data generated from various biosystem components can also be integrated with sensor information for more complete and intelligent assessments of exposure conditions and preventive early warning systems.

Machine learning techniques such as AI, neural networks, and deep learning are applied to aid in the interpretation of molecular and protein data. An inverse model of human exposure using multi-omics data is also described in order to predict specific/subclinical exposure levels when sensor measurement data are correlated with large population biomarker datasets. Integrating data from multiple sensors in a network enables predictive capabilities for external conditions such as air quality, while sensing systems communicable with mobile/cloud servers provide the potential for feedback data generation to notify nearby populations of abnormal exposure conditions. [256, 257, 258, 259]

Signal Processing in Chemical Sensors

Chemical sensors convert a physicochemical quantity into an electrical signal as a measure of the analyte. The resulting signals are usually characterized by changes in potentiometry, conductometry, oscillometry, amperometry, voltammetry, potentiostatic or biosensor systems. Nonetheless, the analyte detection still remained an area of concern, particularly its selectivity and sensitivity to distinguish among species with similar characteristics. Rapid signal understanding makes a chemical sensor valuable in terms of response time. It is most commonly achieved using pattern recognition techniques in both the fully developed sensor systems and in the evaluating stage. When the sensor was developed or is being evaluated is indicated by the analyzer-at-sensor connection. However, in both the cases, it is still a pattern-recognition problem.

The signal can also be interpreted with the knowledge of the linearity of the developed response to the target hence acquiring a calibration plot for the concentration of the analyte under study. Although the signal can correspond to a change in any physicochemical property associated with the electrochemical or other chemical reaction occurring at the sensing layer, it is the sensor's capacity to discriminate among similar species in solution that determines its utility. To accomplish this task, a combination of sensors works effectively; a detection concept of sensor array, an electronic nose, couples several individual sensing elements for qualitative or semi-quantitative investigation of gaseous samples and recognizes a fingerprint signature of a gas mixture. [260, 261, 262, 263]

Pattern Recognition for Pollutant Classification

Pattern recognition offers a powerful approach for analyzing chemical sensor data since it relies not on quantifying individual analytes but rather on recognizing unique chemical signatures associated with specific samples or sample classes. Indeed, the main experimental objective when generating a chemical sensor array is to create a library of sensor responses that contains distinguishing information across sample classes. Such a library may be generated using a single sensor containing a non-specific coating or an array of chemically diverse sensors.

Chemical sensor arrays, referred to as electronic noses or tongues, have been used extensively in identifying and characterizing volatile organic compounds (VOCs) and other compounds soluble in the supporting solvent. These arrays incorporate multiple sensors with a variety of sensing materials designed to yield different physicochemical affinities. Sensor responses are acquired in concentrated phases or as supernatants from solid-phase microextraction. Pattern recognition has been used successfully to classify a number of VOCs, including alkanes, alcohols, aldehydes, ketones, aromatics, and esters. [264, 265, 266, 267]

AI for Molecular and Protein Data Interpretation

Recent advances in artificial intelligence (AI) and machine learning (ML) will allow the development of computational models for the interpretation of molecular- and protein-related environmental exposure data. For actor-response pathway networks, data from two separate sources are integrated not only into a network, as is currently the case for the Barabási–Albert algorithm, but also into an actor-response predictive model aided by the prediction rule discovery technique. Residual analysis, receiver operating characteristic (ROC) curves, and Bayesian probability confirm the quality of the developed models based on predictive-system biology principles. Data sets can be origin non-specific, allowing for a node-response predictive model that gives a response spectrum for a set of actor nodes. In addition, prediction-rule-learning-based models can be established for actor-specific behaviour based on actor-response pathway networks. Machine-learning-based approaches could also be successfully applied for characterizing high-dimensional data, such as multisensor data from chemical odors. This performs combinatorial tests of a large number of pairs of chemical vapors to build an odor classification model that can better resolve individual odors than does a conventional vector machine classification model.

Another area where extern AI capabilities can support environmental health assessment is by merging Big Data, artificial intelligence (AI), and sensor information to better predict which of the multiple known toxic compounds an uncontrolled or accidental release can contain. For that purpose, state-of-the-art Big Data sources are searched to identify compounds based on keywords associated with the event. AI models are then built based on that data and combined with chemical sensor-based detection of actual environmental samples to provide a predictive framework. [253, 268, 269, 250]

Predictive Exposure Modeling

Exposure to environmental contaminants is often estimated through repetitive measurements of pollutants in biological fluids and tissues. However, such analyses are costly, time-consuming, and limited by accessibility to specialized laboratories. A better alternative is the application of predictive exposure models capable of estimating human exposure based on publicly available environmental monitoring data and locations of people in relation to detected pollution sources.

As an example, prediction of blood mercury levels of the U.S. population, aged 1 year or older, was recently achieved by modelling the relationship between human blood concentrations and dietary fish intake rates, by using fish mercury concentrations from the U.S. EPA National Contaminated Fish

Tissue website, and EPA-reported fish consumption rates. The resulting risk model may potentially serve for health risk assessment of mercury in fish and for the identification of dietary groups of concern. In a similar manner, other predictive exposure models have been developed for other hazardous contaminants, including various metals in human hair in relation to industrial activity areas, cancer risk in relation to proximity to Superfund sites, and diabetes probability in relation to proximity to Superfund, NPL, or abandoned hazardous waste sites. [270, 271, 272, 273]

Smart Sensor-Based Environmental Health Systems

Algorithmic or machine learning-based interpretation of raw sensor data for environmental sample classification has gained increasing attention. Fully automated frameworks for the analysis of different types of environmental data based on signal processing and AI techniques have shown promise. Sustainable, efficient, and smart chemical sensor networks can actively monitor local environments, learn normal patterns, and provide early warnings with predictive power. Predictive exposure modeling uses monitoring data as inputs to describe environmental exposures over time, identify population groups at risk, and support epidemiological research.

Cradle-to-grave environmental health issues require a strategic systems approach combining environmental sensing with human exposure assessments and health effect studies to help identify policies that can reduce the burden of health hazards associated with exposures to environmental contaminants. The increasing incidence of environmentally associated human diseases driven by pollution, coupled with advances in multi-omics technologies that can define the effects of exposure and susceptibility pathways, are crucial in providing validation information for exposure-disease link models. [274, 275, 276, 277]

Chapter - 15

Pollutant Exposure and Human Health Outcomes

Research has shown that environmental pollutants can adversely affect all systems of the human body. These systemic impacts can be further substantiated through alterations in well-defined genes involved in various diseases. A comprehensive review of the role of different pollutants in human health and the underlying molecular mechanisms affected by these pollutants are presented. The major contributions include alterations in respiratory, cardiovascular, neurological, endocrine, reproductive, and digestive systems, as well as carcinogenesis, multi-organ damage, diabetes, obesity, and associated pathways, based on the evaluation of several biomarkers along with support from multi-omics studies.

Globally, ambient particulate matter with diameter under 2.5 μm has been linked to higher mortality rates. Even short-term exposure to PM2.5 and PM10 can cause serious cardiopulmonary complications. Several studies have highlighted that acute and chronic exposure to PM2.5 not only increases receptor for advanced glycation end-products expression but also leads to oxidative stress. Marked lungs gene activation of IL-1β, p53, iNOS, and COX-2 has also been noticed in response to PM2.5. Chronic inhalation of concentrated PM2.5 from urban air generates more severe respiratory effects in aged mice, including up-regulated expression of various proinflammatory cytokines as well as Ikk-β and Iκb-α. In addition, PM2.5 induces the expression of inflammatory cytokines IL-8, IL-6, IL-1β, TNF-α, and IL-10, as well as oxidative and endoplasmic reticulum stress along with autophagy impairment in lung epithelium cells.

Epidemiological analyses have identified associations between prenatal exposure to increased concentrations of reactive oxygen species-generating air pollutants and the risk of attention-deficit/hyperactivity disorder and ADHD-like symptoms among children. Several studies have also identified exclusive signatures of ROS in ADHD as well as PM2.5 and PM10-induced alterations in the expression levels of various genes. Furthermore, a limited number of connections have been identified between air exposure to respiratory inflammation-related genes and cardiac risk-related genes, confirming dysregulation in early-life antioxidant mechanisms. The messenger RNA expression profiles induced by PM2.5 and PM10 point toward 강한신다투수의횡단강혈관 lative roles in toxicity pathways, suggesting additional candidate genes for further investigation. [278, 279, 280, 281]

Respiratory and Cardiovascular Effects

Epidemiological studies have increasingly linked ambient air pollution with morbidity and mortality of the respiratory and circulatory systems. Associations are frequently observed for levels of particulate matter, especially for PM2.5 and PM10, but also for particle number, black carbon, total suspended particles, ozone, nitrogen oxides, carbon monoxide, and sulphur dioxide. PM2.5 and PM10 can penetrate deep into lungs and skeleton, reach bloodstream, and cause systemic effects in cardiovascular system. Exposure to PM might affect heart rate variability (HRV) in the population but studies on other cardiovascular variables are relatively few. Increased plasma levels of C-reactive protein (CRP), another non-specific inflammation mark, have been found associated with ambient PM. Immune responses in subjects with adenovirus bronchial infections showed negative correlations with HRV.

Changes in gene expressions, analysed through Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways analyses, were also observed. Genes related to ROS and superoxide metabolism, as well as the KappaB and p53 signalling pathways were upregulated. Protein levels of SOD, CAT and GSH were decreased by PM2.5. A correlation matrix revealed that the expression levels of Hmox 1 and Vcam 1 were closely related to pro-inflammatory cytokines. PM2.5 exhausted antioxidant defence mechanisms, induced an inflammatory response, aggravated adenovirus bronchitis in children, and impaired the body's natural resistance to adenovirus. Particles in the ultra-fine range, including metals, have been demonstrated to activate multiple cellular events and are themselves capable of stimulating the formation of ROS within epithelial cells. ROS can initiate cellular stress responses and modulate gene expression, including expression of genes regulating protein activity involved in inflammation. [282, 283, 284, 285]

Endocrine and Reproductive Toxicity

Continuous exposure to environmental pollutants may disturb the endocrine system and cause reproductive toxicity. Adverse effects of air and water pollution on female and male reproduction have been extensively studied in animals and can be linked to the presence of specific endocrine-disrupting chemicals. Human population studies, however, are more complex, as uncontrolled confounding factors can potentially mask the effects of endocrine disrupters and their biological consequences.

Epidemiological studies reveal an association between pollution exposure during pregnancy and genosomal abnormalities, alterations in DNA repair, pregnancy-related diseases (gestational diabetes and/or pregnancy-induced hypertension), low birth weight and/or preterm birth, and fetal death. Furthermore, PCB and PBDE mixture exposures reduce human reproductive outcomes. In males, high prenatal exposure to phthalate mixtures is associated with an increased risk of being small for gestational age, cryptorchidism, and neuro-developmental effects, while high maternal urinary bisphenol A concentrations during pregnancy are also related to decreased birth weight in boys. [286, 287, 288, 289]

Neurological Impacts of Environmental Contaminants

Pollutants in air, soil, and water are associated with induced neuroinflammation, neurodegeneration, and cognitive impairment. Oxidative stress, mitochondrial dysfunction, and blood–brain barrier disruption may contribute to these effects via environmental exposure-induced epigenetic changes. Environmental contaminants can cause long-lasting toxicity in the developing nervous system, leading to behavioral effects that persist into adulthood. Newly discovered molecular mechanisms include the involvement of hydroxymethylcytosine and 5-formylcytosine in EDCs; miRNA upregulation by the anti-androgenic dibutyl phthalate; an EDC–nuclear receptor–corepressormediated-EUFA signaling pathway; a mechanism underlying uranium-induced neural damage; benzo[a]pyrene exposure-induced dysregulation of mRNA expression; and oxidative stress-induced neurotoxicity via p38 MAPK/JNK.

According to approximately one-quarter of the world's population is exposed to ambient fine particulate matter (PM2.5) concentrations above the World Health Organization Air Quality Guidelines. It has been shown that the total burden of mortality attributable to PM2.5 air pollution is also becoming increasingly concentrated in the developing world. All of these findings clearly demonstrate the importance of environmental factors and pollution in the etiology of disease in humans and animals. [290, 291, 292, 293]

Cancer Risks and Molecular Pathways

Research indicates that hazardous substances in the environment contribute to cancer development through several mechanisms. Peroxynitrite can induce both nitrative and oxidative DNA damage, leading to mutations. Endocrine disruptor compounds (EDCs) play a key role in breast and prostate cancer formation, acting either as promoters or initiators. Case-control studies show that exposure to certain EDCs, like DDT and chlordane, is associated with increased incidence. Phthalates and phenols have also demonstrated carcinogenicity in animal models or cell cultures, with breast and uterus being key organs of concern. Moreover, certain levels of heavy metals, particularly arsenic and cadmium, are linked to cancer. Oxidative stress, multicentric bioactivation of carcinogens, and interaction with the redox status of cells are crucial factors in the carcinogenic processes involved in human diseases.

Integrating multi-omics data could facilitate a more reliable risk assessment of environmental contaminant exposure. Multi-omics approaches encompassing genome, methylome, transcriptome, proteome, and metabolome measurements are particularly promising for deciphering the molecular underpinnings of environmental health. Meta-analyses of human discovery datasets have identified chemical exposure signatures in breast tissues associated with breast cancer outcomes and revealed gene-methylation alterations in response to persistent organic pollutants in the uterus related to uterine cancer. [294, 295, 296, 294, 295, 296, 297]

Integrating Biomarker Data for Health Assessment

Numerous molecular biomarkers of human exposure to environmental pollutants have emerged over the years from efforts to investigate the health effects of complex mixtures of chemical pollutants. However, a gap still exists in applying these biomarker data to evaluate health outcomes in populations exposed to one or more combinations of environmental toxicants. A thorough characterization of the association of biomarker data with outcomes involving the respiratory, reproductive, endocrine and hormonal, cardiovascular, immune, and neurological systems is thus necessary. In addition to single- or multi-pollutant analyses, stratified analyses based on response phenotype aggregation are highly relevant, and development and application of epidemiological modeling techniques that are better suited to account for molecularly detected exposure should also be a priority.

The association of multiple organ systems with the plethora of underlying molecular pathways has opened up the opportunity for the use of propensity scores for modeling, ideally followed by assessing the risk for discrete outcomes pertaining to more than one organ system. Such an approach is expected to add value to the current breadth of health analyses and should inform systems-based modeling of multiple endpoints of environmental exposure. These pathways have been elucidated primarily using expression data sets supplemented with genome-wide association study and open-access toxicogenomics data sets, thus combining information across scales and providing the basis for a broader assessment of human health risk in relation to environmental toxicant exposure.

Chapter - 16

Plant Health and Environmental Stress Responses

Beyond animal and human health, plant wellbeing is also affected by the presence of environmental contaminants. Pesticides, heavy metals, industrial effluents, organic solvents, and other pollutants are shown to have a detrimental effect on plants by inhibiting growth, harvesting efficiency, and crop yield. Chemical responses associated with adverse health are diverse, but the most frequent and informative effects are commonly related to photosynthetic performance, oxidative state, gene expression profiles, and protein response.

Contaminants may inhibit the absorption of important nutrients, producing some important alterations incorporated as biomarkers, e.g., abnormal levels of magnesium, phosphorus, calcium, etc. However, although many studies took into account only the harmful effects on plants, these organisms can be used to monitor pollution levels and health status in aquatic and terrestrial environments. Pollutants may produce specific changes at the metabolic and physiological levels, enabling their use as early warning biosensors. Moreover, plants can metabolize several pollutants and continue their life cycle, resulting in the production of specific metabolites associated with pollutant exposure during the last phase of life.

Sensors have appeared as alternatives for precision agriculture, focusing on real-time analysis of soil properties for proper irrigation and fertilization. The distribution of sensors in the soil or on the plants is essential for analyzing water content, temperature, humidity, and mineral nutrition. In addition to the inorganic and physical conditions of the soil, the use of organic samples can be applied to monitor pollutants using closely related sensor technologies. Plant metabolomics can be used to identify and quantify metabolites, such as alkaloids, phenolics, and flavonoids, with antimicrobial and anticancer activities. Plant regulation of these compounds and the interaction between plant metabolites and contaminants may be used as possible biosensors for environmental malignant sources. [298, 299, 300, 301]

Photosynthetic Alterations Under Pollutant Stress

Photosynthetic responses in plants under pollutant-induced stress conditions are monitored at the molecular level by analysing variations in the transcript levels of photosynthetically important gene families using a natural model system. Expression patterns of genes involved in CO2 fixation, chlorophyll (Chl) a biosynthesis, light-harvesting complex (LHC) saturation, and pigment-pathway regulation are examined in natural populations of two dicotyledonous plants, Ekis5818 and Ekis5819, growing along the eastern coast of Taiwan. The two populations have been exposed to similar types of environmental stressors but different degrees of chemical pollution from industrial activity and residential waste. Transcript quantitation reveals distinct expression patterns. In Ekis5819, which is exposed to heavy metal stress, excess free energy generated from D1-QA photoinhibition leads to photo-oxidative injury and uncouples LHC from the photosystem, resulting in diminished CO2 fixation, downregulated Chl a biosynthesis, and an accumulation of pigments prior to their conversion to Chl_aide. Conversely, Ekis5818, growing in a relatively clean area, exhibits increased LHC and Chl a biosynthetic activity relative to the other genes in the CO2 fixation and pigment regulatory pathways.

Environmental pollutants affect plant systems by altering the structure and functioning of important cell organelles, such as chloroplasts. Chloroplasts are specific organelles housing the entire photosynthetic machinery in plants, through which they can maintain their energy and nutrient needs by producing organic compounds during photosynthesis. The material and energy exchange that takes place through photosynthesis is therefore of utmost importance for both plant life and the entire ecosystem. However, chloroplasts are highly sensitive to environmental pollution. Pollutants such as heavy metals, hydrocarbons, chlorinated pesticides, and acid rain can adversely affect chloroplast structure, endogenous pigments, chloroplast transcription, and even chloroplast-mitochondria interaction. [302, 303, 304, 305]

Oxidative Stress and Antioxidant Enzymes

Oxidative stress (OS) is an imbalance between the production of reactive oxygen/nitrogen species and the organism's ability to eliminate them via antioxidants. Early OS causes membrane lipid peroxidation, protein oxidation, polysaccharide oxidation, enzyme activity alteration, mitochondrial dysfunction, DNA damage, and changes in expression of metal and peroxidase proteins. Indeed, increased or decreased activity of stress-related enzymes has been widely used as a pollution marker in vegetables, fruit trees, and forest trees. Activity variation of peroxidase (POD), catalase (CAT), superoxide dismutase (SOD), ascorbate peroxidase (APX), and glutathione reductase (GR) has been implicated in blueberry, apple, litchi, soybean, hybrid poplar, maize, Cu/CO, and Quercus sect. Ilex increase stress-induced damage, while SOD, CAT and Na+/K+ concentrations protect from high-temperature stress.

Antioxidant enzyme responses can also serve as early warning indicators. SOD, smoothly regulated by salinity fluctuations, is especially sensitive and up-regulated before other stress markers; heat-shock proteins are only induced at long-term (3-day) salinity exposure. In rice, SOD and GR activities, unknown YanX's biological function, and the ratio of RWC can serve as early warnings for hypoxia under flooding stress. APX, GR, and glutathione-S-transferase (GST) are key preventers of soil drought stress; variation in osmotic potential is a sensitive index for detecting soil drought. Additionally, CAT, SOD, and POD responses enable gooseberry bush recognition of early pollution stress. Thus, monitoring these enzymatic changes can inform timely soil-water management for nitrogen-fixing trees under saline-alkali conditions. [306, 307, 308, 309]

Gene Expression Signatures in Polluted Environments

Gene expression profiles produce powerful signatures of environmental changes, such as exposure to persistent organic pollutants and mixtures of traditional and emerging organic pollutants in soil. Changes in the expression of genes related to respiration, signal transduction, cyclic nucleotide metabolism, and membrane transport are indicative of vegetation stress triggered by contrasting atmospheric conditions. Long-term exposure to prolonged temperature stress has contrasting effects on the expression of peptidases and certain heat shock proteins in Pinus avula. Decreases in the expression of genes associated with the chlorophyll biosynthetic pathway and increases in the expression of heme oxygenase, oxidative signal-inducible protein 1, dehydroascorbate reductase, and peroxidase-processing protein transcript suggest an increase in oxidative stress and impairment of chlorophyll biosynthesis. Similarly, oxidative stress, indicated by expression patterns of glutathione reductase, glutathione S-transferase, involucrin, and associated signaling pathways, is linked to long-term photochemical instability in a subtropical scrub ecosystem.

Gene expression signatures hold potential for monitoring environmental health and ecosystem integrity. Expression profiling offers a comprehensive approach to the selection of indicator species, assists in identifying key drivers of biological changes, and enables the reliable prediction of phenological and physiological responses in complex fungal assemblages under simulated climate change. Transcriptomic responses have been explored across multiple life-stage transitions of seven species of fish exposed to temperature and dissolved oxygen extremes in conjunction with sedimentation. Differentially expressed genes associated with cellular responses to iron and oxidative stress, heat shock proteins, and signalling pathways suggest that short, acute temperature-oxygen extremes may compromise cellular functions in fish embryo and early larval life stages, and further experiments highlight the potential impact of explicit changes in sedimentation. Summer warming and reduced autumn flooding of wetlands impact the composition and functioning of diatom assemblages and the leaf-litter decomposition process via interactive effects on latitudinal and altitudinal niche differentiation. [310, 311, 312, 313]

Protein Response Pathways in Plants

Heavy metal pollutants enter the plant through the roots and accumulate in the various cells and tissues. Plant metabolism is adversely affected, causing reductions in growth rate, biomass, leaf area, chlorophyll synthesis, transpiration, nutrient uptake, and photosynthesis. Some of the considered contaminants and their action on molecular and cellular processes in the plants are discussed.

In plants, heavy metals may be taken up and translocated to the aerial parts. The oxidative stress produced by excess metals can cause lipid peroxidation, DNA damage, and protein denaturation. The activity and levels of antioxidant enzymes and nonenzymatic antioxidants can be altered, which promote tolerance in plants. The upregulation of genes related to the oxidative stress response, glutathione metabolism, heat shock proteins, and transporters for heavy metals and maintaining ionic status can also be involved and detected. The proteomic response can indicate the hierarchical activation of processes important for coping with metal toxicity and the mode of action in a specific metal-induced stress situation.

The expression profile of several genes (e.g., involved in cell wall modification, heavy metal transport, detoxification, energy metabolism, and transcription factors) can demonstrate the plant response to heavy eutrophication. The transport activity and expression of heavy metal transporters may be regarded as good indicators of heavy metal contamination. The regulation patterns of Mn2+-sensing transcription factors in response to elevated concentrations of Mn2+ can reveal important insights into how plants sense and respond to excessive external Mn2+. Accumulation studies undertaken at various contaminations of cadmium and copper can help elucidate their distribution pattern and coping mechanism in tolerant plant species for future bioremediation programs. Genes involved in cysteine, methionine, and polyamine metabolism may thus play essential roles in the detoxification of Cu-induced cellular injury. [314, 315, 316]

Role of Sensors in Precision Agriculture

Recent years have witnessed numerous advances in sensor development for the optimization of precision agriculture. Deploying these technologies on a broad scale would enable real-time analyses of fertilizer and pesticide levels in soils and a better understanding of plant stress responses. Such knowledge could provide insights into when crop protection agents should be used and the appropriate concentration for enhancing yield without polluting the environment. Integrated sensor systems measuring multiple environmental parameters, including soil nutrients, weather, and air quality data, could be used in smart farming.

Sensors measuring soil conditions such as temperature, moisture, pH, salinity, and nutrients; plant parameters such as leaf temperature and chlorophyll content; and weather factors such as rainfall, humidity, and air temperature would provide advanced warning of possible plant susceptibility to pests and diseases. In addition, various pathogens release volatile organic compounds that are detectable by sensors. Such monitoring would indicate the probable risks of diseases, pests, or other stresses affecting individual plants or crops, thereby providing enough time for farmers to take preventive measures before yielding losses or declines in quality. [217, 317, 318]

Chapter - 17

Emerging Diagnostic and Sensor Technologies

Recent advances in molecular biology, nanotechnology and sensor development have created new opportunities for the detection and quantification of contaminants and their metabolites in biological samples. The CRISPR/Cas9 system with its flexibility and molecular recognition capability has emerged as a new class of ultra-sensitive environmental diagnosis for gene-editing. The system is now being used to detect DNA from microorganisms with known bioremediation functions, and miRNA as a biomarker of Arabidopsis thaliana in polluted environments.

Wearable and implantable electrochemical sensors are able to determine multiple analytes and ionic species simultaneously, and provide real-time results. Miniaturized lab-on-chip chemical sensors with enzymatic and aptamer-based membranes have been developed for real-time GPS and remote-control operation using smart-phones. These combined characteristics represent a great advantage for the design of biosensors able to give rapid information about environmental quality. New concepts in wearable biosensor technology also offer the possibility for real-time molecular monitoring of internal physiological indicators and for detecting specific external agents in biological fluids such as perspiration. [319, 6, 320, 321]

CRISPR-Based Environmental Diagnostics

Recent advances in CRISPR technology provide new chemistry-based molecular diagnostics tools. CRISPR is capable of detecting various molecules, including proteins and mRNA – from human, animal, plant, and microbial sources – and is also being integrated into novel chemical sensors. CRISPR-Cas technologies compete with cutting-edge molecular-biological methods that have been applied to assess environmental stress impact on humans, plants, and animals for more than three decades.

The appealing aspects of CRISPR systems are their specificity, the rapidity of the reactions (amplified trans-cleavage activities), the generation of an easily readable signal by DNA nanoprobes, and their compatibility with integrated platforms for multiplex detection. Various potential applications in the environmental field are already implemented and numerous other developments are expected in the near future. [322, 323, 324, 325]

Lab-on-a-Chip Sensor Systems

Miniaturized sensing systems that integrate several laboratory processes onto a single chip have created a lot of interest due to their rapidly growing application in real-time detection, especially for point-of-care diagnostics and environmental monitoring. These systems possess high sensitivity and selectivity and can be developed for a variety of analytes using different approaches like electrical, electrochemical, optical, and mass sensing techniques. Recently, CRISPR-based heterogeneous detection has produced a robust development platform with excellent specificity and sensitivity.

CRISPR-based environmental diagnostics are evolving rapidly. Conventional LAMP probes are sensitive, rapid, and simple methods to assess the presence of pathogens and their toxins; however, they lack specificity. Cross-reactivity is a major issue with conventional LAMP probes since sequences are only exhausted in the reaction mixture. Miniaturization of LAMP probes with CRISPR-Cas9 and isothermal amplification can be an alternative strategy. Action of Cas9 endonuclease on a LAMP amplicon results in a fluorescence intensity change. The detection limit is improved by about four times when using CRISPR-LAMP compared to LAMP. [326, 327, 328]

Wearable and Implantable Chemical Sensors

Recent developments in flexible electronic materials have enabled the realization of wearable or implantable chemical sensors that can be placed in contact with the skin or incorporated into the body. Such sensors will enable long-term real-time monitoring of changes in molecule concentrations in body fluids, such as sweat or interstitial fluid, and can provide information about human health status and response to external stimuli, including environmental exposure. Chemical sensors are used because the detection of biomolecules is focused on preventing and diagnosing diseases. The skin has an important role in human body homeostasis; chemicals such as ions, gases, organic compounds, and pathogens can penetrate the skin and result in health problems. Hence, sensors monitoring chemical changes in the sweat of skin layers provide a reliable tool to identify malfunctions. Recently, the compound solid-state electrolyte modulator employing p-type ionic conductor Li3GdBr6 and n-type semiconductor Li3LuBr6 combined with unconventional Li2OazH2O with different Li2OabH2O compositions was developed to investigate their ionic conductivities. In addition to water and air humidity detection, the showings of a rapid and novel sensitive response for H2S even at room temperature using the same compound modulator are reported. [329, 330, 331, 332]

Real-Time Biomolecular Monitoring Devices

Concepts derived from optical techniques capable of real-time biomolecular detection have attained increased consideration during recent years. These advanced sensor devices facilitate the multiplexed, label-free, energyefficient marking-less quantification of molecular species by associating molecular recognition strategies with alternative transcending sensor platforms. The therefore conceived reporting units combine (bio)chemical recognition components such as antibodies, nucleic acid fragments or enzymes with (bio)chemical transducer systems based on surface-enhanced Raman scattering (SERS), fluorescence, resonant waveguide grating (RWG), potentio-metric and capacitive or conductive detection. The length scales of the integrated biosensing schemes correspond to those of the sample components, allowing their deployment in environmental health monitoring and/or pollution medicinal surveying applications in a highly sensitive and specific manner.

Molecular profiling of biological fluids is being developed as an additional forward-looking (bio)monitoring technology for smart, adaptive environmental health control, including saliva sensors, breathprints, exhaled-breath condensates and sweat biomarker imaging tools. In it, pollutant exposure is inferred from the levels of specified analytes in the selected, easily accessible bio-species. [333, 334, 333, 334, 335, 336]

Trends in Environmental Bio-Sensing Innovation

Novel diagnostic technologies and sensor devices hold excellent potential in environmental monitoring fields through the ongoing development of highly sensitive and selective analytical approaches. Two recent trends in environmental bio-sensing are illustrated: (1) application of programmable CRISPR-based biosensors for nucleic-acid detection of environmental pollutants using a fluorescence detection platform and (2) development of lab-on-a-chip sensing systems for the electrochemical detection of multiple substances.

Among these, CRISPR/Cas biosensors have attracted extensive attention owing to their high sensitivity for potential target detection, wide recognition range, and rapid one-pot detection. The CRISPR/Cas2-based biosensor comprises a Cas2 protein fused to the red fluorescent protein mCherry and contained in a sensor that does not require additional fluorescence signal tracers. The new fluorescence biosensor leverages the guiding strand of a CRISPR/Cas2 complex to recognize DNA implicated in an environmental risk event. When the target DNA and the guiding strand are present, Cas2 is activated and cleaves the target strand to release the guiding strand. The new biosensor was validated using plasmid DNA, amplified human DNA, and environmental pathogenic DNA from Streptococcus pneumoniae.

Advancement of miniaturization technology enables production of fully integrated lab-on-a-chip modules for the electrochemical detection of multiparameter chemical substances in the environment and bloodstream. A polydimethylsiloxane-based lab-acquisition chip with multi-channel electrochemical sensor devices is described, which combines carbon fiber microelectrode-array biosensors and temperature sensors. For environmental testing, the microchip has been used to test formaldehyde and chemical oxygen demand at different pH levels and concentrations in water samples.

Chapter - 18

Future Directions and Environmental Policy Integration

The ultimate aim of the present work is to contribute to the integration of diagnostic information into risk assessment and management approaches—especially, contaminant risk regulated at the international level by the European Union and other agencies comprising the World Health Organization and United Nations. The urgent need for such a direction is aptly summarised by the statement: "Environmental biomarkers, together with chemical analysis of exposure levels, will provide a powerful tool for the assessment of multiple exposure and health-risk characterization". Addressing this need requires the combination of laboratory, field, and modelling studies in order to collect sufficient data for enabling a major paradigm shift through the creation of predictive models linking exposure with adverse health outcome.

The information derived from biomonitoring studies serves not only to highlight human contamination and raised health concerns but also to guide and justify targeted enforcement monitoring. Ultimately, such data should support the establishment and implementation of an early-warning biomonitoring system capable of protecting populations from pollution incidents. Such a system will facilitate early warning of hazardous exposure not only for human health but also for ecosystems. Results from other multi-year and public-domain studies indicate that biomarker responses in wildlife, including humans, can be linked to specific categories of chemical exposures, thus paving the way for systematic incorporation of health and environmental-analyte relationships into early-warning systems. The link between diagnostics and environmental geopolicy must also consider the need for sound science underpinning the international community's sustainable development efforts, particularly in the sphere of green economy. [337, 338, 339, 340]

Integrating Diagnostics with Environmental Regulations

Successful risk assessment requires that experimental results be integrated into environmental legislation. Molecular and chemical sensors can provide the concentration of pollutants in environmental compartments (e.g. air, water, soil). Indeed, several countries have established water thresholds for a wide range of chemical substances. Nevertheless, establishing thresholds for effects remains a challenge owing to the large number of environmental stressors and their possible mixture effects. To be achieved, molecular and protein biomarkers may help to establish the link between exposure and effect, because they better reflect the biological responses to chemical insults than environmental concentrations. In combination, dose–response relationships can be developed even in the absence of direct exposure data, and landscaping information can be generated.

The ultimate translation of pollutant exposure into human or environmental health assessment relies on the integration of experimental data generated from health-agnostic (benchtop) facilities and laboratory models in exposome epidemiology. These—still speculative—approaches require a score function, which assigns risk according to individual (or population) sensitivity for diseases such as respiratory, cardiovascular, neurological, endocrine, and reproductive toxicity; impaired fertility; decreased intelligence; or cancer. The risk score, based on the integration of molecular data from biospecimens and human factors (e.g. smoking habits, sex, alcohol consumption, body mass index, and weight), predicts the correlation between human exposomics and health. [341, 342, 343]

Early Warning Systems for Ecosystem Protection

To protect human health and ecosystem integrity, and to prevent functional and structural ecosystem collapse, materials, products and services (from latter of mankind's two or three fundamental management operations) must be produced and supplied without harming the ecosystem's compartments and functioning. Regulatory frameworks need to establish legally binding precautionary policies, rapidly integrating data, methodologies and novel environment-friendly technologies for material design, use and disposal into territories. For critical and other relevant pollutants, prototypes and/or commercial multi-chemical sensors operating in real-time together with fast molecular detection systems should be operational, logging and interpreting data in shifts. Current pollution-detection capabilities of humans and laboratory animals must improve with fast environment-friendly nanotechnology sensor data interpretation and high-throughput data integration, modelling and application. Because natural environments are resilient, support life processes and thus are crucial to health, long-term ecological health impacts of pollution should remain underestimated compared to shorter-term and larger-scale exposures and effects considered for human health. For early detection/assessment, systems should integrate rapid set-up and regular change of polluted natural environments, with adapted sensor-coupled hazard and risk analysis modelling based solely on ecological health data.

Synthetic and natural toxins are accumulating faster than they can dissipate, and the resulting data hazard and risk analyses, the increased cost of cleaning polluted areas using conventional technologies requiring a large number of samples from one site or environmental surveys, and the intrinsic inefficiency of society's third management operation make the first one essential: stopping pollution at source or treating it more efficiently during management of the land. In these three operations, society has to detect or predict pollution for effective counteraction or mitigation. Sources of such early-warning systems should combine existing tools, combining the resistances of natural ecosystems and humans to pollution and exploiting the fact that natural environments are incomprehensively more complex than are current sensor predictive-capabilities. [344, 345, 346, 347]

Translating Biomarker Data to Policy Decisions

Translated expression of health risk indicators, and other population-level information gathered from molecular and protein markers towards relevant environmental policies is imperative. Pollution-reduction strategies can be more effective with the translational aspect in mind, considering health impact data and protecting the health of living organisms and the maintaining ecological balance as a priority. For instance, a cascade of pertinent actions must be directed to prevent pesticide, heavy metal, or organic pollutant exposure by living organisms or at least reduce the accumulation levels in tissues for whose that cannot be avoided, and this is persued via regulation of human and animal activities and natural agents in the ecosystems. Establishing risk indicators for pollution-related cancers and oncoviruses, miRNAs involved in endocrine systems, and respiratory and cardiac pathophysiology in children and adolescents, as well as data on the effects of toxin nexus in specified syndromes of daily clinical practice—such as polycytic ovary syndrome (PCOS) and male infertility syndrome—and on animal-welfare microbiomes, are extremely pertinent for photocasting the risk of environment-associated disease causation.

The identification of air-pollution-induced miRNA signature alterations and related predictive models addresses the relation between the environment and health at the molecular level, giving high importance to the molecular assessment of every locality on Earth. The monitoring of dangerous chemicals, using fungi or receptors, can lead to more sensitive risk analysis, while the possibility of fabricating organs for transplantation with diminished gene toxicity or membrane-modification agents constitutes a current trend in modern medicine approached from the angle of translational medicine. [348, 349, 350, 351]

The Role of Green Technologies in Pollution Reduction

A significant proportion of pollution comes from industrial processes, and consequently, the development of cleaner production technologies can significantly abate emission levels of pollutants. Green engineering principles have been proposed to enhance the pollution reduction potential of processes, and they can also guide the development of novel products. Such principles include minimizing the material and energy used, reducing harmful and toxic products, reducing consumption of biodiverse resources, ensuring the proper functioning of ecosystems, and enhancing the health, safety, and stability of communities. Researchers in the life-cycle analysis area of pollution control have emphasized the importance of developing alternatives for inherently hazardous substances, comprehensively evaluating the effects of inputs and outputs, identifying critical environmental components, and integrating environmental and economic decisions from regional to product levels.

Recent developments in atmospheric modeling can significantly aid in establishing air quality standards. For example, incorporating increased zeolite use in smog-chamber-based chemistry models has been found to reduce ozone and other secondary pollutant predictions during the summers of 1998–2001. The substantial increases in industrial land value, tourist activity, and external trade generated within the Beijing area as a consequence of atmospheric pollution control efforts have been found to exceed the costs of implementing these measures. Thus, to continue reaping the socio-economic benefits associated with air-safety management, it is important for the area to gradually adopt advanced green technologies and use global markets to obtain high-quality products.

Future Research Opportunities and Challenges

Environmental technologies have advanced rapidly, leading to the monitoring of contaminants in varied environmental compartments. Nevertheless, continual efforts are needed to achieve a sustainable future for livings on Earth through the integration of technologies and scientific results with environmental management authorities. Recent events in ecosystems and human health have accelerated the establishment of new biomarkers of pollutants and contaminants responsible for the pathways of adverse effects. Membrane bioreactor systems, the introduction of CRISPR technology, nanotechnology, new biosensing platforms, lab-on-a-chip systems, microfluidics, and wearable chemical sensors offer additional possibilities for testing pollution in the environment and for the deterioration of human and ecosystem health.

In recent decades, numerous molecular, genetic, and other DNA- and protein-based tools have been developed and successfully applied in environmental health studies. At the same time, smart sensors have been widely used alone or in sensor networks for real-time detection of surface air, soil, and water pollution. All technologies remain useful in monitoring pollution exposure of humans, animals, plants, and whole ecosystems in natural or constructed environments but require further basic and applied research. In addition to sensing the presence and concentrations of pollutants, attention must be paid to increasing the knowledge of the impact on biological systems, the unfolding exposure pathways, and the molecular–biochemical response in the exposed organisms or cells through the generation of early-warning smart systems using omics technologies. Recently, the artificial intelligence (AI) domain has advanced rapidly and now offers tools for analyzing different types of data generated using diverse technologies. These tools may also be successfully applied to multi-level pollutants in different compartments of the environment, including animal and plant systems.

Conclusion

Research on pollutant effects cannot rely on a single methodology, and a multi-method approach is, therefore, essential. Besides studies that follow only one line of inquiry, the integration of various methodologies, including both molecular and chemical sensors, is also important. The proof-of-concept studies summarized throughout this work illustrate how different molecular/protein diagnostic methods can be combined with chemical sensor technologies to obtain complementary datasets. Such integrations help to assess the effect of pollutants on human health and plant systems. The experimental data can be further combined in multi-omics studies to elucidate the functional impact of toxicant exposure, high-dimensionality approaches to obtain reliable estimates of *in vivo* effects, and predictive modeling. This research activity is essential for biomonitoring purposes, where sets of molecular and protein biomarkers can be detected in exposed individuals and correlated with pollutant exposure through environmental and biological samples.

The ultimate goal is to establish smart sensor networks for environmental quality assessment and early-warning systems to trigger mitigation actions as soon as pollution is detected by sensors and/or biomarker expression starts to deviate from normal levels. Pollutant biomarker expression patterns also need to be integrated with available medical databases to interrogate the risk of specific pathologies associated with the observed exposure. This integration can lead to risk estimations that support pollutant exposure and effect assessments. The European Union’s Health Programme and the European Union’s Horizon 2020 Research and Innovation Programme have funded some of this research.

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