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Nanosensors for Environmental Applications

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Nanosensors for Environmental Applications

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Preface

Nothing in the world is more exciting than a moment of sudden discovery or invention –
Bertrand Russell, 1950 Literature Prize, Nobel Lecture

Nanosensors are nanoscale miniature devices used for sensing of analyte in ultralow range. These have gained considerable interest in environmental applications such as environmental chemistry and functionalization approaches, environmental engineering, sustainability and green technology for sensing, environmental health monitoring and pesticide, metal and ion detection using electrochemical and wireless sensor.

This book provides a comprehensive overview of the most important types of nanosensor platforms explored and developed in the recent years for efficient detection of environmental/clinical analytes. The chapters cover basic aspects of functioning principles and describe the technologies and challenges of present and future pesticide, metal ions, toxic gases, analytical sensing approaches and environmental sensors.

In Chap. 1, Verma et al. discuss the many bacterial biosensors made by recombinant DNA technology which find their applications in the field of environmental sciences, phenolic compounds detection and biotechnology. In Chap. 2, Mehta et al. review the progress made in biofunctionalized nanostructured materials for sensing of pesticides, and various nanomaterials employed in biosensing of pesticides and the sensitivity and specificity improvement methods along with different means of pesticide remediation have been summarized. In Chap. 3, Materon et al. provide a general overview of the different emerging contaminants, i.e. pesticide, polluters and pharmaceutical products, their negative effects in the environment and the analytical methodologies currently available for their detection.

In Chap. 4, Joshi et al. highlight recent advances in two-dimensional transition metal dichalcogenide nanostructures for gas sensing. The chapter discusses the synthesis and fabrication of these materials and elaborates on their possible use in next-generation electronic and optoelectronic devices, especially gas sensors.

In Chap. 5, Sharma et al. discuss the detailed use of new-generation material carbon dots for the sensing of environmental pollutants, metal ions, anions, chemical

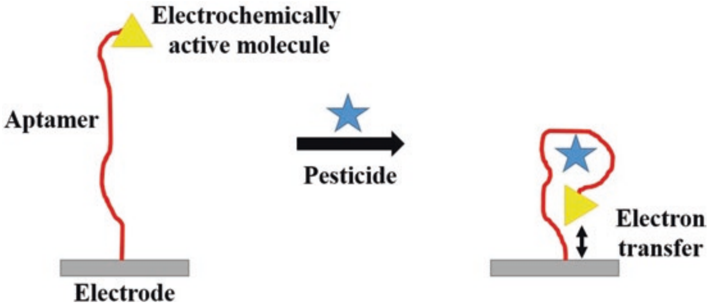

Fig. 1 Electrochemical sensing of pesticide with aptamer as probe. The binding of analyte to the aptamer induces a structural change leading to the change in the position of electrochemically active probe. This alters the electron transfer and is monitored by measuring the current (Chap. 6 by Kalyani et al.)

impurities, microorganisms and carbon dot-based device for running water systems. In Chap. 6, Kalyani et al. describe recent advances in the field of on-site pesticide detection and explain optical- and electrochemical-based biosensor mechanism for pesticide sensing (Fig. 1). In Chap. 7, Mohanta et al. represent the roles of disposable fluorescent point-of-care lateral flow sensor strips as a promising tool for low-cost and rapid sensing of analytes including pesticides.

Finally, in Chap. 8, Kaur et al. focus on understanding the role of sensory materials such as inorganic, organic as well as biomaterials and present wireless sensors using different electrochemical analysis techniques like cyclic voltammetry, linear sweep anodic stripping voltammetry, square wave anodic stripping voltammetry, etc. based on metal nanoparticles, quantum dots, graphene, carbon nanotubes, polymers, enzymes, etc.

We extend our sincere gratitude to all the authors who have put considerable efforts into their contributions and for their timely responses and consistent cooperation during the manuscript writing and revision process. We also extend our thanks to the Springer Nature team for accepting our book proposal and helping to bring it to publication.

We hope this book will be useful to all researchers, students, professors and scientists working in the domain of nanosensors for environmental applications. Finally, we acknowledge almightily God and family members who encourage us to take such venture and motivate us in the completion of this book.

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About the Editors

Satish Kumar Tuteja completed his PhD in Biosensor Engineering at Nanoscience and Nanotechnology Department of CSIR-CSIO, AcSIR, India, in 2016 and completed his Mitacs Elevate Canada Postdoctoral Fellowships at the BioNano Laboratory, University of Guelph, Canada. His PhD thesis was on the development of nanostructure-based ultrasensitive electrochemical, biomedical and environmental biosensors. His research interests are focused on biosensor and diagnostic lab on a chip sensor development, surface functionalization and biointerface development, antibody and aptamer engineering for sensing, diagnostics and nanodevice fabrication. Currently, he is working as Senior Scientist (Alexander Von Humboldt Fellow) at the Institute of Materials in Electrical Engineering 1 (IWE1), RWTH University, Aachen, Germany, and pursuing research on cancer diagnostics.

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Neeraj Dilbaghi completed his doctorate degree in Microbiology from CCS Haryana Agricultural University, Hisar, India, and is presently working as Professor in the Department of Bio and Nanotechnology, Guru Jambheshwar University of Science and Technology, Hisar, India. He is Director of UGC Human Resource Development Centre (HRDC) and Incharge Radio Ecology Centre, GJUS&T, Hisar. He has over 23 years of research and teaching experience. During his professional career, he has guided 11 PhD and over 40 MTech students. Presently, eight PhD students and one PDF are pursuing research under his guidance. His current research focuses on microbial biotechnology, bionanotechnology and nanosensors for healthcare and environmental applications, nanomedicine and drug delivery and toxicological evaluation of nanomaterials. He has published over 130 research papers in peer-reviewed international and national journals of repute and has completed three UGC major research projects, one project funded by BARC-BRNS and three projects funded by DST including the prestigious Indo-Thailand International Collaborative Research Project. Presently, he is handling four sponsored research projects funded by DBT, LSRB-DRDO, HSCS&T, BARC-BRNS, ADAMA-AGAN Ltd Israel, etc. to manage his research activities.

Eric Lichtfouse is Research Scientist at Aix-Marseille University and Invited Professor at Xi'an Jiaotong University. He has invented ^{13}C-dating following the discovery of temporal pools of molecular substances in environmental samples. His research interests include climate change, carbon, pollution and organic compounds in air, water, soils and sediments. He is teaching biogeochemistry and scientific writing. He is the Author of the book *Scientific Writing for Impact Factor Journals*, which include an innovative writing tool, the micro-article, and Chief Editor of the journal *Environmental Chemistry Letters* and the book series "Sustainable Agriculture Reviews" and "Environmental Chemistry for a Sustainable World".

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Chapter 1
Biosensor Applications in the Detection of Heavy Metals, Polychlorinated Biphenyls, Biological Oxygen Demand, Endocrine Disruptors, Hormones, Dioxin, and Phenolic and Organophosphorus Compounds

Varsha Rani and Madan L. Verma

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Abstract Environmental protection is a major issue which should be addressed for the betterment of humankind. The increased number of emerging pollutants from the industries as well as by man-made activities is a threat to the environment. Pesticides, insecticides, dyes, phenols, endocrine disrupters, polycyclic aromatic hydrocarbons, heavy metals and nitrogen compounds are the pollutants in our environment. Recently, farmers, food manufactures and companies are under pressure from the consumers and legislation for providing the essential entities such as food which is higher in quality, free from chemicals and pollutants and having higher nutritional value. A higher number of pollutants in water, soil as well as in food are posing potential hazard to human health. So, a more stringent legislation should be introduced for controlling the release of contaminants as well as for the monitoring of the resources.

Demand for fresh and natural foods which are free from pathogens, having lesser preservatives and additives as well as having higher nutritional value, has fuelled the demand for rapid sensing methods. Biosensors are the tools highly selective and sensitive for detecting the environmental pollutants as well as for monitoring different resources. There are several types of biosensors employed in the field of agriculture, environment and food and biomedical industries for detecting as well as removing the living or non-living contaminants. Detection of microbial invasions in the body as well as in the food, detection of levels of glucose in the body whether higher or lower, detection of heavy metals and insecticides/pesticides in the soil and water and detection of water- and airborne microorganisms can be easily as well as timely monitored via biosensors. In this chapter, we reviewed different issues related to the environment, food as well as human health and found that biosensors are playing a crucial role in monitoring the environment, food materials and human health.

Keywords Sensor · Nanosensor · Contaminant · Adulterant · Monitoring

1.1 Introduction

Sensor-based bioanalytical technology being a broader field is producing major impact on industries like food, healthcare, pharmaceutical and agriculture as well as for environmental monitoring (Verma 2017a; Verma et al. 2010). Biosensors have become an important tool for detecting the biological and chemical components of food and for clinical and environmental monitoring. This is because of the exceptional properties of the biosensors such as rapid response, higher specificity, higher stability, higher selectivity, user-friendly nature, lower cost and compact in size.

Biosensor is a chemical sensing device, combining a recognition entity which is biologically derived with that of a transducer, to develop some complex biochemical parameters quantitatively (Verma 2017b). Biosensor is a combination of two elements, out of which one is biological and another one acts as sensor. The bioelement may be an enzyme, antibody, tissue, living cell, organelle, nucleic acid, cell receptor or microorganism (Jain et al. 2010). The sensing element may be electric current, electric potential and so on. A specific analyte is recognized by a specific biological element, and the process of transduction is done by the sensor into an electric signal. The biological element of the biosensor is highly specific for its analyte to be analysed. Biosensors can be of various types depending on the transducing mechanism used. These can be thermal detection biosensors, resonant biosensors, ion-sensitive field effect transistor biosensors, electrochemical biosensors and optical detection biosensors. Blood glucose sensing is a major application of the biosensors because of its market value (Verma 2017a, b; Guilbault et al. 2004).

Nowadays biosensors are being developed for their use in various fields like environmental applications, quality control of food products, agriculture, bioprocess control and military and medical applications as shown in Fig. 1.1.

Most of the commercially available biosensors are being used in the clinical as well as in the pharmaceutical sector. While in food industry, biosensors are being used in the detection of contaminants in the food products, monitoring of raw material conversion, and product content verification as well as freshness of the product. Biosensors can also be used in the beer industry in the improvement and controlling

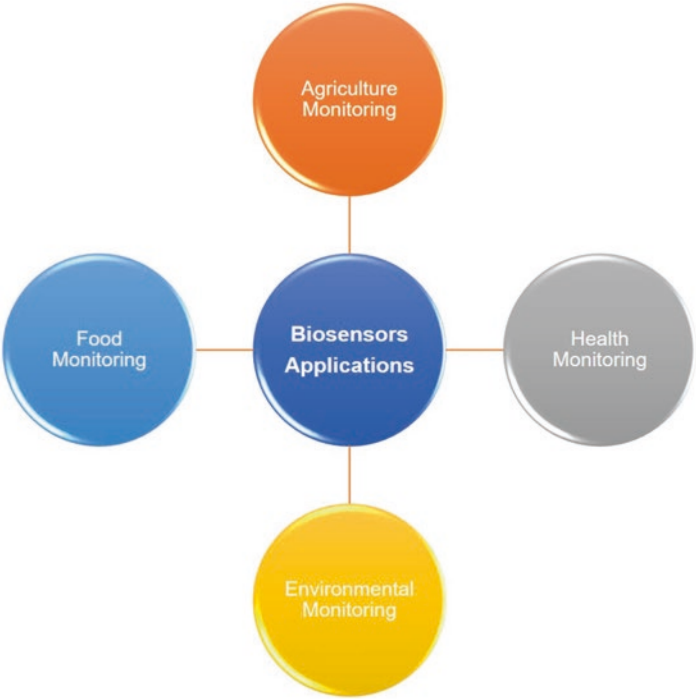

Fig. 1.1 Applications of biosensors in different fields. Biosensors can be used for the monitoring of various toxicants, pollutants and contaminants in various fields like the environment, health, food and agriculture

of the products. Hazardous materials can be detected via using biosensors, so biosensors can be very good defence tools. We can control and monitor the environmental hazards by getting the specified data of the contaminated site via using biosensors. Biosensors can also offer the advantage of measuring pollutants in complex matrices with minimal sample preparation. Biosensors are not only determining the specified chemical, but they can also determine the biological effects of chemicals such as toxicity level and endocrine-disrupting effects (Rodriguez-Mozaz et al. 2004a, b). Exceptional performance and capabilities of the biosensors such as higher specificity, higher sensitiveness, low cost, fast in response, compact in size and user-friendly nature make biosensors an important tool for detecting biological and chemical components as well as for clinical, food and environmental monitoring (Amine et al. 2006; Malhotra et al. 2017).

Biosensor captures the biological signal and then converts it into an electrical signal which can be detectable. Biological entities such as RNA, DNA and proteins are combined with transducers for detecting and observing the biological analytes like antigen-antibody interactions. Several types of biosensors like optical, amperometric, resonance, surface plasmon, phage, DNA, enzymatic and bacterial biosensors are being successfully utilized in the biomedical field, food industries and the environment for detecting and removing the contaminants, whether non-living or living. Detecting microbe invasion inside our body as well as food, glucose level in our body, heavy metals detection in water, soil and air borne microbes, various harmful chemicals produced by the body, pesticides in the water and soil can be easily and timely monitored via biosensors with higher precision and accuracy (Ali et al. 2017). This chapter discusses the biosensors and their applications in the different fields like environmental monitoring, detection of pollutants like heavy metals, phenolic compounds, nitrogen compounds, polychlorinated biphenyls, biological oxygen demand, endocrine disruptors and hormones, pesticides, insecticides, dioxins, organophosphorus compounds and nanotechnology interventions in biosensors.

1.2 Biosensor Applications in Environment Monitoring

Harmful pollutants are increasing day by day in the environment, so fast and cost-effective techniques are needed for the monitoring of these pollutants in the environment. Biosensors can be utilized as quality monitoring tools for the environment in assessing the biological and ecological quality as well as for the chemical monitoring of organic and inorganic priority pollutants. Biosensors are offering advantages over conventional analytical techniques, such as the possibility of portability, work on site, miniaturization and the ability of measuring pollutants in complex matrices with minimal sample (Rogers and Gerlach 1996; Rogers 2006; Sharpe 2003).

Rugged biosensors are needed for the environmental monitoring for detecting the toxic chemicals and pollutants. Electrochemical biosensors are developed via combing two fields of electrochemistry and biology. Biosensors are devices combining the selectivity of the biological molecules with that of the processing power of microelectronics, offering a new approach for monitoring environmental issues via in situ as well as online. Electrochemical biosensor is a combination of a biological recognition element which is immobilized on the surface of an electrode, and the second component is a physicochemical detector. The function of bioreceptor component is to translate the information obtained from the analyte into a chemical or physical output signal having sensitivity for the quantification of the analyte to be monitored, while the function of the transducer is to convert the recognition event into an output signal which is measurable. Some properties like concentration range, reusability, disposability, renewability, accuracy, reproducibility, size of the analyte sample as well as sensor size are very important for considering a biochemical sensor for environmental monitoring (Badihi Mossberg et al. 2007).

Sulphur dioxide (SO_2) is a colourless gas which is a contaminant in the atmosphere. Natural sources which produce sulphur dioxide are oceans, volcanoes, biological decay and forest fires. Fossil fuel combustion, manufacture of sulphuric acid, smelting, wood pulp industry oil and coal burning are the processes which are producing anthropogenic SO_2 pollutants. Acid rains are the main cause of corrosion of buildings and metal objects, and this acidity of the rain is due to SO_2. Higher concentrations of SO_2 are causing respiratory sickness, breathing problems and cardiovascular diseases (Tayanc 2000). Presence of SO_2 in the air is changing the systolic and diastolic blood pressure during the cold weather (Choi et al. 2007). Hart et al. (2002) developed an amperometric biosensor for measuring the SO_2 concentration in flowing gas streams. This amperometric biosensor is based on the enzyme sulphite oxidase having cytochrome c as the electron acceptor with a transducer which is screen-printed.

Herschkovitz et al. (2000) presented an electrochemical biosensor for formaldehyde which is a hazardous air pollutant. Formaldehyde is a compound present in the smoke from forest fires, in exhaust from automobiles and in tobacco smoke which is allergenic and toxic and accumulates in the air. The electrochemical biosensor developed for formaldehyde is based on a flow injection system using formaldehyde dehydrogenase and a redox polymer-poly(vinylpyridine) containing complexed (bpy) 2 OsCl groups and partially quaternized with bromoethylamine, abbreviated POs-EA, a screen-printed electrode.

A bacterial biosensor has been developed for detecting tributyltin using a bioluminescent recombinant *E. coli::luxAB* strain (*E31*). *A. eutrophus* was engineered genetically by inserting a luxCDABE operon from *V. fischeri*. Immobilization of the genetically engineered bioluminescent bacterium (lac::luxCDABE) was done for the development of a whole cell biosensor for detecting toxic gases (Woltbeis 2004). There are some biosensors which are used for the determination of the pollutants in the real samples as shown in Table 1.1.

The most important aspect to deal with the threat of pollutants and contaminants is to monitor the environmental changes. Electrochemical aptamer-based sensors have been reported to be used for the monitoring of food and environmental contamination. Aptamers act as a bio-recognition element, while developing sensor and aptasensors are chemically unchangeable, small in size and inexpensive. Aptamers

Table 1.1 Biosensors for the determination of pollutants in the real samples

Analyte	Matrix	Transducing and recognition element	References
Phenols	Wastewater	Electrochemical and enzymatic	Nistor et al. (2002a, b)
Pesticides and oestrone	River water	Optical and immunochemical	Mallat et al. (1999, 2001) and Rodriguez-Mozaz et al. (2004a, b)
Biological oxygen demand	River water	Optical and pseudomonas	Chee et al. (2000)
Linear alkylbenzene sulphonate	River water	Electrochemical and bacteria	Nomura et al. (1998)
Toxicity	Wastewater	Electrochemical and bacteria	Farre et al. (2001)
Toxicity	Wastewater	Optical and bacteria	Philip et al. (2003)
Oestrogens and xenoestrogens	Lake and sewage water plant samples	Optical and human oestrogen receptor	
Alkanes	Groundwater	Optical and bacteria	Sticher et al. (1997)
Chlamydia trachomatis (DNA)	River water	Electrochemical and DNA	Marraza et al. (1999)
Daunomycin polychlorinated biphenyls, aflatoxin	River water	Electrochemical and DNA	Marraza et al. (1999)

The spectacular applications of different types of biosensors are increased multifold in the determination of pollutants in real samples such as phenols, biological oxygen demand, alkanes, oestrogens, microbial contaminants, pesticides in real samples, etc

showed tremendous selectivity and sensitivity because of their extraordinary properties like expediency in the design and having very good elasticity. Thus, aptamers can be efficiently used as safeguards of the food and our environment (Mishra et al. 2018).

Contaminants from the pharmaceutical industry are inducing adverse effects on our health, and these contaminants became worrisome because their concentration is increasing day by day in surface waters. Besides increasing concentration of pollutants in our environment, we are scarce in having the data about their actual concentrations. Thus, there is a need to regulate as well as to monitor the resources. Therefore, use of enzyme-based and miniaturized biosensors is a promising way to tackle the issues related to environmental monitoring (Campana et al. 2019). Environmental monitoring is a key for the management of pollution. Electronic noses which are formed by a sensor array are the most promising approach for monitoring the pollutants in the atmosphere. Electronic noses play two important roles of monitoring the odour and pollution in the environment. Tin oxide nanofibres are reported to be used in electronic noses. Nanofibres are found to show higher sensitivity towards the major pollutant NO_2 at lower temperature. Thus, nanofibres can be used for the monitoring of NO_2 in the atmosphere (Sayago et al. 2019).

1.2.1 Application of Biosensors in Detecting Heavy Metals

Currently heavy metals are causing very serious pollution problems. Heavy metals even in small concentrations are a threat to the environment as well as the human health because of their non-biodegradable nature (Verma and Singh 2005; Sharpe 2003). Heavy metals are a threat to the environment because they are ubiquitously present in the elements of the biosphere, highly toxic, and available among natural as well as anthropogenic sources.

Exposure of heavy metals is causing severe damage to our health including a significant amount of deaths. Most common metal contaminants in the environment are lead, zinc, mercury, chromium, cadmium and copper (Barrocas et al. 2008; Babai et al. 2000). Sensors based on nano-detection technology like optical sensors and electrochemical sensors and devices are the instruments for tracing the range of heavy metals (Ion et al. 2010). Bacterial biosensors developed for analysing the heavy metals in the environment use specific bacterial resistant genes. Bacterial strains which are resistant to a number of metals such as zinc, tin, copper, silver, cobalt and mercury have been isolated as possible biological receptors (Ramanathan et al. 1997; Rathnayake et al. 2009). An optical biosensor was developed by Durrieu and Tran-Minh (2002) for the detection of heavy metals lead and cadmium. This optical biosensor was developed by inhibiting the enzyme alkaline phosphatase which is present on the external surface of a microalgae named, *Chlorella vulgaris*. Alpat et al. (2007) developed a biosensor for measuring Cu^{2+} volumetrically from microalgae *Tetraselmis chuii*. There are some more examples of biosensors developed for heavy metal determination as listed in Table 1.2.

Application of a chemometric tool for optimizing the performance of electrochemical biosensor has been reported by De Benedetto et al. (2019). Experimental design was made on the basis of the amperometric biosensor performance or response which has been developed for detecting metal ions. The prepared model was validated and successfully employed for the detection of Al^{3+}, Bi^{3+}, Ni^{2+} and Ag^{+} ions. Because of the stability and reversibility of the made biosensor, it can be efficiently used as amperometric detector in the ion chromatographic system for overcoming the lack of selectivity (De Benedetto et al. 2019).

1.2.2 Application of Biosensors in Detecting Biochemistry Oxygen Demand

Parameter which indicates the amount of biodegradable organic material in water is called as biological oxygen demand. Determination of biological oxygen demand is a time-consuming process and also not suitable for online process monitoring. Biosensor-based methods can be used for the fast determination of biological oxygen demand (Rodriguez-Mozaz et al. 2004a, b).

Table 1.2 Examples of biosensors developed for heavy metal determination

Analyte	Recognition biocomponent	Transduction system	Matrix	References
Zinc, copper, cadmium and nickel	*Pseudomonas fluorescens* 10,586 s pUCD607 with the *lux* insertion on a plasmid	Optical (luminometer)	Soil	Mcgrath et al. (1999)
Cadmium	DNA	Electrochemical	Standard solutions	Wong et al. (2007)
Cadmium	Phytochelatins	Optical (localized surface plasmon resonance)	Standard solutions	Lin and Chung (2009)
Mercury, cadmium and arsenic	Urease enzyme	Electrochemical	Standard solutions	Pal et al. (2009)
Zinc, copper, cadmium, nickel, lead, iron and aluminium	*Chlorella vulgaris* strain CCAP 211/12	Electrochemical	Urban waters	Claude et al. (2007)
Cadmium, copper and lead	Sol-gel-immobilized urease	Electrochemical	Synthetic effluents	Ilangovan et al. (2006)
Mercury (II) and lead (II) ions	DNA	Optical	Water	Knecht and Sethi (2009)
Cadmium, copper and lead	Sol-gel-immobilized urease	Electrochemical	Synthetic effluents	
Copper (I) and (II) ions	Red fluorescent protein	Optical	Standard solutions	Sumner et al. (2006)
Cadmium	*Escherichia coli* RBE23–17	Electrochemical	Wastewater	Biran et al. (2000)

Heavy metal detection using different types of biosensors has been employed to determine the quality of a used/unused land

The most common commercial biosensors for the environmental monitoring are biological oxygen demand biosensors. First commercial biological oxygen demand sensor was developed in 1983 by a Japanese company, “Nisshin Electric”, and a number of other commercial biological oxygen demand biosensors are being marketed by Autoteam GmbH, Medingen GmbH and Dr. Lange GmbH in Germany; Kelma (Belgium); and Bioscience, Inc. and US Filter (USA), which are based on microbial cells (Rodriguez-Mozaz et al. 2004a, b, 2005; D’Souza 2001). *Pseudomonas putida*, a bacterium, was isolated from river water and further used for developing biological oxygen demand sensor by Chee et al. (1999). *Pseudomonas putida* was found to degrade the refractory organic compounds such as humic acid and lignin. Nakamura and Karube (2003) had developed a biological oxygen demand measuring system from the cells of recombinant *Escherichia coli* with *Vibrio fischeri* genes lux AE. This system was useful for the real-time analysis of multiple samples. This system was primarily used in the food and pharmaceutical industries. Moreover, an optical biosensor developed by Kwok et al. (2005) is reported to test the biochemical oxygen demand of multiple samples. Dissolved oxygen concentration was monitored by this biosensor in the artificial wastewater via an oxygen-sensing film which was immobilized on the bottom of glass sample vials. Microbial samples were then immobilized on this film, and the biological oxygen demand value was determined from the microorganism's oxygen consumption rate in the first 20 min.

A respirographic biosensor is reported to monitor the waste load and the potential toxicity of the wastewater, both offline in a laboratory or online at the wastewater treatment plant. Based on a reference activity test, toxicity assessment was performed which allowed clear separation of toxic effect from the load variations. The response time for the detection of toxicity was 2 h, but toxicity detection was done readily in case of severe intoxications (Vanrolleghem et al. 1994).

The biological oxygen demand is among the most widely used criteria for the assessment of the water quality and provides information regarding the organic load which is biodegradable in water (Jouanneau et al. 2014). Biological oxygen demand is the most integral characteristic of the quality of water. Biological oxygen demand is the amount of dissolved oxygen which is needed for oxidizing the biodegradable organic matter present in the water. Biological oxygen demand values of surface water layers are generally in the range of 0.5–4 mg/dm^3, and these values vary among different seasons. Pollution in the aquatic bodies has been considerably affecting the biological oxygen demand values. So, there is a need to continuously monitor the biological oxygen demand in the water bodies which can be achieved via biosensors. Biosensor-based biological oxygen demand determination is an advanced step in analytical biotechnology (Ponomareva et al. 2011). A biochemical oxygen demand (BOD) sensor has been reported by Kara et al. (2008). It is based on an immobilized *Pseudomonas syringae* in a microcellular polymer which is highly porous with an electrode having dissolved oxygen. Microcellular polymer disk having *Pseudomonas syringae* offered higher stability as well as longer lifetime to this biochemical oxygen demand sensor.

1.2.3 Application of Biosensors in the Detection of Nitrogen Compounds

Nitrites are widely used for the soil fertilization as well as for preserving the food components. But continuous consumption of nitrites is causing serious implications on the human health, because nitrites react irreversibly with that of the haemoglobin present in the red blood cells (Moorcroft et al. 2001). Aquatic life is also being affected by the increasing levels of nitrates in the groundwater as well as in the surface water.

Chen et al. (2007) developed a biosensor using cytochrome c nitrite reductase from *Desulfovibrio desulfuricans* for amperometric determination of the nitrites. It was achieved by entrapment of redox active hydroxide along with anthraquinone-2-sulfonate (AQS). Khadro et al. (2008) was reported to develop an enzymatic conductimetric biosensor for determining the nitrates in water, validated and used for natural water samples. This biosensor was based on a methyl viologen mediator which is being mixed with nitrate reductase of *Aspergillus niger* and Nafion® cation-exchange polymer. Biosensor was found stable for 2 months and showed good activity when it was stored in the phosphate buffer having pH 7.5 at 4 °C temperature.

Detection of purine metabolites and DNA degradation was reported by using an electrochemical biosensor. This electrochemical biosensor uses a hybrid nanocomposite having an ionic liquid, namely, 1-butyl-3-methylimidazolium hexafluorophosphate, graphene oxide and gold nanoparticles which are stabilized by using chitosan. The developed electrochemical biosensor exhibited the electrochemical activity towards the electro-oxidation of the purine antimetabolites. Besides this, the sensor can also be used to check the double-stranded DNA damage as well as its interaction with that of the anticancer drug 6-mercaptopurine in phosphate buffer solutions at pH 7.4 (Shpign and Andryukhina 2019).

1.2.4 Application of Biosensors in the Detection of Polychlorinated Biphenyls

Polychlorinated biphenyls are ubiquitously present toxic organic compounds and are environmental pollutants (Centi et al. 2006; Pribyl et al. 2006). Polychlorinated biphenyls are highly lipophilic and got accumulated in our food chain, so food is the major source of polychlorinated biphenyl exposure (Gavlasova et al. 2008; Centi et al. 2006). There are about 209 polychlorinated biphenyl congeners which are present worldwide in our environment as well as our food chain. Based on the chlorine moieties orientation, these congeners are divided into three groups, namely, coplanar, mono-*ortho* coplanar and non-coplanar (Centi et al. 2006). Polychlorinated biphenyl analysis is generally based on the gas chromatography coupled with that of the mass spectrometry (Centi et al. 2006; Gavlasova et al. 2008). Immunoassays are another alternative technique to monitor the polychlorinated biphenyls in lab and field. Enzyme-linked immunosorbent assay is the most popular among several immunoassays techniques for the analysis of polychlorinated biphenyls. Biosensors, namely, immunosensors, are highly useful for the detection of the polychlorinated biphenyls which use antigens or antibodies as biological recognition element (Gavlasova et al. 2008).

Polychlorinated biphenyl determination can be performed via a novel piezoelectric immunosensor developed by Pribyl et al. (2006). Polychlorinated biphenyls can be determined directly from the extracts via this piezoelectric immunosensor without any additional purification steps. Gavlasova et al. (2008) had successfully constructed sensors of lower cost for monitoring the environment using real soil. A genetically engineered rhizosphere bacterium, namely, *Pseudomonas fluorescens* F113Rifpcb, is found to have the potential to degrade the polychlorinated biphenyls. It has been reported that F113Rifpcbgfp and F113 L::1180gfp are the biosensor strains which are capable of detecting polychlorinated biphenyl biodegradation as well as the bioavailability by Power B et al. (2011). Alginate beads have been found as effective delivery and storage system for polychlorinated biphenyl biosensors and polychlorinated biphenyls degrading inocula. The alginate bead delivery system was found to facilitate the application of *Pseudomonas fluorescens* F113Rifpcb and the F113 strains as biosensors (Power et al. 2011).

1.2.5 Application of Biosensors in the Detection of Phenolic Compounds

There are considerable amounts of organic pollutants having phenolic structures which are widely distributed in the environment. Phenolic compounds are very well-known for their toxicity and are very common among industrial effluents, plastic production, polymers, antioxidants, dyes, drugs, pesticides, resins, detergents, disinfectants and paper and pulp industries and from the oil refineries (Luong et al. 2008). Nitrophenols and chlorophenols are very toxic to humans as well as to the aquatic world. Degradation of organophosphorus pesticides and chlorinated phenoxy acids produces nitro- and chlorophenols (Su-Hsia and Ruey-Shin 2009). Phenolic compounds produce toxicity in animals as well as in plants via easily penetrating the skin in animals and cell membranes of the plants. Thus, it affected various processes such as biocatalyzed reactions, respiration, photosynthesis, genotoxic effects, hepatotoxicity and mutagenicity (Rodriguez-Mozaz et al. 2006). European Commission and the US Environmental Protection Agency put phenols and their derivatives under the list of hazardous pollutants because of their high toxicity and persistence in the environment.

A biosensing system has been recently realized for detecting the BPA and catechol using tyrosinase enzyme from *Agaricus bisporus* and laccase enzyme from *Trametes versicolor* (Scognamiglio et al. 2012). The catechol (10 μM) and bisphenol A (50 μM) can be detected via this study conducted by the European Commission (1999). Several electrochemical biosensors have been used with improved stability as well as sensitivity of the sensing element via immobilizing the enzymes of various kinds of surface materials like quantum-dot/chitosan composites electrode (Han et al. 2015), graphene oxide electrodes (Reza et al. 2015), magnetic nickel nanoparticles (Alkasir et al. 2010) and boron-doped diamond electrodes (Lv et al. 2010). Reproductive system of aquatic animals has been continuously affected by various oestrogens from the last decade. A BIAcore chip immunosensor has been developed by synthesizing the mono- as well as polyclonal antibodies, and these BIAcore chip immunosensors were found to be fast in their response for the preliminary screening (Samsonova et al. 2004).

Paper biosensor was reported for detecting the phenol from the effluent of paper, wine and plastic industries. This paper biosensor uses Tyr-AuNps (tyrosine and gold nanoparticles) bioconjugate which is produced by a novel isolate *Streptomyces tuirus* DBZ39, and this bioconjugate is found efficient for the detection of phenol because of its biocompatibility. Substrate specificity of tyrosinase enzyme and the unique surface plasmon resonance attribute of the gold nanoparticles are found to be responsible for the efficient detection of the phenol from the effluent of plastic, paper as well as wine industries within 3 min. Tyrosine and gold particle bioconjugate accurately quantifies different types of constituents like dopamine from paper, catechol from plastic and phenol from the wine effluents. Tyrosinase efficiency for the detection of phenol and its constituents was found to be enhanced via using gold nanoparticles because of the optical, magnetic and electron properties (Mazhari et al. 2017). A polyphenol oxidase biosensor has been reported for the detection of phenolic compounds from the textile industry effluent. This polyphenol oxidase biosensor has been developed from jenipapo (*Genipa americana* L.) fruit and was found as a promising tool for phenolic compound quantification and detection (Antunes et al. 2018a).

Plant kingdom is a wide source of enzymes having various biotechnological applications. Enzymes from plants, like polyphenol oxidases, can be used for the development of the biosensors because these enzymes can convert phenolic compounds into quinones. Carbon paste biosensor has been developed using the extract of jurubeba (*Solanum paniculatum* L.) fruits for pharmaceutical applications and analysis (Antunes et al. 2018b).

1.2.6 Application of Biosensors in the Detection of Endocrine Disruptors and Hormones

The endocrine system is made up of glands which secrete hormones for controlling our body’s development, growth, maturation and regulation via binding with the receptors. There are some compounds which can mimic a hormone, and these compounds are called as endocrine-disrupting chemicals. Endocrine-disrupting chemicals enter the hormone receptor and block the normal passage for entering the hormones. Oestrogen is a hormone produced during the process of maturation of female reproductive system by ovaries. Xenoestrogens are endocrine-disrupting chemicals which bind the receptor of oestrogen hormone and mimic its activity. Granek and Rishpon (2002) developed a novel impedance biosensor for monitoring endocrine disruptors which is based on a native oestrogen receptor adsorbed to a synthetic lipid bilayer attached to gold electrodes. During the last few years, endocrine disruptors are altering the normal homoeostasis of the endocrine hormones (Moraes et al. 2008). These endocrine disruptors present in the environment are increasing the incidences of thyroid, testicular and breast cancer. Synthetic as well as natural hormones found in the environment are the result of animal and human excretion and also due to intensive farming. Fully automated immunosensor determined progesterone, testosterone and oestrone along with other organic pollutants (Waring and Harris 2005). Xu et al. (2005) developed an electrochemical biosensor for detecting progesterone in the cow’s milk.

An electrochemical biosensor for progesterone in cow’s milk was developed and used in a competitive immunoassay by Xu et al. (2005). Antiprogesterone monoclo-

Table 1.3 List of endocrine disruptors relative to sensing/biosensing analytical detection methodologies

Endocrine-disrupting chemicals	Analytical methods	References
Paraoxon, aldicarb, carbaryl	Amperometric biosensor based on acetylcholinesterase and butyrylcholinesterase	Arduini et al. (2006)
Chlorpyrifos	Optical biosensor based on acetylcholinesterase	Scognamiglio et al. (2012)
Paraoxon	Cyclic voltammetry and UV-visible methods on the multienzyme carbon nanotube biosensor – polyethylenimine	Zhang et al. (2015)
Atrazine	Optical biosensor based on Photo system II	Giardi et al. (2009)
Diuron, linuron, atrazine, terbuthylazine	Optical biosensor based on Photo system II	Scognamiglio et al. (2009)
Catechol, bisphenol A	Electro-optical biosensor based on tyrosinase and laccase	Scognamiglio et al. (2012)
Oestrone	Surface plasmon resonance assay based on human recombinant oestrogen receptor α	Usami et al. (2002)
Estradiol, estriol, tamoxifen, diethylstilbestrol, BPA, human growth hormone	Surface plasmon resonance immunobiosensor	Kausaite-Minkstimiene et al. (2009)
Diethylstilbestrol	Electrochemical immunosensor based on mesoporous silica-gold nanoparticles-multiwall carbon nanotubes and horseradish peroxidase-antibody-Prussian blue-multiwall carbon nanotubes	Nxusani et al. (2012)
Thiolated-c	Oestrogen receptor-α assembled on the au nanoparticle surface	Senyurt et al. (2015)
Dibutyl phthalate (DBP)	Electrochemical sensor based on biomimetic layers	Noh et al. (2015)

Biosensors has improved multifold detection limit of endocrine disrupting receptors

nal antibody (mAb) was deposited onto the screen-printed carbon electrodes coated with that of the rabbit anti-sheep IgG (rIgG). There is a list of endocrine disruptors and their analytical methods via biosensors shown in Table 1.3.

A Rapid Adaptable Portable In vitro Detection (RAPID) biosensor platform was developed by Salehi et al. (2018) for the detection of chemicals which interact with the human oestrogen receptor β (hERβ). An allosteric fusion protein is present in this RAPID biosensor which can be expressed by using a technology based on cell-free protein synthesis. Cell-free protein synthesis reactions with RNAse inhibitors were also synthesized for enhancing the production yields in the presence of human urine and blood (Salehi et al. 2018)

Intensive farming and growing population increased the risk of harmful synthetic compounds, namely, xenohormones. The European Council has prohibited the use of such substances which are having hormonal or thyrostatic action for animal farming (Muller et al. 2008). Several electrochemical biosensors have been developed analysing hormones which exploited the specific binding ability of natural oestrogen receptors with that of xenohormones (Bahadir and Sezginturk 2015). Surface plasmon resonance-based biosensor has been developed by (Usami et al.) for endocrine receptors' binding capacity without using the fluorescence- and radiolabelled compounds. An electrochemical biosensor was developed by Habauzit et al. (2014) for the detection of 17 β estradiol. This electrochemical biosensor interacts irreversibly with 17 β estradiol based on a receptor molecule which can be an antibody, an aptamer or an oestrogen receptor. This biosensor uses electrochemical impedance spectroscopy and thus achieved the detection limits of picomolar concentrations (Habauzit et al. 2014).

1.2.7 Application of the Biosensors in the Detection of Organophosphorus Compounds

Compounds which are widely used for controlling the pests, weeds in the fields and disease-transmitting vectors in agriculture are termed as organophosphorus compounds. These compounds are being used in huge amounts to enhance the agricultural yield, and the excess amount used is getting into the soil, air as well as in the water, thus contaminating these sources. Organophosphorus compound detection and identification in the sources like air, water and soil is an extremely difficult task (Simonian et al. 2004). Enzymes like organophosphorus acid anhydrolase are being utilized for detecting the organophosphorus compounds. Novel organophosphorus acid anhydrolase was isolated from a halophilic bacterium, *Alteromonas* (Frank and Cheng 1991; Franik et al. 1993). However, organophosphorus acid anhydrolase (OPAA) has been unambiguously identified as a prolidase (E. C. 3.4.13.9) which is capable of hydrolysing the dipeptides with a prolyl residue in the carboxyl terminal position (Cheng et al. 1999).

Solution phase printing of electrodes which are graphene-based is an emerging technique nowadays for creating cost-effective, in-field electrochemical biosensors. Rapid and direct monitoring of organophosphates has been reported by a graphene-based electrode which was developed via using inkjet maskless lithography. Organophosphates are the compounds found in the pesticides as well as in the chemical warfare agents and are highly toxic, polluting water resources and soil in the long term. The biosensor developed via inkjet maskless lithography measures insecticide paraoxon within the response time of 5 s at a detection limit of 3 nM which is quite low. So, this biosensor has been found to be highly sensitive and stable and showed higher longevity (retained 70% of sensitivity after 8 weeks), and with the ability of selectively sensing the organophosphates in the water as well as in soil samples (Hondred et al. 2018). An indium tin oxide-based electrode has been developed for the detection of organophosphorus pesticides. Indium tin oxide-based biosensor was found to detect methyl parathion, chlorpyrifos and fenthion within the concentration ranging from 0.01 to 0.16 μM (Tunesi et al. 2018).

1.2.8 Application of Biosensors in Pesticide Detection

Pesticides have insecticidal properties due to which they are of great use in the agriculture (Mulchandani et al. 2001; Moris et al. 1995). But these pesticides are affecting the environment as well as the human health because of the presence of toxic compounds in them. The toxic compounds present in the pesticides got accumulated in the soil, vegetables, grains and fruits and eventually contaminating the water (Aspelin 1994). These toxic compounds are getting accumulated, and their concentration is increasing in different sources and the environment day by day. Organophosphorus compounds are affecting adversely our health and causing many serious health problems. Organophosphates are not only affecting human health but are very toxic for the bees as well as for the wildlife (Mulchandani et al. 2001). Huge growth in the population leads to limited resources, which exerted an adverse pressure on the agriculture sector, and in order to fulfil the demands of the growing population, use of pesticides for higher yield has been increased via manyfolds. The organophosphorus compounds in the pesticides interfere with the normal functioning of enzyme acetylcholinesterase, which leads to failure of the central nervous system. It is very important to continuously monitor the concentration of these compounds in the environment as well as among the different resources. Acetylcholinesterase-based enzymatic biosensors have been reported for the analysis of these toxic organophosphorus compounds so that the toxicity level can be controlled (Dhull et al. 2013). Environmental Protection Agency has defined pesticide as a substance or a mixture of substances which intend to prevent, repel or destroy pests or used for lessening the effect of a pest (Tothill 2001). Sensors based on enzymes are the most preferred biosensors for the determination of organophosphates (Cock et al. 2009). Parathion (*O,O*-diethyl-*O*-4-nitrophenyl thiophosphate) is a pesticide having broad spectrum in its applications against different insects on different crops. Parathion is used for a wide variety of plants as well as in the greenhouses as a preharvest soil fumigant and for foliage treatment (Patel 2002). Parathion is an organophosphate which is highly toxic either ingested or absorbed by the skin or via inhalation. Parathione entered in our body by all these means leads to human fatalities. Parathion is also inhibiting the function of acetylcholinesterase enzyme like other pesticides (Patel 2002).

The most implemented methods for determining different classes of pesticides are the electrochemical biosensors which are based on inhibition of acetylcholinesterase enzyme (Arduini et al. 2006; Scognamiglio et al. 2009; Rejeb et al. 2009; Compagnone et al. 2010). These electrochemical biosensors which are based on inhibition of acetylcholinesterase enzyme work on a principle which involves the measurement of enzymatic activities before as well as after the exposure of the pollutant. The decrease in enzymatic activity attributes the presence of carbamates and organophosphorus pesticides in the sample. Numerous amperometric biosensors have been developed for the determination of I50 values of different pesticides like paraoxon, carbaryl, aldicarb and chlorpyrifos-methyl oxon (Scognamiglio et al. 2012; Arduini et al. 2010). Zhang et al. (2015) have developed a bi-enzyme biosensor which can discriminate between organophosphorus and non-organophosphorus pesticides among the other compounds. The system of this bi-enzyme biosensor incorporates multi-walled carbon nanotube-organophosphate hydrolase and multi-walled carbon nanotube-acetylcholinesterase with a set of supporting bilayers consisting of multi-walled carbon nanotube-polyethylenimine and multi-walled carbon nanotube-DNA on an electrode made up of glass (Zhang et al. 2015). Hydrazones as mimetic molecules like cyclopropyl methyl ketone hydrazone, 4-[(1E) ethanehydrozanoyl] benzoic acid, hydrazine and 3-methyl-2-butanone hydrazone have been synthesized and characterized by Sgobbi et al. (Sgobbi et al. 2013). These hydrazones exhibited the same catalytic properties as that of the acetylcholinesterase and also has lower synthetic cost as compared to the acetylcholinesterase, which is providing a cost-effective route for the construction of commercial devices which can be disposed of. A novel amperometric biosensor has been developed for the determination of paraoxon, and this biosensor has been reported to determine the paraoxon at ppb level via using cost-effective and automatable bioanalytical approach which is found suitable for *in-field* analysis (Arduini et al. 2015). Cantilever nanobiosensors have been reported via Muenchen et al. (2016) for the detection of various pesticides. These cantilever nanobiosensors have been derived from the technique, namely, atomic force microscopy, and have been proved highly specific in their action as well as highly sensitive.

Cholinesterase inhibitors are the toxic compounds which are being used in the agriculture as pesticides. One biosensor developed in Czech Republic named Detehit, used for the detection of cholinesterase inhibitors, has been reported by Matejovský and Pitschmann (2018).

1.2.9 Application of Biosensors in Herbicide Detection

Herbicides like phenylureas and triazines are found to inhibit the process of photosynthesis in plants. These herbicides can be detected via biosensors designed with the membrane receptors of chloroplasts, thylakoids, reaction centres and photo systems which are employed by amperometric and optical transductors (Velasco-García and Mottram 2003). An immunosensor has been developed for the determination of an herbicide, namely, simazine, and this immune sensor is based on an ion-selective field effect transistor (Starodub et al. 2000).

A direct competitive ELISA method (dcTELISA) based on thermistor enzyme has been established by Qie et al. (2013) for fast detection of an herbicide named atrazine. This biosensor was found responsive, reproducible and stable even after using continuously for 4 months. This fast detection method, direct competitive ELISA, can be used for the detection of pesticide residues inside the large-scale samples. High-quality chemicals as well as renewable biofuel feedstocks can be produced by microalgae (Kim et al. 2018). Detection of pollutants like herbicides and heavy metals can be done by microalgae which inhabit the marine as well as the fresh water offering a versatile solution for constructing novel biosensors. These photosynthetic microbes are highly sensitive towards the environmental changes, enabling the detection of pollutant traces. Microalgae which are helpful for detecting the pollutants belong to diatoms and cyanobacteria groups. Algae respond towards the changes in photosynthetic activity which is due to the presence of herbicides in the water even in lower concentrations (El-Jay 1996). Bacterial biosensors when introduced with the genes responsible for bioluminescence resulted in increased sensitivity when compared with an equivalent system (Vismara and Garavaglia 1997; Kahru et al. 1996).

Electrochemical immunosensors act as analytical tools for monitoring large number of chemical substances. Antibodies can be produced against toxic substances like herbicides and mycotoxins as well as antibodies like proteins, and other molecules can be produced against the nontoxic substances, as long as they are foreign to the immunizing species. Highly specific and sensitive immunosensors can be developed via antibodies because of the higher affinity of the antibodies towards their targets. Electrochemical enzymatic biosensors which are based on peroxidases from plants can also be employed for the determination of the toxic substances like insecticides and mycotoxins. Construction of these biosensors is easy and quick as well as they are cost-efficient. Chemically reduced graphene oxide used while preparing the modified electrodes is an interesting latest option for the development of the third-generation biosensors which avoided the use of redox mediators (Fernández et al. 2017).

1.2.10 Application of Biosensors in the Detection of Dioxins

Dioxins are toxic substances affecting our environment adversely and contaminating our food chain, water and soil as well. Dioxins are toxic, teratogenic, organosoluble and carcinogenic. These are the by-products of various industrial processes, and dioxins can be transported over the long distances mostly via air and also by rivers and sea streams. Dioxins have been widely distributed all over the globe by means of air and water. They are found in such large extent in the environment that if its production will be completely stopped, even then it will take years to diminish the amount of dioxins present in the environment (Yuladev et al. 2001). For the proper monitoring of dioxins, biosensors can be extremely helpful.

Dioxins and compounds like dioxins are persistent pollutants which are mainly found in the animal fatty tissues and food materials (Chobtang et al. 2011). Immunosensors have been constructed by Centi et al. (2007) for the detection of PCBs in the milk samples. Graphite screen-printed low-density arrays and magnetic beads were combined to a solid-phase extraction of the sample, and by doing so, simultaneous measurement of differently processed samples was possible.

Immunosensors have been reported for the detection of 2,3,7,8-tetrachlorodibenzo-p-dioxin in ash samples with limit of detection value of 1 part per trillion, and quartz crystal microbalance has been used as transducer in these biosensors (Kurosawa et al. 2005). Detection of dioxins in food products like eggs, chicken and milk, a biomimetic approach has been used for the production of oligopeptides which mimics the aryl hydrocarbon receptor binding site. Immobilization of these oligopeptides has been done on gold surface, detecting a dioxin mixture, 2,3,7,8-tetrachlorodibenzo-p-dioxin and polychlorinated biphenyls, respectively, in the range of 1–20 parts per billions (Mascini et al. 2004).

1.3 Advances in Biosensors Through Nanotechnology Intervention

Nanotechnology is a multidisciplinary field which is covering a diverse and vast array of devices derived from various fields like physics, engineering, chemistry and biology (Verma 2017a, b; Verma et al. 2012, 2013a, b, c, 2016). Nanotechnology can be very helpful in monitoring the agricultural processes especially by its miniature dimensions. Nanotechnology is highly beneficial for enhancing the quality of food and its safety, reducing agricultural inputs and nanoscale nutrient absorption via soil. Nanotechnology can be utilized in agriculture to reduce the amount of chemicals spreading, which enhances yield through nutrient and pest management, and also minimize the loss of nutrients in fertilization. Soil quality of agricultural fields can be monitored via nanotechnology, and thus nanotechnology acts like sensors for maintaining the agricultural plants' health (Prasad et al. 2017). Nanosensors are used widely for monitoring the contamination in water and soil for to their fast action and strength (Ion et al. 2010; Kuswandi B 2018). A nanosized aqueous dispersion formulation has been released by one of the pesticide companies (Banner MAXX from Syngenta), for controlling blights, rusts, leaf spots and powdery mildews on turf, ornamental plants and other landscape plantings (Wong and Midland 2007). Electrochemical biosensors have been designed by Crumbliss et al., Zao et al. and Xu et al., to identify xanthine, glucose and hydrogen peroxide which use enzyme conjugated with that of the gold nanoparticles.

Nanomaterials synthesized chemically are considered as toxic in nature, so nanomaterials synthesized from the plant materials can be considered as safe and non-toxic and come under the green nanotechnology. Green nanotechnology is a safe and energy-efficient process which reduces waste as well as the emissions from the greenhouse. Using renewable materials for the production of nanoparticles is highly beneficial for environmental monitoring (Prasad et al. 2014, 2016). Nanomaterials which will be developed via renewable materials are environment-friendly and sustainable (Kandasamy and Prema 2015). With the advent of advanced materials, stability of enzyme or microbial system for industrial processes can be improved (Verma and Barrow 2015; Verma 2009; Verma and Kanwar 2008; Verma et al. 2008a, b, 2009, 2010, 2011, 2012).

Human breath is being used for diagnosing the diseases from the longer time. With the advancement in the field of nanotechnology, gas sensors are being employed for predicting, diagnosing as well as for monitoring a wide range of diseases in human beings. Gas sensors specifically designed for analysing human breath are very good alternative method for rapid and accurate disease diagnosis as compared to the current diagnostic methodology. There is a need to treat the diseases like cancer and diabetes at their earliest stages so that treatment costs can be reduced and outcome of the patient can be enhanced. Therefore, gas biosensors can be employed for rapid and accurate disease monitoring. Gas biosensors are highly specific, sensitive and selective in their role (Nasiri and Clarke 2019).

Bioluminescence resonance energy transfer sensing technology is being developed via bioluminescence proteins and luminescence nanomaterials for sensing the biomolecules. This bioluminescence resonance energy transfer technology is found to be highly reliable, selective and easy to use for sensing the biomolecules. Bioluminescence resonance energy transfer is a technique which uses a bioluminescence protein for exciting the acceptor via resonance energy transfer. Bioluminescence resonance energy transfer sensor is able to detect quickly any quantitative change in the target biomolecule without any external electromagnetic field. Development of bioluminescence resonance energy transfer sensors by utilizing the quantum dots made bioluminescence resonance energy transfer sensors more attractive for monitoring the changes in the target molecules as well as bioimaging in vivo (Hwang et al. 2019). Bioelectronics and nanotechnology seem to be growing fields which will have a marked influence for developing the newer strategies of biosensing (Hernandez-Vargas et al. 2018).

1.4 Conclusion

At present, extensive use of agrochemicals to boost agricultural yield has not only polluted the upper layer of the soil but also polluted the underground water. With increasing population, enhanced agricultural productivity is needed, but keeping in mind the damage caused to the ecosystem, new approaches which are eco-friendly should be considered. The damage caused to the environment due to various toxicants like pesticides, insecticides, endocrine disruptors, nitrogenous compounds, phenolic compounds, heavy metals, etc. should be monitored and controlled for healthier lifestyles and safer ecosystem. Analytical technology which is based on sensors is an extremely broader field for environmental monitoring in various sectors such as healthcare, food, pharmaceutical and agricultural industries. Nanotechnology is also becoming an important field for the agricultural sector, showing promising results and applications in the areas like delivery of fertilizers, pesticides, insecticides and genetic material for transformation in the plants. Unique properties of nanomaterials are being used to develop the nanosensors which can detect harmful chemicals and toxicants even at very low concentrations as well as in very less time. Many bacterial biosensors made by recombinant DNA technology have been reported which find their applications in the field of environmental sciences and biotechnology. Portable sensor kits should be developed for the on-site monitoring of environmental issues. There should be the possibility of discriminative as well as simultaneous monitoring of several contaminants in multicomponent systems and biosensing systems such that they can be suitable for large-scale food and environmental applications.

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Chapter 2
Biofunctionalized Nanostructured Materials for Sensing of Pesticides

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Abstract Pesticides constitute to be an integral part of modern agriculture. It has been estimated that approximately 35–45% of crop produce is lost due to infection by different pests, diseases, and growth of weeds. The application of these agrochemicals drastically reduces the effects of pests, weeds, and vector-borne diseases leading to enhanced crop productivity. It has become necessary to use pesticides on crops so as to provide food security to the growing population of the world. However, the indiscriminate utilization of pesticides has led to the persistence of their alarmingly high levels of residues in the environment. The toxicity of these agrochemicals extends largely to nontarget organisms such as humans, birds, and animals. The accurate sensing and efficient removal of these agrochemicals have become crucial due to the presence of their residues in environment and serious health hazards.

Nanoplatforms have drawn a considerable research orientation as alternatives to conventional systems for sensing of pesticide residues. Further, biofunctionalization of nanomaterials with biomolecules provides high specificity to the sensing platforms. The present chapter aims to explore various nanosensors reported till date for the sensing of different pesticides starting with general introduction of pesticides, classification, global scenario, and adverse health effects followed by nanoplatforms that have been investigated for the quantification of pesticides. Next, the nanoplatforms functionalized with specific biomolecules such as whole cells, DNA, antibodies, and enzyme (i.e., biosensors) have been discussed in detail. The chapter tends to highlight the promising properties, advantages, and limitations of the described sensing platforms.

Keywords Biofunctionalization · Biosensors · Nanomaterials · Nanosensors · Pesticides · Sensing

2.1 Introduction

Chemical pesticides are indispensable and have been a boon to the society attributable to their ability to eradicate insects and pests. Pesticides, as described by the United States Environmental Protection Agency (USEPA), are substances used deliberately for preventing, repleeling, destroying, or mitigating any pest ("About Pesticides" 2006). These chemicals are produced and used extensively worldwide to increase crop yields, variety, and preservation. The pesticides are also widely employed in domestic, industrial, and public health domains. According to reports, pest manifestation and vector-borne diseases destroy more than 45% of world's agricultural produce (Abhilash and Singh 2009). The crop losses are severe in tropical countries due to ambient high temperature and humidity which are highly conducive for rapid multiplication of the pests. Therefore to meet food demands of the world, it is essential to apply pesticides during the growth, storage, and transport of crops (Bhatnagar 2001; Rekha et al. 2006).

A Swiss chemist Paul Muller in 1939 discovered the first organochlorine pesticide dichlorodiphenyltrichloroethane (DDT) and was awarded Nobel Prize for the same in the year 1944 (Ware 1974). After that, the hunt for new synthetic chemical pesticides began, and different classes of pesticides such as organophosphates, carbamates, pyrethroids, and other phenols became popular. The distinguishing attributes of these pesticides are broad-range spectrum regarding toxicity to a wide variety of pests, effectiveness even in low quantities, and persistence refraining from frequent applications. Pesticides can be divided into subcategories as insecticides, herbicides, rodenticides, molluscicides, nematicides, fungicides, and virucides according to the target pest on which they act. There are more than 800 pesticides and over 20,000 pesticide-based products that are currently in use.

2.2 Classification of Pesticides

Pesticides are classified structurally, and the major subcategories include organochlorines (OCPs), organophosphates (OPPs), carbamates, and pyrethroids, among others (Vaccari et al. 2006)

2.2.1 Organochlorine Pesticides

Organochlorine pesticides are chlorinated aromatic hydrocarbon-derivatized synthetic organic pesticides. Organochlorines were the first-generation pesticides used expansively from the 1940s to 1960s, and some of the representative pesticide compounds of this group include dieldrin, DDT, methoxychlor, chlordane, endosulfan, and lindane. These chemicals work by disturbing the physiological activities of the target pest resulting in dysfunction and reduced vitality (Jayaraj et al. 2016). They are broad-spectrum pesticides with relatively low toxicity but long residual effects. Due to their slow degradable nature and prolonged use in large quantities, these chemicals led to environmental pollution and bioaccumulation. As a result, they were banned and gradually replaced by other pesticides (Aktar et al. 2009).

2.2.2 Organophosphate Pesticides

Structurally, organophosphate pesticides are esters of phosphoric acid and form the structural basis of many nerve agents, insecticides, and herbicides. Parathion, methyl parathion, malathion, fenitrothion, and phosphamidon are some of the examples of organophosphate pesticides. These are nerve poisons that affect the nerve transmission leading to pest death by irreversible covalent of enzyme acetylcholinesterase (AChE) (Peter et al. 2014). Although the exposure of light and temperature hydrolyzes organophosphate pesticides, the high toxicity toward humans and other animals of their residues has serious, societal, health, and environmental concerns (Bouchard et al. 2011).

2.2.3 Carbamate Pesticides

These organic compounds are carbamic acid (NH_2COOH) derivatives and kill pests by a mechanism similar to organophosphates through inhibition of AChE enzyme and interference with nerve transmission. Aldicarb, propoxur, oxamyl, carbaryl, and terbucarb, among others, are exemplary carbamates. They are mainly insecticides, herbicides, and fungicides. Carbamates are not very stable and breakdown within weeks or months (Goel and Aggarwal 2007). However, higher doses of these chemicals affect microflora and invertebrates and result in bioaccumulation in aquatic organisms.

2.2.4 Pyrethroids

The insecticidal property of these chemicals is attributable to ketoalcoholic esters of pyrethroid and chrysanthemic acids (Reigart and Roberts 1999). Some of the pyrethroid pesticides are allethrin, bonthrin, cyclethrin, dimethrin, tetramethrin, and fenvalerate. They affect the sodium ion channels resulting in paralysis of the target organism. Pyrethroids have comparatively low mammalian toxicity and fast degradation. However, exposure to high levels may cause a headache, vomiting, giddiness, low energy, muscle twitching, convulsions, and unconsciousness (Goel and Aggarwal 2007).

2.2.5 Other Pesticides

There are many other classes of pesticides such as phenylamides, phenoxyalkonates, phthalimides, dipyrids, and heavy metals that are used widely in agricultural practices to control different pests. Phenylamides show antifungal activity through the impact on mitosis and cell division in target fungi (Chao Yang et al. 2011). They have been reported to affect higher organisms as they enter the food chain and inhibit RNA polymerase enzyme (Jayaraj et al. 2016). Herbicides phenoxyalkonates are used to control weeds, and almost all compounds of this group are biodegradable (Vlitos 1952). Phthalimides (captan, folpet, and captafol) are fungicides that react with thiol groups of cysteine and glutathione amino acids. Paraquat and diquat are dipyrids that replace the cations adsorbed in the organisms (Funderburk et al.

1969). Also, elements like lead, sulfur, iron, mercury, tin, and zinc, among others are employed as pesticides in inorganic or organic metal form as methylmercury chloride, calcium arsenate, sodium arsenate, and zinc phosphide, to name a few.

Pesticides, the agrochemicals, are effective means of controlling pests and one of the invaluable inputs for sustainable agricultural production. Therefore, these agrochemicals are immensely produced and used (approximately hundred times more) since the green revolution started.

2.3 Pesticide Usage and Impact

Intentional use of a pesticide started in 2500 BC when the Sumerians rubbed sulfur compounds on their bodies so as to control a variety of insects and mites. Thereafter, marketing of these pesticides started in 1943, and approximately $40 billion/year purchase price is spent to apply about 3 billion kg of different pesticides each year worldwide (“Current pesticide spectrum, global use and major concerns” 2003; Yadav et al. 2015). Europe is the most significant consumer with 45% usage followed by the USA which accounts for 24% of the total consumption, and the rest of the world consumes the remaining collectively (Abhilash and Singh 2009). In the developed nations like North America, Japan, and Western Europe where pesticide application rates are high, herbicides are the majorly used pesticides (nearly 44%) due to lesser toxicity as compared to insecticides (Yadav et al. 2015). Also, the consumption of pesticides is intense in export crops such as bananas, coffee, vegetables, cotton, and flowers.

Although pesticides are agrochemicals that are utilized to control the pests and weeds and to combat losses, only 2–3% of pesticide accomplishes the desired purpose, and the rest causes environmental pollution leading to toxicity. There is a worldwide view that these pesticides have done more damage than benefits to human and ecosystem due to unsystematic use.

According to a joint report of United Nations Environment Programme (UNEP) and World Health Organization (WHO), approximately 200,000 people die, and 3,000,000 are poisoned per year by pesticides worldwide (“Public health impact of pesticides used in agriculture” 1990; “The WHO recommended classification of pesticides by hazard and guidelines to classification 2009” 2010). Food and Agriculture Organization (FAO) inventory has found that nearly 500,000 tons of obsolete and unutilized pesticides are present in the environment as a threat to public health and ecosystem (Abhilash and Singh 2009; “Baseline Study on the Problem of Obsolete Pesticides Stocks” 2001).

Several incidents of pesticide poisoning have occurred in different parts of the world. During the Vietnam War, military forces of the USA sprayed approximately 19 million gallons of herbicides to remove forest cover which resulted in increased cancer risks to locals exposed to pesticides (Frumkin 2003). A study conducted on the affected individuals of Seveso disaster, Italy in 1976, concluded that exposure to herbicide leads to chloracne due to dioxin formation (Bertazzi et al. 1998). Therefore, various global organizations strictly scan the market for these toxic chemicals. European Union has started to establish programs entitled “Monitoring of Pesticides in Products of Plant origin in the European Union” since 1996 to determine the level of pesticide residue contamination in the wide variety of food samples. There are no worldwide standards for permissible pesticide residues in any environmental sample and food commodity. However, the globally accepted safety limits have been set by WHO and FAO in the Codex Alimentarius Commission and Joint Meeting on Pesticide Residues (JMPR) (Fishel 2013; CODEX Alimentarius 2011). If the credits of these pesticides embrace economic development in terms of increased crop productivity, their debits have consequence in serious human health and environment hazards.

2.4 Health Implications of Pesticides

Pesticides have been a boon worldwide to eradicate pests resulting in adequate crop production. Ideally, a pesticide must be detrimental to the target pest only, but this is not so. The controversy over extreme dependency on such chemicals as their excessive use/misuse, volatility, and hydrological system-based long-distance transport has also surfaced. The eventual contamination of environmental resources with pesticide residues poses a risk to human health, results in the death of nontarget organisms, and disturbs the ecosystem (Ashour et al. 1987; Calvert et al. 2010). Various research groups have discussed adverse effects of these agrochemicals that include cancer, respiratory, neurological, and reproductive effects (Chauhan and Singhal 2006; Aslan et al. 2011; Bhatnagar 2001). The pesticides cause irritation and sensory disturbances along with cognitive effects such as learning impairment, language problems, and memory loss (Hart and Pimentel 2002). The exposure to pesticide leads to asthma, chronic sinusitis, bronchitis, reproductive dysfunctions, and birth abnormalities (Baker 1990; Garry et al. 1996; Weiner and Worth 1969; Horrigan et al. 2002). These synthetic chemicals also cause immunopathological effects such as autoimmunity, immunodeficiency, and hypersensitivity reactions like dermatitis, eczema, and allergies (McCarthy 1993). US data has revealed that 90% of all fungicides and 18% of all insecticides are carcinogenic and have been observed to induce tumor growth in laboratory animals (Pimentel and Hart 2001; Maret 1996). Their prolonged contact can also cause neuropathy, hepatotoxicity, and nephropathy (Chauhan and Singhal 2006). Pesticides are endocrine-disrupting molecules that lead to hormonal imbalances and have been linked to breast cancer (Maret 1996). Therefore, the exposure to these chemicals not only results in immediate acute poisonings and allergies but also may prove to have chronic far-reaching consequences.

In the light of scenario mentioned above, the development of pesticide sensing platforms has received research orientation for safety and quality analysis of the environmental samples including water, air, soil, and food commodities.

2.5 Conventional Methods of Pesticide Detection

The detection of pesticide contaminants in various food and environmental samples is necessary to ensure that the exposure to these contaminants is below acceptable levels. Highly sensitive, specific, reproducible, fast, and robust analytical methods are required to carry out the pesticide monitoring programs. The determination of pesticides is carried out by high-performance liquid chromatography (HPLC) and gas chromatography (GC). Their modifications in the form of gas chromatography-mass spectrometry (GC-MS), gas chromatography-ion trap mass spectrometry (GC-ITMS), gas chromatography-tandem mass spectrometry (GC-MS/MS), low-pressure gas chromatography-mass spectrometry (LP-GC/MS), liquid chromatography-mass spectrometry (LC-MS), and liquid chromatography-tandem mass spectrometry (LC-MS/MS), among others, have made a remarkable progress in the area of pesticide monitoring (C-J Tao et al. 2009; Hernández et al. 2006; Cortés et al. 2006; Moreno et al. 2006). A wide variety of detectors such as nitrogen-phosphorus detector (NPD), electron capture detector (ECD), flame photometric detector (FPD), flame ionization detector (FID), and pulsed flame photometric detector (PFPD) have been used in order to improve the sensitivity of detection procedures (Gebara et al. 2005; Salvador et al. 2006; Parveen et al. 2005). These techniques are quite sensitive and selective and allow efficient multi-residue analysis in one run (Hogendoorn and Van Zoonen 2000). However, non-portability due to the involvement of heavy equipment, the requirement of trained personnel, non-applicability for on-site detection, high cost, and time of sample preparation are some of the limitations related to the mentioned conventional methods (Pérez-Ruiz et al. 2005).

Nanosensors employing nanomaterials as transduction and immobilization platform for recognition probes are useful alternatives for the detection of pesticides. Albeit these sensing methods may not offer extremely sensitive detection similar to the aforementioned traditional techniques, they are portable, miniaturized, user-friendly, and enable in situ analysis.

2.6 Nanomaterials for Detection of Pesticides

Nanostructures are the materials having structural elements engineered at nanometer scale with dimensions below 100 nm and possess properties utterly different from that of bulk materials (Luo et al. 2006). The convergence of nanotechnology and analytical techniques paves the path for the development of ultrasensitive, miniaturized, rapid, and inexpensive sensors for real-time in situ and on-site monitoring of environmental contaminants. The characteristics of nano-sized materials such as high surface area-to-volume ratio, physiochemical properties, shape, composition, and good target binding capability advocates their use in sensors. The most commonly used nanomaterials include graphene, quantum dots, carbon nanotubes, metal nanoparticles, metal oxides, and metal-organic frameworks (Yao Fan et al. 2016; Huo et al. 2014; Nair et al. 2003; Pawan Kumar et al. 2014a).

2.6.1 Metal Nanoparticles

Metal nanoparticles, such as silver, gold, titanium, platinum, and iron (Ag, Au, Ti, Pt, and Fe, respectively), are one of the most explored nanomaterials due to their optoelectronic, thermal, and catalytic properties (Shaojun Guo and Wang 2007; Kariuki et al. 2006). Among those, Ag nanoparticles have been used intensively for colorimetric and fluorescence assays along with signal amplification and immobilization of bioprobes (Andreescu et al. 2009).

Ag nanoparticles stabilized through modification with water-soluble calixarene-derivative *p*-sulfonatocalix[*n*]arene (pSC_n) have been employed for designing a simple colorimetric for the sensing of optunal pesticide (Xiong and Li 2008). The detection is due to excellent plasmonic absorbance of the noble metal nanoparticles. Calixarenes are cavity-shaped cyclic organic molecules having unusually high activity toward neutral and ionic molecules, including pesticides (Ikeda and Shinkai 1997). On interaction with the analyte, the introduced organic molecule forms bridging structures between noble nanoparticles and analyte molecules resulting in the change of color and UV-Vis absorption due to aggregation of Ag nanoparticles. The colorimetric probed allows rapid, real-time in situ quantification of optunal down to a concentration 10^{-7} M within linear dynamic range of 5×10^{-6} to 10^{-3} M. In another research, humic acid-capped Ag nanoparticles have been found to be sensitive toward sulfurazon-ethyl herbicide (Dubas and Pimpan 2008). The developed method takes the collaborative advantage of the optical properties of Ag nanoparticles and complex formation capability of humic acid with metal cations as well as herbicides. The adsorption of the target herbicide onto humic acid-modified Ag nanoparticles changes the dielectric constant of the surrounding medium which is well-known to affect the extinction spectrum of spherical noble metal nanoparticles (Frederix et al. 2003). The resulting associated change in color forms the basis of on-site and continuous optical detection of sulfurazon-ethyl in water samples. The solution color changes from yellow to orange-red and then purple with increasing concentration of herbicide from 0 to 500 ppm.

A very similar visual detection strategy quantifies malathion and chlorpyrifos up to a concentration of 100 and 20 ppb, respectively, within seconds using Au nanoparticle-modified alumina surface based on the color change (Lisha et al. 2009). The pesticide adsorption on the nanoparticles results in their aggregation followed by signal enhancement achieved by sodium sulfate. Similarly, Au nanoparticle-modified glass surfaces have been explored for simple spectrophotometric detection of a common pesticide, endosulfan, up to ppm levels (Nair et al. 2003). The nanoparticles aggregate after adsorption of the analyte leading to a change in the surface plasmon resonance (SPR) signal of the metal. Another simple, rapid, and accurate colorimetric sensor has been developed for selective and sensitive detection of carbendazim pesticide in food and water samples with the aid of 4-aminobenzenethiol-functionalized Ag nanoparticles (ABT-AgNPs) in the concentration range of 10–100 M with limit of detection (LOD) of 1.04 M as shown in Fig. 2.1 (Patel et al. 2015). The sensing is based on strong ion-pair and π-π interaction between carbendazim and ABT-AgNPs-based probe forming aggregated large conjugate network due to which color of the probe changes from yellow to orange.

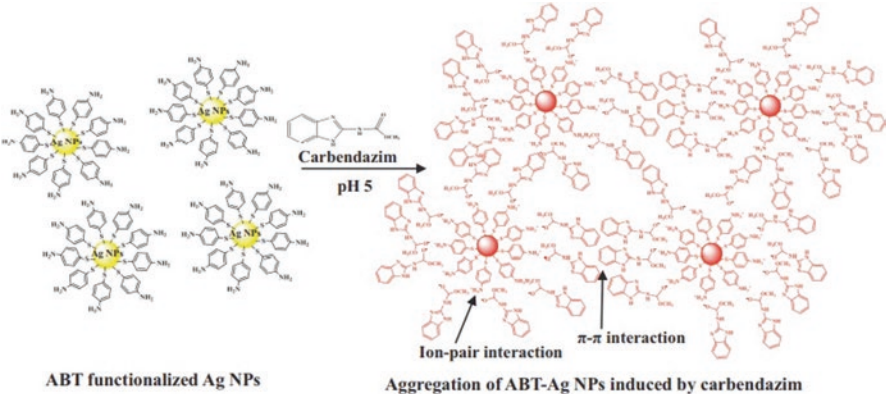


Fig. 2.1 Schematic for aminobenzenethiol-functionalized Ag nanoparticles-based colorimetric sensing of carbendazim: the strong ion-pair and π-π interaction between carbendazim and ABT-AgNPs forms large aggregates resulting into color change from yellow to orange. *ABT* aminobenzenethiol, *AgNPs* Ag nanoparticles, *ABT-AgNPs* aminobenzenethiol-functionalized Ag nanoparticles. (Reproduced from Patel et al. (2015), with permission from Elsevier)

Ag nanoparticle-based simple, facile, and sensitive chemiluminescent sensor array has been reported for detection of five organophosphate and carbamate pesticides, including carbaryl, dimethoate, dipteres, carbofuran, and chlorpyrifos (He et al. 2015). In this work, the researchers propose the use of luminol-functionalized Ag nanoparticles (Lum-AgNPs) which on reaction with hydrogen peroxide (H_2O_2) produces chemiluminescence emission (Fig. 2.2). The different pesticides have been demonstrated to influence chemiluminescence emission of the system with varying degrees which is responsible for the multi-analyte sensing with achievable 24 μg/mL limit of detection. The sensitivity of luminol-based chemiluminescent platforms has been improved using Fe_3O_4 nanoparticles which exhibit intrinsic peroxidase activity and allow magnetic separation (Guan et al. 2012). The Fe_3O_4 nanoparticles catalyze the conversion of dissolved oxygen into superoxide anions resulting in 20 times increase in chemiluminescence intensity. A turn-on sensor fabricated for ethoprophos uses the quenching of luminol chemiluminescence emission by the surface coordinative reaction with the non-redox pesticide. The sensor can detect ethoprophos pesticide down to a concentration of 0.1 nM in a linear dynamic range of 0.1 nM–100 μM. An electrochemical square-wave voltammetry (SWV) sensor for organophosphate, methyl parathion, has been presented using zirconia (ZrO_2) nanoparticles deposited electrochemically onto the gold electrode (Guodong Liu and Lin 2005). ZrO_2 nanoparticles act as selective sorbent, and the platform detects methyl parathion down to detection limit of 3 ng/mL within the linear range of 5–100 ng/mL.

Various reports of pesticide sensors based on surface-enhanced Raman spectroscopy (SERS) active nanoparticles are available in the literature (Vongsvivut et al. 2010; XT Wang et al. 2010; Pengzhen Guo et al. 2015; Kubackova et al. 2014). Wang and co-workers have fabricated Ag nanoparticle-coated silicon nanowire arrays for the quantification of carbaryl pesticide through surface-enhanced Raman scattering (XT Wang et al. 2010). The stability of silicon nanowires in combination

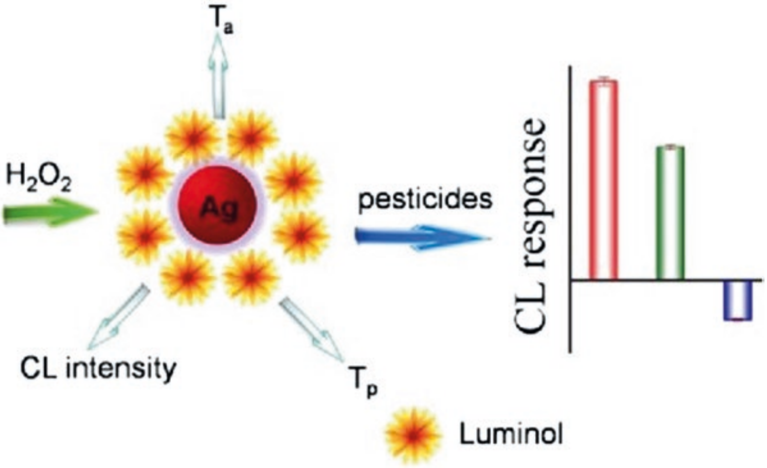


Fig. 2.2 Schematic for the luminol-functionalized Ag nanoparticles-based chemiluminescent sensor for organophosphate and carbamate pesticides: the reaction of Lum-AgNPs with hydrogen peroxide (H_2O_2) produces chemiluminescent emission, and different pesticides demonstrate to influence CL emission with varying degrees responsible for signatures of multi-analytes. *Lum* luminal, *AgNPs* Ag nanoparticles, *Lum-AgNPs* luminal-functionalized Ag nanoparticles, *CL* chemiluminescence. (Reproduced from He et al. (2015), with permission from ACS Publications)

with enhancement effect of appropriately sized and uniform Ag nanoparticles on Raman scattering provides a proper conjugation (Emory et al. 1998; Peng et al. 2008). This resulting SERS-based chemosensor exhibited the sensitivity of 10^{-7} M (0.02 ppm) for carbaryl. A sensor based on the dried films of citrate-reduced silver and gold colloidal NPs records SERS spectra of fonofos organophosphate pesticide down to 10 ppm (Vongsvivut et al. 2010). Also, the orientation geometry of the adsorbed analyte (fonofos, in this case) depends on the type of metal colloid used and results in significantly enhanced SERS spectral profiles.

Another group of researchers has used alkyl dithiol-functionalized silver and gold colloidal nanoparticles to improve the sensitivity of surface-enhanced Raman spectroscopy (SERS)-based sensor for organochlorine pesticide aldrin with an achievable LOD of 10^{-8} M (Kubackova et al. 2014). The functionalization of metal surfaces activates the formation of intermolecular or intramolecular cavities that act as host to the analytes (I López-Tocón et al. 2011). The response intensification occurs if the interaction occurs at hotspots localized in interparticle gaps (Le Ru et al. 2006). Organic molecules such as alkyl dithiol linkers induce the formation of hotspots and also act as molecular hosts for analytes, thereby improving sensitivity and specificity (Isabel López-Tocón et al. 2010). Guo et al. have investigated the shape- and size-dependent SERS response of monodispersed Au@Ag nanocuboids and Au@Ag nanocubes of thickness ranging from 1 nm to 16 nm toward thiram pesticide (Pengzhen Guo et al. 2015). The excitation wavelength discriminates between the shape of particles regardless of their size with maximum attained Raman enhancement at a particular threshold of respective particle size and/or coating thickness. The sensing platform can detect thiram pesticide with a detection limit of 80 pM and 100 pM for nanocuboids and nanocubes, respectively. Similarly, gold-coated SERS nanosubstrates have been used to detect different pesticides such as carbaryl, phosmet, and azinos-methyl with a detection limit of 4.51, 2.91, and 2.94 ppm, respectively, on fruit surfaces (Bin Liu et al. 2013).

Liou and co-workers have used Ag nanoparticle-coated cellulose nanofibers for SERS analysis of thiabendazole pesticides in apples with high sensitivity attributable to the prevented uncontrolled aggregation of Ag nanoparticles on cellulose nanofibers in low-pH environment (Liou et al. 2017). The TBZ is a neutral molecule exhibiting a low affinity for Ag nanoparticles, and the decrease in the pH of thiabendazole solution below its pKa enables the electrostatic attraction between Ag nanoparticles and thiabendazole. However, the use of cellulose nanofibers in low-pH environment prevents the aggregation of Ag nanoparticles and serves as an effective platform for SERS-based quantitative analysis. A simple, sensitive, and selective platform to determine fenitrothion has also been developed using gold (Au) nanoparticles exhibiting nanometal surface energy transfer (NSET) to the fluorescence of fluorescein (Nebu et al. 2018). The “turn-on” fluorescence response of the quenched fluorescein probe in the presence of Au nanoparticles toward fenitrothion has been demonstrated successfully on a paper strip. The strips exhibit LOD of 6.05 nM, 7.84 nM, and 9.41 nM in well water, river water, and tap water samples, respectively. The platform was also successfully employed for the separation of fenitrothion from contaminated water using supramagnetic iron oxide nanoparticles attached to Au nanoparticles.

2.6.2 Metal Oxides

Since the breakthrough regarding semiconducting properties of titanium dioxide (TiO_2), environmental applications have seen the use of a diverse number of semiconducting metal oxides (Andreescu et al. 2009). These include SnO_2, ZnO, CuO, ZrO_2, MnO_2, WO_3, and CeO_2, among others (Oh et al. 1993; Huo et al. 2014; Du et al. 2011; Min Wang and Li 2008; Huang et al. 2003; Schachl et al. 1997; Peral et al. 1997; Zhengxiong et al. 2006).

Oh and co-workers have first reported the sensing behavior of metal oxide, SnO_2 and ZnO, doped with basic oxides of calcium (CaO) and magnesium (MgO) toward dimethyl methylphosphonate organophosphorus compound down to 44 ppb (Oh et al. 1993). The strategy employs the oxidation of adsorbed analyte onto the surface of semiconducting metal oxides for measurement. The enhanced sensitivity achieved by doping with basic oxides is attributed to the strong interaction of their surface hydroxyl groups with dimethyl methylphosphonate, making the dissociative adsorption facile. A SnO_2-based single sensor for pesticide gas mixture operational in the rectangular temperature mode between 250 and 300 °C has also been reported to reduce the power consumption (Huang et al. 2003). The limit of detection achieved using the forementioned sensor for acephate and trichlorfon pesticide gas mixture is 0.1 ppm, each.

In an another literature report, a screen-printed electrode-based electrochemical sensor has been developed for pesticide 3-(3,4-dichlorophenyl)-1,1-dimethylurea (DCMU) up to detection limit of 0.159 μM using highly conductive and catalytic CuO (Pino et al. 2016). It has also been demonstrated that selectivity toward specific pesticide is also dependent on the morphology of CuO nanostructures (Soomro et al. 2016). Among all other morphologies, the glycine-mediated triangular flake-like CuO nanostructures exhibit greater sensitivity toward malathion in the presence of other competitors up to 0.1 nM. The functionalization of CuO with pimelic acid has also resulted in excellent electrochemical behavior of nanomaterial deposited over indium tin oxide (ITO)-based electrode (Tunesi et al. 2018). The platform has been employed for electro-catalytic inhibition-based sensing of organophosphorus pesticides with sensitivity up to nanomolar concentration. The sensitivity of metal oxide-based pesticide sensors improves in the composite form with other metal structures or carbon materials (Huo et al. 2014; Min Wang and Li 2008; Du et al. 2011; Xuanhua Li et al. 2010b; MingYan Wang et al. 2014b; Yonglan Wang et al. 2015). Owing to the high surface area and selectivity of zirconia for phosphate groups, nano-ZrO_2/Au composite-modified alumina electrodes quantify organophosphorus pesticide, parathion (Min Wang and Li 2008). The voltammetry-based detection of parathion using the developed platform has been found to be highly sensitive with a LOD of 3 ng/mL within a linear dynamic concentration range of 10–140 ng/mL. Li et al. have explored Au-coated TiO_2 nanotube arrays for the fabrication of recyclable SERS-based detection platform for a variety of pesticides such as 4-chlorophenol, dichlorophenoxyacetic acid, and methyl parathion (Xuanhua Li et al. 2010b). The electrode exhibits photocatalytic activity toward the analyte, thereby incorporating self-recycling attribute in the sensor. Therefore, the electrode not only decreases the overall cost of the process but also facilitates the degradation of pollutant. The graphene/ZrO_2 nanocomposite voltammetrically detects methyl parathion up to detection limit of 0.1 ng/mL within linear dynamic range of 0.5–100 ng/mL (Du et al. 2011). The rapid electron-transfer kinetics of graphene along with a strong selective affinity of ZrO_2 toward phosphoric moieties incorporates high sensitivity and selectivity to the sensor.

Another group of researchers has investigated the hybrid nanocomposite of CuO nanowires and single-walled carbon nanotubes (SWCNTs) for the quantification of malathion organophosphate pesticide as shown in Fig. 2.3 (Huo et al. 2014). The high stability, electrical conductivity, and affinity of the nanocomposite resulting in detection limit as low as 0.3 nM establish the practical applicability of the sensor. A simple electrochemical detection strategy for methyl parathion has been proposed using zirconia/ordered macroporous polyaniline (ZrO_2/OMP) based on strong affinity of phosphate with ZrO_2 along with high catalytic activity and conductivity of OMP (Yonglan Wang et al. 2015). The sensor works on the square-wave voltammetry and achieves a detection limit as low as 0.23 nM with significant selectivity, reproducibility, and stability in real samples.

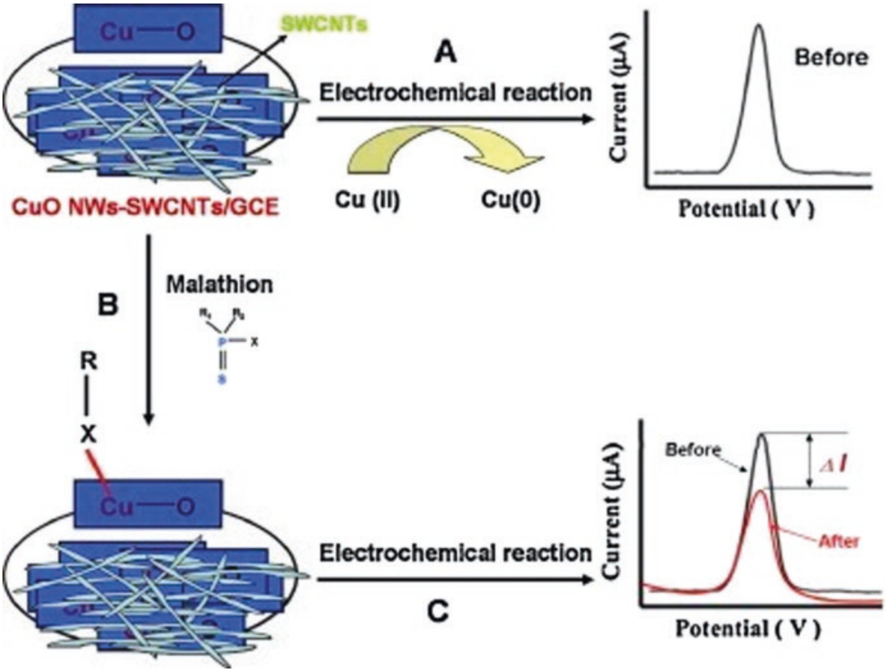


Fig. 2.3 Schematic for electrochemical detection of malathion using CuO nanowires in composite form with single-walled carbon nanotubes deposited over glassy carbon electrode. The high affinity binding of malathion to the nanocomposite creates a barrier to block the electron transfer across the electrode interface and thus decreases the anodic peak current density due to suppression of Cu(II) → Cu(0) reaction so as to quantify the original concentration of malathion. *CuO NWs* copper oxide nanowires, *SWCNTs* single-walled carbon nanotubes, *GCE* glassy carbon electrode. (Reproduced from Huo et al. (2014), with permission from Elsevier)

A novel amperometric sensor composed of cobalt oxide nanoparticle (CoO)-decorated reduced graphene oxide deposited onto glassy carbon electrode (GCE) has been fabricated for carbofuran and carbaryl (MingYan Wang et al. 2014b). The nonenzymatic sensor demonstrates high sensitivity up to detection limit of 4.2 μg/L for carbofuran and 7.5 μg/L for carbaryl in fruit and vegetable samples due to improved electrocatalytic activity of nanocomposite. Further, Khairy and co-workers have explored the nickel oxide nanoplatelets tailored screen-printed electrodes (NiO-SPE) for differential pulse voltammetry-based detection of organophosphate pesticide, parathion. The sensing platform achieves quantification of parathion within the dynamic concentration range of 0.1–30 μM and detection limit of 0.024 μM in real samples of water, urine, and vegetable samples (Khairy et al. 2018).

2.6.3 Quantum Dots

Quantum dots are inorganic colloidal nanocrystalline fluorophores exhibiting unique photophysical properties. The optical characteristics of quantum dots depend on size, composition, structure perturbations, and surface state (Andreescu et al. 2009). Quantum dots are attractive sensing probes for a wide variety of analytes such as metal ions, pesticides, phenols, and nitroaromatic explosives by analyte-induced photoluminescence changes (Costa-Fernández et al. 2006; Constantine et al. 2003b; Yuan et al. 2008; Goldman et al. 2005). Also, the photoluminescence quantum yield of these nanomaterials has been increased by coating core-shell structures with semiconductor materials of the higher band gap (Andreescu et al. 2009).

Li and Qu have proposed the use of a highly luminescent and stable calix[4]arene-coated CdTe quantum dot-based probes for the detection of methomyl pesticide (Haibing Li and Qu 2007). The luminescence of nanocomposite enhances significantly with increasing concentration of methomyl in the range of 0.1–50 μM with an achievable detection limit of 0.08 μM. The sensor is highly selective for methomyl as the cavity of the used calixarene molecules is small and not capable of holding bulk aromatic molecules excluding small linear pesticides, similar to methomyl, and the same is validated by Langmuir-binding isotherm equation. The similar strategy has been employed using another type of calixarene (*p*-sulfonatocalix[4]arene) for coating CdTe quantum dots for highly selective detection of fenamithion and acetamiprid up to concentration down to 12 nM and 34 nM, respectively (Haibing Li and Qu 2007). In the proposed approach, the CdTe quantum dots alone show selectivity to fenamithion. However, it is after functionalization with p-sulfonatocalix[4]arene that CdTe responds selectively to acetamiprid. The entrapment of acetamiprid into the cavity of p-sulfonatocalix[4]arene restricts the disordered orientation of CdTe quantum dots and induces uniform arrangement. This protects the core efficiently and suppresses the trail of quenching from entering into the medium, thereby increasing the luminescence intensity along with providing blueshift to the emission (Konishi and Hiratani 2006).

Zhang et al. have proposed a very simple fluorescence resonance-enhanced transfer (FRET)-based strategy facilitated through the replacement of ligand from the surface of quantum dots for immediate detection of chlorpyrifos up to detection limit as low as 0.1 nM (Kui Zhang et al. 2010b). The employed CdTe quantum dots exhibit green fluorescence near 520 nm, which quenches upon the addition of a bidentate metal chelate, dithizone, due to FRET mechanism. In the presence of chlorpyrifos pesticide, its hydrolysis product, diethylphosphorothionate, replaces dithizone from the surface of quantum dots resulting in fluorescence enhancement. Similarly, a "turn-on" sensor for glyphosate has been designed using FRET between positively charged cysteamine-stabilized Au nanoparticles (CS-AuNPs) and negatively charge thioglycolic acid-capped CdTe quantum dots (TGA-CdTe-QDs) (Jiajia Guo et al. 2014). Figure 2.4 shows the sensing mechanism for glyphosate using the mentioned quantum dot-based platform. Electrostatic interaction between oppo-

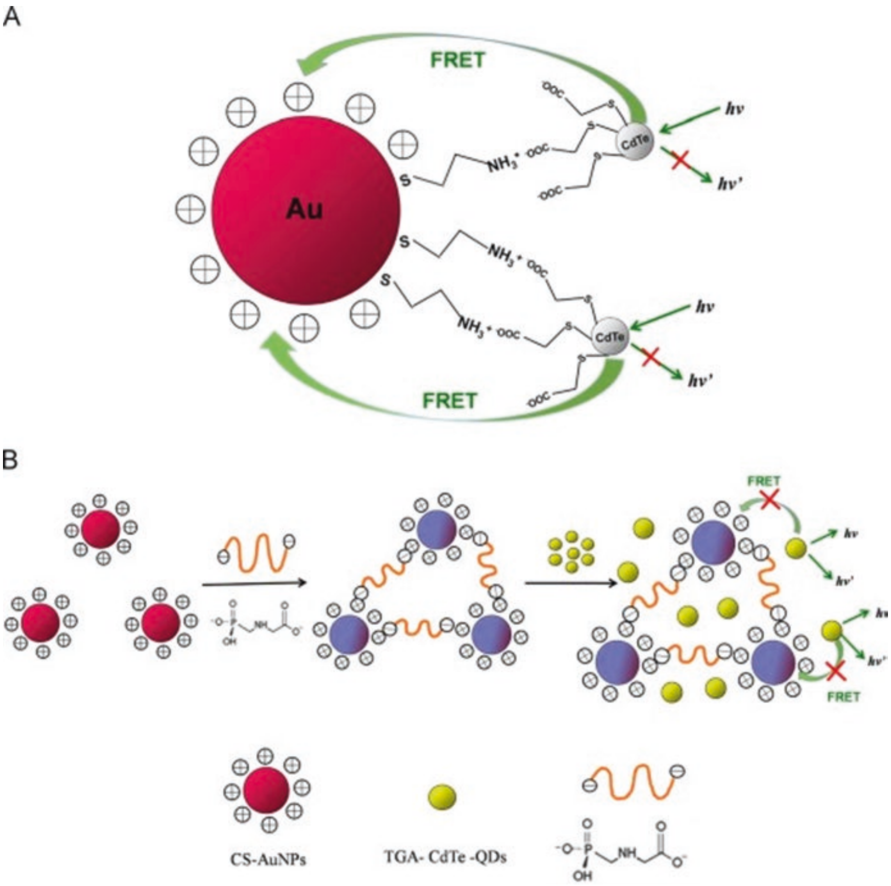


Fig. 2.4 Schematic of a "turn-on" sensor for glyphosate. (**a**) Fluorescence resonance energy transfer between oppositely charged cysteamine-stabilized Au nanoparticles and thioglycolic acid-capped CdTe quantum dots; (**b**) glyphosate-induced attenuation of FRET and the fluorescence recovery of quenched quantum dots due to electrostatic aggregation of CS-AuNPs. *FRET* fluorescence resonance energy transfer, *CS-AuNPs* cysteamine-stabilized Au nanoparticles, *TGA-CdTe-QDs* thioglycolic acid-capped CdTe quantum dots. (Reproduced from Guo et al. (2014), with permission from Elsevier)

sitely charged moieties forms FRET donor-acceptor assembly which quenches the fluorescence of TGA-CdTe-QDs. The presence of glyphosate induces the electrostatic aggregation of CS-AuNPs resulting in the recovery of fluorescence emission of the quenched quantum dots. The obtained detection limit for glyphosate using the developed sensing platform is 9.8 ng/Kg of apples within linear dynamic range of 0.02–2.0 μg/Kg. Likewise, phosphorescent Mn-doped ZnS quantum dots ($ZnS:Mn^{2+}$ QDs) in combination with Ag^+ ions quench the emission of quantum dots for the quantification of thiram pesticide up to 25 nM detection limit. As thiram has high affinity toward Ag^+ ions, the addition of thiram in a solution containing Ag^+ ions quenches quantum dots. The formation of Ag-thiram complex restores the phosphorescence of ZnS:Mn^{2+} quantum dots (Cheng Zhang et al. 2017). The ratiometric fluorescent quantum dots (RF-QDs) also facilitate the development of an optical sensor for acetamiprid in which Au nanoparticles act as fluorescence quencher as well as a colorimetric reporter (Cheng Zhang et al. 2017). Au nanoparticles quench fluorescence intensity of RF-QDs based on inner field effect. The adsorption of acetamiprid on the surface of Au nanoparticles attributable to the strong affinity of its cyano group with gold results in the aggregation of Au nanoparticles and thus restores the fluorescence of quantum dots.

The pesticides, themselves, have a quenching effect on the photoluminescence of quantum dots as shown in work reporting the quantification of pesticides Dipel and Siven in water samples (Bakar et al. 2011). The photoluminescence intensity of ZnCdSe quantum dots quenches with increasing concentration of pesticides solutions. Another group of researchers has also employed the same approach to develop fluorescence "turn-off" pesticide sensing platform by using quenching behavior of pesticides toward water-soluble double ZnCdSe quantum dots (Yao Fan et al. 2016). A similar study elucidating the quenching effect of four pesticides, viz., tetradifon, aldrin, atrazine, and glyphosate, on fluorescence of ZnO quantum dots has been explored (Sahoo et al. 2018). The detection is based on the fact that pesticides having good leaving groups (-Cl) interact with quantum dots with high affinity, and specificity is achieved due to varied binding signatures of quantum dots for the different pesticides. Recently, a new method for simple, highly sensitive visual fluorescence-based sensor has been developed for specific detection of three organophosphate pesticides, namely, dimethoate, dichlorvos, and demeton using "turn-off-on" mode (Qin Wang et al. 2019). The double quantum dots (QD1 for CdTe quantum dots and QD2 for ZnCdSe quantum dots) have been combined with high-activity Zn-nanoporphyrins (nano-ZnTPyP) for signal amplification, reducing environmental interferences and producing color variations for different pesticides. The detection of organophosphate pesticides is based on the quenching of fluorescence of double quantum dots due to energy transfer interactions between quantum dots, nano-ZnTPyP, and organophosphate pesticides via photon-induced energy transfer (PET) and fluorescence resonance energy transfer (FRET).

Researchers have investigated different molecularly imprinted polymer (MIP)-coated quantum dots for the detection of pesticides (Yaoyao Zhao et al. 2011; Haibing Li et al. 2010a). The preparation of MIPs takes place in the presence of analyte via polymerization. The analyte is removed after polymerization to leave nanocavities of exact shape, size, and corresponding functional moieties which are capable of rebinding to the target analyte with high specificity (Aragay et al. 2012). The silica nanosphere-embedded CdSe quantum dot-modified MIP layer (CdSe@SiO2@MIP) has been reported for the detection of lambda-cyhalothrin which is a widely used pyrethroid pesticide (Haibing Li et al. 2010a). Pyrethroid acts as efficient electron or hole acceptor to introduce a novel, nonradioactive decay mechanism for the excitation of quantum dots. The fluorescence of the system quenches in the presence of the analyte which attributes toward and linearly correlates to the concentration of lambda-cyhalothrin within the concentration range of 0.1–1000 μM with a detection limit of 3.6 μM. Similar to the above strategy, Zhao et al. have proposed quantum dot-molecular imprinted polymer (QD-MIP) nanosphere composite for the detection of diazinon pesticides via fluorescence quenching (Yaoyao Zhao et al. 2011). The emission band of quantum dots overlaps with the absorbance band of the pesticide. This results in energy transfer from quantum dots to pesticides, thereby leading to quenched fluorescence of quantum dots. Mn-doped ZnS quantum dots and CdTe quantum dot-embedded SiO_2 coated with an acrylamide-based MIP have also been shown to exhibit specificity and sensitivity toward chlorpyrifos and 2,4-dichlorophenoxyacetic acid down to 17 nM and 2.1 nM concentration, respectively (Ren et al. 2015; Jia et al. 2017). Further, Carrillo-Carrión and group have investigated capillary chromatography-based surface-enhanced Raman spectroscopy (SERS) detection system for excellent analytical detection of different pesticides using Ag quantum dot-based sponge-structured nanocomposite as substrate (Carrillo-Carrión et al. 2012). The detection limit for chlortoluron, diluron, atrazine, and terbuthylazine pesticides ranges between 0.2 and 0.5 μg/mL with high reproducibility.

2.6.4 Carbon-Based Nanostructures

The last two decades have witnessed the extensive use of carbon-based structures such as nanotubes, nanofibers, quantum dots, nanodiamonds, and graphene in analytical applications. Among all other allotropes, carbon nanotubes and graphene attain the primary focus.

Since the discovery of carbon nanotubes in the early 1990s, these nanostructures have been studied extensively as building blocks for sensing platforms (Vinayaka and Thakur 2010; Reiss et al. 2009). The basic structure of carbon nanotubes is composed of sp^2-bonded C atoms, with each C atom bonded to three other C atoms in the two-dimensional x-y plane and the presence of weakly localized π-electrons along the z-axis (Scida et al. 2011). Basically, carbon nanotubes are divided into single-walled carbon nanotubes (SWCNTs) with diameters of approximately 1.5 nm and multi-walled carbon nanotubes (MWCNTs) containing 2–30 concentric layers of graphite each having diameter ranging from 3 to 50 nm (Andreescu et al. 2009). The characteristic high surface area, electronic properties, surface chemistry, high loading capacity, ability to act as a substrate for probes, and electrocatalytic activity advocates the candidature of these nanostructures in this area (Yiping Chen et al. 2010c; Rosenthal 2001).

Carbon nanotubes have been shown to exhibit high adsorption affinity toward inorganic and organic molecules and subsequently develop π-π electrostatic interactions (Asensio-Ramos et al. 2009). Considering this property, Zhou et al. have investigated the use of multi-walled carbon nanotubes (MWCNTs) as solid-phase extraction (SPE) substrates for quantification of three pesticides, namely, imidacloprid, acetamiprid, and thiamethoxam in the water samples (Zhou et al. 2006). The MWCNT-based SPE when coupled with high-performance liquid chromatography can achieve the detection limit of 5.4, 6.7, and 6.1 ng/mL for the respective pesticide pollutants with good linearity in the range of from 0.08 to 100 ng/mL. The technique has also been employed using MWCNTs as a sorbent in gas chromatography-mass spectrometry (GC-MS) in order to analyze the mixture of 12 pesticides with LOD of 0.01 ng/mL over a linear dynamic range of 0.04–4 ng/mL (Shuo Wang et al. 2007). The same strategy has used gas chromatography nitrogen-phosphorus detector (GC-NPD) for the determination of several organophosphate pesticides in soil and fruit juice samples (Asensio-Ramos et al. 2009; Ravelo-Pérez et al. 2008). These findings have demonstrated that several analytes can be detected simultaneously in short-time interval with accuracy. However, these approaches employ the chromatographic separation of the analytes. In this regard, Al-Degs and co-workers have proposed a strategy to determine various pesticides concurrently using MWCNT-SPE along with multivariate calibration instead of chromatography techniques (Al-Degs et al. 2009). The method produces reproducible results at lower cost and exhibits detection limits of 3, 2, and 3 ng/mL for atrazine, methidathion, and propoxur, respectively.

A facile electrochemical sensor made up of a hybrid nanocomposite of copper oxide (CuO) nanowires with single-walled carbon nanotubes (SWCNTs) deposited over glassy carbon electrode (GCE) detects malathion organophosphate (Huo et al. 2014). The sensor combines the selectivity of Cu containing compounds toward thiol group and electrical conductivity of SWCNTs. The so developed platform measures the amount of malathion adsorbed through cyclic voltammetry (CV), electrochemical impedance spectroscopy (EIS), and differential pulse voltammetry (DPV). Under the optimized conditions, sensor shows high specificity and sensitivity with a detection limit of 0.3 nM over a wide linear dynamic range. Another voltammetry-based electrochemical sensor has been developed for diazinon pesticide quantification based on the reduction of analyte on TiO_2 nanoparticles covered multi-walled carbon nanotubes deposited on the glassy carbon electrode (Ghodsi and Rafati 2017). The synthesized nanocomposite exhibits synergistic effect toward electrocatalytic reduction of diazinon resulting in high sensitivity, rapid detection, and LOD of 3 nM.

As compared to carbon nanotubes, graphene consists of one-atom thick sp^2-hybridized carbon sheet made up of interconnected six-membered rings (Tkachev et al. 2011). They exhibit twice surface area as compared to single-walled carbon nanotubes (Pumera et al. 2010). The other significant properties that make graphene promising material for sensing applications are high mechanical strength, elasticity, and absence of metal impurities which affect sensor accuracy (Pumera et al. 2010; Pumera and Miyahara 2009). Graphene is an excellent conductor of electricity. The heterogeneous electron transfer occurs at basal plane defects or edges of the graphene, and its high surface area contributes to numerous defects resulting in multiple electroactive sites (Aragay et al. 2012).

Wu and co-workers have investigated the β-cyclodextrin dispersed graphene (β-CD graphene) as an efficient sorbent for electrochemical detection of nitroaromatic organophosphate pesticide, methyl parathion (Shuo Wu et al. 2011). Many factors advocate the candidature of graphene for highly sensitive and selective detection of organophosphate pesticides. The ultra-high surface area endows graphene with high adsorption capacity, the presence of delocalized π-electrons establishes π-π stacking interaction with aromatic rings, and high conductivity promotes the electron transfer from the electrode to the target molecule (Novoselov and Geim 2007; Jinmei Chen et al. 2010a; Jing Zhang et al. 2010a). Also, the reaggregation of graphene nanosheets during reduction has been overcome by functionalizing graphene with a dispersive reagent, β-cyclodextrin. The proposed sensing platform exhibits LOD of 0.05 ppb which is significantly lower than previously reported sorbent-based electrochemical sensors. The strategy has also employed Au nanoparticle-decorated graphene nanosheet-modified glassy carbon electrode (GCE) for sensing of nitroaromatic organophosphate pesticides (Gong et al. 2011). The developed approach uses electrodes as solid-phase extraction (SPE) matrix for stripping voltammetry-based sensing of methyl parathion with a LOD of 0.6 ng/mL. The designed nanoplatform combines the high catalytic activity and excellent conductivity of Au nanoparticles with the graphene nanosheets for enhanced sensitivity and stability. Another nanocomposite of graphene oxide (GO) with chitosan (CS) has been investigated for electrochemical quantification of methyl parathion (Shanli Yang et al. 2012). Chitosan possesses biocompatibility and high adsorption capacity. The GO-CS nanocomposite-modified GCE can detect methyl parathion down to 0.8 ng/mL concentration within the wide linear dynamic range of 4–400 ng/mL. Ma et al. have explored graphene-armored hollow fiber liquid-phase microextraction (HF-LPME) in combination with high-performance liquid chromatography (HPLC) for detection of some carbamate pesticides in fruit samples (Ma et al. 2014). HF-LPME allow high analyte preconcentration of analytes before detection, facilitate cleanup of pollutant as they act as filters, and can be disposed of after use due to low cost. The achievable LOD of the fabricated sensing platform is 0.2 ng/g for carbaryl within the concentration range of 1–100 ng/g. Magnetic graphene composed of iron counterparts has also been used for SPE/HPLC determination of carbamate pesticides (metolcarb, baygon, and methiocarb) in tomato samples (Zhigang Liu et al. 2016). Furthermore, Shi and co-workers have packed graphene as sorbent material into 1 ml pipette tips for extraction of carbamate pesticides such as isoprocarb, pirimicarb, diethofencarb, and other from fruit juice samples (Shi et al. 2016). The extracted samples have been quantified for different carbamates using tandem mass spectrometry (UHPLC-MS/MS) and ultra-high performance liquid chromatography with LOD in the range of 2.2–3.3 ng/L for different carbamates.

Organophosphate pesticides have been analyzed using an electrochemical impedance-based free-enzyme electronic tongue (e-tongue) composed of four sensing units deposited on graphene hybrid nanocomposites (Facure et al. 2017). The highly conductive nanocomposite has been prepared by the reduction of graphene oxide using gold nanoparticles and conducting polymers (poly(3,4-ethylenedioxythiophene) polystyrene sulfonate (PEDOT:PSS) and polypyrrole) deposited onto gold interdigitated electrodes. The fabricated sensing electrode is shown in Fig. 2.5. Impedance spectroscopy measurements reveal that the electronic tongue is able to detect and discriminate organophosphate pesticides at nanomolar concentration even in real samples. Recently, Au nanoparticle-decorated three-dimensional graphene doped with sulfur and nitrogen atoms exhibiting improved electrical conductivity has been investigated for a nonenzymatic, selective, and sensitive electrochemical sensing of carbaryl (Rahmani et al. 2018). The developed sensor achieves a linear response for carbaryl in the range of 0.004–0.3 μ M with a LOD of 0.0012 μ M in water, fruit, and vegetable based on differential pulse voltammetry.

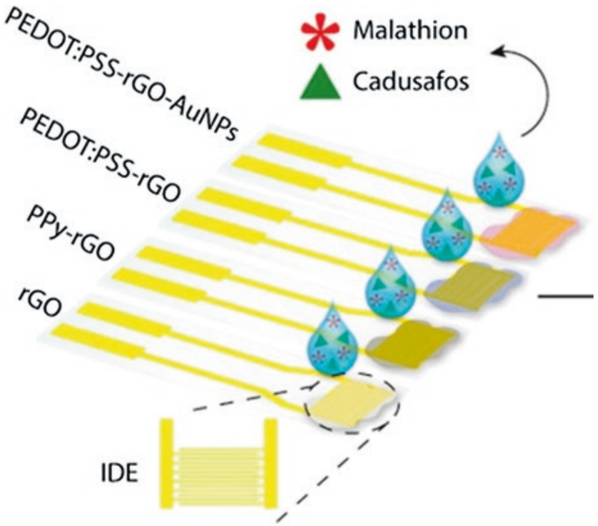


Fig. 2.5 Schematic of electronic tongue for detection of organophosphate pesticides fabricated gold interdigitated electrode modified using gold nanoparticles and conducting polymers poly(3,4-ethylenedioxythiophene) polystyrene sulfonate and polypyrrole in conjugation with reduced graphene oxide. *IDE* interdigitated electrode, *PEDOT:PSS* poly(3,4-ethylenedioxythiophene, *PPy* polypyrrole, *rGO* reduced graphene oxide polystyrene sulfonate. (Reproduced from Facure et al. (2017), with permission from Elsevier)

Molecularly imprinted polymer (MIP)-coated ionic liquid-graphene composite-based glassy carbon electrode has also been explored for the electrochemical detection of methyl parathion (Lijuan Zhao et al. 2013a). MIP is composed of methacrylic acid monomers, ethylene glycol dimethacrylate cross-linkers, and methyl parathion template. The incorporation of ionic liquid promotes the conductivity and solubility of graphene by shielding π-π stacking interaction among graphene nanosheets. The detector can quantify methyl parathion up to detection limit of 6 nM within linear dynamic range of 0.01–7 μM with a sensitivity of 1.25 μA/μM. An analytical square-wave stripping voltammetry-based approach for simultaneous determination of two pesticides, carbendazim and isoproturon, with single drop analysis using graphene has been proposed (Noyrod et al. 2014). The method involves electrochemical detection followed by univariate analysis of the various parameters of the measurement. The portability, low cost, and sensitivity of the sensor support its applicability in real samples up to 0.11 and 0.02 μg/mL for carbendazim and isoproturon, respectively.

Nguyen and group have proposed a surface-enhanced Raman spectroscopy (SERS)-based detection platform for three pesticides, namely, carbaryl, azinphos-methyl, and phosmet using graphene-gold film-gold nanorod (G-Au-AuNR) nanocomposite (Fig. 2.6) (Nguyen et al. 2014). The substrate exhibits excellent Raman signals for the selected analytes and could subsequently quantify carbaryl, azinphos-methyl, and phosmet down to 5, 5, and 9 ppm concentration. The platform shows

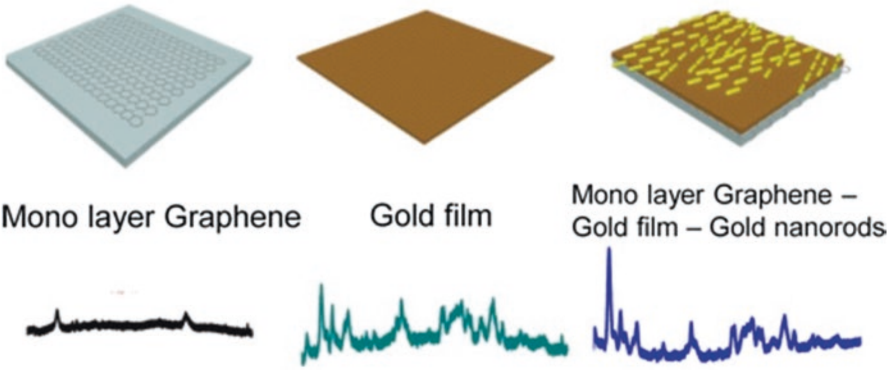


Fig. 2.6 Nanoplatform developed from graphene-gold film-gold nanorod exhibiting excellent Raman signal for surface-enhanced Raman spectroscopy-based detection of three pesticides, namely, carbaryl, azinphos-methyl, and phosmet. (Reproduced from Nguyen et al. (2014), with permission from ACS Publications)

excellent potential to fabricate sensitive, flexible, and lightweight sensors for food safety applications. Another group of researchers has synthesized a ternary particle composed of silver (Ag), graphene oxide (GO), and magnetic ferroferric oxide (Fe_3O_4) nanoparticles (Zhigang Liu et al. 2016). The ternary particles deposited layer-by-layer result in the development of highly adsorptive magnetic graphene SERS substrate. Owing to the exceptional properties of Fe_3O_4@GO@Ag ternary complex, a new technique called surface magnetic solid-phase extraction (SMSPE) has been proposed for detection of pesticides using SERS-based sensor. The sensitivity of the detection process is high enough to detect 0.48 and 40 ng/cm^2 of thiran and thiabendazole pesticides on the fruit peels, respectively.

The electrochemical sensitivity of graphene-based sensors improves by doping of the substrates (Pop et al. 2017; Lihua Wu et al. 2015). Wu et al. have prepared poly(3-methylthiophene)/nitrogen-doped graphene-modified glassy carbon electrode (P3MT/NGE/GCE) through simple drop-casting of NGE and subsequent deposition of the P3MT film (Lihua Wu et al. 2015). The developed electrodes electrochemically detect the trace levels of phoxim pesticide. NGE exhibits good catalytic property, high conductivity, and large surface area. The porous conducting polymer P3MT provides sufficiently high number of active sites for adsorption of the analyte and easily deposits electrochemically. Therefore, with combinatorial effects of NGE and P3MT, the electrode detects phoxim amperometrically up to the detection limit of 6.4 nM within linear ranges of 0.02–2 μM. Graphene-modified boron-doped diamond electrode has also been investigated for the individual as well as simultaneous detection of two pesticides (carbaryl and paraquat) from the buffer as well as natural apple juice samples with high sensitivity (Pop et al. 2017). The boron-doped diamond (BDD) electrode possesses a broad potential window and low background noise along with high stability which enhances the commercial applicability of the developed sensing platform.

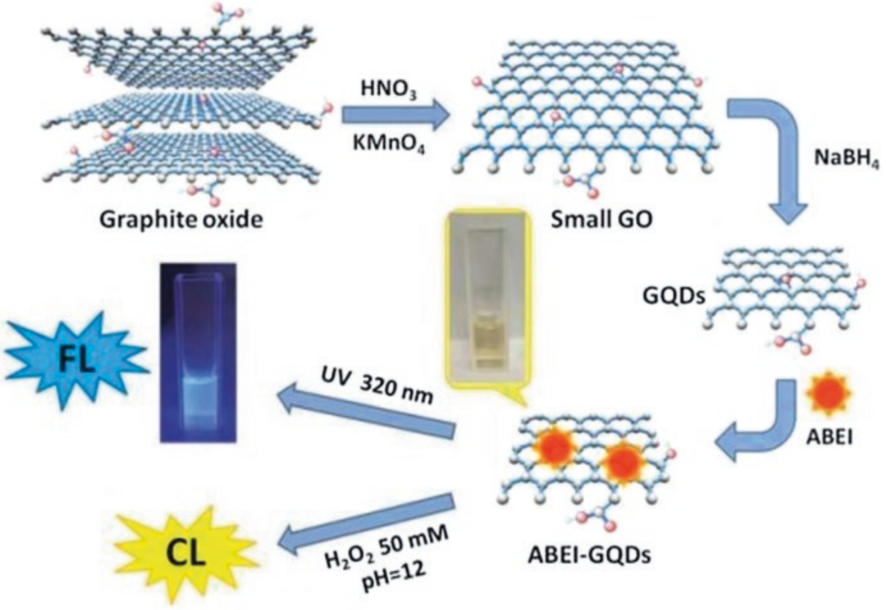


Fig. 2.7 Synthesis of chemiluminescent and fluorescent graphene quantum dots employed for the dual-signal detection of five pesticides, namely, dimethoate, chlorpyrifos, dipteres, flubendiamide, and thiamethoxam. *ABEI* (aminobutyl)-N-(ethylisoluminol), *HNO_3* nitric acid, *$KMnO_4$* potassium permanganate, *$NaBH_4$* sodium borohydride, *GO* graphite oxide, *GQDs* graphene quantum dots. (Reproduced from Gao et al. (2017), with permission from Royal Society of Chemistry)

Apart from carbon nanotubes and graphene nanosheets, graphene quantum dots (GQDs) have been employed for optical sensing of pesticide residues (Zor et al. 2015; Gao et al. 2017). GQDs exhibit low toxicity, resistance to photobleaching, high surface area, functionality, aqueous solubility, and exceptional optoelectronic properties (Shen et al. 2012; Ming Li et al. 2012). A study has reported the use of magnetic silica beads/graphene quantum dots/molecularly imprinted polypyrrole (mSGP) to capture and detect tributyltin pesticide efficiently. The developed mSGP composite exhibits magnetic properties for preconcentration of the analyte, solubility in the aqueous phase, selectivity, and photoluminescence as optical transduction which is quenched by fluorescence resonance energy transfer (FRET) upon the binding of the analyte. The detection system reaches the detection limit of 12.78 and 42.56 ppb for tributyltin in water and seawater, respectively. Another GQDs-based chemiluminescent and fluorescent dual-signal sensor array has been developed five pesticides including dimethoate, chlorpyrifos, dipteres, flubendiamide, and thiamethoxam (Gao et al. 2017). The synthesis strategy of GQDs exhibiting dual signal is shown in Fig. 2.7. The N-(aminobutyl)-N-(ethylisoluminol) (ABEI)-functionalized graphene quantum dots (ABEI-GQDs) exhibit exceptional chemiluminescence and fluorescence emission. The detection strategy with dual-signal efficiently distinguishes varying concentration of different pesticides efficiently.

2.6.5 Metal-Organic Frameworks

Among a myriad of nanomaterials, metal-organic frameworks (MOFs) have surfaced as the promising advanced functional nanomaterials for a verity of the analyte-sensing applications (Gassensmith et al. 2014; Shengyan Wang et al. 2017; Assen et al. 2017; Si-Si Zhao et al. 2016). These are hybrid nanostructures composed of interconnected inorganic metal ions and organic linkers. MOFs possess attributes of stability, high selectivity, luminescence, diverse functionality, the ability of post-synthetic modification (PSM), and suitable signal transduction (Vikrant et al. 2018). Recently, research activity has been dramatically stimulated to promote electron transfer and lower the work over potential along with tuning of luminescent MOFs by host-guest interactions for employing MOFs as electrochemical and optical sensors (Gassensmith et al. 2014; Kuppler et al. 2009).

MOFs contain electron-rich centers in the organic ligand counterpart of their structure. Various research groups have extensively investigated MOFs for the detection of nitro group (electron withdrawing) containing organophosphate pesticides (Rawtani et al. 2018; Rostamnia and Mohsenzad 2018). The Lewis base character of organic ligand allows easy diffusion of guest organophosphate pesticides into MOF pores, allowing their highly sensitive and selective sensing (Qian et al. 2017).

Zheng and co-workers have reported for the first time the potential of luminescent MOF [Zn(pbdc)(bimb)·(H_2O)] for the detection of methyl parathion (Xiaofang Zheng et al. 2014). The incubation of methyl parathion with MOF quenches the luminescence of Zn-MOF in dimethylformamide (DMF) solution. The sensing approach is highly selective toward methyl parathion in the presence of other non-specific pesticides including isocarbophos, acetamiprid, phenamiphos, and methomyl. As observed, MOF's emission completely quenches at 1 mM concentration of the analyte with a detection limit of 2.5 μM. The luminescence quenching is due to the photoexcited electron transfer from organic ligand to electron withdrawing $-NO_2$ group of organophosphate pesticide, methyl parathion. The quenching behavior of nitrotoluene (NT), 1,4-dinitrobenzene (1,4-DNB), and 2,4-dinitrotoluene (2,4-DNT) toward Cd-HDMA and Zn-HDMA MOF (HDMA= protonated dimethylamine cation) also depicts the same fact (Guan-Yao Wang et al. 2014a). Inspired by this work, Kumar and co-workers demonstrated the chemosensing potential of cadmium-based NMOF-1 for quantification of different organophosphate pesticides including methyl parathion, parathion, fenitrothion, and paraoxon (Kumar et al. 2014a). Substantially, a turn-off fluorescence sensor designed by examining the emission of NMOF at 436 nm in the presence of organophosphate pesticides exhibits a very low detection limit of 1 ppb for each of the analyte. Further, the same group of researchers has extended the chemosensing of organophosphate pesticides using another luminescent MOF-5 with an achievable limit of detection of 5 ppb within the concentration range of 5–60 ppb (Pawan Kumar et al. 2014b). The generation of electrons and holes in the conduction and valence is found to be responsible for attenuation of the luminescence emission of NMOF-1 and MOF-5, respectively (Pawan

Kumar et al. 2014b; Allendorf et al. 2009). The interaction of pesticide molecules with trapped or photogenerated carriers initiates the redox processes (Cui et al. 2011). As a result, equilibrium is set up between the pesticide molecules and the uncomplexed or complexed MOF particles leading to quenching. Recently, another group of researchers has explored luminescent Cd-MOF [$Cd_{2.5}$(PDA)$(tz)_3$] (PDA= 1,4-phenylenediacetate and tz= 1,2,4-triazolate) for the sensitive detection of azinphos-methyl in aqueous medium (Singha et al. 2017). The emission of Cd-MOF in the UV region at 290 nm is significantly reduced at 40 μM concentration of the analyte with a LOD of 16 ppb in the presence of interfering non-specific pesticides.

Tao and co-workers have investigated an entangled luminescent Zn-MOF made up of two different ligands possessing pillared-layered structure for the sensing of 2,6-dichloro-4-nitroaniline (DCN) pesticide (Chen-Lei Tao et al. 2017). The luminescence of Zn-MOF has been observed to undergo repressive quenching upon interaction with a trace quantity of DCN resulting in sufficiently low LOD of 0.13 ppm. The luminescence quenching is attributable to the hydrogen-bonding interactions between the amino group of *p*-nitroaniline in DCN and the oxygen of the organic ligand, 4,4′-biphenyl dicarboxylate (bpdc).

Apart from optical-sensing platform, there are various reports of MOF-based electrochemical sensors for pesticides in the literature. One such sensor for glyphosate uses molecularly imprinted polymer (MIP)-MOF thin films prepared by the electropolymerization of *p*-aminothiophenol (PATP) and PATP-modified Au nanoparticles as a template (Do et al. 2015). The so formed films exhibit specificity due to the cavities formed after passive extraction of embedded glyphosate molecules from the template. Also, there is the tendency of glyphosate to form hydrogen bonds with aniline groups of PATP which contributes toward high specificity of the platform. The MIP-MOF sensor exhibits detection limit of 0.8 pg/L for glyphosate in the presence of $[Fe(CN_6)]^{3-/4-}$ redox probe through linear sweep voltammetry. MOFs are excellent sorbent due to the high surface area and exhibit a strong interaction with nitroaromatic compounds through hydrogen bonding and π-π stacking (Wen et al. 2010). Based on both these attributes, Cd-MOF-modified glassy carbon electrode (MOF/GCE) detects the trace level detection of methyl parathion using (Kempahanumakkagari et al. 2018). The Cd(2,2′,4,4′-bptcH_2)]n MOFs (bptc = 2,2′,4,4′-biphenyltetracarboxylic acid) acts as sorbent matrix for preconcentration of the analyte. The result is highly selective and reproducible quantification of methyl parathion up to 0.06 μg/mL detection limit within the linear dynamic range of 0.01–0.5 μg/mL.

The formation of MOF composites with metals and their oxides has been observed to improve the sensing capabilities considerably. For instance, Zhang et al. have explored a nanocomposite of MIL-101 (Fe) with magnetite (Fe_3O_4) nanoparticles prepared via a novel in situ solvothermal process for sensing of six organophosphate pesticides using magnetic solid-phase microextraction (SPME) technique (Suling Zhang et al. 2014). Among the including organophosphate pes-

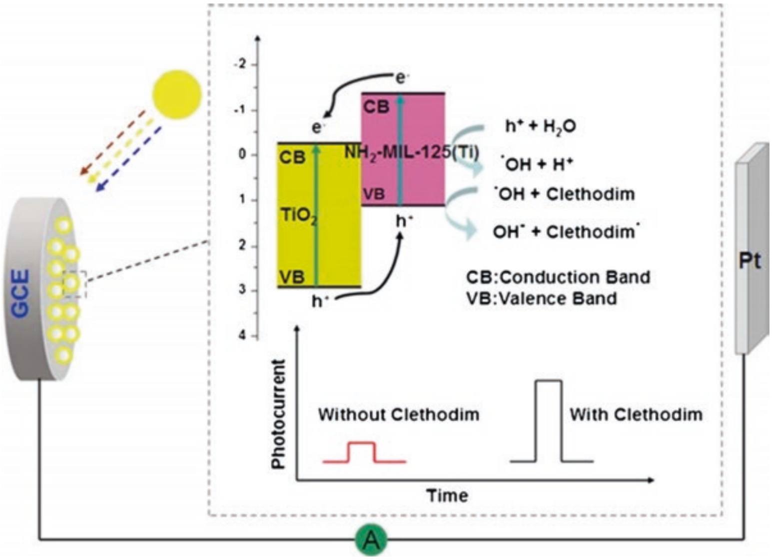


Fig. 2.8 Schematic illustration for the photoelectrochemical mechanism for clethodim oxidation at NH_2-MIL-125(Ti)/TiO_2 modified glassy carbon electrode. On photochemical activation with visible light, the excited electrons are produced and transferred to electrode, and the positive hole generated on the composite surface reacts with hydroxyl radicals which are captured by clethodim resulting into improved charge separation efficiency and photocurrent. *GCE* glassy carbon electrode. (Reproduced from Jin et al. (2015), with permission from Springer)

ticides such as malathion, parathion, methyl parathion, dimethoate, dichlorvos, and methamidophos, the lowest detection limit has been observed for parathion as 0.21 ng/mL in real samples of hair and urine. Another glassy carbon electrode (GCE) modified with nanocomposite made up of gold nanoparticles, L-cysteine, silica, and Cu-MOF (Au-SH-SiO_2NPs@Cu-MOF) has been employed for chronoamperometry-based electrochemical detection of hydrazine in the aqueous phase (Hosseini et al. 2013). The composite electrode demonstrates a significant anodic peak around 0.53 V with a gradual rise in the peak current with increasing concentration of hydrazine. The electrode can quantify hydrazine over broad linear detection range of 0.04–500 μM with very low 0.01 μM detection limit and appreciable stability and reproducibility.

Thereafter, Jin and co-workers have explored the amino-MIL 125 (Ti)/TiO_2 nanocomposite-modified glass carbon electrode (GCE) for photoelectrochemical (PCE)-based detection of herbicide clethodim as shown in Fig. 2.8 (Jin et al. 2015). The TiO_2 nanoparticles exhibit ability to separate source and detector signal, thereby enhancing the signal-to-noise ratio. This improves the sensitivity of amino-MIL 125 (Ti)-based sensor. Following visible-light photochemical activation, the composite produces excited electrons and transfers the excite electrons to GCE. The positively charged holes created on the surface of the composite react with H_2O generating hydroxyl radicals (•OH) which are captured by clethodim, and the charge separation efficiency improves. The enhanced photocurrent is found to increase linearly with the concentration of the analyte over a range of 0.2–25 μM with a detection limit of 10 nM.

The strong candidature of the specified materials in nanosensors is attributed to their nanosized influenced characteristics, high surface area, and intrinsic optoelectronic properties of nanomaterials. Furthermore, the incorporation of bioprobes as recognition elements in nanosensors or functionalization of nanomaterials used in sensors with biomolecules increases the specificity toward analyte and is eco-friendly to use. Biological probes generally employed are nucleic acids, whole cells, antibodies (Ab), and enzymes. Therefore, these nano-biosensors or simply biosensors may offer high sensitivity, selectivity, portability, cost-effectiveness, and in situ detection.

2.7 Biofunctionalized Nanomaterials for Sensing of Pesticides: Biosensors

A biosensor is an analytical device composed of a signal transducer linked to a biological recognition probe, which could be an enzyme, antibody, cell, or nucleic acid (Jin et al. 2015; Du et al. 2008; Grennan et al. 2003; Lei et al. 2004; Nowicka et al. 2010). An explosion of research in the area of sensing has yielded a myriad approaches making use of nanomaterials as transduction substrates for the development of biosensors. The synergy between nanotechnology and biomolecules enhances the specificity and response reproducibility toward analyte. Furthermore, the immobilization on the substrates provides better stability to the biomolecules for leach out prevention and better reusability. Therefore, these nanomaterial-based biosensors may offer high sensitivity, selectivity, portability, cost-effectiveness, and in situ detection. Many such biosensors have been proposed by various research groups to detect different pesticides in food and water samples at trace level.

2.7.1 Whole-Cell Biosensors

Microbial and mammalian cells are increasingly being used as the bioprobes to monitor the different environmental pollutants. Living cells are more stable biomolecules as compared to antibodies, nucleic acids, and enzymes due to the protective envelope. The microbial sensor employs the physiological change of living cells such as oxygen consumption, mobility, genetic activity, and surface electrochemical potential as the sensing mechanism (Kintzios 2007). The use of whole cells for detection of pesticides works on the basis of the catalytic reactions facilitated by large number of membrane-bound enzymes (Chouteau et al. 2005). The enveloping of biocatalysts with cell walls eliminates the diffusional mass transport resistance (Mulchandani et al. 2001).

Rainina and co-workers have developed a microbial organophosphate detection platform with cryoimmobilized recombinant *Escherichia coli* cells entrapped in poly(vinyl)alcohol forming gel spheres (Rainina et al. 1996). The cells express organophosphate hydrolase (OPH) enzyme captured in a flow-through system having a pH-sensitive electrode. The expressed OPH is capable of generating protons from hydrolysis of each molecule of organophosphate pesticide which forms the basis of potentiometric detection of paraoxon organophosphate. The developed biosensor can quantify paraoxon in 20 min within the wide linear detection range of 1–1000 μM. Another group of researchers has fabricated a similar potentiometric biosensor using wild-type non-recombinant strain of *Flavobacterium* sp. (Gäberlein et al. 2000). The work used the cytoplasmic membrane fractions for the construction of biosensor as 90% of OPH activity is limited to cytoplasmic membrane (Mulbry and Karns 1989). The achievable linear detection range using the mentioned sensing platform is 10–470 μM for parathion and chlorpyrifos. Mulchandani et al. have described an amperometric microbial sensor for the direct quantification of paraoxon and methyl parathion down to a concentration of 0.2 μM and 1 μM, respectively (Mulchandani et al. 2001). In this work, the researchers have immobilized genetically engineered cells of *Moraxella* sp. expressing OPH enzyme onto the carbon working electrode of three electrode electrochemical cells. The OPH catalyzes the hydrolysis of organophosphate pesticides into less toxic electrochemically active *p*-nitrophenol. The oxidation current produced with the generation of *p*-nitrophenol is detected and correlated to the analyte concentration. The proposed sensor is highly selective with excellent sensitivity and exhibits excellent reproducibility and stability. Recently, a stable and sensitive *Sphingomonas* sp.-based optical microplate biosensor has been developed by functionalizing silica nanoparticles (SiNPs) with polyethyleneimine followed by integration of functionalized silica nanoparticles (fSiNPs) with *Sphingomonas* sp. cells for methyl parathion sensing (Mishra et al. 2017). The biohybrid of *Sphingomonas* sp. fSiNPs captured on the microplate wells associates with the optical transducer providing linear range of response for methyl parathion (0.1–1 ppm). The biosensor exhibits high storage stability (up to 180 days), sensitivity, and stability.

Chouteau and co-workers have used *Chlorella vulgaris* microalgae to develop a bi-enzymatic conductometric biosensor (Chouteau et al. 2005). The cells of microalgae inherently express two enzymes, namely, alkaline phosphatases and esterases (Durrieu and Tran-Minh 2002). The two enzyme systems either consume or produce charged species, resulting into a change in the composition of the sample. This change in ionic strength is analyzed conductometrically and enables quantification of methyl parathion, methyl paraoxon, and carbofuran. Mammalian neuroblastoma N2a cells entrapped in calcium alginate beads connected to silver working electrode have aided the development of an electrochemical sensor for organophosphate pesticides (Mavrikou et al. 2008). It is well established that organophosphate pesticides inhibit the activity of acetylcholinesterase (AChE) enzyme responsible for nerve conduction which forms the basis of detection. The inhibition of AChE enzymatic activity in the presence of organophosphate pesticides brings about changes in the

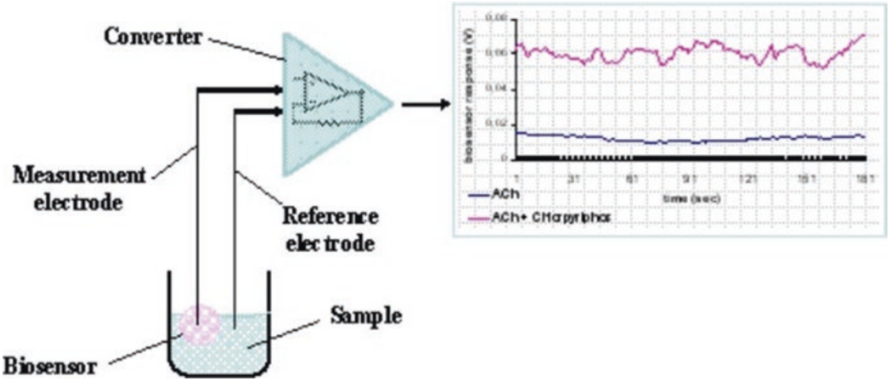


Fig. 2.9 Schematic of the immobilized whole-cell biosensor. In this, mammalian neuroblastoma N2a cells are entrapped in calcium alginate bead which is connected to silver working electrode. The presence of organophosphate pesticides inhibits the enzymatic activity of acetylcholinesterase resulting into change in the membrane potential of the immobilized N2a cells. The reference electrode and the measuring electrode are placed in the liquid sample and the immobilized cell-gel bead (2 mm diameter), respectively. Measurement and reference electrodes are wired to the data converter. The sensor displays voltammetry-based response in the presence of acetylcholine (blue) and acetylcholine + acetylcholinesterase inhibitor chlorpyrifos (red). *ACh* acetylcholine. (Reproduced from Mavrikou et al. (2008), with permission from MDPI Publications)

membrane potential of the immobilized N2a cells measured according to bioelectric recognition assay (BERA) (Fig. 2.9). The sensor response has been tested for organophosphate pesticides, carbamate, and chlorpyrifos instantly in a concentration-dependent pattern down to 1 ppb concentration in tobacco leaf samples.

Various research groups have also investigated the whole-cell-based optical sensors for pesticides. One such example includes entrapment of porous matrix-immobilized microalgae *Chlorella vulgaris* cells on a quartz microfiber filter for sensing of herbicides up to sub-ppb levels (Védrine et al. 2003). The change in the fluorescence emission of algal chlorophyll in the presence of herbicide is collected at the optical fiber tip and sent to fluorimeter for correlated quantification of atrazine. Similarly, Shing et al. have developed a fluorescent biosensor for chlorpyrifos using cyanobacterium *Anabaena torulosa* cells immobilized onto poly(2-hydroxyethyl methacrylate) (pHEMA) with enhanced storability (Wong et al. 2013). *Flavobacterium* sp. expressing OPH enzyme have also been trapped in glass fiber and used as bioprobe for optical fiber-based detection of methyl parathion down to detection limit of 3 μM (Jitendra Kumar et al. 2006). The direct correlation between the concentration of methyl parathion hydrolyzed and chromophoric product, *p*-nitrophenol (λ_{max} 410 nm), forms the basis of detection. Lately, the group has proposed a microbial sensor for organophosphate pesticides composed of a Clark-type electrode and recombinant *p*-nitrophenol degrading/oxidizing OPH expressing bacteria *Pseudomonas putida*. The OPH-mediated catalysis of organophosphate pesticides results in the formation of *p*-nitrophenol which further degrades to CO_2 with consumption of oxygen. The subsequent change in the oxygen reduction current then forms the basis of quantification of analyte (Mulchandani et al. 2006; Lei et al. 2005a, b).

The primary limitation of cell-based biosensors is lower sensitivity and non-selectivity toward individual bioactive compound (Mavrikou et al. 2008). Also, there is limited diffusion of substrates and products across the cell envelope leading to slow response and requirement of environment maintenance for cell viability (Sassolas et al. 2008).

2.7.2 Nucleic Acid Biosensors

Deoxyribonucleic acid (DNA)-based biosensors employ the complementary binding of single-stranded nucleic acid sequences. They are developed by the attachment of single-stranded DNA (ssDNA) probe onto a substrate which can bind to complementary target DNA sequence (Sassolas et al. 2008). The pesticides are well-known mutagenic pollutants. Therefore, in the presence of these pesticides, the target DNA is damaged and cannot bind to immobilized complementary DNA probe. The hybridization of probe and target is quantified and correlated to the initial concentration of the analyte (pesticide, in this case) which forms the basis of DNA biosensors.

An electrochemical DNA sensor has been developed to determine DNA damage caused by various pesticides including 2,4-D, atrazine, carbofuran, paraoxon, glufosinate ammonium, and difluorobenzuron (Nowicka et al. 2010). For this, biotinylated DNA probe immobilized onto the surface of streptavidin-modified gold disk electrode hybridizes with biotinylated complementary DNA target as shown in Fig. 2.10. The hybridized biotinylated DNA then attaches to ferrocene streptavidin. The proximity of electrode to ferrocene molecules induces an oxidation current signal. In the presence of pesticides, hybridized DNA unwinds resulting in the decreased amount of ferrocene in proximity of the electrode surface and subsequent reduction in ferrocene oxidation current.

Ellington and group have discovered “aptamers,” specific nucleic acid sequences that bind with high affinity to specific non-nucleic acid targets such as proteins, pathogens, metal ions, and other molecules (Cox and Ellington 2001). The SELEX (systematic evolution of ligands by exponential enrichment) technique is used to generate deoxyribonucleic acid (DNA) or ribonucleic acid (RNA) oligonucleotide-based aptamers. Aptamers exhibit characteristics of stability, ease of functionalization, reversible denaturation, accuracy, and reproducible chemical production. Fan and co-workers have reported the first use of aptamers immobilized onto an Au nanoparticle-modified gold electrode for highly selective sensing of pesticide acetamiprid (Lifang Fan et al. 2013). The resulting sensing platform has been evaluated using electrochemical impedance spectroscopy (EIS)-based label-free sensing of the pesticide. The enhancement of electron transfer resistance (R_{ct}) increases in the presence of acetamiprid. The rise in Rct value directly correlates to the concentration of the analyte which forms the basis of the proposed sensor with a detection limit of 3.14 nM within linear dynamic range of 5–600 nM. The sensitivity of the above aptamer-based impedimetric biosensor has been significantly enhanced by using Au

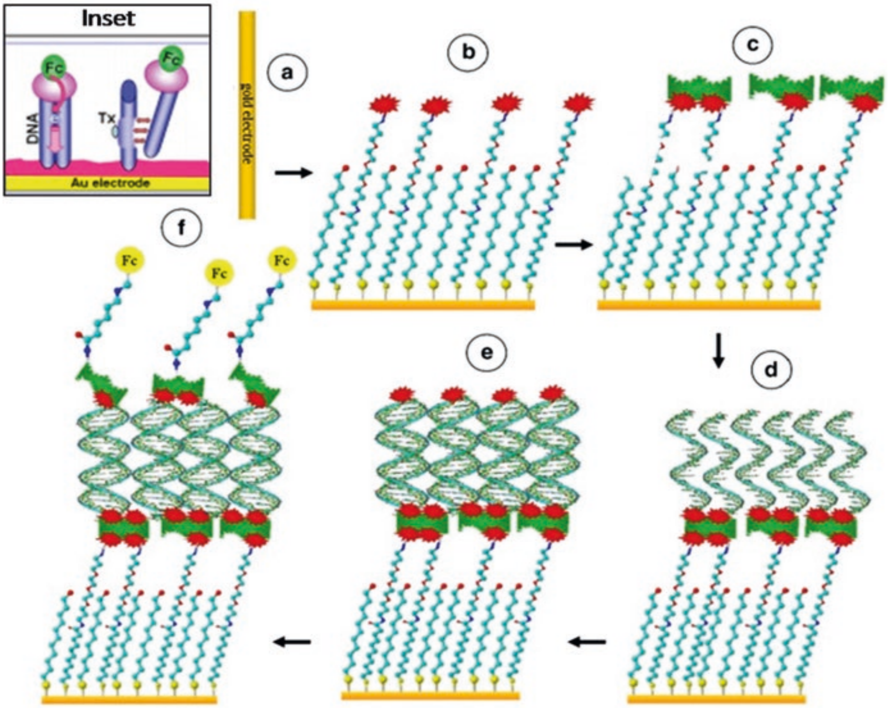


Fig. 2.10 Schematic for development of DNA-hybridization-based sensor. (**a**) A bare gold piezo-electrode; (**b**) electrode after deposition of a mixed self-assembled monolayer of 11-mercapto-1-undecanol and binary 11-mercapto-1-undecanol; (**c**) attachment of streptavidin; (**d**) capture of biotinylated single-stranded probe-DNA; (**e**) hybridization of probe-DNA with single-stranded target DNA from solution on the sensing platform; (**f**) functionalization with a layer of redox transducer ferrocene-labeled streptavidin. Inset: schematic view of the conducting DNA duplex and damaged nonconducting DNA strand. *Fc* ferrocene. (Reproduced from Nowicka et al. (2010), with permission from Elsevier)

nanoparticles, multi-walled carbon nanotubes and reduced graphene oxide (AuNPs-MWCNTs-rGO) composite as immobilization substrate for acetamiprid-specific aptamer (Fei et al. 2015). This aptamer displays extremely low LOD of 17 fM for acetamiprid over the broad linear concentration range of 50 fM–10 μM.

Different research groups have investigated aptamer-based optical detection platforms for monitoring of various pesticides (Weerathunge et al. 2014; Bixia Lin et al. 2016; Tingting Tang et al. 2016). A colorimetric sensor has been developed using the combined intrinsic peroxidase activity of Au nanoparticles exhibiting high specificity and affinity of aptamers to detect neurotoxic acetamiprid pesticide (Weerathunge et al. 2014). The acetamiprid-specific S-18 aptamer molecules have been immobilized onto Au nanoparticles and inhibit the peroxidase activity of gold nanoparticles. In the presence of target analyte acetamiprid, the aptamers are released from the surface of Au nanoparticles in an analyte concentration-dependent manner resulting in reactivated peroxidase activity of gold nanoparticles. The reversible inhibition of peroxidase activity of Au nanoparticles is monitored either directly through visual monitoring or through the formation of changed color reaction product or by using UV-Vis quantification. This approach allows detection of acetamiprid down to a concentration of 0.1 ppm in 10 min. Bala et al. have reported the gold nanoparticle-based aptasensor to detect phorate colorimetrically in apple with high selectivity (Bala et al. 2016). The method is based on the random-coiled structure of aptamer which keeps the nanoparticles well dispersed and provides stability to Au nanoparticles. However, on the addition of pesticide, the aptamer acquires such a conformation which leads to the aggregation of Au nanoparticles. Consequently, the solution color changes from red to blue. The linear response of the method ranges from 0.01 nM to 1.3 μ M with a LOD of 0.01 nM. Moreover, the proposed assay could be applied to real samples for the rapid and efficient screening of phorate. Another colorimetric sensing platform for malathion employs aptamer, cationic peptide in conjugation with unmodified gold nanoparticles. The detection relies on the optical changes of gold nanoparticles on aggregation (Bala et al. 2017). The peptide attached to the aptamer releases the gold nanoparticles free resulting in red color visualization. However, the association of aptamer with malathion renders the peptide free so as to bring about aggregation of the nanoparticles turning the suspension blue. The method delivers a linear response from 0.01 to 0.75 nM concentration of the analyte with detection limit as low as 1.94 pM along with practical applicability in real samples.

The use of quantum dot-DNA aptamer conjugates coupled with capillary electrophoresis has also been explored for the ratiometric sensing of organophosphate pesticides based on laser-induced fluorescence (LIF) (Tingting Tang et al. 2016). Broadly specific aptamers immobilized onto highly fluorescent water-soluble CdTe/CdS core-shell quantum dots through intermediating amino-modified oligonucleotide (AMO) are partially complementary to aptamer probe. The resulting quantum dot-AMO-aptamer duplex is cleaved on the addition of organophosphate pesticides releasing quantum dot-AMO conjugate. The observed change in the ratio of fluorescence peak intensity of quantum dot AMO to quantum dot-AMO-aptamer duplex facilitates the sensing of organophosphate pesticides through capillary electrophoresis laser-induced fluorescence (CE-LIF). The applied strategy detects organophosphate pesticides, namely, phorate, isocarbophos, profenofos, and omethoate, up to a concentration of 0.20, 0.17, 0.10, and 0.23 μM, respectively. Lin and co-workers have proposed a more sensitive quantum dot-aptamer conjugate-based “turn-on” fluorescence sensor for efficient quantification and imaging of acetamiprid pesticide (Bixia Lin et al. 2016). The acetamiprid-specific aptamer-modified ZnS:Mn quantum dots (ZnS:Mn-Aptamer) fluorescent probe is turned off due to multi-walled carbon nanotubes (MWCNTs) facilitated fluorescence resonance energy transfer (FRET). In the presence of acetamiprid, ZnS:Mn-aptamer probe binds specifically to the analyte and is released from MWCNTs, thereby restoring the fluorescence of the probe. By the mentioned principle, the platform is able to quantify acetamiprid in real samples with an achievable LOD of 0.7 nM in the linear dynamic concentration range of 0–150 nM. Nucleic acid-based biosensors offer high specificity. However, their high cost of production limits their commercial application till date.

2.7.3 Immunosensors

Immunosensors employ biochemical assays to quantify the amount of an analyte through the high-affinity molecular interaction of specific antibody (Ab) and corresponding antigen (Ag). The immunoassays offer advantages of speed, reliability, simplicity, cost-effectiveness, and others (Aragay et al. 2012). Various types of nanomaterials such as metal nanoparticles, quantum dots, carbon nanotubes, and graphene, among others have helped to achieve signal amplification resulting in high sensitivity.

Fluorescence-based immunoassays are the most widely reported optical methods of pesticide detection due to high sensitivity and quantum dots being the most commonly used fluorophores. The quantum dots exhibit stability, size-tunable emission and are better than organic dyes in terms of extinction coefficient, brightness, and photostability (Vinayaka and Thakur 2010; Protière and Reiss 2007). An example of CdTe quantum dot-based competitive immunoassay has reported the fluorescent detection of 2,4-dichlorophenoxyacetic acid (2,4-D) (Vinayaka et al. 2009). For this, 2,4-D has been linked to alkaline phosphatase enzyme (ALP) resulting in the formation of 2,4-D-ALP conjugate which further reacts with mercaptopropionic acid-coated quantum dots. The anti-2,4-D antibodies are immobilized in a glass capillary column which bind competitively with free 2,4-D and 2,4-D-ALP conjugates. The higher the concentration of 2,4-D, the more is the displacement of conjugate which then passes through the column. Further, the displaced 2,4-D-ALP conjugate quantified through the fluorescence of quantum dots present in the conjugate correlates to the concentration of 2,4-D. The very low detection limit of 1.1 nM for 2,4-D has been achieved using this strategy. Despite its low limit of detection, this system is relatively complicated and not robust.

Another group of researchers has explored the same approach of a competitive immunoassay for the quantitative determination of chlorpyrifos (CPF) in drinking water down to a concentration of 10 nM (Yiping Chen et al. 2010c). The chlorpyrifos molecules have been treated with 3-mercaptopropyl acid (MPA) and bovine serum albumin (BSA) to form CPF-MPA-BSA conjugate which is physisorbed onto microwell plate. A biotin-modified-specific anti-CPF antibodies mixed with streptavidin-functionalized CdTe quantum dots are then incubated in the CPF-MSA-BSA conjugate coated well in the presence of pesticide containing samples. With the increasing concentration of chlorpyrifos, the amount of Ab-quantum dots conjugate in the plate decreases which is subsequently translated to diminishing output of fluorescence signal. Even though the sensing platform provides high accuracy and sensitivity in drinking water samples, it is limited to laboratory use due to costly integration system. A similar quantum dot-based competitive lateral flow immunoassay (LFIA) platform reports the biosensing of trichloropyridinol which is a biomarker of chlorpyrifos with a further improved detection limit of 5 nM (Zou et al. 2010). The LFIAs are robust, cost-effective, simple, fast, and well-suited for on-site detection of analytes (Posthuma-Trumpie et al. 2009).

There is also a possibility of using different quantum dots as distinct fluorescent labels for development of multi-analyte sensing arrays as different types of quantum dots produce a distinctive fluorescence signal (Rosenthal 2001). Nichkova and co-workers have employed this approach for simultaneous detection of two pesticides, namely, atrazine mercapturate (AM) and 3-phenoxybenzoic acid (PBA) using quantum dots of dissimilar spectral emissions (M Nichkova et al. 2007). The Birch Yellow EviTag and Maple Red EviTag quantum dots having emission at 580 and 620 nm, respectively, have been used for the purpose. This multiplexed micro-immunoassay can detect 4 μg/mL concentration of each analyte.

Apart from quantum dots, different nanoparticles such as Au nanoparticles, Fe_3O_4, and Eu:Gd_2O_3 have also been investigated for optical sensing of pesticides (Mikaela Nichkova et al. 2005; Chunyan Liu et al. 2011; Yi-Rong Guo et al. 2009). Au nanoparticles are one of the most widely used nanoparticles as fluorescent labels in immunoassays for pesticides. Guo's group has reported two Au nanoparticles LFIA formats (strips A and B) for the detection of triazophos and carbofuran simultaneously (Yi-Rong Guo et al. 2009). Strip A is prepared using specific monoclonal antibodies against both the pesticides conjugated to Au nanoparticles for the visual detection of triazophos and carbofuran down to the concentration of 0.03 μM and 0.3 μM, respectively. Strip B formed by the immobilization of AuNP-labeled monospecific antibodies for both the pesticides separately onto the substrate allows no cross-interference. The better LOD of 12 nM and 150 nM for triazophos and carbofuran is observed with the strip B format and therefore used for real sample analysis. Liu et al. have investigated magnetic Fe_3O_4 particle aggregates prepared by cross-linking nanoparticles bearing carbonyl groups with poly-L-lysine for lateral flow immunoassay-based sensing of paraoxon methyl (Chunyan Liu et al. 2011). After coupling with specific antibodies, the probes are settled down in lateral flow chamber followed by measurement of the analyte by optical density analysis. The controlled aggregation of Fe_3O_4 nanoparticles provides signal amplification resulting in much lower LOD of 1.7 ng/mL as compared to that attained using mother nanoparticles. Lanthanide oxide nanoparticles give size-independent emission and high signal-to-noise ratio. Owing to these characteristics, a microarray immunosensor using Eu:Gd_2O_3 nanoparticles as a fluorescent probe has been fabricated for phenoxybenzoic acid, a genetic biomarker for pyrethroid insecticides (Mikaela Nichkova et al. 2005). Firstly, the Eu:Gd_2O_3 nanoparticles are amine functionalized by encapsulating with poly(L-lysine) forming a stable shell. The amine-functionalized reporter nanoparticles are then covalently conjugated to antibodies and used in a competitive fluorescence microassay for phenylbenzoic acid with a detection limit of 1.4 ng/mL.

Further, an upconversion fluorescence nanoparticle-based immunoassay has been developed for the quantification of neonicotinoid insecticide imidaclothiz (You et al. 2017). Upconversion nanoparticles (UCNPs) made up of hexagonal phase NaYF4:Yb,Er functionalized with amino groups are coupled to anti-imidaclothiz antibody with simultaneous labeling of antigen with gold nanoparticles. Competitive binding of Au nanoparticle-labeled IMI and IMI to the anti-IMI

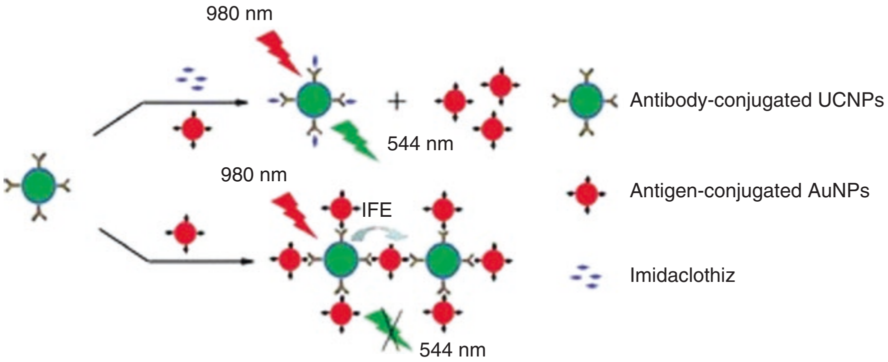


Fig. 2.11 Schematic for working principle of inner filter effect-based competitive immunoassay imidaclothiz developed by using upconversion nanoparticles and gold nanoparticles as labels. The competitive binding of unlabeled and labeled imidaclothiz to the antibody immobilized upconversion nanoparticles results in change in the fluorescent signal of upconversion nanoparticles at excitation and emission wavelengths of 980 and 544 nm, respectively. *AuNPs* gold nanoparticles, *IFE* inner field effect, *UCNPs* upconversion nanoparticles. (Reproduced from You et al. (2017), with permission from Springer)

antibody-immobilized UCNPs brings about the change in fluorescence signal of the UCNPs at excitation and emission wavelengths of 980 and 544 nm, respectively (Fig. 2.11). Under optimal conditions, the sensing platform achieves LOD of 2.1 ng/mL when 18.9 ng/mL of IMI concentration produces 50% signal saturation. The method is sensitive and rapid to determine imidaclothiz in spiked samples of soil, water, rice, apple, pear, pakchoi, tomato, and cabbage.

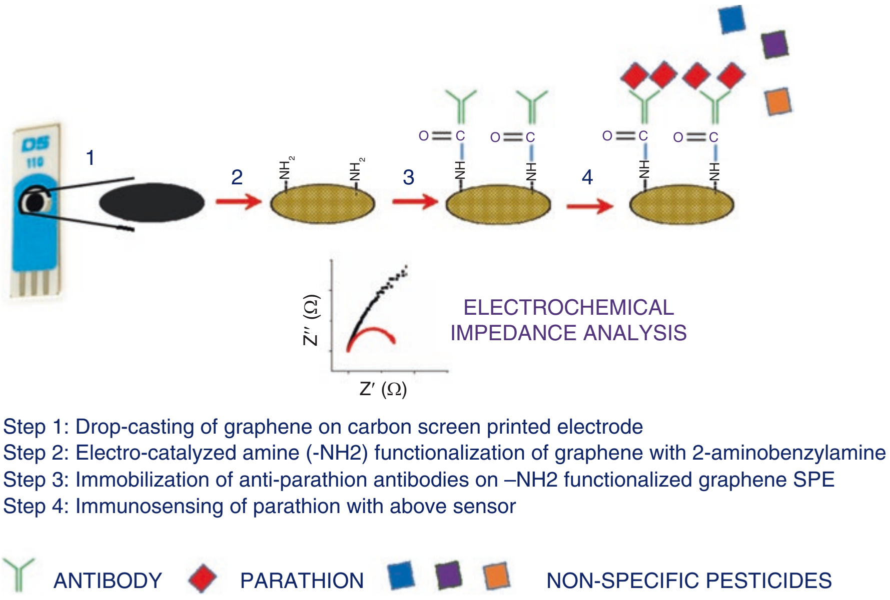
There are many reportings of various other electrochemical immunosensors for pesticides in the literature. The main parameters that advocate the use of electrochemical sensing platforms, especially for pesticides, are sensitivity, selectivity, portability, reproducibility, long-term stability, cost-effectiveness, and ease of use. The colloidal Au nanoparticles in the composite form with chitosan facilitate the electrochemical immunosensing of a commonly used chlorinated herbicide picloram (Lin Tang et al. 2008). The antipicloram antibody is embedded in the colloidal Au nanoparticles composite membrane which is further attached to enzyme horseradish peroxidase (HRP)-tagged secondary antibody in order to quantify the pesticide. The enzymatic electrocatalysis of quinine by HRP and the electron transport shuttled through NPs between the electrode surface and HRP forms the basis of detection. The observed detection limit for picloram using chronoamperometry with high storage stability and precision is 21 nM. A similar electrochemical immunosensor for picloram has been devised using 3D gold nanoclusters instead of Au nanoparticles for the much lower detection limit of 2 nM (Lijuan Chen et al. 2010b). This is attributable to the higher surface area provided by nanoclusters for higher antibody loading and resulting in better electron exchange. Likewise, another group of researchers has investigated Prussian blue-gold nanoparticle (PB-AuNP) film-modified laser-ablated gold electrode for voltammetric quantification of herbicide diuron (Sharma et al. 2011). They have immobilized the specific antibodies onto PB-AuNP film followed by attachment of alkaline phosphatase-conjugated secondary antibody. The sensor gives a response to the analyte in the presence of 1-naphthyl phosphate as a substrate for alkaline phosphatase with a detection limit of 4 pM. Despite very low detection limit, the sensors mentioned above require an additional substrate for HRP to generate a response. In this regard, Valera and co-workers have developed a conductometric immunosensor for atrazine using Au nanoparticles and anti-atrazine antibodies modified interdigitated μ-electrodes (IDμEs) (Valera et al. 2010). The conductometric change brought about by the deposition of secondary antibody-tagged Au nanoparticles onto the electrode gaps after the assay aids the pesticide detection. The gap between IDμEs reduces with these Au nanoparticles which further generates an analytical signal. This approach eliminates the need for an additional substrate and sample pretreatment with achievable LOD of 0.16 μM in wine samples. Also, CdS nanoparticle-labeled paraquat-specific antibodies and magnetic μ-particles functionalized antigen confined on graphite electrodes have been used for immunosensing of pesticide paraquat (Valera et al. 2014). After the Ag-Ab binding, the CdS nanoparticles detach from antibodies followed by the release of metal ions. These ions reduced at the electrode surface are read in the form of signal current using stripping voltammetry. The CdS nanoparticles contribute toward signal amplification resulting in high detectability of 1.4 μg/kg of the crop sample.

Besides optical immunosensors, quantum dots have also facilitated the electrochemical sensing of pesticides. One such CdS@ZnS quantum dot-based magnetic electrochemical immunosensor has been investigated to quantify organophosphate pesticides (Hua Wang et al. 2008). The platform indirectly detects organophosphate pesticides by quantifying organophosphorylated acetylcholinesterase (OPP-AChE) which is synthesized by incubating AChE with model target, paraoxon. The anti-phosphoserine polyclonal antibodies attached onto magnetic nanoparticles capture OPP-AChE and CdS@ZnS quantum dot-labeled anti-AChE monoclonal antibodies recognize the captured OPP-AChE. The sensing platform combines the magnetic preconcentration of the analyte with quantum dot-based sensitive voltammetric detection technique for organophosphate pesticides down to 0.15 ng/mL concentration in human plasma samples. Liu et al. have also detected the OPP-AChE biomarker using the same CdS@ZnS quantum dots as transduction material and ZrO_2 nanoparticles as selective sorbents instead of magnetic nanoparticles (Guodong Liu et al. 2008). The described platform widens the linear detection range for organophosphate pesticides from 10 pM to 4 nM. The last two presented works offer the advantage of detecting an entire group of pesticides rather than a single pesticide and providing a broader detection response for real samples.

Different research groups have reported the use of carbon-based nanomaterials for electrochemical sensing of pesticides. Liu and group have developed a square-wave voltammetry-based immunosensor using chemically assembled vertically aligned single-walled carbon nanotubes (SWCNTs) on functionalized carbon substrate for endosulfan in water samples (Guozhen Liu et al. 2012). The carbon substrates have been amine functionalized using 4-aminophenyl followed by vertical anchoring of SWCNTs through formation of amide bond between amine groups of the substrate and carboxylic groups of SWCNTs. Subsequently, ferrocenedimethylamine (FDMA) is attached to the SWCNTs followed by attachment of endosulfan-specific epitope for antibody binding. On interaction with the analyte, the dissociation of the antibody from the sensing interface modulates the ferrocene electrochemistry. The displacement assay achieves the detection limit of 0.01 ppb for endosulfan over a range of 0.01–20 ppb.

A polyaniline/carboxylated multi-walled carbon nanotubes-chitosan (PANI/MWCNTs/CS) nanocomposite has been used for specific antibody immobilization through Au nanoparticles as a linker (Sun et al. 2013). The developed platform detects chlorpyrifos electrochemically down to 0.06 ng/mL concentration over a wide linear dynamic concentration range of 40 ng/mL–0.1 mg/mL. In this approach, carboxylated MWCNTs allows uniform and thin coating of PANI resulting in an improved electrochemical response. Another group of researchers has investigated graphene sheets-ethyleneimine polymer-Au (GS-PEI-Au) nanocomposite self-assembled with MWCNTs for enhanced sensitivity (Zhu et al. 2013). The modified electrodes exhibit high surface area which enables high loading of carbofuran-specific antibody for quantification of analyte up to detection limit of 0.03 ng/mL. Few reports have demonstrated that site-specific immobilization of antibodies using immunoglobulin along with the addition of single-walled carbon nanotubes (SWCNTs) can further improve the detection limit (Marrakchi et al. 2013). For instance, Wang et al. have used this approach for the determination of atrazine down to detection limit of 100 pg/mL, which is 20 times better than that obtained by using non-oriented antibody immobilization. The oriented immobilization of specific antibodies onto graphene sheet-multi-walled carbon nanotube-gold nanoparticles-chitosan (GS-MWCNTs-AuNPs-CS) nanocomposite film has also been reported using protein A (SPA) combined with Au nanoparticles (Xiangyou Wang et al. 2014c). The platform can detect chlorpyrifos down to concentration as low as 0.037 ng/mL with high stability, reproducibility, and potential for the real sample application. A multiplexed immunoassay to detect seven pesticides (namely, fenpropathrin, triazophos, carbendazim, methyl-parathion, chlorothalonil, fenpropathrin, thiacloprid, and carbofuran) simultaneously has been investigated (Lan et al. 2016). The method employs 16 pairs of pesticide antigens and their respective pesticide antibodies with a microarray chip containing nitrocellulose membrane-immobilized 7 antigens. Nanogold label has been employed for signal amplification to bring sensitivity down to 0.02–6.45 ng/mL, in order to meet requirements for detection of pesticide residues.

An electrochemical impedance immunosensor has been developed for parathion using cadmium- based nanometal organic framework (NMOF) deposited on a 2-aminobenzylamine (2-ABA)-functionalized indium tin oxide (ITO) slide (Deep et al. 2015). The anti-parathion antibodies are conjugating to the pendent carboxylic functional groups present on the assembled NMOF film to obtain a pesticide immunosensor. The proposed immunosensor is specific to parathion with sensitivity in the concentration range of 0.1–20 ng/mL and the detection limit of 0.1 ng/mL. Another MOF-based immunosensor has been fabricated using the assembled thin films of a silica (SiO_2)-coated Cu-metal organic framework ($Cu_3(BTC)_2@SiO_2$)



Step 1: Drop-casting of graphene on carbon screen printed electrode
Step 2: Electro-catalyzed amine (-NH2) functionalization of graphene with 2-aminobenzylamine
Step 3: Immobilization of anti-parathion antibodies on –NH2 functionalized graphene SPE
Step 4: Immunosensing of parathion with above sensor

Fig. 2.12 Schematic for the development of impedance-based screen-printed immunosensor for parathion. (Reproduced from Mehta et al. (2016), with permission from Elsevier)

on a conducting substrate composed of amine-functionalized polyaniline (PANI) (Bhardwaj et al. 2015). The assembled thin films exhibit electrical conductivity of approximately 35 μA, and their conjugate with anti-atrazine antibodies resulted in conductometric detection of atrazine with LOD of 0.01 nM.

Mehta et al. have investigated graphene-based nanostructures for highly sensitive and selective immunosensing of ethyl parathion (Mehta et al. 2016, 2017). The graphene sheet-modified screen-printed electrodes (SPEs) have been investigated for impedimetric immunosensing of ethyl parathion with detection limit of 52 pg/L in a linear detection range of 0.1–100 ng/L (Mehta et al. 2016). The immunosensor has been fabricated by the modification of carbon SPEs with carboxylated graphene sheets followed by the electrochemical deposition of amine functionality using 2-aminobenzylamine (2-ABA) (Fig. 2.12). The amine functionalization provides stable and oriented immobilization of specific antibodies resulting in high sensitivity. The same group of researchers improved the sensitivity of the fabricated SPE immunosensor for ethyl parathion using graphene quantum dots (GQDs) in place of graphene sheets (Mehta et al. 2017). The sensitivity, stability, and linear detection range improves with the use of GQDs due to monodispersity and higher conductivity of GQDs as compared to graphene sheets.

Despite the promising sensitivity and selectivity of immunosensors, there are several associated limitations such as the requirement of expensive nonrenewable materials, interference of complicated ligand interactions, and prior knowledge of analyte (Rainina et al. 1996).

2.7.4 Enzymatic Biosensors

Enzymatic biosensors are composed of enzymes as recognition elements present in proximity to the transducer. They provide ease of immobilization, robustness, and fast response as compared to immunosensors (Arduini et al. 2016). These sensors detect analytes through (i) an inhibition mechanism, where the extent of inhibition is measured and, subsequently, correlated to the analyte concentration to be detected, and (ii) a catalytic mechanism, in which the analyte itself acts as a substrate and generates a transduction signal on the formation of reaction products. The most commonly used enzymes for the development of enzymatic biosensors for pesticides are acetylcholinesterase (AChE) and organophosphate hydrolase (OPH).

Acetylcholinesterase (AChE) enzymes are a class of catalytic proteins that hydrolyze acetylcholine which is a neurotransmitter (Stenersen 2004) according to the equation: acetylcholine + H_2O → choline + acetate. The organophosphate and carbamate pesticides phosphorylate the serine amino acid residue presents in the active site of AChE, thus inhibiting the enzyme irreversibly (Fukuto 1990). The quantification of enzyme inhibition then forms the fundamental principle of AChE-based biosensors for pesticides. The procedure includes measurement of the initial enzymatic activity, followed by the incubation of enzyme in pesticide containing sample and subsequent quantification of inhibited enzyme activity. Liu and co-workers have reported multi-walled carbon nanotubes and graphene oxide (MWCNT/GO) nanocomposite which exhibits a better catalytic activity for fabricating AChE biosensor for carbaryl detection (Qian Liu et al. 2015). Also, various biosensors exploit nonnatural substitute of acetylthiocholine, i.e., thiocholine for measurement due to its high electroactivity. The resulting biosensor exhibits LOD of 1.7 nM for carbaryl within linear dynamic range of 5–5000 nM. The composite of carbon nanotubes with conducting polymer polyaniline (PANI) has been investigated for quantification of carbaryl and methomyl in real samples of liquefied cabbage, apple, and broccoli (Cesarino et al. 2012). The conducting layer of PANI offers coverage of the entire active surface of the electrode and film thickness control resulting in enhanced sensitivity and reproducibility. The sensor detects methomyl and carbaryl voltammetrically down to the concentration of 0.95 μM and 1.4 μM, respectively, which is far below the permissible maximal residual limit. The nanosized electrochemical mediators have also been employed for detection measurements at a low potential to achieve much lower detection limits. For instance, a nanocomposite of Prussian blue nanocube/reduced graphene oxide has been reported for the fabrication of an AChE biosensor for monocrotophos (Lin Zhang et al. 2012). The so-developed sensing platform can achieve a detection limit of 0.1 ng/mL for monocrotophos. The electrocatalytic activity of Prussian blue toward oxidation of the thiocholine results in high sensitivity and rapid response of the biosensor. Apart from carbonaceous materials, researchers have investigated nanoparticles and quantum dots for the preparation of pesticide biosensors. Self-assembly of AChE enzyme on the surface of Au nanoparticles/reduced graphene oxide nanohybrid-modified glassy carbon electrode (GCE) has resulted in the ultra-

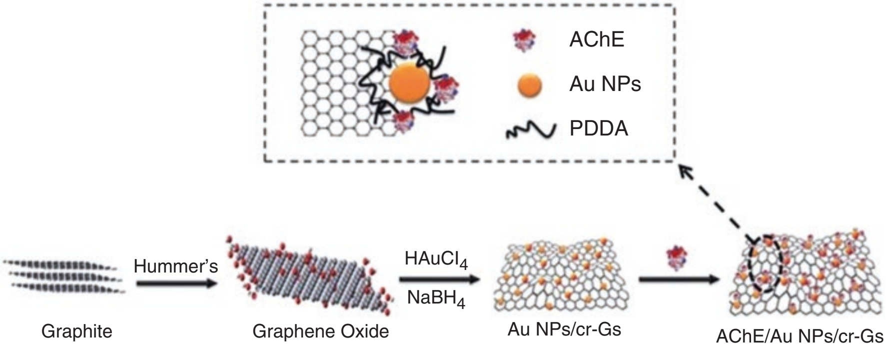


Fig. 2.13 Schematic for the Au nanoparticles and chemically reduced graphene oxide nanosheets hybrid synthesis and development of acetylcholinesterase inhibition-based sensor assembly generation by polydiallyldimethylammonium chloride polymer. Graphene oxide was synthesized from graphite by Hummer's method, and hybrid was obtained by reduction of tetrachloroauric(III) acid on graphene oxide. Further, acetyl was stabilized on the surface of nanohybrid by self-assembling. *AChE* acetylcholinesterase, *AuNPs/cr-Gs* Au nanoparticles/chemically reduced graphene oxide nanosheets hybrid, *PDDA* polydiallyldimethylammonium chloride, *$HAuCl_4$* tetrachloroauric(III) acid. (Reproduced from Wang et al. (2011), with permission from Royal Society of Chemistry)

sensitive electrochemical sensor for paraoxon as shown in Fig. 2.13 (Ying Wang et al. 2011). The scattering effects of nanosized Au nanoparticles on reduced graphene oxide nanosheets greatly improve the electrochemical signal by including a negative potential shift in operation which is responsible for signal amplification resulting in higher sensitivity. The detection platform is sensitive to 0.1 pM for paraoxon and exhibits excellent stability. Another research group has employed the same approach of AChE-immobilized carbon nanotube-modified electrode with achievable LOD of 0.4 pM for paraoxon (Guodong Liu and Lin 2006). Du et al. have proposed AChE-based electrochemical biosensor for monocrotophos using CdTe quantum dots/Au nanoparticle-modified GCE (Du et al. 2008). The CdTe quantum dots/Au nanoparticles composite has been found to promote the electron transfer in AChE enzyme catalyzed oxidation of thiocholine, thereby amplifying the sensor sensitivity. The electrochemical response for monocrotophos-mediated inhibition of AChE is proportional to the concentration of an analyte in the range of 9–67 nM with observed LOD of 1.34 nM.

Bi-enzymatic platforms have also facilitated quantification of the pesticides. In a bi-enzymatic system, AChE facilitates catalytic hydrolysis of acetylcholine neurotransmitter into acetate and choline, further converting choline into aldehyde and hydrogen peroxide (H_2O_2) with the aid of choline oxidase (ChO) (Yuehe Lin et al. 2004). The so produced H_2O_2 is detected amperometrically. Using this approach, a biosensor co-immobilizing bi-enzymes, namely, AChE and ChO onto CdTe quantum dot-modified electrode, has been reported (Meng et al. 2013). The sensor can quantify of dichlorvos with a detection limit of 4.49 nM in linear dynamic range of 4.49–6780 nM.

Various research groups have reported the fabrication of AChE-based optical sensors. An indirect visual method of pesticide detects paraoxon down to a concentration of 10 nM by thiocholine-mediated growth of Au nanoparticles (Pavlov et al. 2005). The thiocholine produced as a result of AChE-mediated hydrolysis catalyzes the growth of Au nanoparticle seeds in the solution of $AuCl_4^-$. The presence of a pesticide inhibits AChE activity and results in reduced production of thiocholine. Consequently, monitoring of fewer formed Au nanoparticles by UV-Vis absorbance aids in sensing of the analyte. The sensor also provides a visual aid as the glass surface is blue colored in the absence of paraoxon and losses color due to plasmon band blueshift in the presence of analyte pesticide. The same group has employed CdS quantum dots instead of Au nanoparticles in combination with AChE enzyme for fluorescent detection (Saa et al. 2010). The thiol group containing molecules (such as thiocholine) are known to promote the decomposition of sulfoxide ions to hydrogen sulfide which forms fluorescent nanocrystal of CdS from Cd^{2+} ions. Thus, the formation of CdS quantum dots is indicative of the inhibited AChE enzyme activity in the presence of pesticides and the subsequently reduced fluorescent response of quantum dots. The LOD observed for AChE inhibitor using the mentioned strategy is 50 nM. Thiocholine has also been reported to quench the fluorescence of CdTe quantum dots embedded in AChE multilayer platform (Zhaozhu Zheng et al. 2011b). The quantification of organophosphate pesticides has been done up to the improved detection limit of 0.01 nM using this approach. The AChE enzyme activity is inhibited in the presence of organophosphate pesticides resulting in reduced production of thiocholine and subsequently diminished the rate of fluorescence quenching. Zheng et al. have devised a similar CdTe quantum dot-based bi-enzymatic sensor for organophosphate pesticides up to pM levels over a wide linear dynamic range of $1–10^{-6}$ μM employing acetylcholinesterase and choline oxidase (Zhaozhu Zheng et al. 2011a). However, the quenching mechanism differs as the H_2O_2 produced by choline oxidase-mediated catalytic reaction etches the surface the surface of quantum dots leading to more surface defects and consequent decrease in size and fluorescence of CdS nanocrystals. Acetylcholinesterase enzyme inhibition has also been quantified using Au nanoparticle-modified fiber-optic sensing platform for paraoxon based on localized surface plasmon resonance (LSPR) (Tsao-Jen Lin et al. 2006). The presence of organophosphate pesticides inhibits the enzyme activity, thereby altering the light attenuation and subsequently enabling the quantification of pesticide down to a concentration of 0.9 nM.

A label-free biosensing platform has been reported for highly sensitive detection of organophosphate pesticides using dual mode of detection (fluorescence and colorimetry) based on acetylcholinesterase (AChE)-directed quenching of carbon dots fluorescence (Hongxia Li et al. 2018). The sensing strategy involves catalytic hydrolysis of acetylcholine with AChE resulting into the production of thiocholine which triggers the decomposition of 5,5-dithiobis (2-nitrobenzoic acid) into yellow-colored 5-thio-2-nitrobenzoic acid (TNBA). The so produced TNBA acts as quencher for carbon dots fluorescence through dynamic quenching process. However, in the presence of organophosphate pesticides, the enzymatic activity of

AChE is inhibited leading to the fluorescence signal recovery and decrease in absorbance intensity along with color variation. The dual-mode output assay provides high sensitivity for paraoxon down to 0.4 ng/mL concentration.

A colorimetric method based on enzymatic hydrolysis of acetylcholinesterase (AChE) and the formation of gold nanoparticles suspension in Au^{3+}-cetyltrimethylammonium bromide (Au^{3+}-CTAB) solution has been developed for organophosphorus pesticides (OPPs) analysis (Shuo Wu et al. 2017a). In the absence of OPPs, thiocholine formed as a product of enzymatic hydrolysis reduces Au^{3+} and prevents the formation of Au nanoparticles suspension by Au^{3+}- CTAB. However, in the presence of OPPs, the activity of AChE is inhibited resulting into the production of only small amount of thiocholine for Au^{3+}consumption. Thus, the large residual amount of Au^{3+} dissolves Au nanoparticles resulting in decrease of both the size and concentration of Au nanoparticles, leading to change in color from red to colorless or red to light pink. Under optimal conditions, the method quantifies the presence of OPPs down to 0.7 ppb concentration colorimetrically. Further, a highly sensitive Au nanoparticle-coated dipstick has been fabricated by immobilizing Au nanoparticles onto a cellulose paper for organophosphate pesticides detection with achievable LOD of 35 ppb. The monitoring of organophosphate pesticides in apple washing solution, tap water, and seawater has been successful using colorimetric method even in the saline solution containing 5 M of NaCl, and the method is applicable for the on-site detection of organophosphate pesticides in complex systems. The other enzymes less extensively investigated enzymes for the development of inhibition-based enzymatic biosensors for pesticides are butyrylcholinesterase (BChE), alkaline phosphatase (ALP), acid phosphatase, laccase, and tyrosinase. The detection platform developed using BChE as biocomponent on Prussian blue-modified screen-printed electrodes (SPE) detects paraoxon with LOD of 3.6 nM (Arduini et al. 2015). The sensors work on the principle similar to AChE-based platforms and exhibit good sensitivity owing to electrocatalytic properties of Prussian blue nanoparticles. Carbon dots have been used in combination with manganese dioxide (MnO_2) quencher in the presence of acetylthiocholine (ATCh) and butyrylcholinesterase (BChE) enzyme for the detection of organophosphate pesticides (Yan et al. 2018). The detection is based on quenching of fluorescence of carbon dots due to MNO_2 nanosheets which is recovered after the MNO_2 nanosheets decomposition in the presence of BChE and ATCh. However, organophosphate pesticides act as inhibitor for the activity of BChE enzyme, thereby preventing the thiocholine generation and subsequent nanosheets decomposition resulting in fluorescence "turn-off." The developed fluorescence-based platform has been demonstrated to detect paraoxon within dynamic range of 0.05–5 ng/mL with a LOD of 0.015 ng/mL. Using a similar approach, a fluorescent sensor based on natural carbon quantum dots (CQDs) derived from chlorophyll and BChE enzyme has been investigated for detection of organophosphate pesticides (Xiaoli Wu et al. 2017b). The tunable fluorescence emission of CQDs is effectively quenched by gold nanoparticles via fluorescence resonance energy transfer (FRET). Thiocholine produced as a result of catalytic activity of BChE results in Ag nanoparticles aggregation and corresponding recovery of CQDs fluorescence. However, in the presence of organophosphate pesticides, the recovery effect is reduced due to irreversible inhibition of BChE enzymatic activity. The sensing platform displays a linear response in the concentration range of 0.05–50 μ g/L for paraoxon with achievable LOD of 0.05 μ g L^{-1}.

Another group of researchers has exploited a plant esterase immobilized on chitosan/gold nanoparticle-graphene nanosheets. The nanocomposite-modified electrode can quantify malathion and methyl parathion up to a concentration of 1.51 nM and 0.19 nM, respectively (Bao et al. 2015). The factors such as strong inhibition of esterase by pesticides, high-probe surface area for high loading of enzyme, and favorable environment provided to the enzyme by chitosan are responsible for the excellent performance of sensing platform. A reversible tyrosinase inhibition by chlortoluron has formed the basis of herbicide biosensing in cereals (Haddaoui and Raouafi 2015). In this regard, tyrosinase immobilized onto ZnO nanoparticle-modified screen-printed electrode (SPE) is able to detect chlortoluron with an observable limit as low as 0.47 nM. A similar biosensor has been investigated using multi-walled carbon nanotubes (MWCNTs) or graphene-modified SPE as transducer and immobilization substrate for tyrosinase. The mentioned inhibition biosensor reaches to the detection limit of 1.4 μM for atrazine (Tortolini et al. 2016). However, the extensive interference studies have to be performed in tyrosinase-based biosensors due to reversible inhibition of the enzyme in the presence of pesticides (Arduini and Amine 2013). Various research groups have investigated the use of laccase enzyme as bioprobe for sensing of pesticides. For instance, an inhibition biosensor for formetanate hydrochloride has been reported using laccase-immobilized Au nanoparticle-modified gold electrodes (Ribeiro et al. 2014). The sensor exhibits detection limit of 95 nM for the analyte without the need of incubation time resulting in a rapid response. However, the sensor requires aminophenol as an additional substrate for facilitating electrochemical sensing. A few alkaline phosphatase (ALP) enzyme inhibition-based biosensors have also been explored for sensing of different classes of pesticides using screen-printed electrodes, platinum electrodes, optical fibers, and other transduction and immobilization substrates (Del Carlo et al. 1997; Ayyagari et al. 1995). However, some pesticides have been shown to activate ALP instead of their inhibition due to which their extensive use in biosensors is limited. In spite of being able to detect organophosphate pesticides with a LOD of 0.5 ng/mL, the use of ALPs is also restricted in biosensors due to the requirement of low pH for catalysis.

All the abovementioned enzymatic biosensors are inhibition-based sensors; direct catalytic biosensors employing organophosphate hydrolase (OPH) enzyme are receiving research orientation. The major limitations of inhibition-based sensing platforms include the requirement of the additional substrate and the multistep procedure involved in detection (measurement of enzyme activity, incubation with an analyte-containing sample followed by quantification of enzyme activity inhibition in terms of analyte concentration). Therefore, the inhibition-based enzymatic biosensors result in increased cost, time consumption, and non-robustness. However, in the direct catalytic biosensors, the analyte itself acts as substrate, and product of the reaction facilitates detection of a pesticide in one step contributing toward non-complexity of the platforms. These sensors are well-suited for continuous monitoring of pesticide concentration which is not possible with inhibition-based biosensors.

Organophosphate hydrolase (OPH)-based biosensors work on the principle of hydrolysis of organophosphate pesticides into *p*-nitrophenol which can be detected both electrochemically and optically. Pedrosa and co-workers have demonstrated the OPH single-walled carbon nanotubes (SWCNTs) and multi-walled carbon nanotubes (MWCNTs) for amperometric detection of *p*-nitrophenol for quantification of paraoxon (Pedrosa et al. 2010). The OPH-immobilized SWCNTs exhibit better activity attributable to the low electrical percolation thresholds and high surface area of SWCNTs as compared to MWCNTs. Thus, the OPH@SWCNTs-based sensing platform detects the analyte down to the concentration of 0.01 μM over the concentration range of 0.5–8.5 μM. A similar amperometric biosensor for paraoxon employs OPH as biocatalytic recognition probe and carbon nanotubes (Deo et al. 2005). The sensor can measure paraoxon and methyl parathion with a detection limit as low as 0.15 μM and 0.8 μM, respectively. The carbon nanotubes greatly improve anodic detection of generated hydrolysis product, *p*-nitrophenol, resulting in higher sensitivity and stability. Du et al. have reported an amperometric biosensor for the monitoring of methyl parathion due to dual-signal amplification facilitated by OPH-immobilized CdTe quantum dots loaded to MWCNTs/Au nanoparticles (Du et al. 2010). The high surface area of electrode allows high loading of enzyme, and synergistic catalytic effects of nanoparticles with enzyme improve the sensitivity and selectivity toward analyte. Due to the two enhancement factors, LOD of 1 ng/mL is observed using the developed biosensor. It has also been established that the amperometric response of carbon black and mesoporous carbon is better than carbon nanotube-modified glassy carbon electrode for quantification of organophosphate pesticides (Lee et al. 2010). The factors such as edge-plane-like defects, well-ordered nanopores, and high surface area of mesoporous carbon/carbon black anodic layer result in detection of pesticide paraoxon down to nanomolar range. A functional nanocomposite consists of elastin-like-polypeptide-organophosphate hydrolase (ELP-OPH), bovine serum albumin (BSA), carboxylic acid functionalized multi-walled carbon nanotubes (c-MWCNTs), and titanium dioxide nanofibers (TiO_2NFs) (Bao et al. 2016). ELP-OPH serves as biocatalyst for organophosphate pesticides, while BSA stabilizes enzymatic activity of nanocomposite-immobilized OPH. TiO_2NFs concentrate organophosphate pesticides in the composite attributable to their strong affinity with phosphoric group of organophosphate pesticides, and c-MWNCTs improve the electron transfer to facilitate sensitive amperometric detection of organophosphate pesticides. ELP-OPH/BSA/TiO_2NFs/c-MWCNTs nanocomposite shows a wide linear range and low detection limit of 1 nM and 12 nM for ethyl parathion and methyl parathion, respectively. The enhanced sensing performance of the nanocomposite has been applied for selective monitoring of organophosphate pesticides in spiked lake samples with good accuracy. Another group of researchers has proposed the use of magnetic nanoparticles of Fe_3O_4@Au nanocomposite for methyl parathion hydrolase (MPH) self-assembly to develop a biosensor for organophosphate pesticides (Yuting Zhao et al. 2013b). The magnetic nanoparticles facilitate easy construction of biosensor by simple application of the magnetic field and regeneration of the electrode through the magnet removal. The biosensor shows the rapid response for methyl parathion in the linear range of 0.5–1000 ng/mL with LOD of 0.1 ng/mL. A polyelectrolyte-based architecture using polycationic OPH and chitosan in combination with polyanionic thioglycolic acid-capped CdSe quantum dots has been fabricated for optical sensing of organophosphate pesticides (Constantine et al. 2003a). In this system, the entrapment of quantum dots between the layers of polycations improves the photoluminescence of the functionalized quantum dots. The sensor not only detects paraoxon up to 1 μM concentration through photoluminescence quenching but also exhibits the ability to detoxify the pesticide. Another fluorescence-based sensor has been developed for the detection of paraoxon using OPH bioconjugated (CdSe)ZnS core-shell quantum dots (Ji et al. 2005). The coupling of OPH to quantum dots occurs through the electrostatic interaction of positively charged amine groups and side chains of enzymatic protein with negatively charged quantum dots. In the presence of a pesticide, surface passivation of quantum dots occurs due to a conformational change of the enzyme resulting in the quenching of quantum dots fluorescence. The achievable LOD for paraoxon using the developed detection platform is 10 nM.

Recently, a very simple UV-visible absorption-based optical sensing platform has been investigated and proposed for detection of methyl parathion using hexahistidine-tagged organophosphate hydrolase (OPH^{6His}) enzyme in situ encapsulated within the framework of terbium-BTC (BTC = 1,2,4-benzenetricarboxylic acid) metal-organic framework (MOF) (Mehta et al. 2019a). The enzymatic activity and stability of the enzyme enhances remarkably post encapsulation in the MOF. The developed enzyme-MOF composite (OPH^{6His}@Tb-BTC) acts as a dual platform for detection and hydrolytic catalysis of organophosphate pesticides. The detection is based on the quantification of UV-visible absorption of catalytic product of methyl parathion, *p*-nitrophenol, at 410 nm formed in the presence of OPH^{6His} enzyme. The developed enzyme-MOF platform exhibits high stability, reusability, and a very low detection limit of 2.6 nM. Simultaneously, organophosphate pesticides are converted into less toxic product supporting the strong candidature of the synthesized composite for the remediation of pesticide-laden environmental samples. In another report, the same enzyme OPH^{6His} has been immobilized on the chemically activated UiO-66-NH_2 MOF surface to form OPH^{6His}/UiO-66-NH_2 composite employed to detect methyl parathion optically down to 10 ng/mL concentration (Mehta et al. 2019b). The authors have explored coumarin 1 (7-diethylamino-4-methylcoumarin) as a fluorescent reporter molecule, for achieving signal amplification and rapid response with good sensitivity. The detection is based on the fact that the fluorescence of coumarin 1 is quenched in the presence of degradation product of methyl parathion, *p*-nitrophenol, in the presence of OPH^{6His}/UiO-66-NH_2 as shown in Fig. 2.14. The quantification of fluorescence quenching is correlated with the initial concentration of analyte. The development of OPH-based sensors is still in its infancy as compared to other enzymatic detection platforms for pesticides due to the high cost of protein extraction. However, they offer promising prospects due to high specificity toward organophosphate pesticides as compared to inhibition-based sensors. Also, OPH is a relatively stable enzyme able

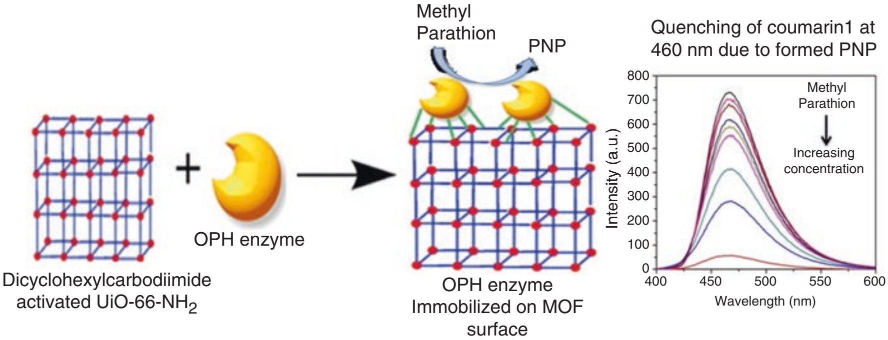


Fig. 2.14 Schematic for synthesis and detection strategy for methyl parathion using enzyme/metal-organic framework nanocomposite. Firstly, the enzyme is immobilized onto the surface of chemically activated UiO-66-NH$_2$ MOF which is used for quantification of methyl parathion. The degradation product, *p*-nitrophenol, formed as a result of catalytic hydrolysis of methyl parathion in the presence of surface-immobilized OPH enzyme quenches the fluorescence of coumarin-1 reporter molecule and can be correlated to initial concentration of methyl parathion. *OPH* organophosphate hydrolase, *PNP p*-nitrophenol, *UiO-66-NH$_2$* zirconium MOF. (Reproduced from Mehta et al. (2019b), with permission from Elsevier)

to work within a pH range of 8–10 and up to 50 °C temperature. The activity, stability, and recyclability of OPH enzyme improve after immobilization on suitable nanomaterials resulting in an overall reduced cost of the system. As the sensing mechanism of OPH biosensors involves hydrolysis of organophosphate pesticides into less toxic compounds, these platforms can facilitate simultaneous detection and biodegradation of organophosphate pesticides.

2.8 Conclusion

This chapter discussed the literature available on usage, contamination, sensing, and removal of pesticides, i.e., the status of different conventional detection techniques, their limitations, and the advancements realized in biosensing of pesticides employing nanomaterials and biomolecules in conjugation. Nanomaterials exhibit high surface area, varied morphology, and chemical functionality along with optoelectronic properties which results in the development of robust and sensitive new-age sensing systems for pesticides. Metal nanoparticles, metal oxides, quantum dots, carbon-based materials, and metal-organic frameworks are the extensively explored advanced nanostructures for the detection of various pesticides. Further, biosensors fabricated by stable immobilization of biomolecules on nanomaterials have emerged as efficient alternatives to conventional methods of pesticide detection due to portability, robustness, on-site applicability, high sensitivity, and specificity. Various whole cell, DNA, antibody, and enzyme- based pesticides biosensors are also reported in the literature. Therefore, the various nanomaterials employed in biosensing of pesticides, the sensitivity, and specificity improvement methods along with different means of pesticide remediation have been summarized in this chapter. The future prospects of the biosensors for pesticides lie in the development of simple-specific biomolecule-immobilized nanoplatforms exploring different nanomaterials for highly sensitive and specific multiplexed detection of pesticides. For this, nanomaterials can be post-synthetically modified to facilitate stable immobilization of bioprobes to improve sensitivity. The developed nanoplatforms can also be explored to develop portable electrochemical and paper-based sensors for pesticides to monitor the safety of food and environmental samples. The proposed nanoplatforms can further be investigated to enhance activity of biocatalytic platforms for use in environmental remediation.

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Chapter 3
Analytical Detection of Pesticides, Pollutants, and Pharmaceutical Waste in the Environment

Elsa M. Materon, Gisela Ibáñez-Redín, Nirav Joshi, Débora Gonçalves, Osvaldo N. Oliveira Jr, and Ronaldo Censi Faria

Contents

Abstract The rapid population growth and industrialization have led to widespread use of pesticides, drugs, personal care products, and dyes, some of which are so-called emerging contaminants (ECs). These compounds have obviously brought great benefits in controlling diseases and for increasing agricultural and industrial production, but their indiscriminate use has caused problems to human health and the environment. They can be found in surface water and groundwater at concentrations from ng L^{-1} to mg L^{-1}, which may seem negligible. However, some

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contaminants can accumulate or transform in other more toxic products in the human body and induce such problems as antibiotic resistance. Unfortunately, since there is no regulation for some emerging contaminants, they are not monitored in the environment or cannot be detected with conventional analytical techniques.

The purpose of this chapter is to present the state-of-the-art methodology for detecting the emerging contaminants, e.g., pesticides and pharmaceutical products. The chapter will be divided into subtopics – pesticides, pollutants, and pharmaceutical waste – with adverse environment effects also commented upon. The analytical methodologies for detection will be highlighted, with emphasis on recent advances in sensors and biosensors that may offer low-cost, sensitive, selective, and accurate analysis.

Keywords Sensors · Biosensors · Pesticides · Pollutants · Pharmaceutical waste · Emerging contaminants

3.1 Introduction

Contamination in the environment is generally linked with global warming, being mainly caused by extensive industrialization, high population density, and highly urbanized areas (Akpor and Muchie 2011). Negative consequences to human and animals' health arise from improper discarding of pharmaceutical waste, endocrine disrupting compounds, personal care products, and household care products. They may include hormones, glucocorticoids, analgesics – ibuprofen, estriol, additives in drugs, etc. – and cosmetics containing siloxanes and parabens. Figure 3.1 shows a flowchart depicting sources and fate of the so-called emerging contaminants (ECs) (Gogoi et al. 2018). Unfortunately, since there is no regulation for emerging contaminants, they are not monitored in the environment (Noguera-oviedo and Aga 2016). Hence, pesticides are detected in groundwater and drinking water, even though there is a growing effort of environmental protection companies to replace these products with environmentally friendly substitutes (Aamand et al. 2015). Furthermore, existing treatments of wastewater or drinking water are not efficient to remove estrogens, androgens, or detergent compounds (Adeel et al. 2017; Kot-wasik et al. 2007).

Potential health problems have been usually associated with excessive amounts of emerging contaminants in drinking water, as illustrated in Fig. 3.2, including breast and prostate cancer. The effects of prolonged hormone exposure in aquatic ecosystems, even at low levels (<0.001 mg L^{-1}), can lead to adverse effects on aquatic organisms (Jennifer et al. 2017; Kot-wasik et al. 2007) such as estrogens which may affect fish physiology and reproductive maturity in domestic and wild animals. Estrogens and steroid precursors affect roots, flowering, and germination of plants (Adeel et al. 2017). The awareness about environmental issues is crucial to forge environmentally friendly technologies according to the rules of sustainable

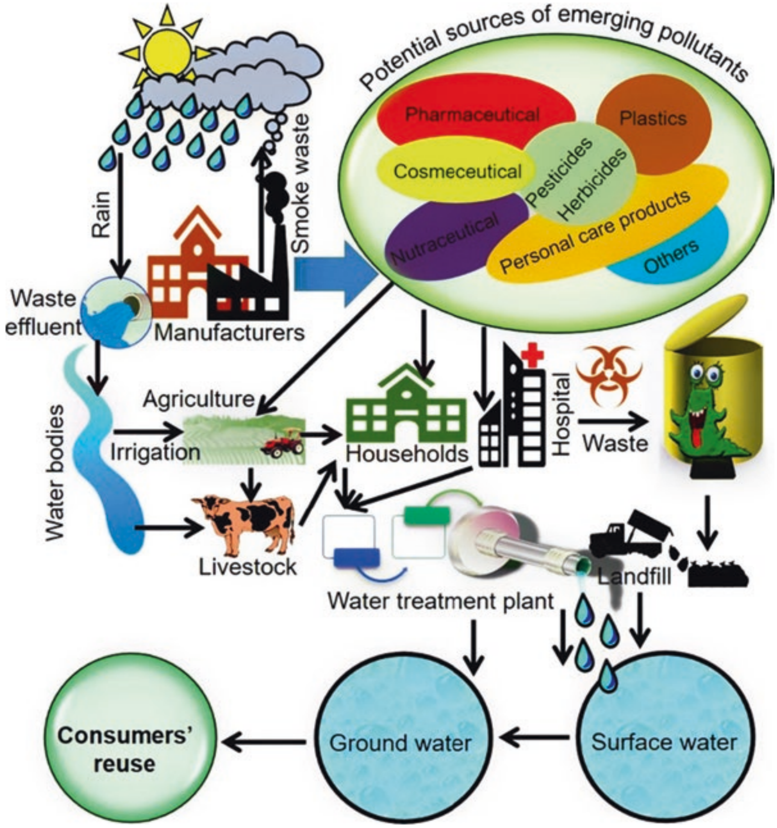


Fig. 3.1 Schematic design with the potential sources of emerging pollutants in the environment. (Reproduced from Ref. (Rasheed et al. 2019) with permission from Elsevier, 2018)

growth (in other words, green chemistry plus green technology). In this context, also relevant are the analytical methodologies to detect trace concentrations of a broad spectrum of pollutants (Kot-wasik et al. 2007).

This chapter reviews the state of the art of groups of emerging contaminants (pesticides, polluters, and pharmaceutical chemicals) and their negative impacts on the environment. In addition, a brief description of standard analytical methodologies is provided, with emphasis on biosensors and sensors to detect emerging contaminants.

3.2 Side Effects of Pesticides

Pesticides are used in agriculture to prevent and control the spread of weeds, bacteria, insects, and rodents. Their use has increased agricultural productivity, helping to secure nearly one-third of the global crop production (Samsidar et al. 2018). In

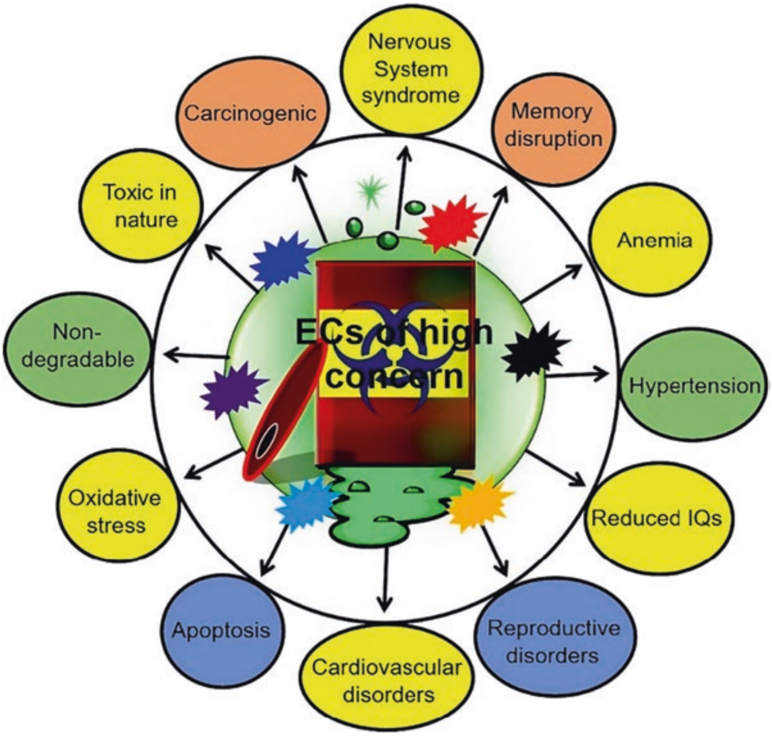


Fig. 3.2 Schematic design on side effects of emerging contaminants. (Reproduced from Ref. (Rasheed et al. 2019) with permission from Elsevier, 2018)

addition, pesticides are useful for controlling vegetation growth, in pet care products, and preventing disease vectors from spreading. More than 1000 pesticides are commercialized, and this number keeps increasing owing to the emergence of resistant pests (Rejczak and Tuzimski 2015). Unfortunately, most of these compounds are toxic, and their indiscriminate use yields major risks to human health, especially for agricultural workers and people living close to farms. Also, exposure to pesticides can cause long-term health effects such as cancer, Parkinson's, Alzheimer's, multiple sclerosis, and cardiovascular diseases (Mostafalou and Abdollahi 2013).

Pesticides are classified based on the target pests and their origin – chemical or biological (Rawtani et al. 2018) – as shown in Fig. 3.3. Biopesticides are derived from natural sources, including animals, plants, bacteria, and minerals. Chemical pesticides have been synthesized to kill different types of pests and are classified as insecticides, herbicides, fungicides, rodenticides, and nematicides (Samsidar et al. 2018). Organophosphates, carbonates, and organochlorines are among the most known chemical pesticides. Compounds such as dichlorodiphenyltrichloroethane (DDT), atrazine, malathion, and parathion have been related to adverse effects on the environment, which include destruction of the habitat of different species (Rawtani et al. 2018).

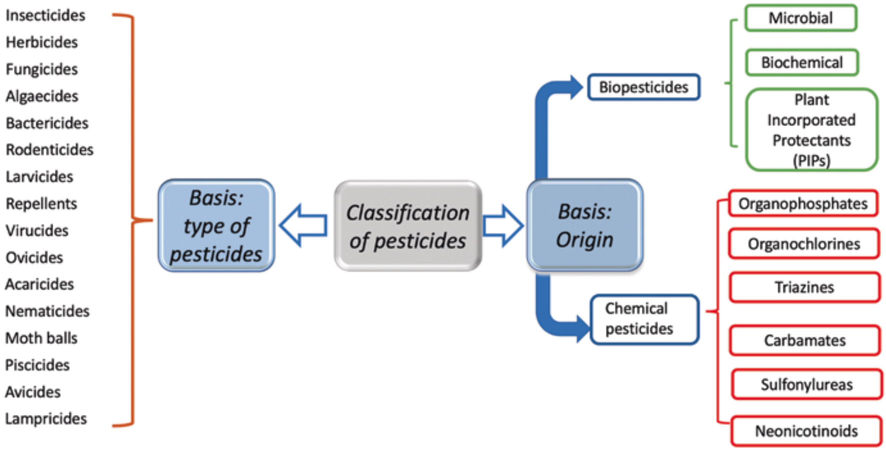


Fig. 3.3 Classification of pesticides. (Figure based on Rawtani et al. (2018))

3.2.1 *Analysis of Pesticides*

Many countries have established regulations to control the level of pesticides in the environment, especially in water, raw vegetables, and fruits (Samsidar et al. 2018; Yan et al. 2018). In order to enforce these regulations, there is an increasing demand for sensitive and accurate analytical tools to detect low concentrations of pesticides. Analytical methods have been based on conventional techniques – high-performance liquid chromatography (LC) (Picó et al. 2004; Thurman et al. 2001), capillary electrophorese (CE) (Hsu and Whang 2009), and gas chromatography (GC) (Guan et al. 2010). These techniques can be used in combination with several detectors depending on the pesticide and sample analyzed (Rejczak and Tuzimski 2015). For instance, nonvolatile pesticides have been detected using LC coupled to UV detectors, fluorescence detectors, diode-array detectors (DAD), and mass spectrometry (MS). Polar and easily vaporizable compounds are normally detected using GC coupled to detectors such as flame photometric detector (FPD), flame ionization detector (FID), and nitrogen phosphorus detectors (NPD) (Rejczak and Tuzimski 2015).

A crucial step toward the efficient detection of pesticides in complex matrices, e.g., soil, natural waters, and food, is a sample pretreatment to remove potential interferents that may impair an accurate analysis. Efforts have been made to develop procedures for sample extraction and purification, including liquid-liquid extraction (LLE), solid-phase extraction (SPE), matrix solid-phase dispersion (MSPD), solid-phase microextraction (SPME), stir bar sorptive extraction (SBSE), and quick, easy, cheap, effective, rugged, and safe (QuEChERS) extraction (Rejczak and Tuzimski 2015). In addition to removing impurities, many of these methodologies allow one to concentrate the analytes, which is more suitable to detect trace concentrations. An alternative to pretreatment methods is to employ molecularly imprinted polymers (MIPS), which are 3-D polymeric matrices with complementary cavities designed for a template molecule (Sarafraz-yazdi and Razavi 2015). They are suitable for this protocol owing to their high selectivity, relatively low cost, stability, and easy preparation. MIPs have been used as sorbents for SPE, MSPD, and SPME methods for selective extraction of pesticides from food (Djozan et al. 2009) and human serum (Zhang et al. 2019a). Magnetic MIPs have also been used (Karimian et al. 2017), and these hybrid materials show high selectivity, with their magnetism effect allowing an effect of sample separation without requiring additional filtration or centrifugation steps.

Combining sample pretreatment approaches and analytical characteristics from more conventional techniques has made it possible to detect single molecules and mixtures of pesticides, as illustrated in Table 3.1. It should be mentioned, however, that many experimental methods require sophisticated equipment and trained operators and usually are time-consuming, limiting their application for real-time and on-site detection.

Table 3.1 Analytical methods for detecting pesticides residues

Analyte	Detection technique	Extraction method	Sample	LODs	References
Organophosphates	LC-MS/MS	Liquid-liquid extraction	Fruits and berry juice	3×10^{-4} mg L^{-1} – 3×10^{-2} mg L^{-1}	Timofeeva et al. (2017)
Organochlorine	GC-EDC	Solid-phase extraction	Water	1.7 ng L^{-1}	Moawed and Radwan (2017)
Pyrethroids	GC-ECD	Solid-phase microextraction	Fruits and vegetables	0.1–0.5 ng L^{-1}	Zhang et al. (2017)
Organophosphates	LC-DAD	–	Water	32.8 ng L^{-1} – 104.5 ng L^{-1}	Mahajan and Chatterjee (2018)
Carbamates	LC- MS/MS	Solid-phase extraction	Water	0.5–6.9 ng L^{-1}	Shi et al. (2014)
Multiclass pesticides	GC-FID	Liquid-liquid extraction	Water	0.34–5 μg L^{-1}	Farajzadeh et al. (2015)
Diazinon	LC-UV	Magnetic molecular imprinted polymers	Water	2.19 mg L^{-1}	Karimian et al. (2017)
Ametryn	LC-UV	Magnetic molecular imprinted polymers	Tomato, capsicum, and strawberry	25 nmol L^{-1}	Khan et al. (2018)

LC-MS/MS high-performance liquid chromatography mass spectroscopy, *GC-ECD* gas chromatography-electron capture detector, *LC-DAD* high-performance liquid chromatography with diode-array detection, *GC-FID* gas chromatography-flame ionization detector, *LC-UV* high-performance liquid chromatography with UV detection, *LOD* limit of detection

3.2.2 *Sensors and Biosensors for Pesticide Detection*

The growing need for analytical methods for a rapid, selective, and accurate detection of pesticides has motivated the development of relatively low-cost sensors and biosensors. These devices normally contain nanomaterials: carbon nanotubes (Kaur et al. 2019), graphene derivatives (Hashemi et al. 2019), quantum dots (Wang et al. 2019b), and metal nanoparticles (Jiang et al. 2018). Transduction methods for these sensors include electrochemistry (Velusamy et al. 2019), fluorescence (Wu et al. 2019), surface-enhanced Raman scattering (SERS) (Jiang et al. 2018), and surface plasmon resonance (SPR) (Cakir et al. 2019). A large enhancement in SERS signal may arise from plasmonic nanostructures, then permitting detection of analytes at very low concentrations. For example, a SERS sensor containing Ag-coated Au nanoparticles (Au@Ag NPs) detected insecticide residues in peach simultaneously (Yaseen et al. 2019). Figure 3.4 shows the results for Au@Ag NPs with 26 nm Au core size and 6 nm Ag shell yielded to enhance Raman signals for pesticides, in which the limits of detection were 0.1 mg kg^{-1} for thiacloprid and 0.01 mg kg^{-1} for profenofos and oxamyl.

Biosensors have been preferred for detecting pesticides due to their selectivity provided by biological components acting as recognition units, viz., enzymes, antibodies, nucleic acids, microorganisms, biological tissues, and organelles. They can be used in combination with a physical transducer to generate intense signals due to changes in concentration of a specific analyte (Madrid et al. 2017). The selectivity of biosensors may allow for analyte detection even in complex matrices (Saini et al. 2017). Enzymes are utilized in electrochemical biosensors to detect pesticides since many products of enzymatic reactions show electroactive responses. Enzymes are

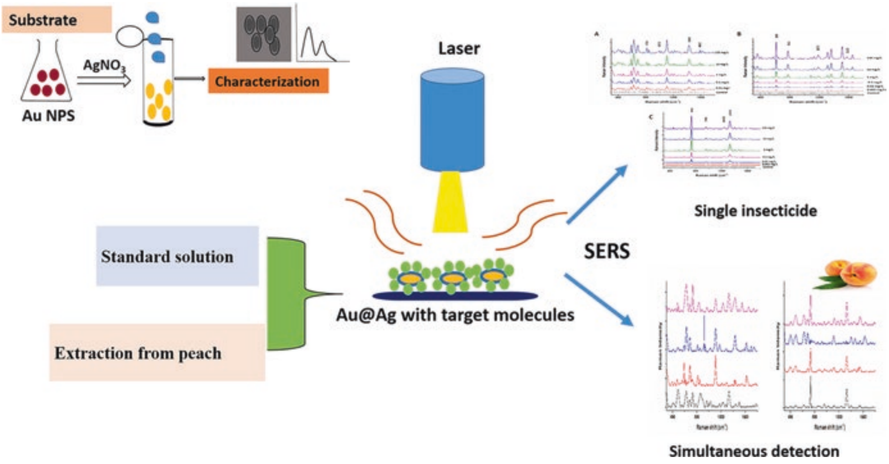


Fig. 3.4 Schematic design for a surface-enhanced Raman scattering (SERS) sensor for detecting thiacloprid, profenofos, and oxamyl in peach. (Reproduced with permission from Yaseen et al. 2019)

usually more stable and less expensive than other common biomolecules such as antibodies (Fabiana Arduini et al. 2016). The detection protocols using enzymatic biosensors involve monitoring changes in pesticide concentration by means of either enzymatic reactions or enzyme-inhibition mechanisms.

Many catalytic biosensors contain organophosphorus hydrolase (OPH), which catalyzes the hydrolysis of organophosphorus compounds, including parathion and methyl parathion, by breaking P-O, P-S, and P-CN bonds (Sassolas et al. 2012). The hydrogen ions and alcohols generated as enzymatic products can be monitored by electrochemical and optical techniques (Sassolas et al. 2012). Wearable potentiometric tattoo biosensors have been built with OPH immobilized onto screen-printed transducers to detect diisopropyl fluorophosphate (DFP) (Mishra et al. 2018). Figure 3.5 shows the principle of detection for these biosensors made with electrodes printed onto a temporary tattoo paper after being modified with a pH-sensitive polyaniline (PANI) film. This PANI film helps to monitor hydrogen ion released from the enzymatic hydrolysis of DFP. This biosensor was also efficient to detect other organophosphates. Catalytic biosensors, nonetheless, have drawbacks that restrict their widespread use, including a limited number of enzymes available for catalyzing the hydrolysis of pesticides. For example, OPH-based biosensors detect only some organophosphorus compounds, since large molecules with more complex structures do not interact effectively with active enzymatic sites (Mulyasuryani and Prasetyawan 2015).

Biosensors based on enzymatic inhibition mechanisms, where the analyte is quantified through its ability to inhibit enzyme function, are more sensitive for detecting pesticides than catalytic biosensors. Figure 3.6 shows the operation principle in which the enzymatic activity can be monitored. After addition of the inhibitor, the catalytic activity decreases and so does the analytical signal (Amine et al. 2015). The properties and operation parameters for these biosensors depend on the enzyme-inhibitor interaction, which is classified as reversible or irreversible. When the interaction is irreversible, covalent bonds are formed between the inhibitor and the active site of the enzyme leading to permanent loss of enzymatic activity (Aziz Amine et al. 2006). For biosensors based on reversible inhibition, on the other hand,

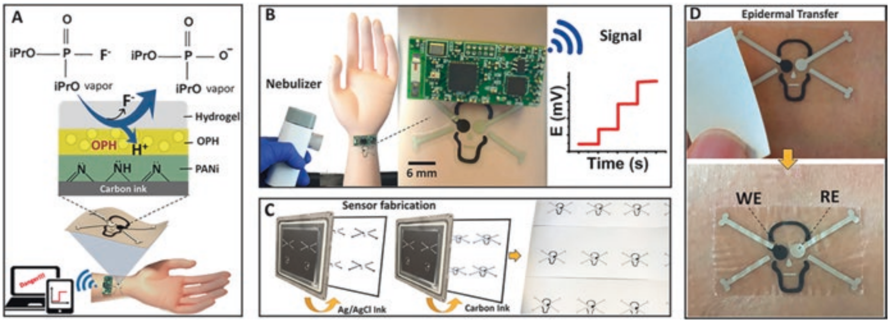


Fig. 3.5 Illustration of tattoo biosensors for detecting nerve agents. (Reproduced with permission from Mishra et al. 2018)

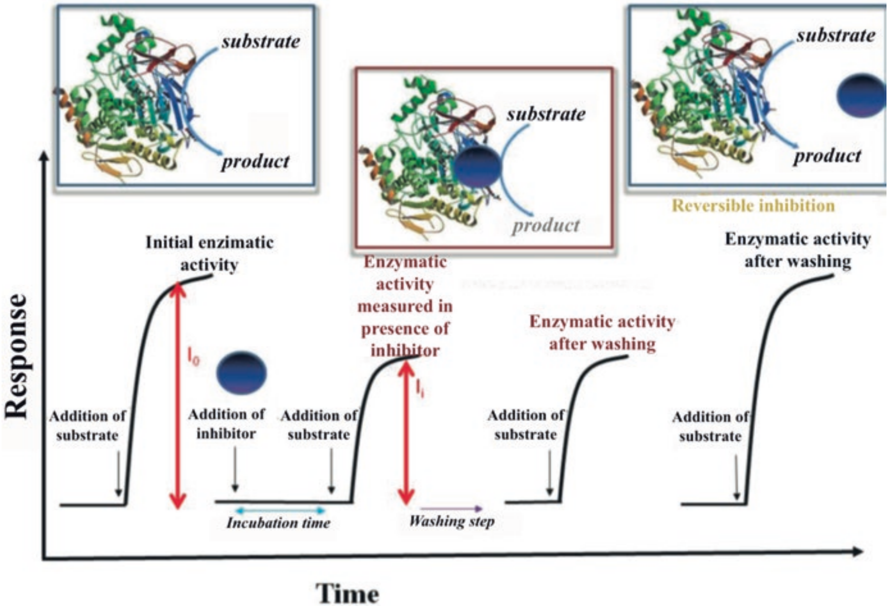


Fig. 3.6 Reversible and irreversible inhibition detection using biosensors based on enzyme inhibition mechanism. (Reproduced with permission from Amine et al. 2015)

the enzymatic activity can be restored by washing them with water or buffer solutions, which allows one to perform multiple measurements with a single device (Amine et al. 2015).

The activity of cholinesterase is inhibited irreversibly by organophosphorus and carbamate pesticides (Fabiana Arduini et al. 2010; Pundir and Chauhan 2012). These enzymes are found in insects and vertebrates, being responsible for catalyzing the hydrolysis of the acetylcholine neurotransmitter, a crucial step in the transmission of nerve impulses. Two types of cholinesterase are known, which are mainly distinguished by their substrate specificity: acetylcholinesterase (AChE), which has a higher catalytic activity toward acetyl esters, e.g., acetylcholine, and butyrylcholinesterase (BChE), which preferentially hydrolyzes butyrylcholine (Saini et al. 2017). The reaction products can be monitored using potentiometry or optical methods with pH-sensitive indicators (Sassolas et al. 2012). A simpler methodology involves artificial substrates such as acetylthiocholine and butyrylthiocholine, whose hydrolysis product – thiocholine – can be detected electrochemically at relatively low potentials. Bi-enzymatic and tri-enzymatic biosensors have also been developed, in which enzymes such as choline oxidase and peroxidase can be used to produce electrochemically detectable species (Andreescu and Marty 2006).

Paper-based biosensors relying on enzymatic inhibition have been reported for low-cost, user-friendly determination of pesticides. Arduini et al. (2019) developed paper-based biosensors using butyrylcholinesterase, alkaline phosphatase, and tyrosinase on screen-printed electrodes modified with carbon black and Prussian blue nanoparticles to improve sensitivity. Paraoxon, 2,4-dichlorophenoxyacetic acid, and atrazine were detected in standard solutions and river water samples using amperometry. A relevant limitation of biosensors based on enzymatic inhibition is the low selectivity for several enzymes, and this may impair pesticide detection in complex matrices of environmental interest owing to the presence of other, competitive inhibitors. Therefore, most of these sensors are used for screening purposes and not for detecting specific molecules (Jiang et al. 2008).

Immunosensors and aptasensors are useful to detect pesticides, since antibodies and aptamers are able to recognize analytes. For immunosensors, the interaction between antibodies (Ab) and antigens (Ag) is affected by the concentration of a specific analyte (Jiang et al. 2008). In addition to their use for detecting biomarkers of various diseases, immunosensors serve to detect pesticides and other compounds through advances in biotechnology where antibodies are generated which are specific for several molecules (Fernández-Benavides et al. 2019; Jiao et al. 2018). Aptasensors are promising for performing selective, fast, and sensitive detection of pesticides at low concentrations. They can be used in sensors as recognition elements as short oligonucleotides of RNA or DNA synthetized using the selection evolution of ligands by exponential enrichment (SELEX) technique (Liu et al. 2019). With SELEX, molecules can be obtained which possess high binding affinity and selectivity against a target analyte without using animals or cell cultures. In addition to the advantages in the production process, aptamers are more stable than antibodies and enzymes, allowing the use of aptasensors under harsh conditions. Aptasensors exploiting electrochemical techniques (Fu et al. 2019; Xu et al. 2019) and fluorescence (Cheng et al. 2018) have been used to detect pesticides.

3.3 Pollutants and Side Effects

The rapid population growth and industrialization have led to discarding a huge number of contaminants into the environment, which is why the twenty-first century was coined the Century of the Environment (Azam et al. 2016). Most pollutants are hazardous and poisonous, as the case of volatile organic compounds (VOCs) (Liu et al. 2018; Malik et al. 2018), heavy metals (Kamilari et al. 2018), toxic inorganic gases (Joshi et al. 2018), dyes (Nguyen and Saleh 2016), food preservatives, and personal care products. They pose severe threats for human beings and the environment. VOCs, for instance, can easily evaporate from household products such as paints, cleansers, and furnishings, causing short- and long-term adverse effects (Spinelle et al. 2017). Real-time monitoring of VOCs is now required for several types of industries, including cosmetics, medical diagnosis, food, and beverages, and long-term exposure can cause damage to the liver, kidney, and central nervous system (Jung et al. 2012).

The International Agency for Research on Cancer (IARC) has stated that online monitoring of formaldehyde should be performed in indoor environments because formaldehyde has been linked to cancers in the nasal cavity, mouth, throat, skin, and digestive tract (Mandayo and Castaño 2013). A major concern is water contamination in community services, particularly with heavy metals (Tchounwou et al. 2012). Metals such as Hg, Pb, As, and Cd are known as bioaccumulative compounds in the human body, resulting in multi-organ disruption (Jaishankar et al. 2014; Karri et al. 2016). Another class of pollutants includes additives and dyes in foods and textile industries (Sorouraddin et al. 2015). A synthetic diazo colorant, allura red, used in beverages, ice cream, and bakery products, is known for its carcinogenic effect, also being the main cause of hyperactivity in children. In addition to those linked to air and water quality systems (Scotter 2015), there are pollutants such as brominated flame retardants (Darnerud 2003) and textile dyes used for dyeing and finishing operations. Table 3.2 shows a list of air and water pollutants and adverse effects on mankind and animals.

3.3.1 Analytical Techniques for Pollutant Detection

Quantitative and qualitative measurements of pollutants are necessary to control air and water pollution. However, these measurements are not straightforward, especially owing to the presence of interferents (Qin et al. 2013). Moreover, managing pollution requires detection of pollutants at low concentrations (Gauquie et al. 2015), which depend on mainly on:

- Pollutant state (liquid, gaseous, aerosols, or particulate matter)
- Sample preparation and concentration level
- Measurement period (short or long term)
- Measurement site (in lab or on-site)
- Temperature and humidity effect and control
- Cross-sensitivity with other analytes
- Reliability and stability check with commercial sensor

For monitoring air quality, there are methods to detect hazardous analytes in the environment, as illustrated in Table 3.3. However, stability and selectivity are still a challenge for current sensor technologies. Optical and electrochemical sensors can offer high sensitivity, but bulky dimensions and high-power consumption do not allow them to be widely applied for health-care or mobile applications.

There are also analytical techniques to detect pollutants such as heavy metals, VOCs, food dyes, and brominated flame retardants, as depicted in Table 3.4.

3.3.2 Sensors and Biosensors to Detect Pollutants

The need to detect pollutants in air, soil, and water has sparked research into analytical techniques (Goradel et al. 2017) to replace conventional chromatography that requires expensive, time-consuming sample preparation. Cost-effective, robust, and

Table 3.2 Examples of air and water pollutants – sources and effects (Kaur and Nagpal 2017; Muralikrishna 2017)

No	Pollutants	Sources	Effects
1	Carbon monoxide (CO)	Incomplete combustion of fuels in road transport. Wood stoves, cigarette smoke, and forest fire	Interfering with the blood's ability to carry oxygen, slowing reflexes, and causing drowsiness, headaches, and stress on heart in high concentrations – CO can cause death
2	Sulfur dioxide (SO_2)	Burning fossil fuels (gasoline, oil, natural gas) Released from petroleum refineries, paper mills, chemical, and coal-burning power plants	It is easily dissolved in water and forms acids, contributing to acid rain in lakes and forests. Metals and stones can be also damaged by acid rain
3	Nitrogen oxides (NOx)	Burning fuels in motor vehicles, power plants, industries, and residences that burn fuels	Make the body vulnerable to respiratory infections, lung disease, and possibly cancer
4	Volatile organic compounds	Emitted as gases (fumes) by burning fuels, cleaning supplies, paints, and solvents	Smog formation and can cause serious health problems. They may also harm plants
5	Heavy metals (lead, mercury, cadmium, etc.)	Waste incineration Production of nonferrous metals, iron, steel, and cement	Cause organ and neurological damage in humans and animals. It can also slow down growth rate in plants
6	Organic pollutants Oil and grease pesticides/weedicides Plastics Detergents	Automobile and machine waste, tanker spills, and offshore oil leakage Chemicals used for better yield from agricultural, industrial, and household waste	Disruption of marine life, aesthetic damage Toxic effects (harmful for aquatic life) Possible genetic defects and cancer Kill fish, eutrophication aesthetics
7	Textile dyes	Natural or synthetic coloring substance which is used in textile industries	They are dangerous and have toxic and carcinogenic effects
8	Brominated flame retardants (BFRs)	Flame retardants containing brominated organic compounds that are applied to combustible materials, such as plastics, wood, paper, electronics, and textiles to meet fire safety regulations	Severe pneumonia by respiratory syncytial virus (RSV) infection to birds and animals. Toxic (acute and chronic) and ecotoxic effects of some BFRs have been observed

portable biosensing and gas sensing devices have been proposed (Materón et al. 2019) with the majority of biosensors incorporating nanomaterials to enhance sensitivity and selectivity (Hernandez-Vargas et al 2018). Electrochemical biosensors, in particular, can detect biological analytes at low concentrations with various techniques, including potentiometric, amperometric, voltammetric, and conductometric measurements (Hernandez-Vargas et al. 2018; Justino et al. 2017). Air pollution caused by hazardous gases from textile and automobile industries has become a serious issue. The major gases that cause air pollution are carbon monoxide and nitrogen oxides, and their main source is fossil fuel combustion (Joshi et al. 2018).

Table 3.3 Air quality sensors and detection principle (Aswal and Gupta 2006)

Type of sensors	Sensor	Detection principle
Solid-state sensors	Chemiresistive	A change in conductivity of semiconductor is measured when it interacts with the analyte gas
	Chemical field-effect transistors (ChemFET)	Current-voltage (I-V) curves of a field-effect transistor (FET) are sensitive to a gas when it interacts with gate
	Calorimetric	The concentration of a combustible gas is measured by detecting the temperature rise resulting from the oxidation process on a catalytic element
	Potentiometric	The signal is measured as the potential difference between the working electrode and the reference electrode. The working electrode's potential must depend on the concentration of the analyte in the gas phase
	Amperometric	Diffusion limited current of an ionic conductor is proportional to the gas concentration
Mass-sensitive sensors	Acoustic	Change in frequency of surface acoustic waves (SAW) excited on a quartz or piezoelectric substrate upon absorption of gas in a suitable sorption layer (e.g., metals, polymers)
	Microelectromechanical systems (MEMs) based	Change in mechanical bending of micro- or nanocantilevers upon adsorption of gas
Optical sensors	Surface plasmon resonance (SPR)	Change in SPR signals is proportional to the refractive index close to the sensor surface and is therefore related to the amount of bound gas molecules
	Optodes	The change of optical properties measured can base on absorbance, reflectance, luminescence, light polarization, Raman, and others

Volatile organic compounds (VOCs) are produced by construction materials and paint industries, which may even cause headache and skin trouble for people moving into a new apartment (Campos and Sarkis 2018). For example, formaldehyde is produced in industries in the manufacture of resins, as a disinfectant, or as a preservative in consumer products; it is a dangerous indoor pollutant as it can harm all kinds of organisms (Chung et al. 2013; Lawal et al. 2017). The allowed concentration of formaldehyde is only 0.1 ppm in Netherlands and Germany (Chmielewski 2011). Also, the US Environmental Protection Agency (US EPA) has imposed strict regulations on the concentrations of environmental contaminants in air and water. In this section we will discuss the sensors and biosensors for detecting heavy metals, hazardous gases and VOCs, food dyes, and brominated flame retardants.

- *Heavy Metal Detection*

Due to increasing industrial activity, heavy metals such as Hg, AS, Pb, and Cd have been entering into the environment which are highly toxic and carcinogenic

Table 3.4 Detection techniques and detection principles for heavy metals, food dyes, VOCs, and brominated flame retardants (Holbrook et al. 2012; Hori et al. 2013; Zhu et al. 2017).

Type of analytes	Detection method	Detection principle
Heavy metal ions	Inductively coupled plasma (ICP) by mass spectrometry (MS)	The ICP is used to ionize the sample, while the mass spectrometer is used to separate and quantify those ions. Calibrating the instrument with known standards allows for an unknown sample to be quantified
	Cold vapor atomic absorption (CV-AA)	This analysis detects mercury by measuring the absorption of light by mercury in an elemental gaseous state
	Optical	Optical sensors can be described as small devices that respond to the presence of heavy metals by generating an optical signal proportional to the type and concentration of the heavy metal
	Electrochemical	The working principle of such sensors is based on having a transducing element covered with recognition element, which can be either a biological or a chemical element
	Microelectromechanical systems (MEMs) based microspectrometers	Microspectrometer is a tool designed to measure the spectrum of microscopic areas or microscopic samples to measure the transmittance, absorbance, reflectance, polarization, and fluorescence of sample areas smaller than a micron
Volatile organic compounds	Electrochemical (amperometric) sensors	In these sensors, analyte particles diffuse through a membrane and the internal electrolyte toward the surface of working electrode suitably polarized with respect to a reference electrode
	Chemiresistive	Change in conductivity on exposure to analyte gas
	Nondispersive infrared sensors (NDIR)	Sensor consists in arranging a source of infrared radiation along an optical line with a detector. When an analyzed gas appears in a measurement chamber, it absorbs radiation of a particular wavelength and decreases in radiation which is converted into electrical signal.
Food dyes	Paper chromatography (extraction techniques)	The principle involved is partition chromatography, wherein the substances are distributed or partitioned between liquid phases
	Ultraviolet-visible (UV- VIS) spectrophotometer	Principle of UV-visible spectrophotometer is mainly based on Beer's law and Lambert's law

(continued)

Table 3.4 (continued)

Type of analytes	Detection method	Detection principle
Brominated flame retardants	Gas chromatography/mass spectrometry (GC/MS)	The GC works on the principle that a mixture will separate into individual substances when heated. The heated gases are carried through a column with an inert gas (such as helium). As the separated substances emerge from the column opening, they flow into the MS

even at a trace level. They are not biodegradable and will therefore remain for decades once released in the environment and appear at detectable levels in food resources (Tangahu et al. 2011). The sensitive conventional methods to detect heavy metals include atomic absorption spectroscopy and atomic emission spectroscopy. These methods require laborious preparation and pretreatment procedures and professional personnel (Chinna et al. 2018).

Electrochemical, optical, and field-effect transistor (FET)-based sensors have been developed using nanostructures and nanomaterials (Fig. 3.7). Luo et al. (Luo et al. 2009) used silicon nanowires (SiNWs) in FET sensors for detecting toxic heavy metal cations with a LOD of 10^{-7} mol L^{-1} for Hg^{2+} and 10^{-4} mol L^{-1} for Cd^{2+}. The chemical gating effect and strong chelation between thiol groups with positively charged cations is the main reason for the high sensing behavior, and sensors could also be recycled with nearly the same sensitivity as before. Figure 3.7a shows the measuring setup, while Fig. 3.7b shows the I-V behavior of the SiNW before and after thiol modification. The ohmic contacts are formed between electrodes and SiNW, and the modification induces slight decreases in the conductance of SiNW. Figure 3.7c indicates the current change by varying Cd^{2+} concentration in solution. Compared to distilled water (pH = 4), the change in current was increased by 10%. When Cd^{2+} ion of 10^{-4} mol L^{-1} was introduced and as Cd^{2+} concentration further increased to 1×10^{-3}, 3×10^{-3}, 1×10^{-2}, 2×10^{-2}, and 4×10^{-2} mol L^{-1}, the current increased by 28.1%, 40.2%, 56.6%, 66.7%, and 67.4%, respectively. Similarly, the current changed with the Hg^{2+} concentration, as illustrated in Fig. 3.7d.

Optical sensors to detect heavy metals can exploit various principles, including colorimetry, surface plasmon resonance (SPR), and surface-enhanced Raman scattering (SERS) (Meyer et al. 2011; Prabowo et al. 2018; Jiangcai Wang et al. 2017). SERS sensors have been used for chemical and biological sensing and medical diagnostics, but few reports exist of detection of heavy metals. SERS is the molecular spectroscopy which provides spectral fingerprints of target analytes. It is unable to detect heavy metals directly, so the plasmonic nanostructures are functionalized with organic ligands that bind specifically to heavy metal ions. Jinglian Li et al. (2011) developed SERS sensors for As^{3+} detection in aqueous media with glutathione (GSH)/4-mercaptopyridine (4-MPY)-modified silver nanoparticles (AgNPs). Figure 3.8a shows increased SERS signal with addition of As^{3+} ions owing to the As-O linkage established when the distance among AgNPs was shortened with a moderate amount of GSH and 4-MPY. The sensor achieved a limit of detection

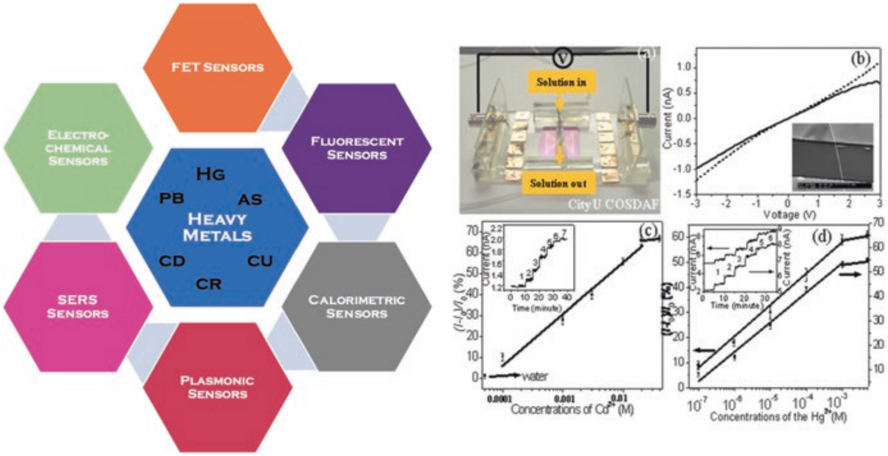


Fig. 3.7 Sensors for detecting heavy metals (**a**) Sensing setup system; (**b**) I-V characteristics of a SiNW before (dotted line) and after thiol modification; (**c**) current changing with increasing Cd^{2+} concentration; (**d**) current variation with increasing Hg^{2+} concentrations. (Reproduced with permission from (Luo et al. 2009), Copyright 2009, American Institute of Physics)

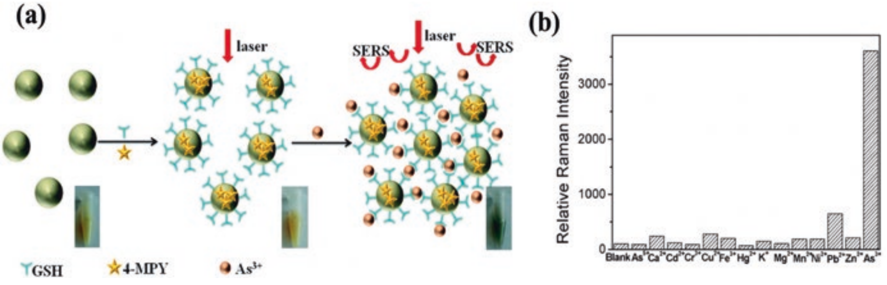


Fig. 3.8 (**a**) Representation of glutathione (GSH) and 4-MPY-modified AgNPs; (**b**) SERS sensor for selective As^{3+} detection using silver nanoparticles. (Reproduced with permission from Jinglian Li et al. (2011). Copyright 2011, American Chemical Society)

(LOD) of 0.76 ppb with selectivity over various metal ions (Fig. 3.8b). However, long-term stability and repeatability of the SERS-based sensors are still a major concern.

- *Chemical Sensors for Detection of Toxic Pollutants*

Chemical sensors are a crucial part of modern life with applications in environmental monitoring, domestic safety, public security, and food quality assessment among others (Swager and Mirica 2019). They are increasingly being integrated into mass-market applications, for instance, in air quality control in buildings and motor vehicles and in traditional areas of toxic and explosive gas detection. The market for gas sensors is growing with new applications driving innovation, for instance, the analysis of gases from the gut and breath for noninvasive diagnosis of diseases (Bogue 2017). Chemiresistive sensors comprise an important part of the gas sensor market, against a host of competing technologies, due to their low cost, high sensitivity, fast response, and relative simplicity (Liu et al. 2012). The materials used in these sensors are typically wide-bandgap semiconducting metal oxides, such as tin oxide, tungsten oxide, indium oxide, or zinc oxide (Domènech-gil et al. 2017; Joshi et al. 2016; Jinwei Li et al. 2015b; Sayago et al. 2019). They function as gas sensors because adsorbed gaseous species form surface states in the metal oxide by exchange of electrons with the bulk material. The concentration of the surface states is proportional to the partial pressure of the gas impinging on the metal oxide, and hence the conductivity of the material changes in response to changes in gas concentration. These chemically induced changes can then be transduced into electrical signals by means of simple conductivity measurements.

Metal oxides are the most common and even commercially available sensors; however, they rely on high temperature modulation to achieve high sensitivity and selectivity which decreases the sensor lifetime and makes the system more complex (Zhou et al. 2014b). In order to obtain room temperature sensing, 2D materials have been investigated owing to their high surface to volume ratio, but the speed of recovery is still a limitation. Liu et al. (2018) demonstrated new AC phase sensing of graphene FETs for chemical vapors with fast recovery, with a new concept illustrated in Fig. 3.9. To get rid of the effects of trap states and defects, those authors used the reversible and stable phase change as the sensing parameter instead of the vulnerable DC resistance (see Fig. 3.9a). The phase lag between channel resistance and the gate voltage was detected with the AC voltage applied on the gate electrode, as shown in Fig. 3.9b. The recovery speed is ten times faster than with DC resistance signals. Figure 3.9c illustrates the key difference between AC and DC measurements where AC measurements are more sensitive to weak adsorption of vapor molecules, while DC measurement results are sensitive to a strong adsorption-desorption process. Malik et al. (2018) employed Au-TiO_2@g-CN nanohybrids to detect volatile organic amines (VOAs), such as triethylamine (TEA), using a two-step method (hydrothermal and nanocasting). The average times for response and recovery of the Au-TiO2@m-CN sensor toward TEA gas are 9–16 and 6–12 s for 1–50 ppm range.

- *Detection of Food Dyes*

Manufacturing industries use large amounts of cost-effective artificial ingredients for improving their consumer characteristics and appearance (Leo et al. 2017; Lipskikh et al. 2018; Nambiar et al. 2018; Zhu et al. 2017). Monitoring the quality of food dyes in drinks has therefore become of paramount importance. Brilliant Blue (E133), Tartrazine (E102), Sunset Yellow (E110), and Amaranth (E123) (molecular structure and commercial name and details in Table 3.5) are synthetic dyes added to nonalcoholic beverages. The Brazilian Agency for Public Surveillance (ANVISA) has issued legal provision in 2002 to regulate the use of food dyes, since their high consumption could induce skin allergies and bronchial asthma. The maximum level allowed is 0.01 g/100 mL for Sunset Yellow, Tartrazine, and

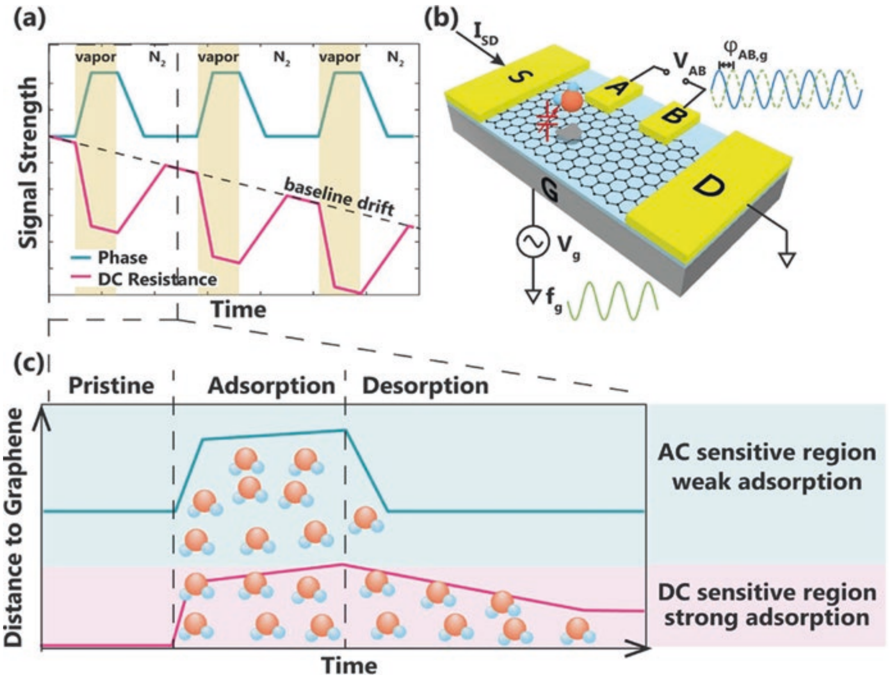
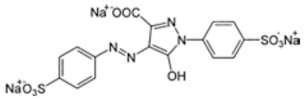
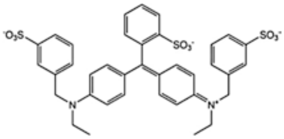
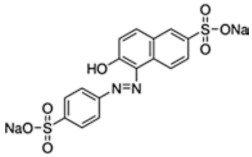
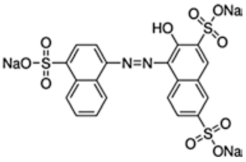


Fig. 3.9 (**a**) Schematic of gas sensing performance using the phase lag detection method with fast recovery compared to the DC resistance method. (**b**) Schematic of phase lag $\varphi_{AB,g}$ between V_{AB} and V_g on a CVD graphene FET sensor under the exposure to chemical vapor. (**c**) Vapor adsorption process and desorption on the graphene surface illustrating that the AC sensing scheme is more effective to detect weakly adsorbed gases away from the graphene surface, while the DC sensing scheme is more effective to detect molecules close to the surface. (Reproduced with permission from (Liu et al. 2018) Copyright 2018, Elsevier)

Brilliant Blue in nonalcoholic beverages, while the value for Amaranth is 0.005 g/100 mL.

The analytical techniques to determine concentrations of food colorants include thin-layer chromatography (TLC), spectrophotometry in the visible region, high-performance liquid chromatography, and capillary electrophoresis. Reverse phase LC and ion-pair high-performance liquid chromatography (LC IP) are the most used in drinks. For instance, sulfonated azo dyes used in 330 commercial samples of orange and grape carbonated soft drinks were determined using ion-pair LC combined with photodiode array and thin-layer chromatography (TLC) (Andrade et al. 2014). A liquid chromatography diode-array detector (LC-DAD) was utilized to distinguish natural and synthetic colorants in dairy samples such as milk shakes, yogurts, and ice creams (Gallego and Valca 2003). Second-order derivative linear sweep voltammetry was used to detect tartrazine where glassy carbon electrodes were coated with a TiO_2-reduced graphene oxide composite (He et al. 2018).

Table 3.5 Food colorants and their structures and commercial names. European Community (EC) number, and food (F) and drug (D) number (Oplatowska-stachowiak and Elliott 2015)

Molecular structure	Commercial name	EC number	FD&C number
	Tartrazine	E102	Yellow #5
	Brilliant Blue FCF	E133	Blue #1
	Sunset Yellow FCF	E110	Yellow #6
	Amaranth	E123	Red #2

- *Detection of Brominated Flame Retardants*

Brominated flame retardants (BFRs) such as polybrominated diphenyl ethers (PBDEs) and hexabromocyclododecane (HBCD) are mainly used in plastics and electronic equipment to prevent combustion. Exposure to PBDEs may lead to endocrine disruption and neurodevelopmental toxicity in humans and hepatotoxicity, endocrine disruption, gene expression, and impaired reproductive physiology in animals. They have been banned in Europe, North America, and Australia (Mcgrath et al. 2017). Most BFRs are detected with gas chromatography/mass spectrometry (Geng et al. 2017).

3.4 Pharmaceutical and Personal Care Products (PPCPs)

Pharmaceutical (human and veterinary therapeutic drugs) and personal care products (PPCPs) comprise a well-known group of emerging contaminants (Boxall 2004; Boxall et al. 2012; Jennifer et al. 2017). Some of this pollution comes from human excretion of contraceptives and other medicines (e.g., acetaminophen, acetylsalicylic acid, ibuprofen, naproxen, and carbamazepine), which are eventually found in water (Boxall 2004). These drugs are absorbed, metabolized, and excreted to the sewage system, with some metabolized products being even more toxic than the non-metabolized drugs. Furthermore, many of the water treatment systems are not capable of removing the drugs and may transform the products into more toxic ones (Boxall 2004; Boxall et al. 2012; Jennifer et al. 2017; Kümmerer 2009; Vieno and Sillanpää 2014). The main sources of environmental pollution from pharmaceutical products are:

- Effluents from manufacturing and hospital waste
- Excretion by animals treated with antibiotics or other drugs
- Human excretion of pharmaceutical and personal care products (Richardson and Bowron 1985; Rzymski et al. 2017)

The traditional methods to treat water include adsorption, solvent extraction, reduction, flocculation, coagulation, chemical or biological oxidation, ultrasound, and membrane filtration (Fan et al. 2018; Jing Wang et al. 2019a). The reported concentrations of pharmaceutical products are low, between ng L^{-1} (groundwater) and μg L^{-1} (wastewater), but many drugs can have cumulative effects and bring health problems, such as cancer (Boxall 2004; Christou et al. 2018).

3.4.1 Current Analysis of Pharmaceutical Products

The large number of recent reports of emerging pollutants in the environment may give the impression that this is a new problem. However, this is not new, and such pollution was simply ignored in the past owing to the lack of analytical methods with sufficient sensitivity to detect trace amounts (Buchberger 2011). Indeed, already in 1977 Hignite and Azarnoff found clofibric acid (used to lower plasma triglycerides and cholesterol concentrations in humans) and salicylic acid at low ppb levels in sewage treatment plant effluents (Hignite and Azarnoff 1977). Kolpin et al. (2002) detected 95 pharmaceutical contaminants such as hormones and other organic wastewater contaminants (OWCs) in water resources in the USA in 1999 and 2000 (Kolpin et al. 2002). Ternes reported the discovered drugs in the aquatic environment at concentrations up to approximately 1 μg l^{-1} in the UK (Ternes 1998). Pharmaceutical and chemotherapeutic drugs were found in the sewage, sewage effluents, river, and potable water (Richardson and Bowron 1985). Unfortunately, some drug residues could survive the various water treatment processes and remain at low concentrations <μg L^{-1} (Richardson and Bowron 1985; Ternes 1998).

In a review about ecotoxicity of hospital waste effluents, Orias and Perrodin (2013) listed a variety of toxic substances (Jean et al. 2012; Orias and Perrodin 2013), and human and veterinary pharmaceutical substances were found in surface water, groundwater, tap/drinking water, and soil (Beek et al. 2016). The anti-inflammatory drug diclofenac was found in higher-than-expected concentrations in 50 countries (aus der Beek et al. 2016). Also relevant are the effects of cocktails of drugs released in the environment after human consumption or/and incomplete removal at the waste treatment plant, which increase ecotoxicity (Vasquez et al.

2014) that is increasing over the years owing to their availability in town pharmacies (Parrella et al. 2014), (Besse et al. 2012). Ferrando-Climent and co-workers found tamoxifen and ciprofloxacin in the river upstream the sewage discharge (Ferrando-Climent et al. 2014), and Miller et al. (2018) discussed bioaccumulation of pharmaceuticals and its metabolite products in aquatic fauna, including anticancer drugs (Miller et al. 2018).

The increasing environmental contamination with pharmaceutical products requires alternative analytical techniques (Webb et al. 2003) to liquid (LC) and gas chromatography (GC) coupled to mass spectrometry (MS) (Fatta et al. 2007; Miller et al. 2018). Other methodologies to detect emerging pollutants are given in Table 3.6, including titrimetric measurements, UV-vis spectroscopy, near-infrared spectroscopy (NIRS), fluorometry, phosphorimetry, and nuclear and magnetic resonance spectroscopy (NMR) (Turci et al. 2003).

3.4.2 Sensors and Biosensors to Detect Pharmaceutical and Personal Care Products (PPCPs)

Pharmaceutical products and derivatives are among the most demanding contaminants to detect in the environment. Highly frequent are the antibiotics introduced into the ecosystem via excretion from humans and animals (Khor et al. 2011). Antibiotics have been found in water resources, effluent from industries, sludge, manure, soil, plants, and organisms, the most common being b-lactams, sulfonamides, monobactams, carbapenems, aminoglycosides, glycopeptides, lincomycin, macrolides, polypeptides, polyenes, rifamycin, tetracyclines, chloramphenicol, quinolones, and fluoroquinolones (Gothwal and Shashidhar 2014). Negative effects from antibiotics include reduction of the growth, photosynthesis, content of photosynthetic pigments, chlorophylls, and carotenoids in plants. Moreover, fluoroquinolones inhibit DNA synthesis in eukaryotic cells, and b-lactams affect the plastid division in lower plants (Gothwal and Shashidhar 2014). In humans, fluoroquinolones may cause side effects such as nausea, dyspepsia, vomiting, dizziness, insomnia, and headache (Norrby 1991). The most serious problem, though, is the potential resistance development in human and animal pathogens (Norrby 1991; Larsson 2014).

Detection of pharmaceutical products has also been performed with electrochemical techniques that may offer low cost, robustness, easy miniaturization, low detection limits, small analyte volume, and real-time monitoring (Wang et al. 2008). Electroanalytical methods may also be combined with standard techniques to improve sensitivity (Brett 2001). They employ enzymes, antibodies, nucleic acids, or whole cells immobilized onto amperometric or potentiometric electrode transducers, without requiring sample pretreatment (Joseph Wang 2002). Biosensors with a chemically selective layer (Stradiotto et al. 2003) may encompass immunosensors, such as the one to detect the fluoroquinolone antibiotic enrofloxacin in milk

Table 3.6 Methods to detect pharmaceutical products in the environment

Drug determined	Technique	LOD	Real sample	References
Acetaminophen	UPLC-MS/MS	3.5 ng L^{-1}	Wastewater	Hong et al. (2015)
Amoxicillin	LC-ESI-MS/MS	9.49 ng L^{-1}	Hospital Wastewater	Gros et al. (2013)
Amoxicillin	LC-ESI-MS/MS	2.65 ng L^{-1}	Urban Wastewater Effluent	Gros et al. (2013)
Amoxicillin	LC-ESI-MS/MS	3.32 ng L^{-1}	Urban Wastewater Influent	Gros et al. (2013)
Amoxicillin	LC-ESI-MS/MS	1.32 ng L^{-1}	River Water	Gros et al. (2013)
Caffeine	UPLC-MS/MS	3.4 ng L^{-1}	Wastewater	Hong et al. (2015)
Cefalexin	LC-ESI-MS/MS	4.32 ng L^{-1}	Hospital Wastewater	Gros et al. (2013)
Cefalexin	LC-ESI-MS/MS	1.43 ng L^{-1}	Urban Wastewater Effluent	Gros et al. (2013)
Cefalexin	LC-ESI-MS/MS	3.40 ng L^{-1}	Urban Wastewater Influent	Gros et al. (2013)
Cefalexin	LC-ESI-MS/MS	0.77 ng L^{-1}	River Water	Gros et al. (2013)
Clindamycin	LC-ESI-MS/MS	4.89 ng L^{-1}	Hospital Wastewater	Gros et al. (2013)
Clindamycin	LC-ESI-MS/MS	1.48 ng L^{-1}	Urban Wastewater Effluent	Gros et al. (2013)
Clindamycin	LC-ESI-MS/MS	3.13 ng L^{-1}	Urban Wastewater Influent	Gros et al. (2013)
Clindamycin	LC-ESI-MS/MS	0.48 ng L^{-1}	River Water	Gros et al. (2013)
Chloramphenicol	LC-MS	0.03–0.83 ng g^{-1}	Mussels	Fedeniuk et al. (2015)
Ciprofloxacin	U-LC-Q-Extractive Orbitrap	12.6 ng L^{-1}	River water	Lidia et al. (2015)
Diclofenac	UPLC-MS/MS	8.6 ng L^{-1}	Wastewater	Hong et al. (2015)
Doxycycline	LC-ESI-MS/MS	33.65 ng L^{-1}	Hospital Wastewater	Gros et al. (2013)
Doxycycline	LC-ESI-MS/MS	77.49 ng L^{-1}	Urban Wastewater Effluent	Gros et al. (2013)
Doxycycline	LC-ESI-MS/MS	59.79 ng L^{-1}	Urban Wastewater Influent	Gros et al. (2013)
Doxycycline	LC-ESI-MS/MS	11.23 ng L^{-1}	River Water	Gros et al. (2013)
Diclofenac	U-LC-Q-Extractive Orbitrap	5.0 ng L^{-1}	River water	Lidia et al. (2015)
Erythromycin	UPLC-MS/MS	0.22–0.26 ng g^{-1}	Fish	Liu et al. (2014a)

(continued)

Table 3.6 (continued)

Drug determined	Technique	LOD	Real sample	References
FQs	LC-FLD	0.3 ng g^{-1}	Fish liver and muscle, sediment	He et al. (2012)
FQs	LC-MS	0.5–3.9 ng g^{-1}	Frog legs, fishes	Turnipseed et al. (2012)
FQs	LC-MS/MS	0.06–0.9 ug kg^{-1}	Mollusks	Li et al. (2012a)
FQs	LC-MS/MS	0.31–38.4 ng g^{-1}	Plants	Sabourin et al. (2012)
FQs	LC-MS/MS	0.08–0.25 ng g^{-1}	Fish	Liu et al. (2015)
FQs	UPLC-MS/MS	Nd	Fish	Zhao et al. (2015a)
Ketoprofen	UPLC-MS/MS	5.0 ng L^{-1}	Wastewater	Hong et al. (2015)
Metronidazole	LC-ESI-MS/MS	6.49 ng L^{-1}	Ho spital Wastewater	Gros et al. (2013)
Metronidazole	LC-ESI-MS/MS	1.80 ng L^{-1}	Urban Wastewater Effluent	Gros et al. (2013)
Metronidazole	LC-ESI-MS/MS	4.45 ng L^{-1}	Urban Wastewater Influent	Gros et al. (2013)
Metronidazole	LC-ESI-MS/MS	0.43 ng L^{-1}	River Water	Gros et al. (2013)
Naproxen	U-LC-Q-Extractive Orbitrap	3.7 ng l^{-1}	River water	Lidia et al. (2015)
Oxacillin	UPLC-MS/MS	5.5 ng L^{-1}	Wastewater	Hong et al. (2015)
Oxytetracycline	LC-MS	2.6–4.4 µg kg^{-1}	Plants	Lidia et al. (2015)
Penicillin G	LC-ESI-MS/MS	2.55 ng L^{-1}	Hospital Wastewater	Gros et al. (2013)
Penicillin G	LC-ESI-MS/MS	3.48 ng L^{-1}	Urban Wastewater Effluent	Gros et al. (2013)
Penicillin G	LC-ESI-MS/MS	8.62 ng L^{-1}	Urban Wastewater Influent	Gros et al. (2013)
Penicillin G	LC-ESI-MS/MS	4.00 ng L^{-1}	River Water	Gros et al. (2013)
Penicillin V	LC-ESI-MS/MS	11.31 ng L^{-1}	Hospital Wastewater	Gros et al. (2013)
Penicillin V	LC-ESI-MS/MS	7.04 ng L^{-1}	Urban Wastewater Effluent	Gros et al. (2013)
Penicillin V	LC-ESI-MS/MS	22.82 ng L^{-1}	Urban Wastewater Influent	Gros et al. (2013)
Penicillin V	LC-ESI-MS/MS	5.37 ng L^{-1}	River Water	Gros et al. (2013)

(continued)

Table 3.6 (continued)

Drug determined	Technique	LOD	Real sample	References
PCs	LC-UV/VIS	11.0–20.4 ug kg^{-1}	Fish	Evaggelopoulou and Samanidou (2013)
Piroxicam	U-LC-Q-Extractive Orbitrap	3.9 ng L^{-1}	River Water	Lidia et al. (2015)
QLs	LC-MS/MS	Nd	Fish, crustacean	Na et al. (2013)
QLS	LC-MS/MS	0.81–4.60 ug kg^{-1}	Crustacean	Na et al. (2013)
Roxithromycin	UPLC-MS/MS	0.25–0.35 ng g^{-1}	Fish	Liu et al. (2014b)
SAs	LC-MS/MS	0.01–0.1 ng L^{-1}	Aquatic plants	Li et al. (2012b)
SAs	LC-MS/MS	0.01–1 μg kg^{-1}	Fish, sediment	Gao et al. (2012)
SAs	LC-MS/MS	Nd	Plants	Tanoue et al. (2012)
Sulfadiazine	U-LC-Q-Extractive Orbitrap	2.3 ng L^{-1}	River Water	Lidia et al. (2015)
Sulfadiazine	LC-MS/MS	5 ng L^{-1}	Plants	Michelini et al. (2012)
Sulfadiazine	LC-FLD	Nd	Plants	Li et al. (2013)
Sufamethoxazole	LC-MS	9.28–16.07 g g^{-1}	Plants	Holling et al. (2012)
Tetracycline	LC-ESI-MS/MS	24.30 ng L^{-1}	Hospital Wastewater	Gros et al. (2013)
Tetracycline	LC-ESI-MS/MS	13.42 ng L^{-1}	Urban Wastewater Effluent	Gros et al. (2013)
Tetracycline	LC-ESI-MS/MS	16.25 ng L^{-1}	Urban Wastewater Influent	Gros et al. (2013)
Tetracycline	LC-ESI-MS/MS	4.72 ng L^{-1}	River Water	Gros et al. (2013)
Triclosan	UPLC-MS/MS	16 ng L^{-1}	Wastewater	Hong et al. (2015)
Tylosin	LC-ESI-MS/MS	11.97 ng L^{-1}	Hospital Wastewater	Gros et al. (2013)
Tylosin	LC-ESI-MS/MS	28.11 ng L^{-1}	Urban Wastewater Effluent	Gros et al. (2013)
Tylosin	LC-ESI-MS/MS	34.00 ng L^{-1}	Urban Wastewater Influent	Gros et al. (2013)
Tylosin	LC-ESI-MS/MS	2.37 ng L^{-1}	River Water	Gros et al. (2013)
Vancomycin	LC-MS/MS	8.8 ng L^{-1}	Wastewater	Hong et al. (2015)
Warfarin	UPLC-MS/MS	14 ng L^{-1}	Wastewater	Hong et al. (2015)

nd no data, *FLD* fluorescence detection, *LC* high-performance liquid chromatography, *ESI* electrospray ionization, *UPLC* ultra-performance liquid chromatography, *LC-MS/MS* liquid chromatography mass spectroscopy

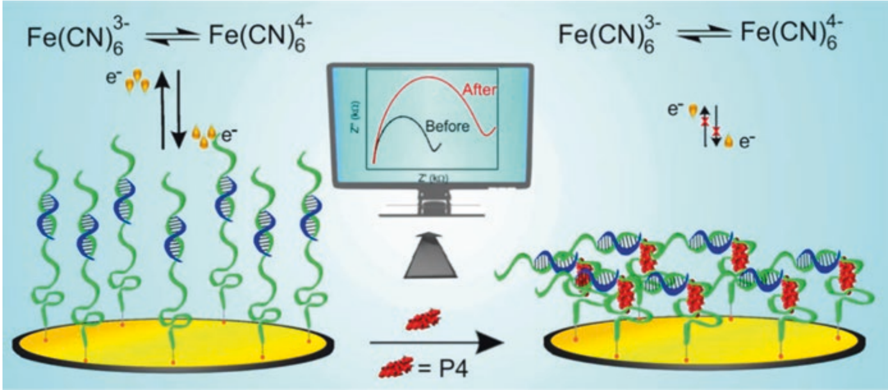


Fig. 3.10 Design of the impedimetric aptasensor to detect progesterone (P4). (Reproduced with permission from (Jiménez et al. 2014). Copyright 2019, American Chemical Society)

and waters (Khor et al. 2011). An immunosensor prepared in a microfluidic device modified with antibodies was used to detect ibuprofen in water from various sources with a limit of detection at 0.25 pg mL^{-1} (Nagaraj et al. 2014), where the principle of detection was impedance spectroscopy. Aptasensors have been used to detect the hormone progesterone (P4) in a concentration range from 10 ng mL^{-1} to 60 ng mL^{-1} with a detection limit of 0.90 ng mL^{-1} (Jiménez et al. 2014). This impedimetric aptasensor was fabricated by immobilizing an aptamer on gold electrodes, as depicted in Fig. 3.10.

Illicit drugs have also been found in sewage and wastewater (Mccall et al. 2015). Huerta-fontela et al. determined cocaine and metabolites in wastewater at concentrations from 4 ng L^{-1} to 4.7 μg L^{-1} and from 9 ng L^{-1} to 7.5 μg L^{-1}, respectively, while concentrations of amphetamine type stimulatory drugs ranged from 2 to 688 ng L^{-1} (Huerta-fontela et al. 2008). Drugs found in tap water included ecstasy, caffeine, paraxanthine, fentanyl, and methadone (Boleda et al. 2011). Fentanyl exemplifies the risk because it causes death owing to overdoses (Ciccarone 2017). Goodchild and co-workers (2019) developed a sensor to detect fentanyl made with screen-printed carbon electrodes (SPCE) modified with the ionic liquid (RTIL) 1-butyl-1-methylpyrrolidinium bis(trifluoromethylsulfonyl)imide $[C_4C_1PYrr][NTF_2]$ using cycling square voltammetry (Goodchild et al. 2019). Data for this sensor, whose limit of detection was 5 μmol L^{-1}, are illustrated in Fig. 3.11:

Table 3.7 shows other examples of sensors and biosensors used for pharmaceutical detection in the environment. The presence of emerging pollutants in the environment, mainly in potable water, is already a worrying reality in many countries. Novel sensors and biosensors need to be developed to detect pollutants, pesticides, and pharmaceutical products in the environment.

As mentioned above, there is no doubt that electroanalytical techniques are an outstanding alternative to monitor contaminants due to low-cost and excellent detection limits.

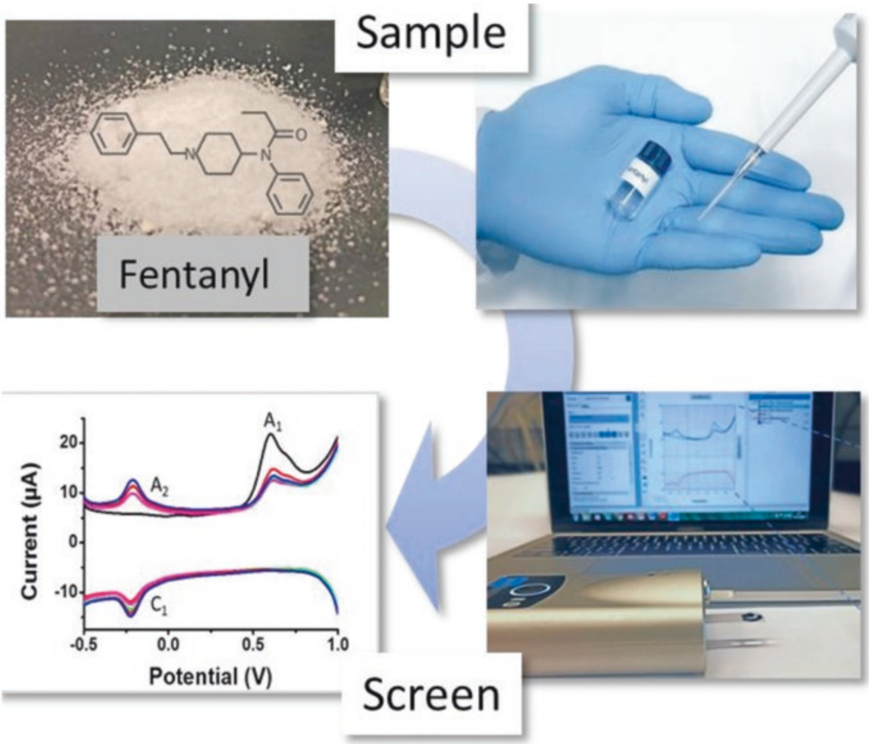


Fig. 3.11 Fentanyl sensor based in screen-printed modified with the room temperature ionic liquid (RTIL). (Reproduced with permission from (Goodchild et al. 2019). Copyright 2019, American Chemical Society)

3.5 Final Remarks

The problem of emergent contaminants has been ignored for an extended time because many environmental entities consider lower concentrations to be harmless. Consequently, these low concentrations lead to serious health problems in humans and animals, due to many products that are accumulated or can cause compounds to be more toxic when metabolized by the body.

Undoubtedly, the emergent contaminants are a significant problem that should be resolved by new regulations about the environmental quality that support green chemistry and the development of devices to monitor these product toxics in the environment – followed by more toxicity studies and rigorous control of products that will be brought to market.

As mentioned in this chapter, the electrochemical techniques have been postulated as a tool for detection of pollutants, pharmaceutical products, and pesticides with a low price, simplicity, and selectivity, rather low detection limits and multiple

Table 3.7 Electrochemical methods to detect pharmaceutical products in the environment

Drug determined	Technique	LOD	Real sample	References
17b-Estradiol	Electrochemical impedance	5.0×10^{-9} μmolL^{-1}	Water sample	Ke et al. (2014)
Acetaminophen	Differential pulse voltammetry	4.4 μg L^{-1}	River water	Berto et al. (2018)
Amiloride hydrochloride	Square wave voltammetry	0.09 μmolL^{-1}	Tap water	Moraes and Salamanca-neto (2017)
Amlodipine besylate	Square wave voltammetry	0.30 μmolL^{-1}	Tap water	Moraes and Salamanca-neto (2017)
Ampicillin	Differential pulse voltammetry	1.09×10^{-9} molL^{-1}	Milk	Wang (2015)
Ampicillin	Differential pulse voltammetry	4.0×10^{-9} molL^{-1}	Milk	Wang et al. (2016)
Ampicillin	Square wave voltammetry	2.8×10^{-10} molL^{-1}	Lake water	Yang et al. (2017)
Ascorbic acid	Cyclic voltammetry	1 μmolL^{-1}	Lemon juice	Emran et al. (2018)
Atenolol	Square wave voltammetry	0.06 μmolL^{-1}	Tap water	Moraes and Salamanca-neto (2017)
Bisphenol-A	Square wave voltammetry	0.6×10^{-9} mol L^{-1}	Tap water	Liu et al. (n.d.)
Bisphenol-A	Square wave voltammetry	0.19×10^{-9} molL^{-1}	Tap water	Yu et al. (2016)
Bisphenol-A	Differential pulse voltammetry	2.1×10^{-11} molL^{-1}	Environmental water	Derikvand et al. (2016)
Bisphenol-A	Differential pulse voltammetry	5.0×10^{-6} molL^{-1}	milk	Zhou et al. (2014a)
Cefalexin	Differential pulse voltammetry	0.01 μmolL^{-1}	River water	Feier et al. (2017)
Cefalexin	Cyclic voltammetry, electrochemical impedance spectroscopy	3.2 nmolL^{-1}	River water	Feier et al. (2019)
Cefalexin	Differential pulse voltammetry, amperometry	1.0×10^{-7} molL^{-1}	Spike river water	Feier et al. (2017)

(continued)

Table 3.7 (continued)

Drug determined	Technique	LOD	Real sample	References
Chloramphenicol	Electrochemical impedance spectroscopy	1.8×10^{-6} molL^{-1}	Buffer solution	Pilehvar et al. (2014)
Chloramphenicol	Square wave voltammetry	1.0×10^{-12} mol L^{-1}	Fish	Chen et al. (2015)
Chloramphenicol	Square wave voltammetry	4.6×10^{-10} mol L^{-1}	Milk	Yan et al. (2016)
Chloramphenicol	Cyclic voltammetry	1.0×10^{-5} mol L^{-1}	Milk	Munawar et al. (2017)
Chloramphenicol	Differential pulse voltammetry	1.0×10^{-10} mol L^{-1}	Milk and honey spiked samples	Yang and Zhao (2015)
Chloramphenicol (CAP)	Square wave voltammetry and cyclic voltammetry	2.0×10^{-7} mol L^{-1}	Milk powder, bee pollen samples spiked with CAP	Sun et al. (2017)
Ciprofloxacin	Differential pulse voltammetry	0.005 µmolL^{-1}	Wastewater effluent	Gayen and Chaplin (2015)
Ciprofloxacin	Electrochemical impedance spectroscopy, cyclic voltammetry	0.5 ng L^{-1}	Milk	Li et al. (2018)
Clenbuterol	Electrochemical impedance spectroscopy	1.3×10^{-12} molL^{-1}	Pork	Chen et al. (2016)
Clonazepam	Differential pulse adsorptive cathodic stripping voltammetry	0.65 µgL^{-1}	Natural rivers	Nunes et al. (2017)
Dexamethasone	Square wave voltammetry	2.8 10^{-8} molL^{-1}	Wastewater	Oliveira et al. (2015)
Diazepam	Differential pulse adsorptive cathodic stripping voltammetry	0.27 µgL^{-1}	Natural rivers	Nunes et al. (2017)
Diclofenac	Square wave voltammetry	1.8×10^{-7} mol L^{-1}	Wastewater	Oliveira et al. (2015)
Dopamine	Flow injection analysis system coupled to multiple pulse	0.011 µmolL^{-1}	Waste river samples	Wong et al. (2018)
Flutamide	Square wave voltammetry	0.21 µmolL^{-1}	Water	Švorc et al. (2017)

(continued)

Table 3.7 (continued)

Drug determined	Technique	LOD	Real sample	References
Flutamide	Cyclic voltammetry	0.016 μmolL^{-1}	Tap water	Kubendhiran et al. (2018)
Hydrazine	Amperometry	0.23 μmol L^{-1}	Natural lake and tap water	Deroco et al. (2018)
Hydrochlorothiazide	Square wave voltammetry	0.08 μmolL^{-1}	Tap water	Moraes and Salamanca-neto (2017)
Hydroquinone	Square wave voltammetry	0.05 μmolL^{-1}	Water samples	Soltani et al. (2016)
Hydroquinone	Flow injection amperometry	0.1 μmolL^{-1}	Water samples	Upan et al. (2015)
Ibuprofen	Differential pulse voltammetry	2.0×10^{-10} molL^{-1}	Wastewater	Roushani and Shahdost-fard (2016)
Kanamycin	Differential pulse voltammetry	8.7×10^{-13} molL^{-1}	Food	Xiong et al. (2012)
	Square wave voltammetry	1.4×10^{-10} molL^{-1}	Milk	Zhou et al. (2015)
	Differential pulse voltammetry	7.6×10^{-12} molL^{-1}	Milk	Sheng et al. (2017)
	Differential pulse voltammetry	0.87×10^{-6} molL^{-1}	Milk	Qin et al. (2015)
Kanamycin	Differential pulse voltammetry	5.8×10^{-9} molL^{-1}	Milk	Sun et al. (2013)
	Square wave voltammetry	1.0×10^{-9} molL^{-1}	Milk	Xu et al. (2015)
	Differential wave voltammetry	9.5×10^{-12} molL^{-1}	Milk	Xu et al. (2014)
Kanamycin	Cyclic voltammetry, electrochemical impedance spectroscopy	0.11 ng mL^{-1}	Spiked milk samples	Sharma et al. (2017)
Levofloxacin	Differential pulse voltammetry	3.61 ng mL^{-1}	Milk	Huang et al. (2016)
Metronidazole	Cyclic voltammetry	1.8×10^{-11} molL^{-1}	Tablets, fish samples	Li et al. (2015a)

(continued)

Table 3.7 (continued)

Drug determined	Technique	LOD	Real sample	References
Metronidazole	Differential pulse adsorption square voltammetry	1.6×10^{-8} molL^{-1}	Milk, honey spiked samples	Chen et al. (2013)
Metronidazole	Linear sweep voltammetry	2.8×10^{-8} molL^{-1}	Lake water	Emran et al. (2018)
Ofloxacin	Differential pulse voltammetry	0.4 ng mL^{-1}	Water, plant sewage	Pilehvar et al. (2016)
Oxacillin	Differential pulse voltammetry, amperometry	1.0×10^{-5} molL^{-1}	Spike river water	Feiera et al. (2017)
Oxytetracycline	Square wave voltammetry	2.2×10^{-10} molL^{-1}	Milk	Rapini and Marrazza (2017)
Paracetamol	Square wave voltammetry	0.01 µmolL^{-1}	Water samples	Kumar et al. (2019)
Paracetamol	Differential pulse voltammetry	1.3×10^{-8} molL^{-1} 8.0×10^{-9} molL^{-1}	Natural water from creek	Raymundo-Pereira et al. (2017)
Penicillin G (beta-lactams)	Amperometry	1.0×10^{-10} molL^{-1}	River wastewater	Merola et al. (2014)
Piroxicam	Square wave voltammetry	0.16 µmolL^{-1}	Tap water	Augusto et al. (2018)
Ractopamine	Electrochemical impedance spectroscopy	1.0×10^{-10} molL^{-1}	Pork	Chen et al. (2016)
Streptomycin	Differential pulse voltammetry	14.1×10^{-6} molL^{-1}	Rat serum, milk	Danesh et al. (2015)
Streptomycin	Differential pulse voltammetry	5×10^{-10} molL^{-1}	Porcine, kidney, honey (spiked samples)	Wen et al. (2017)
Sulfadimethoxine	Square wave voltammetry	7.0×10^{-9} molL^{-1}	Lake water	Yang et al. (2017)
Sulfaguanidine	Impedance spectroscopy, differential pulse voltammetry	0.20 pg mL^{-1}	Honey samples	El et al. (2018)
Sulfamethoxazole	Square wave voltammetry	0.024 µmolL^{-1}	Surface water samples	Zhao et al. (2015b)
Sulfamethoxazole	Electrochemical impedance	1.0×10^{-12} molL^{-1}	Seawater	Ait-lahcen et al. (2016)

(continued)

Table 3.7 (continued)

Drug determined	Technique	LOD	Real sample	References
Sulfamethoxazole	Square wave voltammetry	0.024 μmolL^{-1}	Lake water	Zhao et al. (2015b)
Sulfamethoxazole	Electrochemical impedance spectroscopy	1.0×10^{-12} molL^{-1}	Spiked seawater	Ait-lahcen et al. (2016)
Sulfanilamide	Amperometry	0.016 μ molL^{-1}	Pork	He and Chen (2016)
Sulfathiazole	Amperometry	0.001 μg mL^{-1}	Milk	Bueno et al. (2014)
Sulfonamides	Cyclic voltammetry	0.12 ng mL^{-1}	Water samples	Zhang et al. (2019b)
Tetracycline	Cyclic voltammetry	0.035 μgL^{-1}	Water samples	Alawad et al. (2019)
Tetracycline	Voltammetry	0.22 fM	Honey	Bougrini et al. (2016)
Tetracycline	Differential pulse voltammetry	5.6×10^{-12} molL^{-1}	Milk	Guo et al. (2015)
Tetracycline	Differential pulse voltammetry	4.5×10^{-11} molL^{-1}	Milk	Mohammad, et al. (2016)
Tetracycline	Linear sweep voltammetry	2.2×10^{-16} molL^{-1}	Honey	Bougrini et al. (2016)
Tetracycline	Adsorptive stripping differential pulse voltammetry	3.6×10^{-7} mol L^{-1}	River water	Wong et al. (2015)
Theophylline	Differential pulse voltammetry	1.2×10^{-9} molL^{-1}	Tea	Gan et al. (2017)
Timolol maleate	Pulse adsorptive anodic stripping voltammetry	7.1×10^{-10} mol L^{-1}	Tap water	Mohammed et al. (2018)
Triclosan	Cyclic voltammetry	0.23 pg mL^{-1}	Water samples	Motia et al. (2019)

designs that allow miniaturization. These techniques also have the possibility of being coupled with conventional measurement methods improving their sensitivity.

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Chapter 4
Two-Dimensional Transition Metal Dichalcogenides for Gas Sensing Applications

Nirav Joshi, Maria Luisa Braunger, Flavio Makoto Shimizu, Antonio Riul Jr, and Osvaldo Novais Oliveira Jr

Contents

Abstract The fast-growing earth population and the industrial growth of developing economies in Latin America and Asia have generated increasing air, water, and agricultural pollution in urban regions with consequences to human health. Most industrial sites are in urban regions, thus creating a challenge to ensure air quality and environment monitoring. Despite a growing diagnostic toolkit and a plethora of therapeutic interventions, a key challenge remains in the control of widespread diseases like cancer and diabetes. In the last decades, several semiconducting oxides

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have been used to detect dangerous or toxic gases. The excellent gas sensing performance of these gas sensor devices has been observed at high temperatures, which forbids their use for the detection of flammable and explosive gases. To overcome the problems such as selectivity, high sensitivity, and operation temperature, atomically thin transition metal dichalcogenides, which are two-dimensional (2D)-layered materials with large surface areas and tunable bandgaps, have emerged as a candidate for gas sensors. In the present book chapter, the recent advancement in the gas sensors, based on two-dimensional (2D) transition metal dichalcogenides, has been comprehensively discussed. In the first section, the recent advances on synthesis process and the properties of these materials have been discussed. The next section depicts the layered transition metal dichalcogenides (TMDs) and their recent advances for application in the field of gas sensors. The challenges and opportunities in gas sensing are discussed, with emphasis on the sensing mechanisms. The third and fourth sections highlight the functionalization of TMDs with noble metals and other metal oxides to investigate the gas sensing properties. Finally, as summary, the prospects of these two-dimensional transition metal dichalcogenides have been outlined for the development of highly efficient future generation gas sensors for accelerating the commercialization of the same.

Keywords Transition metal dichalcogenides · Gas sensors · Heterojunction · Charge-transfer · Mechanism · Noble metal decoration

4.1 Introduction

Since the second half of the twentieth century, chemical gas sensors have become an indispensable part of modern society with broad applications in healthcare, food products, indoor monitoring, industrial safety, and environmental monitoring. Chemical sensors are used for diagnostics and monitoring purposes in different aspects of human life (Tomer et al. 2019; Joshi et al. 2018b; Malik et al. 2018). They are not limited to on-body applications but have a much broader scope when integrated with other surfaces, such as in buildings or vehicles as illustrated in Fig. 4.1 (Meng et al. 2019). It has been realized that chemical sensors are also crucial for the Internet of Things (IoT) which requires real-time data acquisition and is expected to have an economic impact on the healthcare of over 1 trillion dollars in 2020 (Gubbi et al. 2013). Only a few gas sensor systems are available in the market which are cost-effective, portable, and fully functional. This is due to their respective inherent limitations (Bârsan et al. 2013).

The sensing material is responsible for the interaction with gas molecules and inducing change in its properties which is then transformed into electrical signals by a transducer (Wu et al. 2019; Gusain et al. 2017; Nie et al. 2019). For the effective and selective sensing toward target gases, these sensing materials should have large

Fig. 4.1 Chemical sensors for environmental monitoring in different aspects of human life. (Reproduced with permission from Meng et al. 2019. Copyright 2019, American Chemical Society)

surface-to-volume ratio, suitable active sites, and better electrical and processing properties (Sun et al. 2012; Joshi et al. 2018b).

Functional nanomaterials such as metal oxides, conducting polymers, graphene, and derivatives have been exploited for chemical gas sensors (Joshi et al. 2014, 2016a, 2018a; Liu et al. 2018b)(Singh et al. 2013a, b, c, d; Mekki et al. 2014; Kumar et al. 2015a). Wide-bandgap semiconducting metal oxides, in particular, are used to detect toxic gases because of their good sensitivity and low cost. These sensors, nevertheless, still exhibit problems with selectivity and require operation at high temperatures (Ponzoni et al. 2017). Most studies have focused on improving their sensitivity, and little efforts have been made to improve their selectivity. Regarding this, conducting polymers in sensing devices have the ability to work at room temperature, but they are limited by the effects of humidity and degradation with a sluggish response and recovery time (D'Arsié et al. 2018). Gas sensors produced with carbon nanotubes can operate at room temperature, but the long recovery time and setup complexity still affect their applications (Wang and Yeow 2009). Graphene and derivatives such as graphene oxide and reduced graphene oxide are the most studied materials for chemical gas sensors due to their enhanced electron transport properties, low electrical noise, and sub-ppb (part per billion) detection (Liu et al. 2018a, b; Materón et al. 2019). Their main drawback, however, is the long recovery time which indicates that at room temperature gas molecules are firmly attached to graphene and the complete recovery is possible only by using ultraviolet illumination or external heating (Schedin et al. 2007; Yavari and Koratkar 2012). Thus, a reliable strategy to obtain scalable and controlled synthesis of certain sensing materials is a primary need for reliable and robust microsensors.

Recently, transition metal dichalcogenides with the formula of MX_2 including MoS_2, WS_2, $MoSe_2$, and WSe_2, and layered group III–VI semiconductors (GaS, GaSe, and SnS_2), phosphorene, h-boron nitride, etc., have attracted interest due to their outstanding physical and chemical properties. Several applications have been proposed, as schematically shown in Fig. 4.2, including gas sensors, biosensors, photodetectors, energy storage, and optoelectronics (Chhowalla et al. 2013; Tan and Zhang 2015; Li and Chen 2016; Yim et al. 2016; Fahad et al. 2017; Hu et al. 2017). Like graphene, these layered inorganic analogues have a large surface-to-volume ratio and atomic-level thickness. In addition, they have rich surface chemistry and exceptional electrical properties with an appropriate bandgap to modulate the transport characteristics, which make them suited to detect hazardous analytes.

In this chapter, our main motivation is to discuss and elaborate the gas sensing applications and mechanism on transition metal dichalcogenides and related layered inorganic analogues. Our intention is not only to help the readers grasp and assess the latest advancements in the chemical sensing of two-dimensional TMDs but also to compare the essential parameters like sensor response, selectivity, stability, and response/recovery speed and importantly their gas sensing mechanism across the broad range of materials. Finally, we will conclude the overall challenges, opportunities, and commercialization perspectives of two-dimensional transition metal dichalcogenide-based gas sensors that lie ahead toward personalized environmental monitoring.

4.2 Recent Advances in Two-Dimensional Transition Metal Dichalcogenide Nanostructure Fabrication

Two-dimensional transition metal dichalcogenides can be synthesized using two approaches: top-down in which the bulk forms are exfoliated into a few layer structures and monolayers and the bottom-up that employs growth methods using chemical vapor deposition (Bergeron et al. 2017; Tao et al. 2017). Work is progressing in various labs to scale up the fabrication of large-area arrays. Two-dimensional transition metal dichalcogenide nanostructures such as nanosheets, hierarchical structures, nanorods, and microspheres have been synthesized using wet chemical synthesis, chemical vapor deposition, epitaxial growth, chemical or electrochemical Li-intercalation exfoliation, and liquid phase exfoliation. With such a diversity of methods and types of nanostructures, it is always recommended to find the right fabrication method suitable for distinct applications (Lv et al. 2015).

The fabrication of 2D nanomaterials, including MoS_2 and WS_2, using mechanical exfoliation was inspired on graphene by Novoselov et al. (2004) (Novoselov et al. 2004). The process is simple since it does not require sophisticated equipment, being

Fig. 4.2 Typical two-dimensional transition metal dichalcogenide nanostructures and their applications as gas sensors, biosensors, chemical sensitive-field effect transistors, and photovoltaic devices. (Reproduced with permission from Sharma and Kim 2018, Copyright 2018, Nature; (Liu et al. 2015), Copyright 2015, American Chemical Society; (Nam et al. 2015), Copyright 2015, AIP Publishing; (Hu et al. 2014), Copyright 2014, American Chemical Society; (Zhou et al. 2017), Copyright 2014 Wiley-VCH; (Gao et al. 2017), Copyright 2017 The Royal Society of Chemistry; (Liu et al. 2017), Copyright 2017 Springer Nature; (Zhao et al. 2014), Copyright 2014 The Royal Society of Chemistry)

suitable to yield nanosheets or highly crystalline monolayers. Lin et al. (Yuan et al. 2016) reported a reliable way to mechanically exfoliate large-scale two-dimensional materials, whose properties could be studied with atomic force microscopy and Raman spectroscopy, as seen in the results in Fig. 4.3a. Yanying et al. (Lu et al. 2016) used a facile spraying synthesis to produce mesoporous MoS_2/C microspheres for sodium-ion batteries (Fig. 4.3b). The as-synthesized mesoporous MoS_2/C microspheres show that ultrathin MoS_2 nanosheets (~2 nm) with expanded interlayers (0.64 nm) are distributed uniformly in the carbon microspheres. The batteries exhibited excellent

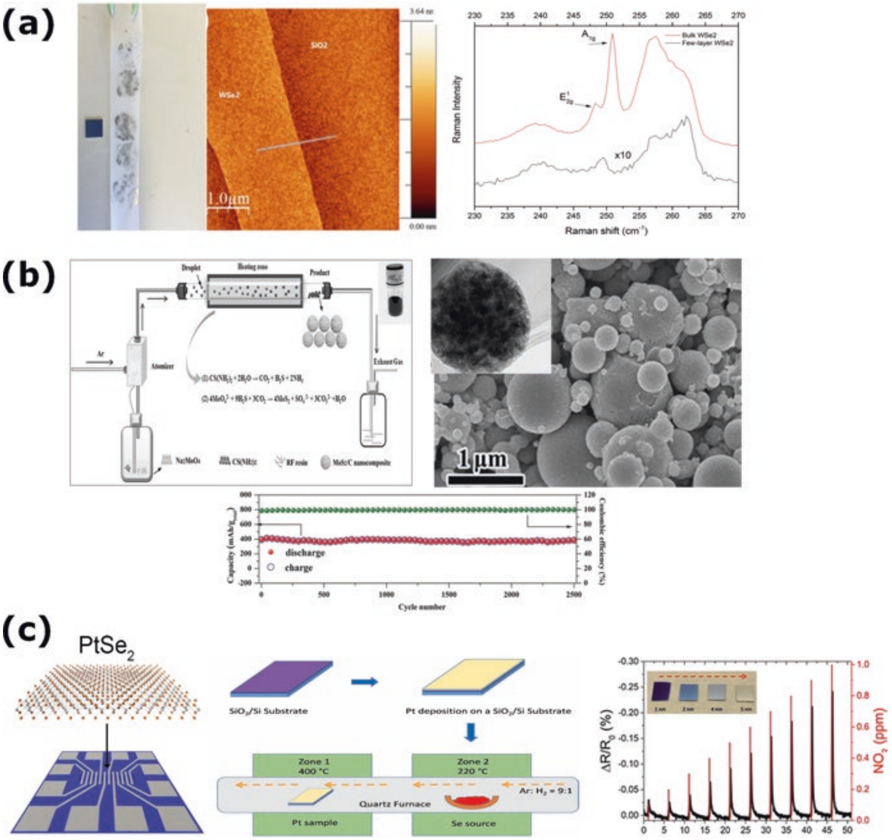

Fig. 4.3 (**a**) Mechanical exfoliation of WSe_2 flakes and the substrate with topography image by atomic force microscopy and Raman spectra of few and bulk layers. (Reproduced with permission from Yuan et al. 2016. Copyright 2016, AIP Publishing). (**b**) Fabrication and morphology of mesoporous MoS_2/C microspheres. (Reproduced with permission from Lu et al. 2016. Copyright 2016, WILEY-VCH). (**c**) High-performance $PtSe_2$ films for gas sensors and photodetectors with facile and scalable fabrication process on SiO_2 (300 nm thick)/Si substrates. (Reproduced with permission from Yim et al. 2016. Copyright 2016, American Chemical Society)

cycling stability (390 mAh g^{-1} after 2500 cycles at 1.0 A g^{-1}) and high rate capability (312 mAh g^{-1} at 10.0 A g^{-1} and 244 mAh g^{-1} at 20.0 A g^{-1}). A large-scale synthesis method was used to obtain thin films of platinum diselenide ($PtSe_2$) (Yim et al. 2016) used in high-performance gas sensors, photodetectors, and photovoltaic cells. Figure 4.3c depicts some of the results for the $PtSe_2$ thin films prepared via thermally assisted conversion, with atomic structure examined by electron microscopy analysis. The Raman spectra of $PtSe_2$ thin films with different thickness show two prominent peaks at ~176 and 210 cm^{-1}, which correspond to the E_g and A_{1g} Raman active modes, respectively. The gas sensing study showed the ultrafast NO_2 response at room temperature. The estimated response and recovery times are 2.0 and 7.4 s for 0.1 ppm of

NO_2 exposure, which is considerably smaller than the previous metal oxide sensors (Wetchakun et al. 2011; Kumar et al. 2015b).

4.3 Two-Dimensional Transition Metal Dichalcogenide-Based Gas Sensors

Concerns about environmental pollution to human health make it urgent to develop reliable tools for air quality monitoring. Environmental hazardous gases include ammonia (NH_3) and nitrogen oxides (NO_x = nitric oxide (NO) and nitrogen dioxide (NO_2)) used in petroleum, food, and textile industries, which are found to cause severe diseases in the respiratory tract. The main challenge is to detect such gases at the ppb level or lower, according to the World Health Organization (WHO) guidelines (WHO 2006). Typical commercial devices are based on electrochemistry, while chemiresistive sensors are promising next-generation gas sensors due to their high sensitivity, good selectivity, and low power consumption.

Various strategies to enhance the response of chemiresistive gas sensors employ novel materials and nanoarchitectonics for sensing layers (Ariga et al. 2016; Raymundo-Pereira et al. 2019)(Joshi et al. 2019). Chemiresistors made of metal oxides (Joshi et al. 2016b; Zappa et al. 2018), carbon allotropes (Joshi et al. 2018b; Li et al. 2018), and conducting polymers (Zhang et al. 2018c) are highly sensitive and selective (Chen et al. 2016). But TMD nanomaterials have advantages owing to their semiconducting properties (Schmidt et al. 2015) (a bandgap ranging from 1.5 to 3 eV, contrary to gapless band structure of graphene (Chen et al. 2016)), rapid response, high sensitivity, stability, and ability to operate at room temperature. Moreover, theoretical research and machine learning (Paulovich et al. 2018; Abbasi and Sardroodi 2019) can assist the discovery of novel composites, characterize doped TMD (Zhang et al. 2019a), and even predict the response efficiency (Zhang et al. 2018b; Wu et al. 2018). A list of TMD chemiresistive gas sensors is given in Table 4.1, which will be further discussed in the next sections.

4.3.1 Two-Dimensional MoS_2-Based Gas Sensors

MoS_2 is the most studied two-dimensional transition metal dichalcogenides as sensing layer for gas sensors. Zhang et al. (2018b) developed transition metal dichalcogenide nanocomposite as sensing layer to work at room temperature either by drop-cast films of Pd-decorated TiO_2/MoS_2 (4 wt% Pd loading) suspensions or outside nanoarchitectonics (Ikram et al. 2018) layer-by-layer (Raymundo-Pereira et al. 2019) (LbL) films of Fe-TiO_2/MoS_2 (Wu et al. 2018) and In_2O_3/MoS_2 (Zhang et al. 2018a) for the detection of different gases (benzene, ethanol, formaldehyde) with superior response (up to eight times) than pure MoS_2 films. Ikram et al. (2019b)

Table 4.1 Literature review on two-dimensional transition metal dichalcogenide chemiresistive gas sensors

TMD	Material/ morphology	Synthesis process	Working temp. (°C)	Analyte gas	Conc. (ppm)	Gas response $\Delta R/R_0(\%)$	Response/recovery time (s)	References
MoS_2	2D	CE	RT	NO_2	100	22	45/–	Yun et al. (2017a)
	Nanoflakes	CVD	RT	NH_3, NO_2	10.8, 4	18, –60	~400/–	Kang et al. (2017)
	Nanowires	CVD	160	NO_2	5	18.1	16/172	Kumar et al. (2018a)
	3D flowerlike nanospheres	HT	100	NO_2	50	60	15/12	Zhang et al. (2018d)
	Hollow spheres	HT	150	NO_2	100	40.3	79/225	Li et al. (2019)
	Microspheres	HT	120	H_2	700	27.5	30/60	Zhang et al. (2018e)
MoS_2	Pt-TiO_2	HT	100	H_2	2000	74.9	150/370.2	Luo and Zhang (2018)
	Bi_2O_3-Bi_2S_3	HT	RT	NO_x	50	10.7	1/–	Ikram et al. (2019a)
	Flowerlike @In_2O_3	HT	RT	NO_x	100	–	1.6/–	Ikram et al. (2019b)
	rGO-CdS	HT	75	NO_2	0.2	27.4	25/34	Shao et al. (2019)
	SiO_2/nanorods	CVD	RT	NO_2	50	390	~1000/–	Shim et al. (2018)
	@ZnO/nanowires	HT	200	NO_2	50	31.2	3600_{cycle}	Zhao et al. (2018)
	ZnO/nanowires	HT	RT	NO_2	0.2	188	3600_{cycle}	Zhou et al. (2018)
	ZnO/nanoparticles	WCR	RT	NO_2	5	3050	40/1000	Han et al. (2018)

	MoO_3	CVD	RT	NO_2	10	33.6	19/182	Kumar et al. (2018b)
	rGO	CE	RT	NO_2	0.45	28	–	Yun et al. (2017b)
	3D rGO	HT	80	NO_2	10	2483	–	Chen et al. (2019)
	SWCNT	CVD	RT	NH_3, NO_2	40	34.5, 54	–	Kim et al. (2018)
	rGO	US	RT	Humidity	85%	2494.25	6.3/30.8	Park et al. (2018)
	$SmFeO_3$@	HT	RT	Humidity	11%	–	1.5/29.8	Zhang et al. (2018f)
	PANI/MWCNTs	COP	RT	NH_3	0.25	11	32/36	Chen et al. (2016)
	CuO	DCMS	RT	NH_3	100	47	17/26	Sharma et al. (2018)
	Co_3O_4	LbL	RT	NH_3	0.1	10.3	98/100 (5 ppm)	Zhang et al. (2017a)
	Cu_2O/ microspheres	HT	100	NH_3	100	43	90/100	Zhang et al. (2019b)
	Fe-TiO_2/QDs	HT	RT	Ethanol	5	150	62/49 (1 ppm)	Wu et al. (2018)
	In_2O_3@	HT	260	Ethanol	50	41	8/20	Liu et al. (2018c)
	Pd-TiO_2	HT	RT	Benzene	50	64	13/10	Zhang et al. (2018b)
	In_2O_3/nanocube	HT	RT	Formaldehyde	50	75.2	14/22	Zhang et al. (2018a)
WS_2	Nanosheets	HT	–	Ethanol	100	~47	40_{cycle}	Cao (2016)
	Nanosheets	HT	RT	NO_2	0.1	9.3	–	Xu et al. (2018)
	2D	CE	RT	Humidity	85	1300	140/30	Leonardi et al. (2018)

(continued)

Table 4.1 (continued)

TMD	Material/ morphology	Synthesis process	Working temp. (°C)	Analyte gas	Conc. (ppm)	Gas response $\Delta R/R_0(\%)$	Response/recovery time (s)	References
WS_2	@MTCNFs		RT	NO_2	1	15	2400_{cycle}	Cha et al. (2017)
	Graphene/aerogel		180	NO_2	2	3.2	100/300	Yan et al. (2018)
	rGO	HT	RT	NH_3	10	121	60/300	Wang et al. (2019)
	Co-N-HCNCs		RT	NO_2	5	48.2	–	Koo et al. (2018)
	Pt/QDs	HT	RT	NH_3	250	~10	$-/1200_{cycle}$	Ouyang et al. (2018)
	SnS_2/SnO_{2-x}	WCR	130	NH_3	50	1.4	~60/300	Leonardi et al. (2019)
	PANI	Polymerization	RT	NH_3	200	81	260/790	Jha et al. (2018)
$WS_{0.96}Se_{1.04}$		TTFS	RT	NO_2	500	2621	1200/3000	Ko et al. (2018a)
WSe_2	Nanosheets	ALD	RT	NO_2	100	4140	390/43	Ko et al. (2018b)

RT room temperature; *CE* chemical exfoliation; *CVD* chemical vapor deposition; *HT* hydrothermal; *COP* in situ chemical oxidative polymerization; *DCMS* DC magnetron sputtering; *US* ultrasonication; *WCR* wet chemical route; *QDs* quantum dots; *LbL* layer-by-layer; *ALD* atomic layer deposition; *TTFS* tube-type furnace system; *MTCNF* multiple tubular pore carbon nanofibers; *TE* thermal evaporation; *Co-N-HCNCs* Co, N-doped hollow carbon nanocages; *Au* gold; *Pt* platinum; *Fe* iron; *Pd* palladium; TiO_2 titanium dioxide; Bi_2O_3 bismuth oxide; Bi_2S_3 bismuth sulfide; In_2O_3 indium oxide; *rGO* reduced graphene oxide; *CdS* cadmium sulfide; *SWCNT* single-walled carbon nanotube; *MWCNT* multi-walled carbon nanotubes; *CuO* copper (II) oxide; Co_3O_4 cobalt tetraoxide; Cu_2O copper (I) oxide; *PANI* poly(aniline); In_2O_3 indium(III) oxide; SnS_2 Tin(IV) sulfide; MoO_3 molybdenum trioxide; SiO_2 silicon dioxide; *ZnO* zinc oxide developed a ternary heterojunction with MoS_2-Bi_2O_3-Bi_2S_3 that provided an ultrafast response of 1 s at room temperature with response of 10.7% to 50 ppm of NO_x gas.

External stimuli are also an interesting strategy to enhance gas sensor response as reported by Agrawal et al. (2018). A heterostructure MoS_2 sensor presented fast response (8.51 s) and high sensitivity (∼10.36% for 10 ppm of NO_2 at room temperature), but with incomplete recovery because adsorption energy of MoS_2-NO_2 is very high at room temperature. To overcome the slow recovery time problem, an external thermal energy (125 °C) was applied to the sensor which decreased the response time to 4.44 s and enabled a complete recovery within 19.6 s. Despite that, it reduced the adsorption rate of NO_2 and consequently the sensor sensitivity (~7.79%). Replacing the heater by ultraviolet light, the room temperature condition could be maintained, and a complete recovery was achieved within 146.49 s. Since the surface is photoactivated by light, the response signal increased to ~21.78% which also increased the time response to 6.09 s. They proposed the gas sensing mechanism depicted in Fig. 4.4a. Without ultraviolet light the charge-transfer mechanism prevails (Cho et al. 2015a), in which NO_2 (oxidizing gas) molecules accept electrons from the n-type MoS_2 surface. Figure 4.4b shows that under ultraviolet light illumination, the generation of photoexcited carriers (electron and hole pairs) is triggered in mixed MoS_2 flakes. The adsorbed oxygen takes the holes from the MoS_2 film and desorbed from the mixed MoS_2 flakes. The desorbed oxygen created new active sites on MoS_2 flakes for the NO_2 molecule adsorption. The same enhancement effect was observed for the MoS_2/ZnO nanocomposite (Zhou et al. 2018).

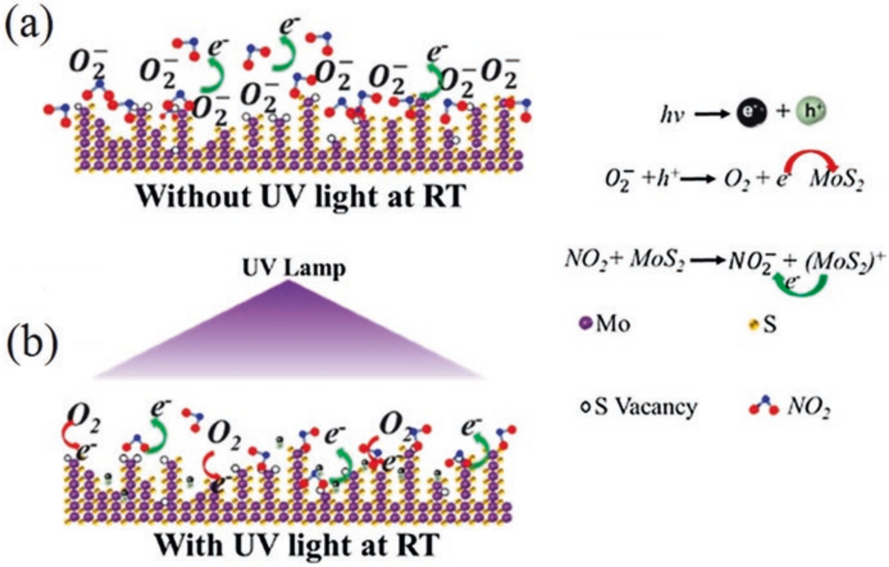

Fig. 4.4 Schematic illustration of the interaction of NO_2 molecules: (**a**) at room temperature with the mixed MoS_2 flakes and (**b**) at room temperature with ultraviolet light illumination. (Reproduced with permission from Agrawal et al. 2018. Copyright 2018, American Chemical Society)

Density function theory studies (Li and Shi 2018; Zhang et al. 2019a) have supported experimental results and strengthen the chemiresistor mechanisms of detection. Li and Shi theoretically predicted the high performance of NO sensing with MoS_3-vacancy and S-vacancy defects explained by the stronger chemisorption and greater electron transfer effects than pure MoS_2 monolayer. Using density function theories, Zhang et al. (2019a) investigated MoS_2 monolayer doped with B, N, P, and Al elements and concluded that for SO_2 gas molecules, Al/MoS_2 is the best candidate as sensor due to the strong oxidation of Al. Cho et al. (2015b) demonstrated that vertically aligned MoS_2 layers have a fivefold higher response than horizontal ones because gas adsorption occurs strongly on edge sites and weakly on the basal plane. This observation confirms theoretical predictions of a preferential gas adsorption on molybdenum atoms as shown in the scheme of Fig. 4.5. Shim et al. (2018) applied this strategy to enhance the sensitivity by 90 times using vertically aligned MoS_2 along the SiO_2 nanorods. In spite of the strong response in these cases, the recovery is still a problem. Cho et al. (Ikram et al. 2019b) reported MoS_2 vertically aligned on mesoporous In_2O_3 nanocubes increasing the exposure of active edges which not only allowed a response of 10.3% to 100 ppm NOx at room temperature but also had an ultrafast response time of 1.6 s. However, the enhancement effect does not occur for all vertically aligned MoS_2 (Zhao et al. 2018).

4.3.2 Two-Dimensional WS_2-Based Gas Sensors

WS_2 has a similar layered structure as MoS_2, with a bandgap slightly higher for both bulk and monolayer, being 2.03 and 1.88 eV, respectively (against 1.23 and 1.88 eV for MoS_2) (Gusakova et al. 2017). As shown in Table 4.1, highly sensitive gas sensors

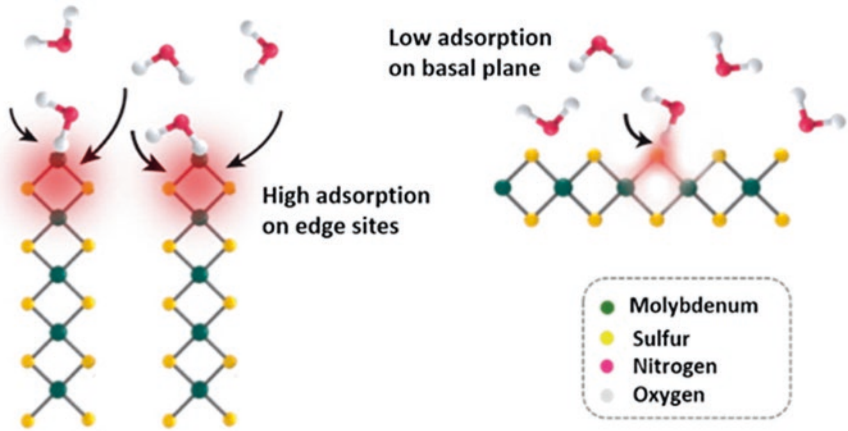

Fig. 4.5 Schematic illustration of gas adsorption mechanism on edge sites and basal plane of MoS_2. (Reproduced with permission from Cho et al. 2015b. Copyright 2015, American Chemical Society)

have been reported with the nanoarchitectonics strategy, but in some cases, it is difficult to achieve complete recovery at room temperature. Enhancing recovery has been tried with the thinning method (Ouyang et al. 2018) (few or monolayer) and with external thermal energy which requires a heating system and increases costs. Ko et al. (2018b) reported an outstanding NO_2 (500 ppm) gas response of 4140% for 2D WSe_2. They also proposed a method to reduce the recovery time from 85 min to 43 s by simply adding NH_3 gas that spontaneously reacts with adsorbed NO_2 causing their desorption from the WSe_2 surface at room temperature.

Light as external stimulus has been used by Polyakov et al. (2018) that prepared WS_2 nanotubes decorated with Au nanoparticles as sensing layer and obtained a photoresistive response to NO_2 gas under 530 nm light illumination at room temperature. An increase of ~20% was observed with gold-modified WS_2 nanotubes compared to pristine WS_2 nanotubes, owing to the photogeneration of electron-hole pairs, since the green photon energy (2.34 eV) exceeds both indirect (1.3–1.4 eV) and direct (2.0–2.1 eV) bandgaps of WS_2. Using the same principle, Gu et al. (2018) investigated the response of ammonium gas sensors with ultraviolet (UV, 365 nm), green (525 nm), yellow (580 nm), and infrared (IR, 850 and 940 nm) light sources. Figure 4.6a shows the increase in sensor response with decreasing light wavelength. The highest response was obtained for 365 nm, with ~3.5%, as expected because the photon energy is 3.4 eV, i.e., much larger than that of NH_3 (1.9 eV), facilitating electron transfer from the highest occupied molecular orbital of NH_3 to WS_2. Surprisingly, the second highest value was obtained with the lowest photon energy 1.3 eV (940 nm) which approximates to the indirect bandgap of WS_2 (1.3–1.4 eV) with ~3% response. The interferent gas experiment, using the light sources of 365 and 940 nm, is interestingly driven to a selective response enhancement solely to NH_3 gas, keeping constant the response for formaldehyde, methylbenzene, methanol, acetone, benzene, and ethanol as shown in Fig. 4.6b.

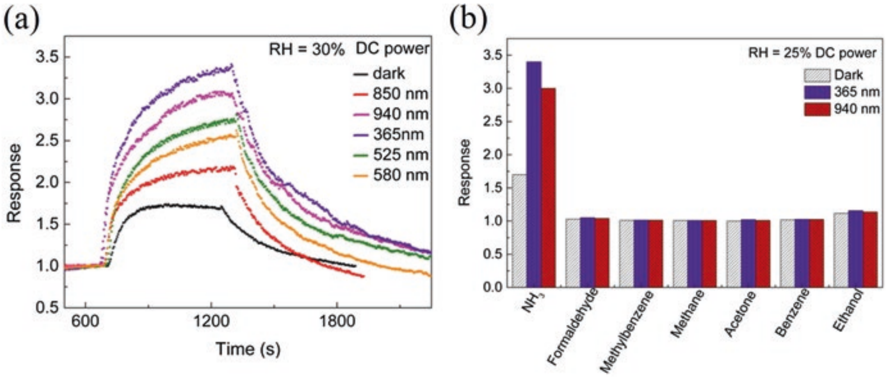

Fig. 4.6 (**a**) Response curves of WS_2-based chemiresistive sensors under different light illuminations driven by DC power to 10 ppm NH_3. (**b**) Comparison of the sensor response under light (365 nm, 940 nm) driven by DC power and in the dark, for several possible interferents at 60 ppm, including formaldehyde, methylbenzene, methanol, acetone, benzene, and ethanol. (Reproduced with permission from Gu et al. 2018. Copyright 2018, Elsevier)

4.4 Transition Metal Dichalcogenides and Metal Oxide Hybrids for Gas Sensing

The incorporation of metal oxides into two-dimensional transition metal dichalcogenides is an approach for improving the gas sensing performance of volatile organic compounds due to the synergistic hybridization efffects in these materials (Lee et al. 2018). In this section we will present some examples of metal oxides with well-known properties, such as ZnO and SnO_2, recently incorporated into transition metal dichalcogenide-based composites for sensing.

Figure 4.7a shows the response of sensors made with ZnO and ZnO-coated MoS_2 nanosheets for ethanol, from 50 to 1000 ppm (Yan et al. 2016). The responses increase according to the ethanol concentration and return close to zero after the volatile organic compounds are consumed in the testing chamber (quick and reversible response). The composite sample presented the higher response, which was attributed to the reduced energy barrier that facilitates electron transfer, promoted by the MoS_2 matrix in contact with the ZnO nanoparticles [96]. Moreover, MoS_2 nanosheets provide direct conduction paths for charge carriers from the junction to the external electrode, rapidly propagating the electrical signal. The sensors were also tested for methanol, acetone, ammonium, benzene, and methylbenzene, with significantly higher sensitivity for ethanol, as shown in Fig. 4.7b. Therefore, these sensors are selective to detect ethanol compared to other volatile organic compounds. Zhang et al. reported an ammonia gas sensor with an MoS_2/ZnO layer-by-layer film onto interdigitated electrodes in a printed circuit board substrate (Zhang et al. 2017b). Two bilayers of PDDA/PSS (poly(diallyldimethylammonium chloride)/poly(sodium 4-styrenesulfonate)) were deposited onto interdigitated electrodes as precursor layers for charge enhancement. The device performance as ammonia sensor was tested against comparable structures formed by pure ZnO drop-cast and MoS_2/PDDA layer-by-layer films (Fig. 4.7c). The MoS_2/ZnO device exhibits higher response from 0.25 to 100 ppm of ammonia gas. Figure 4.7d shows the responses of the MoS_2/ZnO nanocomposite film sensor toward ammonia, carbon monoxide, carbon dioxide, hydrogen, and dimethyl methane at room temperature. The high selectivity to ammonia is clear in comparison with other volatile organic compounds at the same concentration (5 ppm). The authors correlate these results to the more polarized structure of ammonia.

Qiao et al. fabricated a P-N heterojunction of MoS_2 nanosheets and SnO_2 nanofibers to be tested as a gas sensor for trimethylamine (Qiao et al. 2018). To improve the sensorial response, several tests were performed to adjust the molar ratio of the MoS_2/SnO_2 heterojunction device. Additional experiments were performed using devices formed by pure SnO_2 and compared to the MoS_2/SnO_2 heterojunction to test the selectivity of the sensors for distinct volatile organic compounds, such as trimethylamine, ethanol, acetone, formaldehyde, and methanol at 200 ppm. Figure 4.8a shows that the device with the MoS_2/SnO_2 heterojunction presents

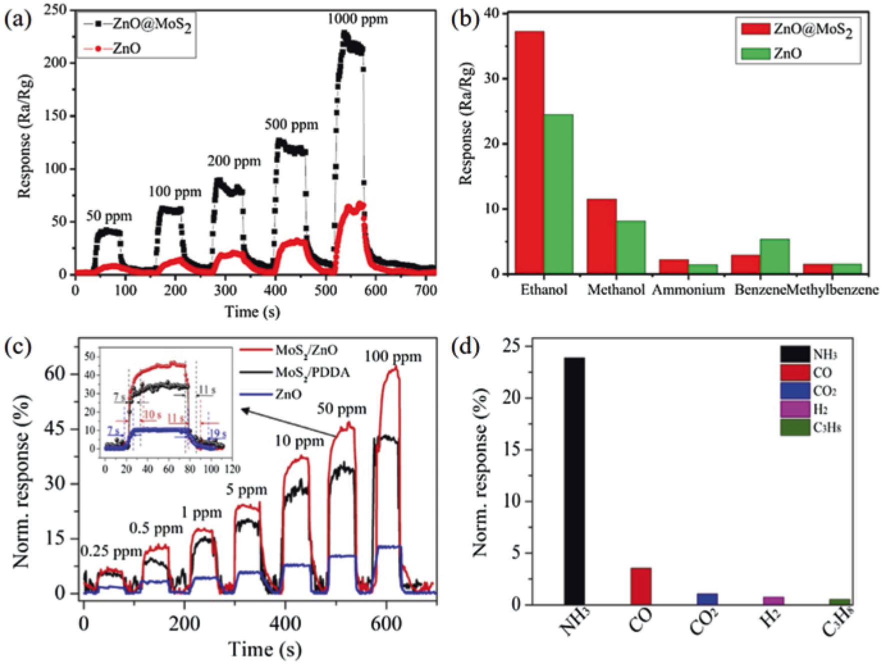

Fig. 4.7 Gas sensing devices made with hybrids of two-dimensional transition metal dichalcogenides, MoS_2, and metal oxide, ZnO. (**a**) Dynamic responses of ZnO and ZnO-coated MoS_2 samples to different ethanol concentrations (50–1000 ppm) and (**b**) the ZnO-coated MoS_2 response to different VOCs, highlighting the selectivity to ethanol. (**c**) Dynamic responses of MoS_2/ZnO, MoS_2/PDDA and ZnO film sensors exposed to various ammonia gas concentrations (0.25–100 ppm) and (**d**) the MoS_2/ZnO device response to 5 ppm of different VOCs, highlighting the selectivity to ammonia. (Reproduced with permission from Yan et al. 2016; Zhang et al. 2017b. Copyright 2016 and 2017, Elsevier)

excellent selectivity to detect trimethylamine among other volatile organic compounds when compared to the pure SnO_2. The selectivity is ascribed to the stronger electron-donating ability of trimethylamine compared to the other volatile organic compounds, in addition to the Mo ions that are more likely to be adsorbed onto Lewis acid sites.

Also using SnO_2 as metal oxide in the device structure, Gu et al. applied SnO_2/SnS_2 heterojunction as gas sensor for NO_2 (Gu et al. 2016). The composite was fabricated by oxidizing pristine SnS_2 in air at 300 °C. Figure 4.8b presents the sensor response to 8 ppm of NO_2, with a higher response by the heterojunction. The higher sensitivity can be attributed to the extra charge transfer between SnO_2/SnS_2 interfaces. The SnO_2/SnS_2 device was also tested with other volatile organic compounds such as formaldehyde, methanol, acetone, benzene, ethanol, and methylbenzene. The results in Fig. 4.8c point to the selectivity to NO_2.

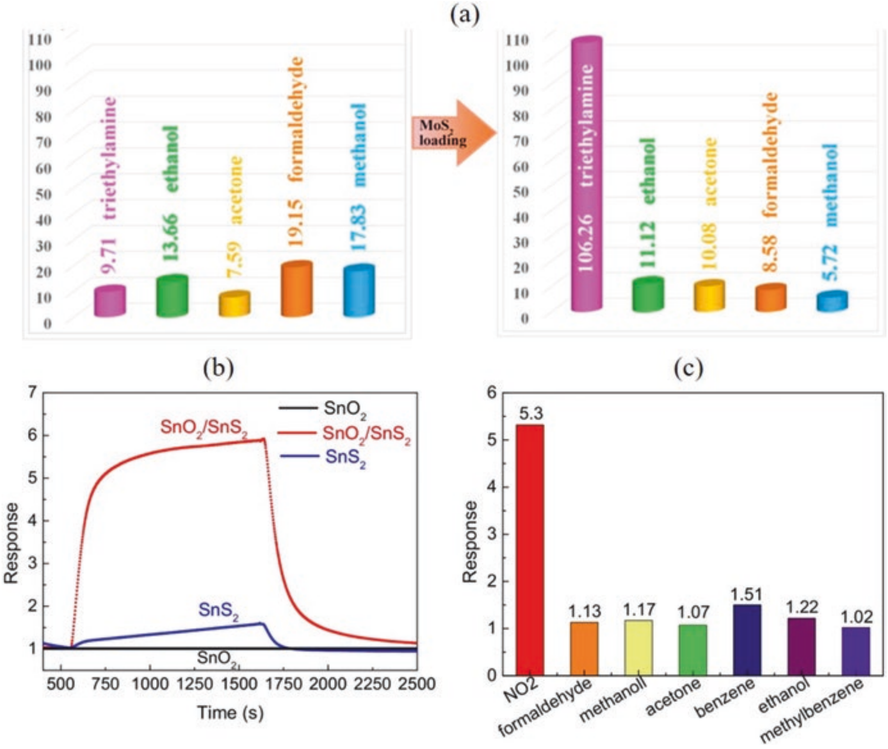

Fig. 4.8 Literature results for gas sensorial devices based on hybrid materials based on SnO_2 as the metal oxide and two different two-dimensional transition metal dichalcogenides. (**a**) Gas responses of pure SnO_2 compared to the MoS_2/SnO_2 heterojunction sensors to different volatile organic compounds, highlighting the selectivity to trimethylamine. (Reproduced with permission from Qiao et al. 2018. Copyright 2018, American Chemical Society). (**b**) Response of SnO_2, SnS_2, and SnO_2/SnS_2 devices to NO_2 and (**c**) comparison for the sensor based on the SnO_2/SnS_2 heterojunction to different volatile organic compounds, highlighting the selectivity to NO_2. (Reproduced with permission from Gu et al. 2016. Copyright 2017, Elsevier)

4.5 Functionalization of Transition Metal Dichalcogenides with Metallic Nanoparticles and its Gas Sensing Properties

Combining noble metal nanostructures with two-dimensional transition metal dichalcogenide materials is an effective way to obtain high catalytic efficiency for electrochemical hydrogen generation (Ping et al. 2017), providing a significant enhancement in sensing applications. In this section we will present some examples of metallic nanoparticles, such as Pd and Au, recently incorporated into transition metal dichalcogenide materials and applied to gas sensors.

Sarkar et al. configured a MoS_2-based field effect transistor functionalized with Pd nanoparticles as a sensor for hydrogen gas (Sarkar et al. 2015). Figure 4.9a, b presents

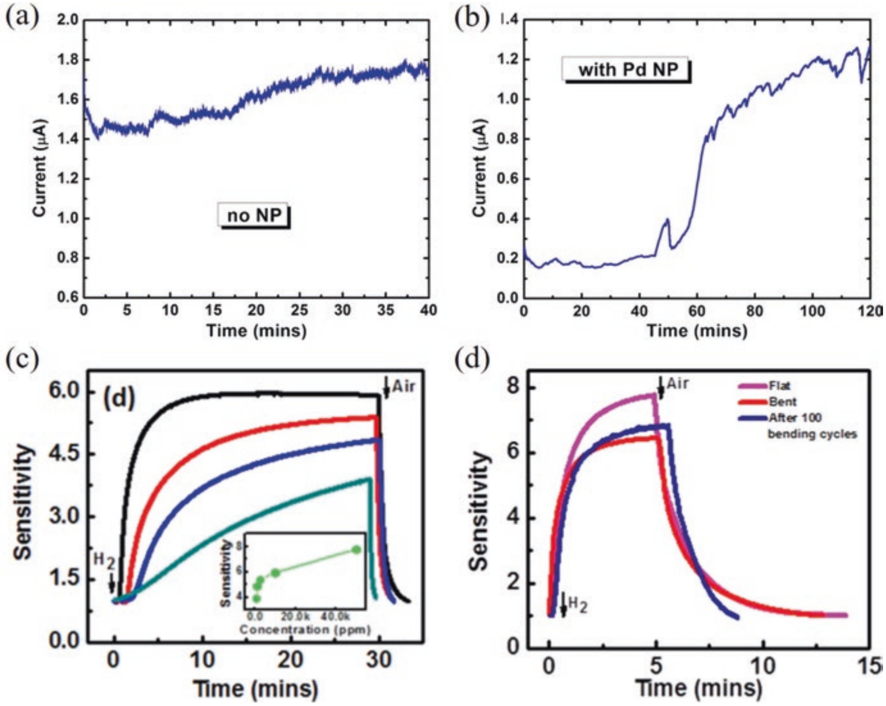

Fig. 4.9 Results for gas sensing devices made with two-dimensional transition metal dichalcogenide materials functionalized with Pd nanoparticles. (**a**) Responses of MoS_2 field effect transistor of pure and (**b**) functionalized with Pd nanoparticles, upon exposure to hydrogen. (Reproduced with permission from Sarkar et al. 2015. Copyright 2015, American Chemical Society). (**c**) Response of the WS_2 functionalized with Pd nanoparticles sensor upon H_2 exposure from 500 ppm (green curve) to 10,000 ppm (black curve). The inset presents the device sensitivity as a function of H_2 concentration. (**d**) Comparative sensing performance to hydrogen of the WS_2-Pd composite film in flat and bent geometry. (Reproduced with permission from Kuru et al. 2016. Copyright 2016, IOP Publishing)

the response of the MoS_2 pure and with Pd nanoparticles to hydrogen exposure, respectively. For the pristine MoS_2 device, only a small change in the current is observed upon hydrogen exposure, while for the functionalized material, the current response increases substantially. The result is explained (Sarkar et al. 2015) in terms of a decrease in the Pd work function owing to hydrogen adsorption, leading to a decrease in the p-type doping, thus increasing the current in the n-type MoS_2 transistor. Kuru et al. also used Pd nanoparticles to functionalize a transition metal dichalcogenide material and be applied as hydrogen sensor, using WS_2 nanosheets instead of MoS_2 (Kuru et al. 2016). Also, worth mentioning is the flexible polyimide substrate that offers advantages such as lightweight and mechanical durability, compared to hard substrates. Sensing measurements with different concentrations of H_2 from 500 ppm to 50,000 ppm were performed on the WS_2-Pd composite device as shown in Fig. 4.9c, and the results exhibit an increasing sensitivity with H_2 concentration. To evaluate the flexible structure, the sensing tests were also performed under mechanical deformation by bending the device around a cylindrical surface. The responses are presented in Fig. 4.9d under 50,000 ppm H_2 exposure, for tests with WS_2-Pd composite device flat, bent and after 100 bending cycles, resulting in slight variations in the sensor performance. After the bending cycles, the device was evaluated by scanning electron microscopy, and no obvious structural change was observed, indicating high mechanical durability of this flexible sensor based on WS_2-Pd nanoparticle composite film (Kuru et al. 2016).

Y. Cho et al. tested the sensitivity of MoS_2 films covered with Au nanoparticles to ambient gas, such as N_2, H_2/N_2, and O_2 (Cho et al. 2016). Although current versus voltage measurements on MoS_2 pure and functionalized with nanoparticles are distinct, no significant change in the electrical resistance under exposure of the three gases was observed. According to the authors, charges transferred from the gas may be insufficient to induce a measurable resistance change or may be trapped in defect states. S.-Y. Cho et al. enhanced the performance in volatile organic compound sensing with MoS_2 devices functionalized with Au nanoparticles (Cho et al. 2017). The devices responded to different volatile organic compounds at 1000 ppm, such as acetone, acetaldehyde, ethanol, hexane, and toluene. The Au nanoparticles on MoS_2 induced n-doping effects, significantly modifying its response. In conclusion, gas selectivity is still a problem, and further studies are required to address this limitation in sensors made with two-dimensional transition metal dichalcogenide materials functionalized with metallic nanoparticles.

4.6 Conclusion

In this chapter, some properties and applications were compiled for two-dimensional transition metal dichalcogenides and their heterostructures, with emphasis on the synthesis methods and gas sensing. With this literature survey, it was possible to identify the strategies adopted to enhance the gas sensing performance of two-dimensional transition metal dichalcogenides, which include functionalization with noble metals, integration with metal oxides shrinking the sensor to the micro- and nanoscales, and use of molecular filters and ultraviolet illumination. A selection of representative results was presented for the most studied transition metal dichalcogenides (MoS_2 and WS_2) used in gas sensors. In many cases, the sensing performance in terms of sensitivity and selectivity was promising even for operation at room temperature. There are, nevertheless, important challenges to exploit these two-dimensional transition metal dichalcogenide in practical sensing applications. For instance, key issues to be addressed include the need of large-area low-temperature synthesis and charge carrier transfer at the contacts and interfaces.

The outlook for two-dimensional transition metal dichalcogenide materials and their structures for gas sensing looks bright, considering the possible leveraging combination with other materials such as metal oxides and noble metals. Research into these novel materials is still at an embryonic stage, especially with the need to understand sensing mechanisms which may benefit from advances in molecular dynamics simulations. Important challenges to be faced are related to achieving fast recovery after sensing with 2D materials, e.g., by introducing photoreactive materials into the heterostructure or using ultraviolet illumination. Another avenue to be pursued is with AC sensing measurements (Liu et al. 2018b), as phase changes are only sensitive to the weak adsorption of gas molecules which warrants fast desorption. It is hoped that with such developments, gas sensors made with two-dimensional transition metal dichalcogenide materials may be instrumental for the next-generation electronics and the IoT.

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Conflicts of Interest The authors declare no conflict of interest.

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Chapter 5
Carbon Nanolights as Optical Nanosensors for Water Contaminants

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Abstract The environmental contaminants are a leading cause of various health hazards. There is a huge amount of effort that has been devoted for detection and decontamination. The ever-growing pollutants have brought significant attention toward development of sensors which can act at high specificity and sensitivity. The water pollution worldwide is a public health threat, and on-site detection is of great interest.

The exciting fluorescence properties of carbon dots have established them as an important sensing material of optical regime. A plethora of sensors have been reported in the last decade using the fluorescence switching of carbon dot in the presence of an analyte. This chapter provides a detailed overview of different environmental pollutants classified as metal ions (arsenic, lead, mercury, cadmium, chromium, and palladium), anions (sulfide, phosphate, thiosulfate), and chemical moieties (phenols) and their detection using carbon dot-based optical sensors. The performance of these optical sensors is compared on the basis of limit of detection and the linear working range of the sensor. The health hazards caused by these contaminants are briefly discussed. The chemical and green synthesis methods along with structural and optical properties of these carbon nanolights are also discussed.

Keywords Carbon dot · Biosensor · Fluorescence · Optical · Metal ion

5.1 Introduction

Carbon dots (c-dots) are the glowing member of carbon family with size below 10 nm and with interesting optical properties including high quantum yield, wavelength-tuned emission, potential to up-convert, etc. The fluorescent nature of c-dots has helped them emerged as the rapidly growing and most sought after material in the carbon family recently. The electrophoretic separation of carbon nanotubes led to the discovery of these fluorescent dots (Xu et al. 2004) which were later coined as carbon dot or carbon quantum dot (CQD) (Sun et al. 2006).

It is established that the optical properties of c-dots synthesized from different carbon precursor vary significantly. The abundance of carbon precursors led to the synthesis of c-dots using various precursors ranging from chemical small molecules to natural carbon sources (Sharma et al. 2017). The easy functionalization of carbon dots has seen a tremendous interest in developing doped carbon dots with the intent of further tuning the optical behavior of these nanolights. A great amount of effort has been devoted for the development of c-dots doped with elements like nitrogen, phosphorus, sulfur, and even metals like Zn and Fe.

The area of fluorescence-based sensor has exploited the extreme potential of optical nature of carbon dots. A range of fluorescence switch sensor has been developed for metal ions and anions using carbon dot. The water-soluble nature of carbon dots makes it feasible to employ them in real water sample, and hence these sensors have been used in detecting the presence of trace metal contaminates in environmental samples. The sensors have been employed in real water samples with satisfactory selectivity, sensitivity, and recovery. A variety of carbon dot-based composites have been used for removing metal pollutants from water. In a nutshell, the excellent optical nature, low inherent toxicity, high water solubility, easy synthesis, and convenient functionalization make the carbon nanolights as an ideal optical nanosensor for metal contaminants in water samples.

The non-biodegradable nature of heavy metals makes them a dangerous water pollutant. The vast use of metals in industrial revolution has increased their circulation to water bodies making them a leading and lethal water pollutant. The increased presence of metal contaminants in water is not only an environmental concern but also a public health threat. The metals are important for certain biochemical and physiochemical activities, but their concentration higher than a certain threshold is toxic. The most common water-polluting heavy metals are zinc, chromium, arsenic, lead, cadmium, copper, and nickel.

This chapter discusses the use of c-dot-based optical sensors for determination of metal ions, anions, and chemical pollutants in environmental samples. The synthesis strategies of c-dots are discussed, and the relevant optical properties are highlighted. Moreover, the detection of these pollutants are discussed in terms of dynamic range, limit of detection, and selectivity of the c-dot sensor. The toxic impacts of the environmental pollutants are also discussed in respective sections.

5.2 Synthesis of Carbon Dot-Sensing Material

Ever since the discovery of c-dots, the synthesis of these nanolights is of prime interest, and hence various methodologies are being explored. The top-down approaches utilized for the synthesis of c-dots include laser ablation, arc discharge, ultrasonication, chemical and electrochemical oxidation, etc. The bottom-up approaches include plasma treatment, hydrothermal carbonization, microwave pyrolysis, thermal decomposition, and template-based synthesis. A summarized representation is shown in Fig. 5.1.

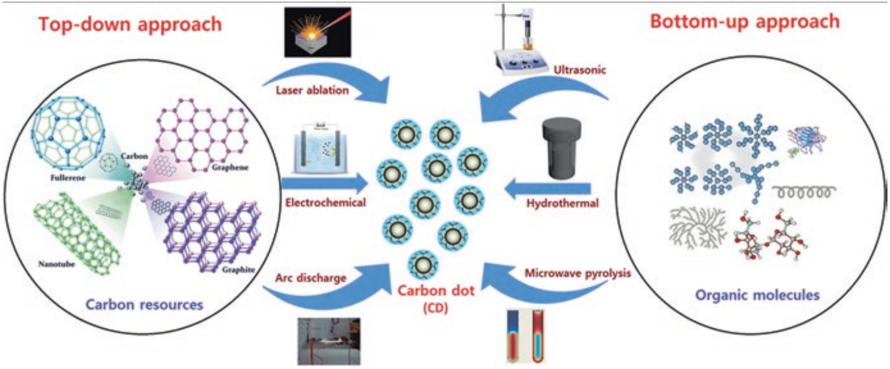

Fig. 5.1 A representation of synthetic approaches for carbon dot. (Reproduced from Sciortino et al. (2018) with permissions from the Royal Society of Chemistry)

A great amount of effort has been put in the exploration of various precursors for synthesis of c-dots. A variety of chemical precursors as well as various green precursors is employed for synthesizing c-dots (Tiwari et al. 2019). Interestingly, the properties of c-dots are greatly affected with synthesis conditions including the precursor, dopant, temperature, and the method of synthesis.

On the basis of carbon precursor used, it can be classified as chemical synthesis and green synthesis.

5.2.1 Chemical Synthesis

In order to explore various starting materials for c-dot synthesis, various chemical precursors have been utilized. The precursor used so far includes citric acid, urea, thiourea, benzene, ammonium citrate, ethylene glycol, phenylenediamine, phytic acid, EDTA, etc. Zhai et al. (2012) used citric acid for microwave pyrolysis and synthesized c-dots with a QY of ~30%. The carboxylic group on citric acid aids in dehydration and carbonization of the precursor. The authors also used various amines such as di-ethyleneamine, tri-ethyleneamine, ethylenediamine, and butanediamine for surface passivation. Yang et al. (2014c) employed ammonium citrate for synthesis of carbon-rich dots. A hydrothermal carbonization at 160 °C was carried out. The resultant product was run through silica gel column and eluted with methanol and di-chloromethane. The obtained QY was 13.5%.

Zhou et al. (2013) carbonized EDTA at 400 °C in order to obtain c-dots with a QY of 11%. Wang et al. (2013c) used phytic acid as a source of carbon and ethylenediamine as passivation agent for microwave treatment at 700 W resulting in phosphorous-containing c-dots. In order to extract the c-dots, organic solvents like methanol, acetonitrile, tetrahydrofuran, ethanol, and acetone were used, and the QY was obtained in the range of 11.1–19.5%. Li et al. (2011) employed an ultrasonic methodology for synthesis of c-dots where glucose was used for alkali/acid-assisted ultrasonication. Kasprzyk et al. (2018) used citric acid and urea in a microwave-assisted synthesis for synthesis of c-dots. In a typical synthesis, mixture of citric acid and urea was heated using microwave in a sealed vessel and an open vessel. Both synthesis conditions result in different emission properties of c-dots. The c-dots synthesized in an open vessel result in green emission, while the one synthesized in sealed vessel results in blue-emitting c-dots (Fig. 5.2).

5.2.2 Green Synthesis

The abundance of carbon-containing species in nature opens natural sources as an avenue for c-dot synthesis. Soon after the discovery of c-dots, the green carbon precursor was explored resulting in a plethora of green c-dots (Sharma et al. 2017). The initial green sources used for c-dot synthesis were coffee grounds and grass (Hsu et al. 2012; Liu et al. 2012).

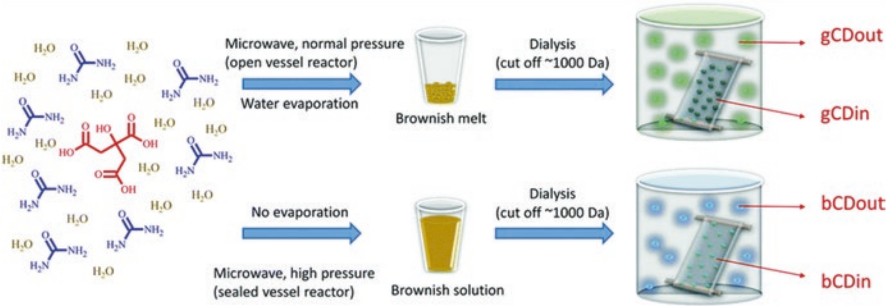

Fig. 5.2 Schematic synthesis of c-dots. The microwave pyrolysis of citric acid and urea results in c-dot synthesis. The dialysis helps in cutting off different molecular weight fragments. A closed and an open vessel condition results in blue carbon dot (bCD) and green carbon dot (gCD), respectively. (Reproduced from Kasprzyk et al. (2018) with permission from the Royal Society of Chemistry)

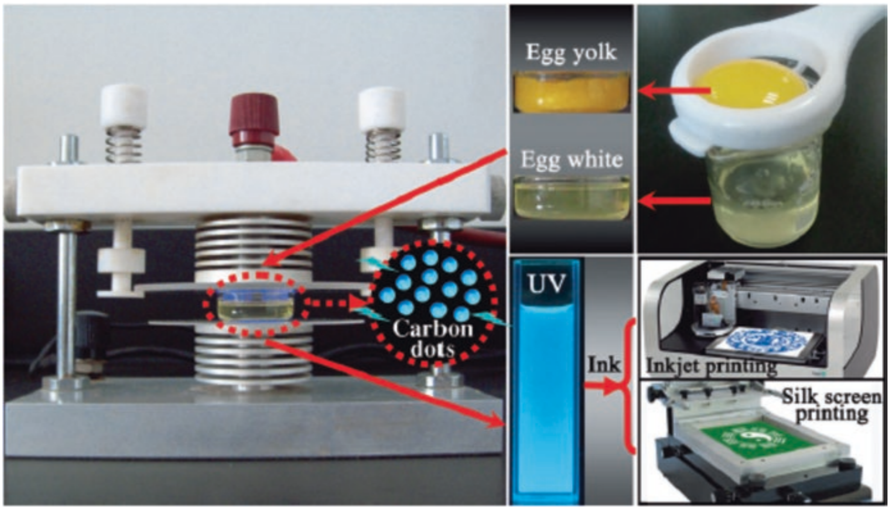

Fig. 5.3 Plasma-assisted synthesis of c-dots using egg white and egg yolk as carbon precursor. The c-dots were employed for multicolor printing. (Reproduced from Wang et al. (2012) with permissions from John Wiley & Sons)

The self-passivation offered by green precursor is an attractive feature for c-dot synthesis which also results in inherently doped c-dots. Wang et al. (2012) used a one-step strategy for synthesizing self-passivated nitrogen-doped c-dots using chicken egg as a carbon precursor (Fig. 5.3). The QY obtained using this process was 6–8%.

A variety of edible green sources including fruits like papaya, mango, strawberry, lychee, watermelon, apple, grapes, sugarcane, orange, banana, etc. (Zhou et al. 2012a; Sahu et al. 2012; De and Karak 2013; Huang et al. 2013, 2014;

Prasannan and Imae 2013; Jeong et al. 2014; Xu et al. 2015b; Kasibabu et al. 2015; Mehta et al. 2015; Xue et al. 2015; Kumawat et al. 2017; Vandarkuzhali et al. 2017; Yang et al. 2017; Sharma et al. 2018b); vegetables like potato, tomato, yam, onion, cabbage, carrot, radish, etc. (Lu et al. 2013; Mehta et al. 2014; Alam et al. 2015; Li et al. 2015; Bandi et al. 2016; Liu et al. 2017; Hu et al. 2017; Jin et al. 2017; Shen et al. 2017; Bankoti et al. 2017); and beverages like milk, tea, coffee, beer, etc. (Zhu et al. 2012b; Jiang et al. 2014; Wang and Zhou 2014; Wang et al. 2014, [CSL STYLE ERROR: reference with no printed form.]; Wei et al. 2014; Saravanan and Kalaiselvi 2015; Wang et al. 2015c, 2016b; Campos et al. 2016; Song et al. 2017) were explored for the synthesis of carbon dot. Even human- and animal-associated carbon precursors were employed for development of c-dots. A few examples are human hair and urine, beef meat, shrimp, honey, feathers, *Bombyx mori* silk, silkworm chrysalis, pig skin, prawn, crab shell, etc. (Wu et al. 2013; Wang et al. 2013b; Sun et al. 2013; Liu et al. 2014b, a; Yang et al. 2014b; Essner et al. 2015; D'souza et al. 2016; Guo et al. 2016; Wen et al. 2016; Yao et al. 2017).

5.3 Properties of Carbon Dots

The properties of carbon dots are known to be dependent on the carbon precursor due to the presence of inherent combination of carbon, attached functional groups, and heteroatom dopants (Sharma et al. 2019). The most common synthesis method for carbon dot formation involves "carbonization or pyrolysis" of carbon precursor. The carbon precursor usually undergoes condensation, polymerization, carbonization, and passivation during the synthesis of c-dots (Liu et al. 2019). In the condensation reaction, carbon precursor forms chain compound precursor; then in subsequent step, the carbon precursor gets polymerized. The polymerized carbon gets carbonized and forms carbon core. This carbon core formation usually occurs at high temperature. Then, through surface passivation the functional groups get attached on carbon core and modify the carbon dots. This section describes briefly the structural and optical properties of the c-dots.

5.3.1 Structural Properties

The carbon dot possesses size less than 10 nm leading to mostly amorphous or sometimes crystalline structure. Mostly powder X-ray diffraction (PXRD) and high-resolution transmission electron microscopy (HR-TEM) are used for structural characterization of carbon dots. A broad hump in $2\theta = 20°–25°$ arises in PXRD pattern of carbon dots (Essner et al. 2015) due to its amorphous nature. The electron microscopy confers spherical morphology of these nanodots. Moreover, at a very high magnification, lattice fringes can be seen in some carbon dots. The c-dots synthesized by cellulose waste paper by Jeong et al. (2018) exhibit a size in the range of 2–9 nm. The lattice fringe and corresponding “d” value of 0.24 nm were found that was attributed to (100) graphitic plane. The selected area electron diffraction (SAED) pattern corresponds ring pattern and supports high crystallinity. The Raman spectra of carbon dot exhibit mostly two broader peaks at values “1300 cm^{-1}” and “1580 cm^{-1}” attributing disordered “D” band arising from either structural defect or doping agent and “G” band arising from ordered sp^2 hybridized carbon atoms (Mazrad et al. 2018). The carbon dots mainly composed of C, H, and O elements along with doped elements such as N, S, P, etc. The most common methods used for surface functionality studies of c-dots are X-ray photoelectron spectroscopy and Fourier-transform infrared spectroscopy which help in determining the elemental percentage and presence of surface functional groups (Sharma et al. 2017).

5.3.2 Optical Properties

The c-dots are known to show exciting optical behavior leading to the greater interest in them. The absorption spectra of c-dots mostly exhibit $n\text{-}\pi*$ and $\pi\text{-}\pi*$ transitions. The π states arise from sp^2 hybridized carbon core, whereas the n states arise due to the lone pairs containing functional groups (Wang et al. 2017). In the UV-vis absorption spectra of c-dots, the peak in between 230 and 280 nm attributed to $\pi\text{-}\pi*$ transitions (C=C) bond, whereas peak around 300–320 nm arises because of $n\text{-}\pi*$ transition (C=O) bond (Ramanan et al. 2016; Wang et al. 2016c). Apart from these transitions, the most exciting property of c-dots is the fluorescence nature. The fluorescence behavior in carbon dots arises through various mechanisms such as quantum confinement (Kim et al. 2012; Jiang et al. 2015a), degree of surface oxidation (Shen et al. 2013a; Shi et al. 2016), and molecular fluorescence (Essner et al. 2018).

Ding et al. (2016) observed multicolor emission ranging from blue to red emission in c-dots by increasing the degree of surface oxidation. It was observed that due to the increase in surface oxidation, the bandgap gets reduced on carbon dot surface which leads to the red shift in emission behavior (Fig. 5.4a). Zhang et al. (2017) reported tunable and multicolor emission in nitrogen-doped carbon dots. In this case, the fluorescence origin occurs due to the surface functional group present on c-dots, and the doped element introduces a new energy level and ultimately new transitions which shifts the electron to higher wavelength (Fig. 5.4b). Kim et al. (2012) synthesized different sizes (5–35 nm) and morphologies, which exhibited size-dependent absorption and fluorescence spectra. It was demonstrated that the increase in particle size leads to red shift in emission wavelength. Meanwhile, some reports suggest that both quantum confinement and surface state provide a synergistic effect toward fluorescence of carbon dots.

In some recent studies, the formation of fluorescent impurities of carbon dots becomes fluorescent. Schneider et al. (2017) studied the contribution of distinct molecular fluorescence by preparing three different types of carbon dots from citric acid. They showed that fluorophore attached with carbon dots significantly influenced the optical behavior of carbon dots.

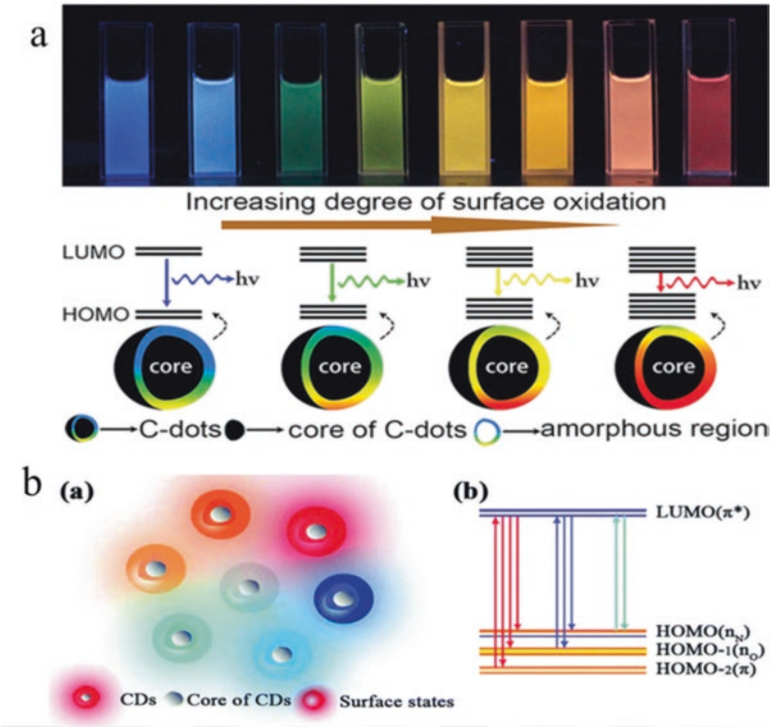

Fig. 5.4 The optical transitions in c-dots. (**a**) Fluorescence origination from the degree of surface oxidation. (**b**) Structure and electronic transition diagram of carbon dots. (Reproduced from Ding et al. (2016) and Zhang et al. (2017) with permissions from the Royal Society of Chemistry and the American Chemical Society)

The c-dots are shown to have fluorescence up-conversion. The up-conversion in c-dots attributes to multiphoton activation process, where absorption of two or more photon leads to emission at shorter wavelength. This interesting property of carbon dots has significant potential applications especially in biomedical imaging (Wang and Hu 2014).

5.4 Carbon Dot-Based Nanosensor for Water Contaminants

A variety of c-dot sensors have been reported for water contaminants. This section describes the contaminant, associated toxicity, and the c-dot sensor with limit of detection (LOD) of the said sensor.

5.4.1 Detection of Metal Contaminants

Metals are the entities having high electrical conductivity, malleability, lustrous nature and have the potential to lose their electron-forming cations. Heavy metals (having specific density ~5 g/cm^3) have the potential to severely affect environment and living organism (Järup 2003). These heavy metals such as arsenic, cadmium, lead, chromium, zinc, etc. are significant pollutants which can cause very high toxicity and are risky for the environment and human health (Nagajyoti et al. 2010; Theodore 2012; Jaishankar et al. 2014a).

Nanosensor for Arsenic

Arsenic having semimetallic properties is the twentieth most abundant element, is prominently toxic and carcinogenic, and is lethal for living creatures and environment. Arsenic contamination to drinking water has become a serious global problem around all corners of world (Hughes et al. 1988). According to the World Health Organization, arsenic content in drinking water must not be higher than 10 µgL^{-1} (Shen et al. 2013b). As(III) and As(V) species of arsenic possess high toxicity to humans (Samanta et al. 1999).

The arsenic-induced toxicity mainly arises from oxidative stress through induction of heat shock or stress protein (Keyse and Tyrrell 1989). Earlier reports concluded generation of $O_2^{\cdot-}$ and H_2O_2 due to arsenic exposure in various cell lines (Wang et al. 1996; Jing et al. 1999; Corsini et al. 1999; Lynn Shugene et al. 2000; Liu et al. 2001; García-Chávez et al. 2003). The inorganic arsenicals induce oxidative stress by hindering mitochondrial respiration, leading to mutations in DNA and resulting in cancer (Rana 2008). The toxicity of arsenic has already caused severe threat (Fig. 5.5); thus its detection and removal are very important.

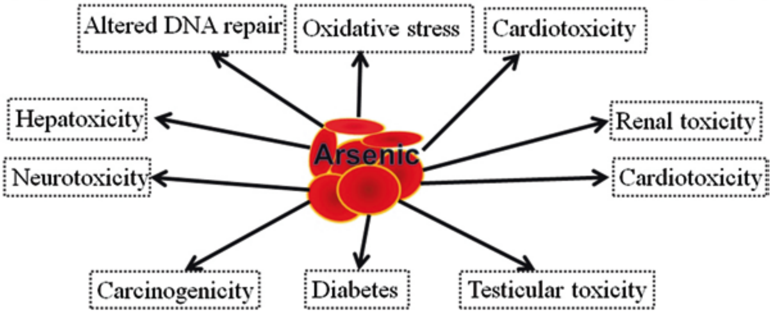

Fig. 5.5 The toxic impacts of arsenic. (Adapted from Ghosh and Sil (2015))

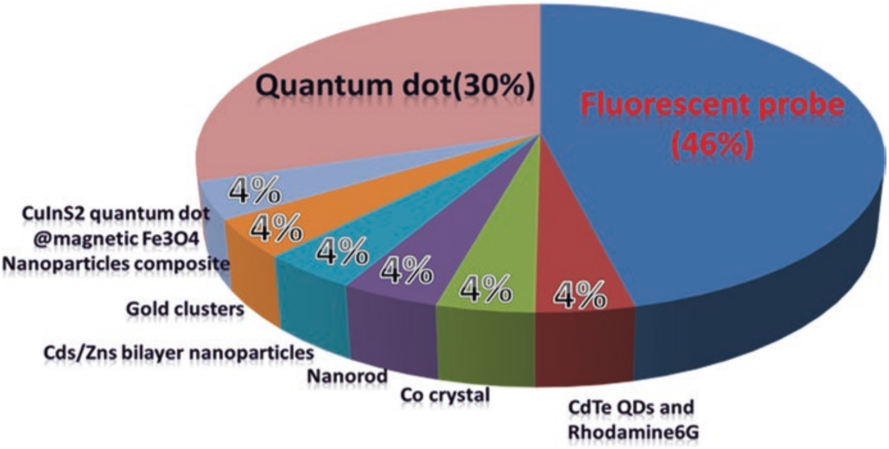

Fig. 5.6 Different groups of materials for optical detection of arsenite (2010–2016). (Adapted from Pooja et al. (2017))

The analytical tools developed for arsenic detection include its quantification using spectroscopic techniques such as atomic absorption spectroscopy (Pohl 2009; Gasparik et al. 2010), ICPMS (Caroli et al. 1999), calorimetric detection using fluorescence (Prestel et al. 2000), and cyclic voltammetry (Bhanjana et al. 2016). However, very high instrumental cost, tedious sample preparation, and complex instrumental handling limit their applicability. Thus colorimetric detection has the potential to bypass the drawbacks of earlier methods (Sirawatcharin et al. 2014). Gupta et al. (2016) synthesized carbon dots using trisodium citrate as carbon precursor and employed it for sensing As(III). The synthesized carbon dots exhibit ultrasensitive sensing behavior with limit of detection value of 32 pM. The carbon dots from citric acid and cysteamine, functionalized with ditheritheritol, were also employed for selective detection of toxic arsenite with limit of detection of 0.086 ppb (Pooja et al. 2017). The optical detection of arsenite using nanomaterials is summarized in Fig. 5.6.

Carbon dots synthesized from green “prickly pear cactus” source were used for sensing of As(III) through fluorescence turnoff in the presence of As(III) (Fig. 5.7). The linearity was in the range 2–12 nM with limit of detection value of 2.3 nM (Radhakrishnan and Panneerselvam 2018). Further, the quenching mechanism toward As(III) sensing was studied; the average lifetime gets increased to 3.0653 ns with addition of As(III) as compared to bare carbon dots having lifetime value of 2.752 ns. Further, the sensing ability was also demonstrated in tap water, river water, pond water, and industrial water having recovery of more than 99%.

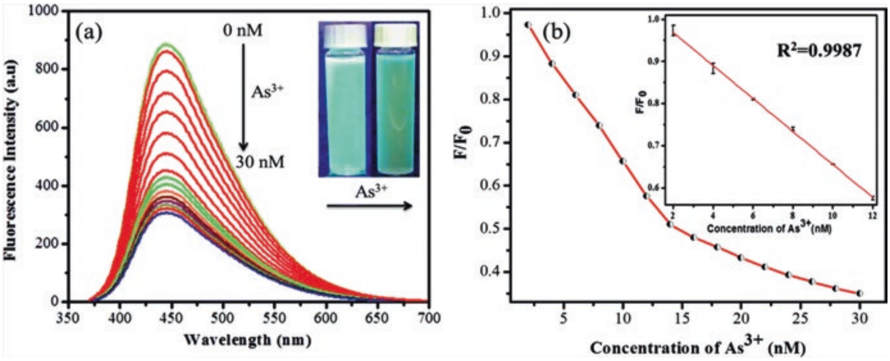

Fig. 5.7 The fluorescence decay in c-dots with subsequent addition of As3+. (Reproduced from Radhakrishnan and Panneerselvam (2018) published by the Royal Society of Chemistry)

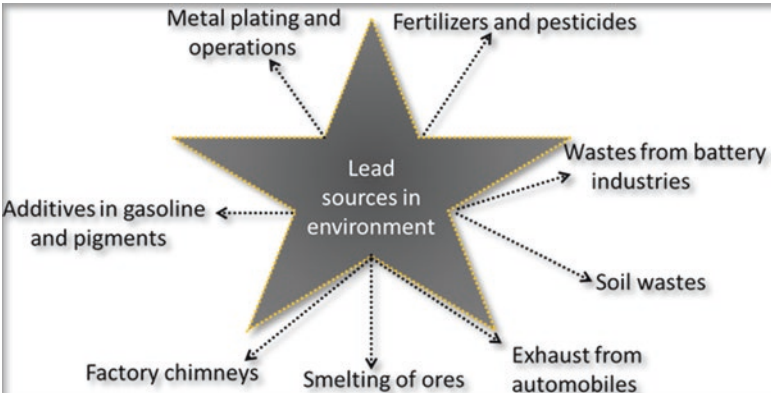

Fig. 5.8 Different sources of lead pollution in the environment

Nanosensor for Lead

Lead-based pollutants have caused extensive environmental contamination causing serious health problems. The primary lead sources include industrial processes, drinking water, smoking, plumbing pipes, storages batteries, etc. Figure 5.8 shows different sources of lead which has the potential to cause pollutions (Sharma and Dubey 2005). Various human activities like mining, manufacturing, and fossil fuel burning result in lead accumulation. Lead has a carcinogenic effect on the human body. Toxicity from lead can be divided into two types: (1) acute and (2) chronic. The acute toxicity causes loss of appetite, headache, renal dysfunction, fatigue, arthritis, etc. However, chronic exposure leads to mental retardation, autism, dyslexia, brain damage, etc. (Barbosa Fernando et al. 2005; Gracia and Snodgrass 2007).

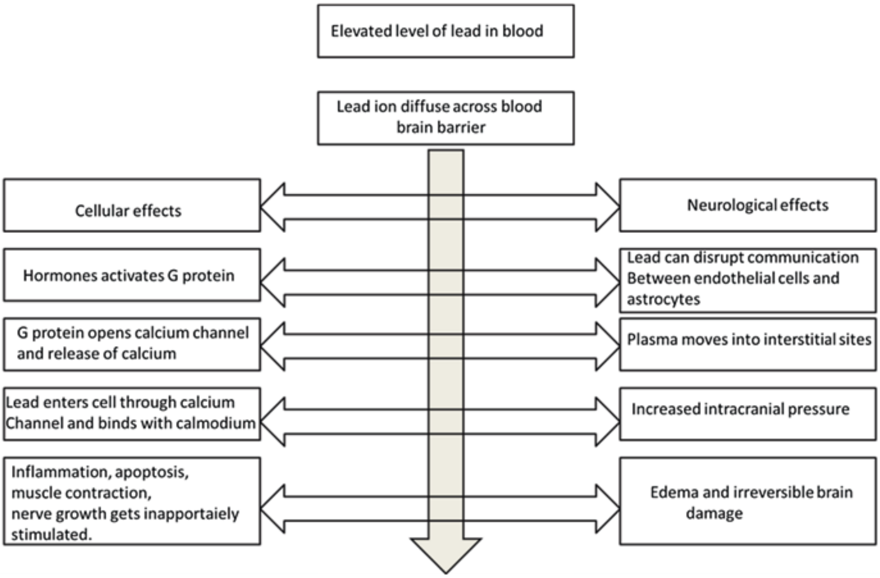

Fig. 5.9 Effect of increased concentration of lead in blood. (Adapted from Brochin et al (2008))

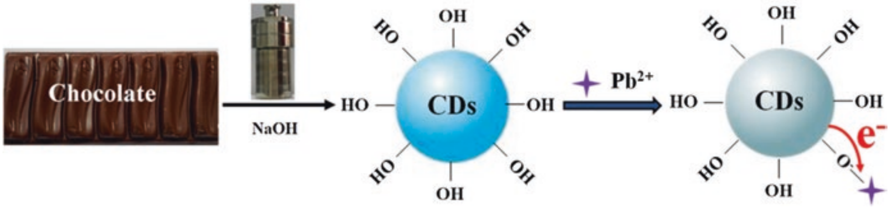

Fig. 5.10 Carbon dots as nanosensor for Pb^{2+}. (Reproduced from Liu et al. (2016) with permission from Elsevier)

As shown in Fig. 5.9, high lead concentration in blood causes serious toxicity hazards, i.e., neurological, reproductive, cardiovascular, and developmental can occur which may lead to permanent neurological damage (Brochin et al. 2008). According to US Environmental Protection Agency, the maximum contamination level of lead in water must not be greater than 72 nM (Wang et al. 2013a). Thus, severe health threat due to lead accumulation must be monitored and quantified. Earlier atomic absorption spectroscopy, atomic emission spectroscopy, and mass spectroscopy were used for lead analysis.

Carbon dots were explored for highly selective sensing of lead recently. The chocolate-derived carbon dots were used for highly selective sensing of Pb^{2+} with limit of detection value 12.7 nM (Fig. 5.10) by fluorescence quenching effect. To

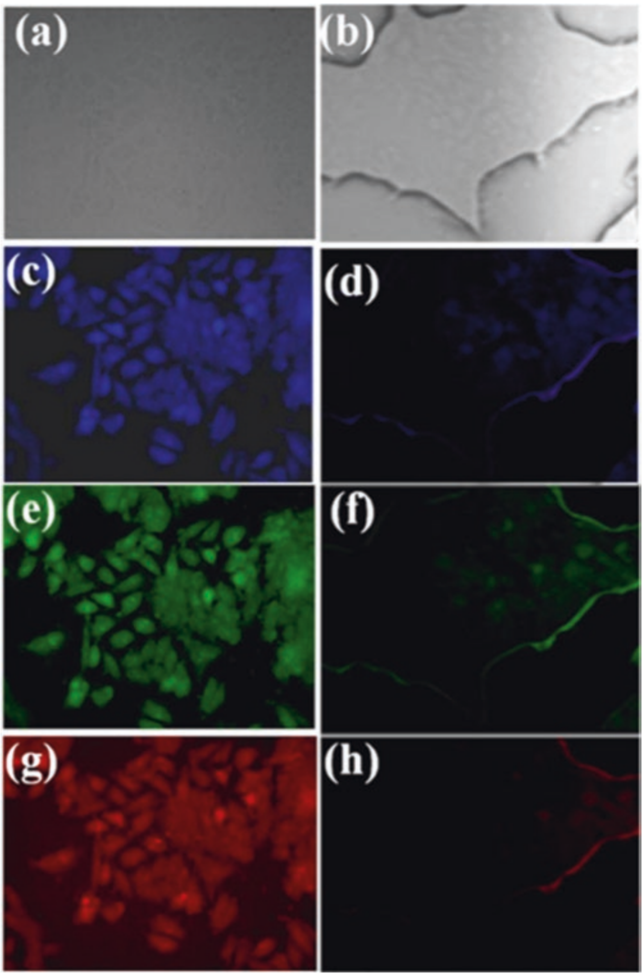

Fig. 5.11 Fluorescence microscopy image of MDA-MB 468 cells incubated with CDs [(**a**) bright field and (**c**, **e**, and **g**) at 330–385 nm, 450–480 nm, and 510–550 nm excitation wavelengths], and (**b**, **d**, **f**, and **h**) represents the corresponding fluorescence quenching after addition of lead ions (10 µM). (Reproduced from Kumar et al. (2017) with permission from Elsevier)

further authenticate the sensing capability, the sensing behavior was also checked on real water samples, and good recoveries were achieved (Liu et al. 2016).

In another report by Kumar et al. (2017), a green source "*Ocimum sanctum*" was used to synthesize carbon dots by hydrothermal method. The as-synthesized carbon dots had size in between 4 and 7 nm. Further, the obtained carbon dots were explored as label-free sensor for Pb^{2+}. The limit of detection value of Pb^{2+} was 0.59 nM. Further, Pb^{2+} ion detection was also performed on MDA-MB 468 cells (Fig. 5.11). The synthesized carbon dots internalize into the cells which can easily be confirmed from the fluorescence microscopy image. The carbon dot-treated cells exhibit multicolor emission (i.e., blue, green, and red color emission). However, when Pb^{2+} (10 μM) was present, the fluorescent intensity gets quenched suggesting suitable Pb^{2+} detection in living cells. The sensor was also shown to have good recovery in real water samples.

The cellulose-based fluorescent nanoparticles were also found successful in sensing Pb^{2+} with detection limit of 24 nM (Yun-fei et al. 2017).

Nanosensor for Mercury

Mercury is bioaccumulative and toxic. Mercury poisoning is known as acrodynia or pink disease. There are various sources such as paper-pulp preservatives, chlorine and caustic soda production, etc. through which mercury gets released in the environment (Morais et al. 2012). The increased level of mercury has the potential to alter brain function which can lead to shyness, memory problems, irritability, and change in vision and hearing. Similarly, metallic mercury exposure causes lung damage, vomiting, diarrhea, nausea, and increased heart rate. According to the World Health Organization (WHO), the mercury level in drinking water must be less than 0.001 mg/L (Gray et al. 2015). Various molecular sensors were developed for Hg^{2+} detection and were based on chemical bond formation such as Hg-O, Hg-Se, Hg-C, Hg-S, hydrogen bond formation, and nanomaterial-based sensors like carbon nanomaterials, gold nanoparticles, silver nanoparticles, micelles, strips, metal complexes, etc. (Chen et al. 2015); a summarized view is shown in Fig. 5.12. A highly selective and sensitive technique for Hg^{2+} detection using DNA-functionalized AuNPs and OliGreen was developed (Liu et al. 2008). The Hg^{2+} interacts with "T" units of DNA molecule which results in conformational change in DNA derivative. Further, some of DNA molecules gets released from the AuNP sur-

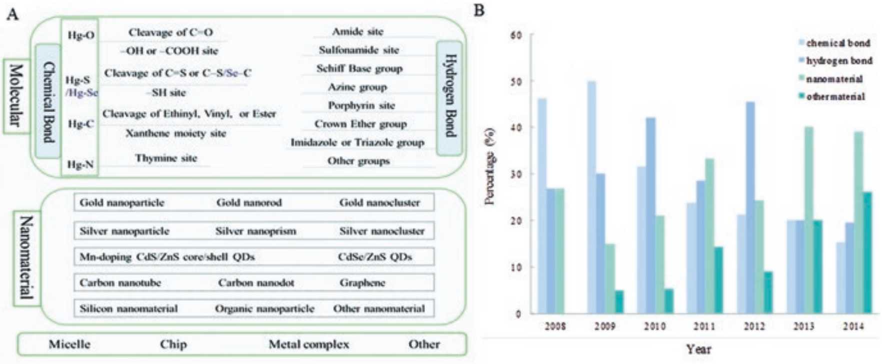

Fig. 5.12 (**a**) Various sensors for mercury detection. (**b**) Percentage of literature published from 2008 to 2014 on various sensors for mercury detection (Chen et al. 2015). (Reproduced from (Chen et al. 2015) with permissions from the Royal Society of Chemistry)

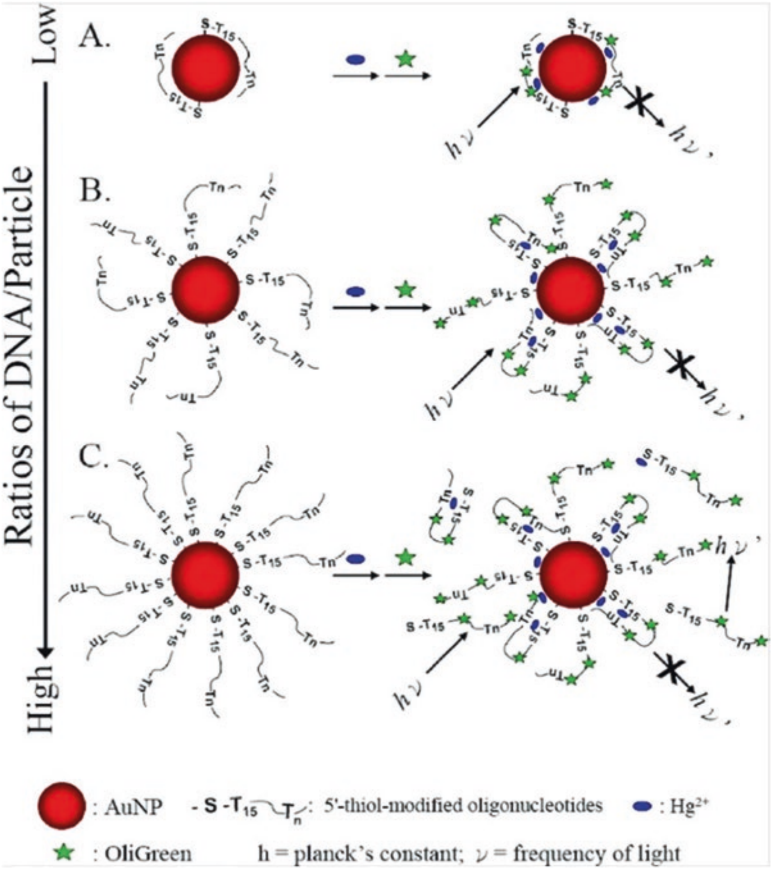

Fig. 5.13 Schematic representation of Hg^{2+} nanosensors at various DNA to AuNP molar ratios: (**a**) <30, (**b**) 30–50, and (**c**) ≥60. (Reproduced from Liu et al. (2008) with permission from the American Chemical Society)

face and reacts with OliGreen which leads to formation of OliGreen-DNA complex, and enhancement of fluorescence intensity at 525 nm with increase in Hg^{2+} concentration was used as a detector of mercury concentration (Fig. 5.13). The limit of detection of the sensing system was 25 nM, and linearity was in the range 0.05–2.5 μM.

The fluorescence-sensing system offers several advantages like high selectivity, sensitivity, fast sensing response time, and nondestructive nature. A green carbon source, "pomelo peel"-based carbon dots, was employed for Hg^{2+} sensing. The inherent fluorescent behavior of carbon dots was quenched with Hg^{2+} introduction. The LOD of this method was 0.23 nM. Further, the fluorescence of carbon dots was recovered by using cysteine as a chelator (Lu et al. 2012). A novel nanohybrid ratio metric fluorescence sensor was developed by combining fluorescent carbon

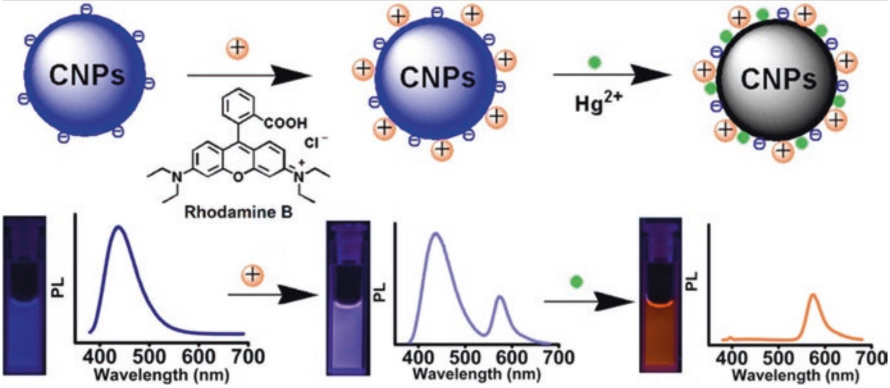

Fig. 5.14 Dual-emission fluorescence sensing of Hg^{2+} based on a CNP-RhB nanohybrid system. (Reproduced from Lan et al. (2014) with permission from the American Chemical Society)

nanoparticles and rhodamine (CNP-RhB). The photoluminescence of the hybrid system gets completely quenched by Hg^{2+} via electron transfer process which further results in distinguishable fluorescence color variation from violet to orange as shown in Fig. 5.14. The detection limit of the present method was 42 nM (Lan et al. 2014). Further, the intracellular sensing activity was studied with A549 cell lines. It was observed that the CNP-RhB nanohybrid shows good cell permeability and dual-emission nature (blue and red color emission). However, when 20 μM Hg^{2+} was added in CNP-RhB nanohybrid, no blue fluorescence was observed, and only strong red fluorescence was observed.

A nitrogen and sulfur co-doped graphene quantum dot system synthesized by one-pot hydrothermal method was employed for highly selective and sensitive detection of Hg^{2+} (Anh et al. 2017). Nitrogen doping results in enhanced quantum yield (41.9%), and sulfur provides high selectivity toward Hg^{2+} through strong interaction. The LOD was around 0.14 nM which was obtained in DI water. Further, the sensing ability was also checked in sewage and dye wastewater with good linear range 0.1–15 μM and recovery of 96–116%. Moreover, N,S-GQD-based paper strips were made using low-cost cellulose papers. These paper strip sensors were used in wastewater Hg^{2+} detection by reduced fluorescence behavior as shown in Fig. 5.15. The developed paper strips have the potential to act as a platform for efficient and robust detection of Hg^{2+} (with wide concentration range) in wastewaters.

Nanosensor for Cadmium

Cadmium is the seventh most toxic element and is classified as group 1 carcinogens for humans (Bernhoft 2013). Cadmium gets exposed to humans by various sources such as fossil fuel and iron-steel productions (Fig. 5.16). Cadmium gets accumulated in proximal tubular cells and affects the kidney severely. Earlier studies

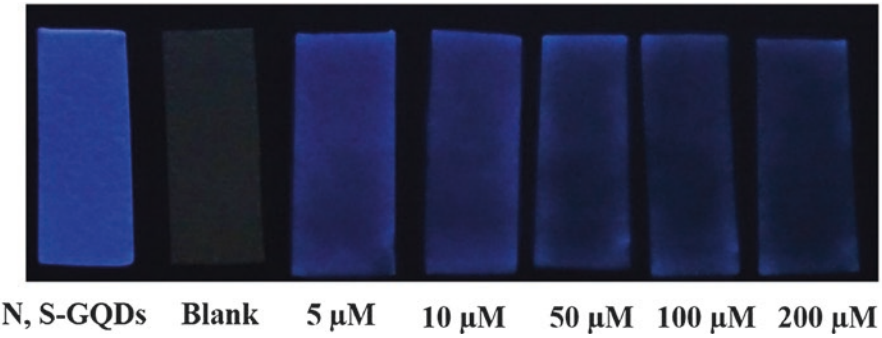

Fig. 5.15 N,S-GQD-based papers with varying concentration of Hg^{2+} in wastewater. (Reproduced from Anh et al. (2017) with permission from Elsevier)

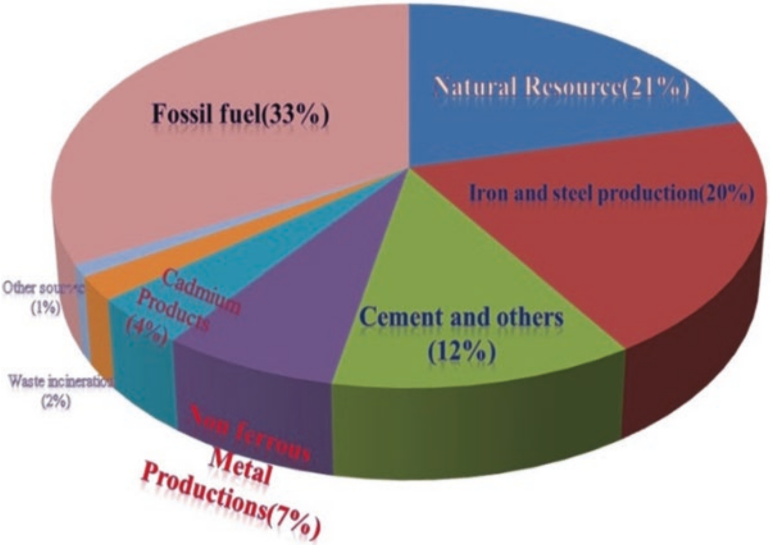

Fig. 5.16 Contribution from various sources of cadmium exposure. (Adapted from Regoli (2005) and Jaishankar et al. (2014b))

revealed that cadmium exposure results in skeletal damage, lung damage, and stomach irritation.

A nanohybrid of carbon quantum dot and Au nanoclusters was developed for ratiometric sensing of Cd^{2+} ion with LOD as low as 32.5 nM. The sensing behavior was attributed to static fluorescence quenching at inner filter effect (Niu et al. 2016). A simultaneous detection of Pb^{2+} and Cd^{2+} was devised using a nitrogen-doped carbon dot and graphene oxide hybrid. This method was based on anodic strip voltammetry (Fig. 5.17). The method was tested on lake water and tap water with satisfactory recoveries (Li et al. 2018).

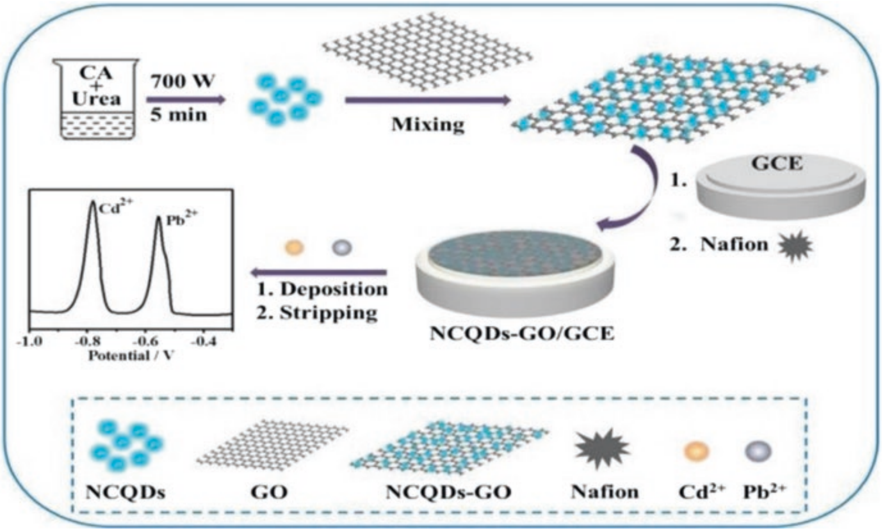

Fig. 5.17 A c-dot- or graphene-based electrochemical sensor for simultaneous detection of Pb^{2+} and Cd^{2+}. (Reproduced from Li et al. (2018) with permission from Elsevier)

Nanosensor for Chromium

Chromium is the seventh most abundant element present on earth and occurs in the environment in oxidation state ranging from Cr^{2+} to Cr^{6+} (Monalisa and Kumar 2013). In aqueous form chromium exists in a trivalent (Cr^{3+}) and hexavalent form (Cr^{6+}). The Cr^{3+} form of chromium plays a significant role in glucose and fat metabolism (Shinde et al. 2004). However, Cr^{6+} has been proven very toxic and may cause carcinogenic and mutagenic effects. According to the World Health Organization (WHO), the maximum concentration of Cr^{6+} in drinking water must not be greater than 1 μM (Blowes 2002). In the last two decades, a number of analytical techniques were developed for Cr^{6+} detection such as chromatography, atomic absorption spectrometry, etc.; however, these methods are not convenient because of the high cost of equipment and complicated sample pretreatment (Zheng et al. 2013). The fluorescent-based Cr^{6+} monitoring has the potential to become a good alternative. Bu et al. (2016) developed Cr^{6+} sensor using phosphate-derived carbon dot probes. The inherent fluorescent nature of as-synthesized carbon dots gets quenched in the presence of Cr^{6+}. The detection limit was 0.24 μM, and linearity was in the range 1–400 μM. Further, Cr^{6+} concentration was determined in river water and tap water. The recoveries of 104.5% and 98.42% were found supporting the accurate and feasible monitoring of Cr^{6+}. Recently, N,S co-doped carbon dots (N,SCDs) were also used for detection of Cr^{6+} (Yang et al. 2018). The fluorescence of N,SCDs gets quenched by Cr^{6+} due to inner filter effect. Moreover, the fluorescence of

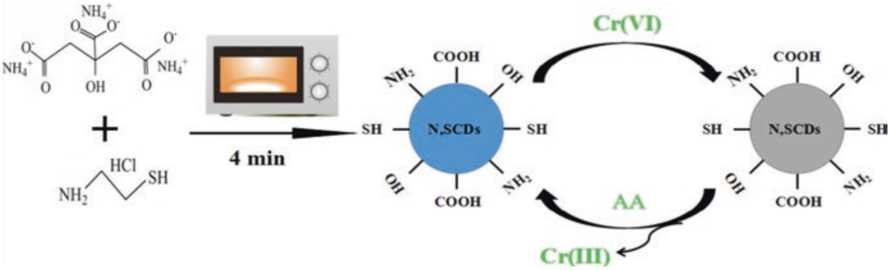

Fig. 5.18 Synthesis of N,SCDs and detection of Cr^{6+} and ascorbic acid. (Reproduced from Yang et al. (2018) with permission from Elsevier)

N,SCDs-Cr gets recovered with the addition of ascorbic acid (Fig. 5.18). The liner range and limit of detection of present method were 0.35–126 μmolL^{-1} and 0.11 μmolL^{-1}, respectively. Interestingly, a molecular logic gate was constructed based on fluorescence recovery.

Nanosensor for Iron

Iron is the second most abundant element present in the earth crust. Iron is very important biologically because it is the cofactor for several vital enzymes and proteins. Also Fe^{3+} ions play a very crucial role in biological system such as in cellular metabolism, oxygen transport in hemoglobin, and enzyme catalysis (Hentze et al. 2010). The imbalance in iron concentration may disturb cellular equilibrium and may cause various diseases like anemia, liver kidney dysfunction, heart failure, diabetes, and cancer (Weinstein et al. 2002; Agarwal et al. 2004; Hörl 2007; Narayanaswamy and Govindaraju 2012; Zhang et al. 2014b). Thus, highly precise sensing system is needed for monitoring of Fe^{3+} ions. Fluorescent probes such as semiconducting quantum dots, metal nanoclusters, and metal organic framework were earlier used for Fe^{3+} detection. However tedious synthesis approach, toxicity, and hydrophobicity were the major concern. The carbon dots synthesized from a “black tea” by one-step hydrothermal method were used for Fe^{3+} detection (Song et al. 2017). As-synthesized carbon dots exhibit excellent photostability, biocompatibility, low toxicity, and high sensitivity. Further, as-synthesized carbon dots selectively sense Fe^{3+} by quenching the fluorescence. The limit of detection of 0.25 μM was achieved. Further, sensing of Fe^{3+} was also performed in living cells and in human serum. The *Vigna radiata* sprouts were also used as sole carbon precursor to synthesize nitrogen-doped carbon dots. The synthesized carbon dot exhibits quantum yield of ~58%. Further as-synthesized carbon dots were used for Fe^{3+} sensing. The LOD and linear range of sensing system were 140 nM and 100–1000 and 1000–2000 μM, respectively (Kaur et al. 2019).

Nanosensor for Palladium

Palladium (Pd^{2+}) a rare transition metal belonging to platinum group of metals plays a very crucial role in various biological and chemical activities. However, residue of Pd^{2+} left in water, food, and drugs has the potential to cause severe health issues. Earlier several conventional methods were employed for Pd^{2+} detection such as X-ray fluorescence, atomic absorption spectroscopy (AAS), high-performance liquid chromatography, and plasma emission spectroscopy (Ren et al. 2012). However expensive instruments and rigorous experimental protocol limit their applicability. To nullify the above problems, fluorescent carbon dot-based probe was used. The citric acid-derived carbon nanoparticles (CNP) were used for palladium sensing through "fluorescence turn-off" mode (Sharma et al. 2016). The limit of detection for Pd^{2+} was 58 nM, and linearity was in the range 5–100 μM. Moreover, the sensing capability was tested on real samples. The CNP sensor provides excellent recovery of more than 97% in RO water and tap water.

The red-emissive carbon dots synthesized from citric acid and neutral red via one-step hydrothermal method were also used for Pd^{2+} detection. The as-synthesized carbon dots sense Pd^{2+} with detection limit of 3.29 μM (Gao et al. 2018).

5.4.2 Detection of Anion Contaminants

There has been an extensive interest in cation sensing through fluorescence quenching of c-dots. However, in some cases, the quenched fluorescence is recovered by addition of an anion in c-dot/cation pair due to cation-anion interaction.

Nanosensor for Sulfide Ion

The sulfide ion is produced in various biological processes, and hence its sensing has a significant interest. The sulfide ion pollutant can affect respiratory functions and mucous membrane. A cyclam-functionalized carbon dot sensor was recently developed for detecting sulfide by recovering the Cu^{2+}-induced quenching of c-dot fluorescence. The LOD of this method is reported to be 130 nM (Chen et al. 2016).

A sulfide ion-induced direct increase in c-dot fluorescence was observed in rose petal-derived carbon dot. The rose petal-derived c-dots were doped with nitrogen and sulfur, and resulting QY was 9.6%. The sulfide detection using this method shows linearity in range 0–500 μM, and LOD is as low as 63.1 nM. Interestingly, the addi-

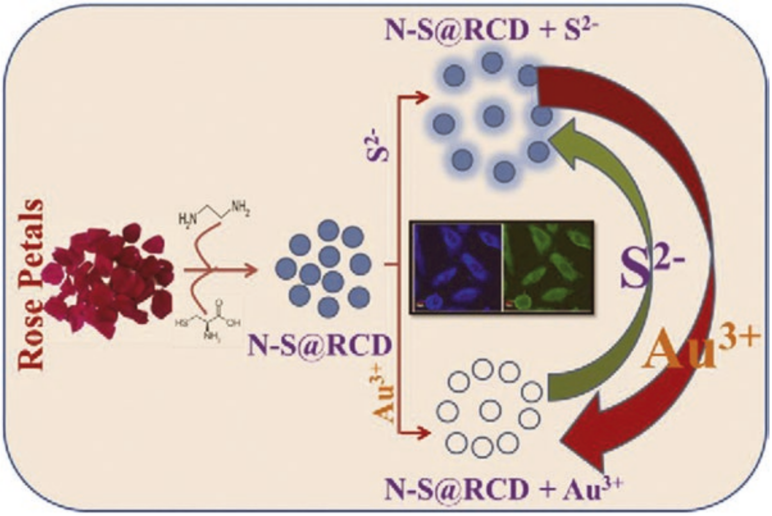

Fig. 5.19 Rose petal-derived c-dots for fluorescence "on-off-on" sensing of Au^{3+} and S^{2-} with bioimaging. (Reproduced from Sharma et al. (2018a) with permission from Elsevier)

tion of sulfide increased the QY from 9.6% to 25.3% (Sharma et al. 2018a, 2019). It was also observed that the fluorescence of these c-dots is quenched by addition of Au^{3+} which could be recovered up to 93% by addition of S^{2-} (Fig. 5.19).

A citric acid-derived c-dot-based sulfide ion sensor was also reported with LOD of 0.78 μM and validated physiological milieu along with running water and live cells. This method detects the sulfide ion by measuring the recovery of Cu^{2+}-induced quenched fluorescence of c-dots (Hou et al. 2013).

Nanosensor for Phosphate Ion

The phosphate ion sensors based on c-dots also use the principle of recovery of quenched fluorescence of c-dots. Europium-adjusted c-dots were reported to be an efficient sensor for phosphate ion in the linear range of ~1–12 μM with LOD of 5.1×10^8 mol L^{-1}. It was observed that the presence of Eu3+ aggregates the c-dots leading to the quenched fluorescence. The presence of phosphate ion disrupts the aggregation and results in recovery of fluorescence intensity. A total of 93% of initial intensity could be recovered by addition of phosphate which makes the basis of phosphate detection using this sensor (Zhao et al. 2011).

Nanosensor for Thiosulfate Ion

A fluorescence switching in rice-derived c-dot was reported by Dhenadhayalan and Lin (2015), where the quenched fluorescence in a c-dot/Fe^{3+} system is recovered by addition of thiosulfate ions. A total of 80% of initial fluorescence intensity could be recovered. The thiosulfate sensor responded in a wide concentration range with LOD obtained to be 8.47×10^{-6} M.

5.4.3 *Degradation of Dye Pollutants in Environment Using Carbon Dots*

Apart from metal and anion contaminants, various dye contaminants enter aqueous system from sources like painting, dyeing, textile industries, etc. These dyes cause serious toxic and carcinogenic problems; hence exploration and validation of efficient methods are needed for dye degradation (Ghorai et al. 2008; Hankare et al. 2011; Yu et al. 2012; Zhan and Zeng 2016; Raman and Kanmani 2016). Initially, Fenton oxidation method was used for dye removal, e.g., a solution containing iron ions, and H_2O_2 generates hydroxyl ions for the removal of dyes (Kallel et al. 2009; Chu et al. 2012). However narrow active pH range (mostly acidic) and presence of pollution from metal ion limit their applicability. Metal-free catalytic system like carbon nanomaterials especially carbon dots has the potential to overcome these problems.

The carbon dots synthesized by thiourea and citric acid were used for degradation of thymol blue (TB) (Zheng et al. 2017). These carbon dots mimic "Fenton-like" catalyst and degrade in H_2O_2 solution at room temperature. The catalytic degradation occurs because of generation of $\cdot O_2^-$ and OH·. Further it was found that the addition of KI in carbon dot-H_2O_2 system significantly improves the degradation efficiency (Fig. 5.20).

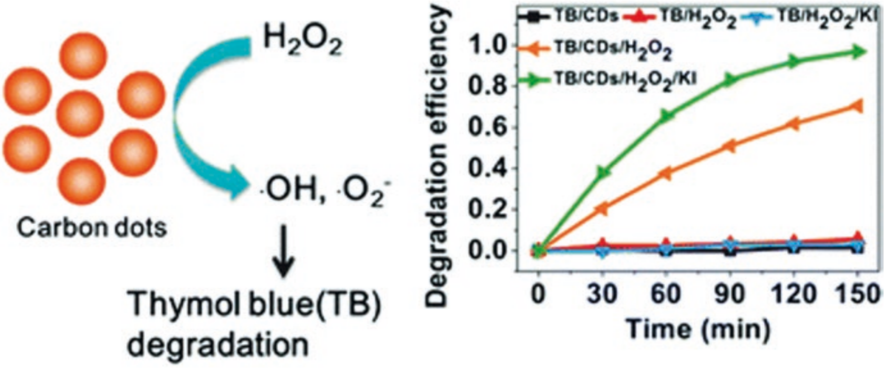

Fig. 5.20 Degradation of thymol blue using carbon dots and the degradation efficiencies. (Reproduced from Zheng et al. (2017) with permission from the Royal Society of Chemistry)

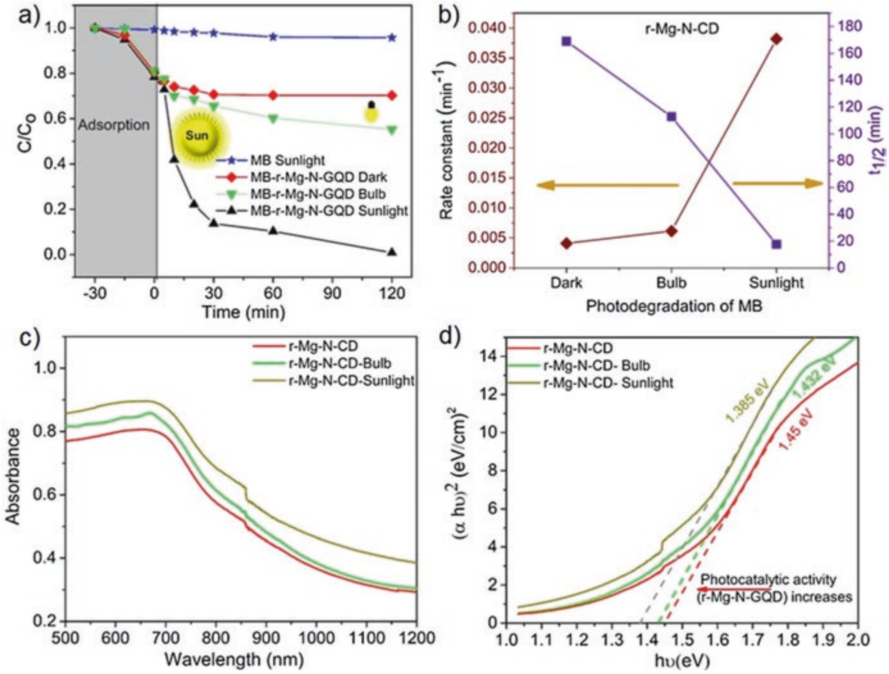

Fig. 5.21 (**a**) C/C_o v/s time for methylene blue under different conditions. (**b**) Rate constant and $t_{1/2}$ value. (**c**) Absorbance value. (**d**) Tauc plot v/s photoenergy in different light source. (Reproduced from Bhati et al. (2018) with permission from the American Chemical Society)

In another report, *Bougainvillea*-derived and magnesium-nitrogen-embedded carbon dots were used for degradation of methylene blue under sunlight. The carbon dot was synthesized using simple domestic microwave (Bhati et al. 2018). Further, excitation-independent emission at wavelength ~678 nm was observed with quantum yield of ~40%. The catalytic activity of ~99.1% was achieved with as-synthesized carbon dots under sunlight irradiation, whereas just 45% was achieved with 100 W tungsten bulb under 120 min. A significant effect of sunlight can easily be seen for photodegradation (Fig. 5.21a). The rate constant and half-life ($t_{1/2}$) value of methylene blue degradation at different photodegradation conditions is shown in Fig. 5.21b. The lower $t_{1/2}$ value in sunlight leads higher rate constant, whereas in the dark, degradation rate constant was lowest. Interaction of carbon dot with methylene blue was investigated using *UV-vis* spectroscopy (Fig. 5.21c). In the presence of sunlight, the absorbance value was highest, whereas control carbon dot-methylene blue had least absorbance. Further, bandgap of carbon dots-methylene was investigated at various conditions (Fig. 5.21d). The bandgap was highest with sunlight confirming the higher absorbance value. The bandgap values were consistent with photodegradation rate constant and half-life values.

5.4.4 *Nanosensors for Other Chemical Pollutants*

Nanosensor for Water pH

It is well known that the most common side effect of pollution is change in pH of groundwater. The pH indicates activity of hydrogen ion (H^+) in any specimen. The pH of natural water must not be less than 6. Any significant change in pH, i.e., too low or too high, causes threats to aquatic animals.

As shown in Fig. 5.22, a slight change in the pH value leads to death of many aquatic animals. The conventional methods for pH determination were based on electrochemical approach which includes voltammetric, amperometric, and potentiometric (Ang et al. 2008; Lu and Compton 2014; Galdino et al. 2015). The colorimetric monitoring of pH provides advantages in comparison to other methods. The dual-emissive N,S co-doped carbon dots (N,SCDs) having the emission peak at 648 nm synthesized via solvothermal method were used for pH sensing (Zhang et al. 2019). The synthesized N,SCDs exhibit reversible pH-responsive fluorescence behavior in pH range 1–13. The increase in pH from 1 to 13 leads to the decrease in fluorescence intensity which gets restored when reverting the pH from 13 to 1. The N,SCDs shows excellent reversible pH performance and supports the robustness toward present sensing method.

The sugarcane-derived carbon dots were also successfully demonstrated to detect alkaline pH in range 9–13 with good reversibility (Sharma et al. 2018b).

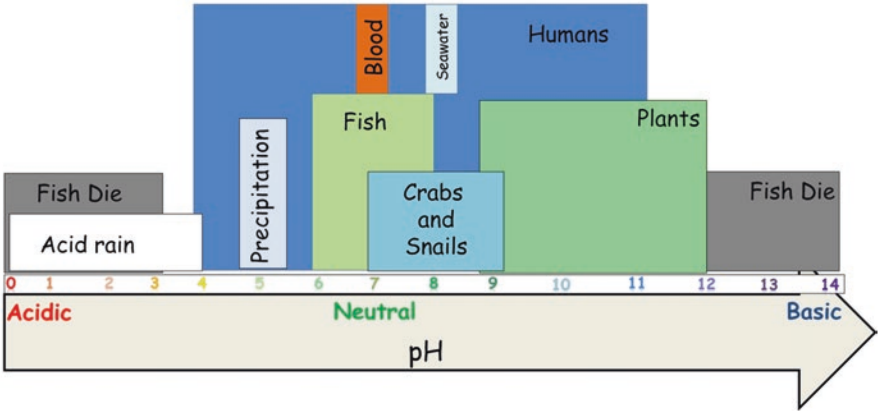

Fig. 5.22 The physiological pH level for different biological system

Nanosensor for Phenols

The nitro-aromatic constituent is an important class of perspective pollutant due to their use in security, environmental, and healthcare. The P-doped c-dots derived from sucrose and phosphoric acid were employed for detection of 2,4,6-trinitrophenols (Fig. 5.23). The QY of as-synthesized c-dots was found to be 21.8%. The fluorescence of P-doped c-dots shows a quenching of fluorescence in linear range of 0.2–17.0 μM with LOD of 16.9 nM (Shi et al. 2015).

The use of coal as carbon precursor was also explored for synthesis of c-dots for phenol sensing (Xue et al. 2018). A one-step ozone oxidation of coal leads to synthesis of c-dots with average particle size of 4.2 nm. These c-dots act as a selective sensor for phenols in water having a linear range in phenol concentration 0–40 μM with LOD of 0.076 μM. Table 5.1 summarizes the carbon dot-based nanosensors for environmental pollutants.

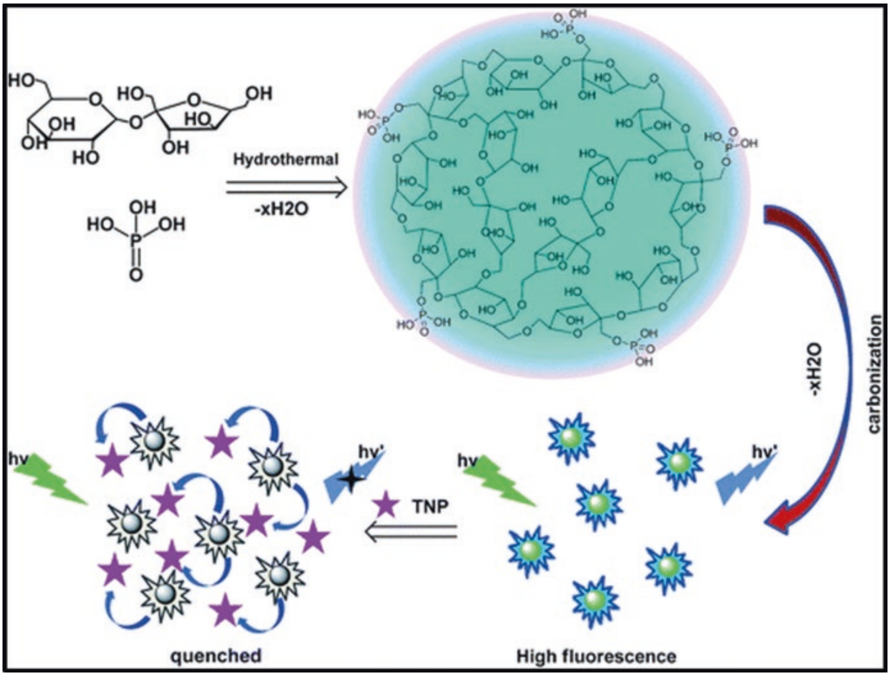

Fig. 5.23 The sensing of 2,4,6-trinitrophenol using P-doped c-dots derived from sucrose. (Reproduced from Shi et al. (2015) with permission from the Royal Society of Chemistry)

Table 5.1 Representative carbon dot nanosensors reported for different pollutants

Environmental pollutant	Carbon source	LOD	Linear range	Reference
Hg^{2+}	Pomelo peel	0.23 nM	0.5–10 nM	Lu et al. (2012)
Hg^{2+}	EDTA salts	4.2 nM	0–3 μM	Zhou et al. (2012b)
Hg^{2+}	Citric acid	0.93 nM	0.03–8 μM	Xu et al. (2015a)
Hg^{2+}	Folic acid	0.23 μM	0–25 μM	Zhang and Chen (2014)
Hg^{2+}	Citric acid	226 nM	0–12 μM	Yan et al. (2014)
Hg^{2+}	Citric acid	0.18 μM	0–20 μM	Wang et al. (2015b)
Hg^{2+}	Sodium citrate	0.65 μM	0.001–5 μM	Ren et al. (2018)
Hg^{2+}	Citric acid	2.47 × 10–6 M	0–35 μM	Ma et al. (2018)
Hg^{2+}	Human hair	3.7 nM	10–100 nM	Hou et al. (2014)
Hg^{2+}	Strawberry	3 nM	10 nM–50 μM	Huang et al. (2013)
As^{3+}	Citric acid	0.086 ppb	5–100 ppb	D. et al. (2017)
As^{3+}	Prickly pear cactus	2.3 nM	2–12 nM	Radhakrishnan and Panneer selvam (2018)
Cd^{2+}	Camphor	–	–	Gaddam et al. (2014)
Cd^{2+}	Alanine and histidine	32.5 nM	4×10^{-2}–1.5×10 μM	Niu et al. (2016)
Cd^{2+}	Scallion	15 nM	5–30 μM	Gu et al. (2018)
Zn^{2+}	Citric acid	6.4 nM	0–2 μM	Zhang et al. (2014c)
Zn^{2+}	Camphor	–	–	Gaddam et al. (2014)
Zn^{2+}	Glucose	2 μM	2–100 μM	Yang et al. (2015a)
Pd^{2+}	Citric acid	58 nM	35–100 μM	Sharma et al. (2016)
Pd^{2+}	Citric acid	3.29 μM	20–160 μM	Gao et al. (2018)
Cu^{2+}	Graphite rods	5×10^{-6}–2×10^{-4} M	–	Zhu et al. (2012a)
Cu^{2+}	Citric acid	0.09 μM	0–1.55 μM	Salinas-Castillo et al. (2013)

(continued)

Table 5.1 (continued)

Environmental pollutant	Carbon source	LOD	Linear range	Reference
Cu^{2+}	Citric acid	6 nM	10–1100 nM	Dong et al. (2012)
Cu^{2+}	Prawn shells	5 nM	0–5 μM	Gedda et al. (2016)
Fe^{3+}	Glucose	0.55 ppm	–	Yang et al. (2014a)
Fe^{3+}	Ethanol	0.04 μM	1–800 μM	Miao et al. (2015)
Fe^{3+}	Bovine serum albumin	0.5 μM	0–1.5 mM	Yang et al. (2015b)
Fe^{3+}	Citric acid	2.5 nM	0.01–500 μM	Zhang et al. (2014a)
Fe^{3+}	Citric acid	20 μM	20–200 μM	Chandra et al. (2016)
Fe^{3+}	Citric acid	0.1 μM	–	Wang et al. (2016a)
Fe^{3+}	Chitosan hydrogel	0.5 nM	–	Gogoi et al. (2015)
Fe^{3+}	*Vigna radiata*	140 nM	100–1000 μM 1000–2000 μM	Kaur et al. (2019)
Ag^{+}	CCl_4	–	1–100 μM	Qian et al. (2014)
Ag^{+}	Lactose	385.8 nM	–	Algarra et al. (2014)
Ag^{+}	1,2,4-Triaminobenzene	0.20 μM	1–7 μM	Jiang et al. (2015b)
Ag^{+}	MWCNT	0.55μgmL^{-1}	0.8–20 μgmL^{-1}	Cayuela et al. (2016)
Ag^{+}	DNA	0.31 μM	0–10 μM	Song et al. (2015)
Au^{3+}	Black forest honey	0.48 μM	0–75 μM	Gu et al. (2015)
Au^{3+}	Peach gum	6.4×10^{-8} M	0–50 μM	Liao et al. (2016)
Au^{3+}	Polystyrene	53 nM	0–18 μM	Ramanan et al. (2018)
Au^{3+}	Rose petal	63.1 nM	50–750 μM	Sharma et al. (2018a)
Cr^{6+}	Citric acid	–	0.01–50 μmol/L	Zheng et al. (2013)
Cr^{6+}	Glucose	0.05 μM	5–100 μM	Zhang et al. (2015)

(continued)

Table 5.1 (continued)

Environmental pollutant	Carbon source	LOD	Linear range	Reference
Cr^{6+}	Citric acid and L-cysteine	20 nM	0.5–125 mM	Dong et al. (2013)
Cr^{6+}	Candle soot	0.21 μg L^{-1}	–	Liu et al. (2015)
Cr^{6+}	Chitosan	1 pM		Gogoi et al. (2015)
Bi^{3+}	Ascorbic acid	150 nM	0.5–30 μM	Qu et al. (2015)
Pb^{2+}	Glycerol	15.0 nM	0.1–6 μM	Jiang et al. (2015c)
Pb^{2+}	Bovine serum albumin	5.05 μM	–	Wee et al. (2013)
Pb^{2+}	Kerosene soot	5.05 μM	–	Wang et al. (2015a)
Ni^{2+}	Sago wastes	13.9 μM	–	Tan et al. (2014)
Pt^{6+}	Folic acid	657.4 nM	–	Campos et al. (2016)
Sn^{2+}	Sago starch nanoparticles	0.36 μM	0–4 mM	Mohd Yazid et al. (2013)
F^-	Citric acid	–	1–25 ppm	Singhal et al. (2017)
F^-	N-Octylpyridinum hexafluorophosphate	1.1 × 10–4 M	0–26.7 mM	Shamsipur et al. (2015)
S^{2-}	Lime juice	0.32 μM	2–10 μM	Barati et al. (2016)
2,4,6-Trinitrophenols	Sucrose	16.9 nM	0.2–17.0 μM	Shi et al. (2015)
pH	Sugarcane		pH 9–14	Sharma et al. (2018b)

5.5 Conclusion and Future Outlook

It is evident that carbon nanodots have established themselves as an exciting new-generation material which has a lot to offer. The sustainability of c-dots for environmental applications is not only stimulated by their biocompatibility and nontoxic nature, but also their enriching optical potential makes them an ideal material for high-throughput applications. The availability of a vast range of carbon precursors and the precursor-triggered optical properties opens up a broad horizon to simulate the desired optical response from these nanolights. Moreover, the impact of heteroatom functionalization opens up another dimension for fine-tuning the optical response of c-dots. There is no wonder that hundreds of precursors are continuously being explored for optical tuning of these nanodots.

C-dots have shown enormous applicability toward the detection of environmental pollutants. The range of analytes that can be detected using c-dots is vast and includes metal ions, anions, chemical impurities, and even microorganisms. The extensive research in c-dot has led to development of metal ion sensors for heavy metal impurities in water up to sub-nanomolar concentrations. Similarly, a variety of pollutant anions are successfully detected using c-dots at ultralow concentrations. In such sensing capabilities, c-dots have shown considerably good sensitivity and selectivity. The research in exploration of c-dots for several other pollutants is growing rapidly.

The existing challenge for c-dot-based sensors is to move from a laboratory environment to a natural scenario. C-dots are expected to see industrial application and commercial production in times to come. Moreover, the existing sensing methods using c-dots are dominated by fluorescence-based switching off; other phenomena such as fluorescence lifetime imaging, shift in emission wavelength, ratiometric sensors, and FRET need to be explored further.

The last decade has seen a tremendous upsurge in employment of c-dots-based sensor in real water samples showing its extraordinary potential for environmental applicability. More efforts still need to be made toward development of a c-dot-based device for running water systems.

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Chapter 6
Point-of-Care Sensors for On-Site Detection of Pesticides

Neeti Kalyani, Surbhi Goel, and Swati Jaiswal

Contents

Abstract As the population of the world grows, the demand for food and other agricultural resources has led to escalation of pesticide poisoning and environmental hazards. Thus, an efficient system of pesticide detection is a constant endeavor, and a number of technologies are working hand in hand to generate effective biosensors for various classes of pesticides. Many commercial biosensors for detection of pesticides are available based on amperometric or fluorescence detection. Yet more innovative technologies are being developed which overcome issues by reducing time and costs involved in sample preparation. In addition to that, improvements in ease of operation

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with minimum expertise and better sensitivity have been achieved using various techniques such as optical, colorimetric, fluorescence, chemiluminescence, photoluminescence, SERS, and electrochemical. The essential characteristics of biosensors include limit of detection (LOD) and recovery.

A number of tools such as aptamers, gold nanoparticles, quantum dots, molecularly imprinted polymers, bispecific antibodies, etc. are used to develop hybrid biosensors where the sensitivity is increased several folds and limit of detection is as low as 0.1 pM. The time of detection is reduced to 22 min along with simultaneous detection of increasing number of pesticides by the biosensors. Thus, integration of more than one technique overcomes the limitation encountered by one, leading to increased sensitivity, high precision, and broadened applications in pesticide detection. Also, the goal is to accelerate the path toward commercial implementation with point-of-care setting which has the added advantage of cheaper, portable, and handy biosensing technology with much stable recognition element or substrate, which can stay useful and active even at environmental conditions for in-field analysis. Thus, the review encompasses all the above innovations and criteria in detailed and up-to-date analysis.

Keywords Point-of-care · Pesticide · Organophosphates · Pesticide detection · Biosensor · Electrochemical sensors · Optical sensors

Abbreviations

AChE	Acetylcholinesterase
CHOx	Choline oxidase
CL	Colorimeter
EIS	Electrochemical impedance spectroscopy
FRET	Fluorescence resonance energy transfer
GC-MS	Gas chromatography-mass spectroscopy
GNPs	Gold nanoparticles
GQDs	Graphene quantum dots
HPLC	High-performance liquid chromatography
ITS	Immunochromatographic test strip
MIP	Molecularly imprinted polymer
MOGs	Metal-organic gels
MWCTs	Multi-walled carbon nanotubes
POC	Point-of-care
Ppb	Parts per billion
Ppm	Parts per million
QDs	Quantum dots
RBCs	Red blood cells
SERS	Surface-enhanced Raman scattering

TLC	Thin-layer chromatography
UCNPs	Upconversion nanoparticles
USEPA	US Environmental Protection Agency
VPH	Volume phase hologram
WHO	World Health Organization
ZnS-Mn	Mn-doped ZnS

6.1 Introduction

More than 1000 pesticides are used around the world to control pests and prevent crop damage of which annual consumption of pesticide has been estimated to be 2 million tonnes worldwide. Europe's consumption of pesticide is highest, i.e., 45%, followed by the United States (25%), and the rest is consumed by other countries (Aktar et al. 2009). According to USEPA (US Environmental Protection Agency) report of 2012, a total of $ 55,000 million were spent worldwide on pesticides. Among different classes of pesticides, herbicide consumption was reported to be highest, i.e., 44%, followed by insecticides (29%), fungicides (26%), and fumigants (1%) (Atwood and Paisley-Jones 2017). According to the World Health Organization (WHO), pesticides are one of the leading causes of death by self-poisoning, particularly in middle- and low-income countries. Every year approximately 3 million incidents of pesticide poisoning happen worldwide, resulting in the mortality of 250,000 people (Bertolote et al. 2004).

Pesticides are utilized primarily due to their lucrative effects to eliminate, prevent, and control weeds, worms, insects, and pests, thereby increasing the production and decreasing the crop damage in agriculture which in turn increase the crop yield by a number of times. On the contrary, the pesticides inflict abominable effects to the ecosystem, exposing the living organisms to various risks. Even the small amount of residual pesticide in the food causes severe problems and endangers human life (Guruge and Tanabe 2001; Lee et al. 1997; Sivasankaran et al. 2007). Though the pesticides present in food are detected within the recommended amount, still their regular exposure and accumulation are detrimental and pose serious hazard to people's health (Yan et al. 2018). Pesticides are toxic compounds which pose chronic and acute health effects depending on the quantity, ways, and time for which the person is exposed. The adverse effect of the pesticides can be observed only after certain level of exposure. Therefore, regular monitoring of pesticide residues in food and environment is required.

Pesticides are being used much widely in crop production for (1) curtailing the growth of weeds; (2) the protection of crops from the insects, rodents, and fungi; (3) increasing productivity; and (4) slashing the postharvest losses (Fang et al. 2009; Meng et al. 2013; Odukkathil and Vasudevan 2013). Pesticides can be classified on the basis of chemical composition into organophosphates, organochlorines, pyrethroids, neonicotinoids, carbamates, and inorganic pesticides. On the basis of target, they can be classified into insecticides, weedicides, fungicides, bactericides, rodenticides, and nematocides (Table 6.1). Naturally, the pesticides get degraded by

Table 6.1 List of various pesticides with their uses and WHO category

Type	Category	Name	Effect	Use	WHO category
Insecticide	Organophosphate	Phorate	Acetylcholinesterase inhibitor	Food grains, tomato, fruits, sugarcane, milk and milk products, and meat	1a extremely hazardous
		Dichlorvos	Acetylcholinesterase inhibitor	Wheat, rice, vegetable, fruits, milk, and household pests	1b highly hazardous
		Methamidophos	Acetylcholinesterase inhibitor	Potato, rice, broccoli, Brussel sprouts, cauliflower, grapes, celery, sugar beets, cotton, tobacco	1b highly hazardous
		Heptenophos	Acetylcholinesterase inhibitor	Tomatoes, cucumber, mushrooms, ornamental crops	1b highly hazardous
		Cadusafos	Acetylcholinesterase inhibitor	Banana, citrus, maize, potatoes, sugarcane	1b highly hazardous
		Omethoate	Acetylcholinesterase inhibitor	Fruits including citrus, apples, plum, hops, sugar beet, potatoes, cereals, ornamentals	1b highly hazardous
		Paraoxon	Acetylcholinesterase inhibitor, fetotoxin	Field crops, fruit, vegetables, vines, hops, ornamentals	1a extremely hazardous
	Phenylpyrazole	Fipronil	Neurotoxicant and both an eye and skin irritant	Rice, chilli, sugarcane, cabbage, grapes, milk and its products, and meat	II moderately hazardous
	Pyrethroids	Allethrin, permethrin	Neurotoxic effects and Na^+-K^+ ion channels	Cucumber, cottonseed, soya bean, sunflower seed	II moderately hazardous
	Carbamate	Carbofuran	Cholinesterase inhibitor		1b highly hazardous
		Carbaryl	Acetylcholinesterase inhibitor	Citrus, fruit, cotton, forests, lawns, nuts, ornamentals, shade trees	II moderately hazardous
Fungicide	Organochlorine	Edifenphos	Acetyl cholinesterase inhibitor	Rice	1b highly hazardous
	Thiophosphoric acid esters	Iprobenfos	Low toxic to mammals	Rice, chilli, tomato, potato, onion	II moderately hazardous
	Triazole	Tebuconazole	Carcinogen and reproduction toxin	Wheat, barley, oat, rye, grapes, peanuts, onions, peas, pepper, banana, sugarcane	II moderately hazardous

	Dicarboximide	Mancozeb	Endocrine disruptor	Chilli, cauliflower, groundnut, cumin, black pepper, mustard seed, gherkin, onion, milk and milk products, meat and meat products, mango, grapes, citrus, cucumber, tea, rice	U unlikely to present acute hazard in normal use
Herbicide	Triazine	Atrazine	Endocrine disruptor, carcinogenesis, and birth defects	Sorghum, maize, sugarcane, lupins, pine, and eucalypt	III slightly hazardous
	Sulfonylurea	Ethoxysulfuron	Very toxic to aquatic organisms	Rice	U unlikely to present acute hazard in normal use
		Halosulfuron-methyl	Postnatal developmental neurotoxicity in rats	Sugarcane, maize, and bottle gourd	U unlikely to present acute hazard in normal use

number of ways, but they can perdure in the environment for longer duration of time, even for multiple years because they are highly stable and poorly soluble in water. For example, parathion (organophosphate) and dichlorodiphenyltrichloroethane (organochlorine) can be found in soil samples even after 20 years of their application (Stewart et al. 1971; Tanabe et al. 1994). The use of pesticides in huge quantity leads to drifting of their considerable amount in soil, food, air, and water (Verma and Bhardwaj 2015). When these pesticides enter the food chain, it induces harmful effects to a number of organisms and presents severe toxicological effects.

Pesticides, while inhibiting the proliferation of insects, weeds, or fungi, simultaneously impede the biological processes of other organisms (Amaral 2014; Skládal et al. 1997). Most of the pesticides are neurotoxic in nature and inactivate the acetylcholinesterase enzyme which plays an important role in the central nervous system. The inhibition of this enzyme leads to the increased concentration of acetylcholine in the nerves which obtrude muscular movements and working of the organs and sometimes result in death (Chapalamadugu and Chaudhry 1992; Donarski et al. 1989). In addition, pesticides also affect the human liver, red blood cells (RBCs), endocrine system, immune system, and reproduction system (Farag et al. 2010; Fendick et al. 1990; Gold et al. 1991; Rawlings et al. 1998; Suwalsky et al. 2005), and few are known to be carcinogens and mutagens (De Flora et al. 1993). Some pesticides also get transmitted from the mother to the child via breastfeeding (Muñoz-de-Toro et al. 2006). In the United States, Europe, and other developed countries, most of the harmful pesticides are banned because of their longer persistence in the ecosystem, proclivity of bioaccumulation, and undesirable effects which they impose on nontargeted life forms (Leung et al. 2010; Poon et al. 2005). But they are still in use in some developing countries and in the countries facing food shortages to improve agricultural yield. Therefore, the prompt and accurate detection and quantitation of pesticide are pivotal to prevent their hazardous effects to the environment and organisms.

Each pesticide is chemically different and hence has different properties, mode of action, and toxicological effects. Insecticides are relatively having more harmful effects on human than the herbicides. The toxic effect of pesticide also depends on the route by which the person is exposed, i.e., swallowing, ingestion, or direct contact with the skin, and on the dose of the pesticide. The harmful effects of the low dose of the pesticide can be seen in months, while the high dose of the same pesticide can show similar effect even in few days.

In recent years, due to extensive utilization of pesticides in agriculture, the rapid detection of pesticide has become crucial. In order to assess the quality of crops, environment, food, beverages, and animal products, these samples are required to be tested routinely (Pang et al. 2016). Conventionally, the detection of pesticides has been done by various chromatographic techniques such as liquid chromatography/gas chromatography-mass spectroscopy, high-performance liquid chromatography (HPLC), and thin-layer chromatography (TLC) (Grimalt and Dehouck 2016; LeDoux 2011; Sherma 2015). These techniques are automated, sensitive, and highly reproducible but are time-consuming, laborious, and expensive and require tedious sample preparation and skilled personnel. In addition, these methods require

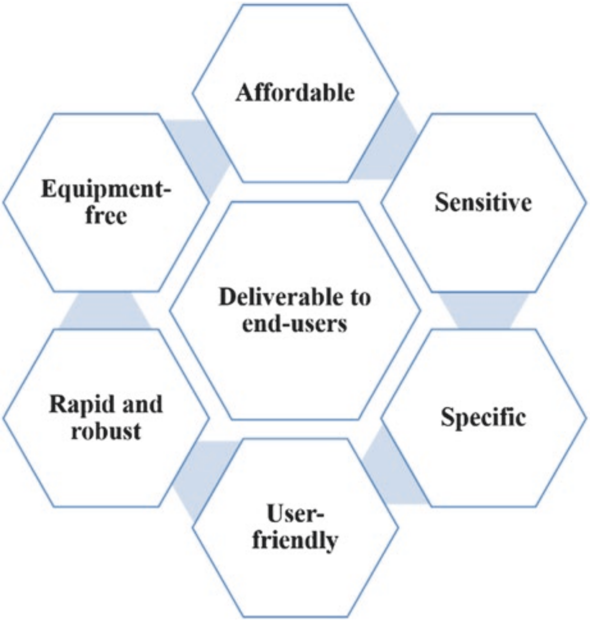

Fig. 6.1 The World Health Organization's "ASSURED" criteria for point-of-care testing device

multiple steps leading to increased analysis time and chances of error, thus cannot be used for the on-site detection and real-time applications, specifically in emergency cases (Jiang et al. 2008; Velasco-Garcia and Mottram 2003). Hence, vast endeavors are being dedicated to find the reliable alternative techniques and assays for the analysis of pesticides in a simple, facile, and speedy manner. Point-of-care (POC) testing is helpful for reducing time and costs involved in sample preparation and result generation, and provides ease of operation with minimum expertise and better sensitivity. Also, in-field pesticide detection will help in regulating the utilization as well as in ensuring its proper disposal, thus overall minimizing its toxic effect to the environment. For this, the World Health Organization coined the acronym "ASSURED" to express the principal criteria of point-of-care testing (Fig. 6.1): affordable, sensitive, specific, user-friendly, rapid and robust, equipment-free, and deliverable to end-users (Kosack et al. 2017).

Biosensors offer commendable performance due to simplicity, ease in operation, field portability, and compact size. A number of different biosensors are evolving throughout the globe which have several advantages over conventional techniques like rapid detection, user-friendliness, accuracy, portability, and cost-effectiveness and can be utilized for easy on-site detection in the field (Patel et al. 2019; Yan et al. 2018). These biosensors integrate the various recognition elements and nanomaterials to achieve excellent selectivity and high sensitivity for the real-time detection of pesticides. Different recognition elements or capture probes like enzymes, aptamers, antibodies, and molecularly imprinted polymers have been employed for pesticide biosensor showing marvellous superiority for bio-monitoring of clinical, food, and environmental samples. Biosensors are promising tools for ascertaining the amount of pesticides by transforming the identification of analyte into a physically measurable signal such as optical, magnetic, and electronic (Verdian 2018).

Recent progress in nanobiotechnology displays the potential of nanomaterials as the fundamental unit and signalling component for the development of biosensors exhibiting excellent behavior (Boken et al. 2017; Syedmoradi et al. 2017; B. Wang et al. 2017a). Nanomaterials have unique morphology, nanoscale size, and large surface area which provide peculiar optical, chemical, and electronic properties which can be utilized for different purposes like imaging, targeting, separating, and sensing (Chao et al. 2016). Lately, various nanomaterials including nanorods, nanoflowers, nanosheets, nanotubes, and quantum dots (QDs) are used for the fabrication of biosensors (Chen et al. 2017; Kurt et al. 2016; Shawky et al. 2017; Tian et al. 2016; Yoon et al. 2016; Zor et al. 2015). Biosensors based on nanomaterials are capable of successfully identifying various pesticide molecules present in very low amount due to large amplification of signals (Verdian 2018).

6.2 Optical Sensors

Optical sensing method for pesticide detection is the simplest technique, which involves fluorescence, ultraviolet-visible, Raman, or chemiluminescence for studying signal change. An optical sensor constitutes of a recognition element which interacts specifically with the target analyte and a transducer component that is required for signalling the interaction. The recognition elements have gained attention to improvise the performance of biosensors (Yan et al. 2018). A number of optical sensors have been reported based on various recognition elements like aptamers (Bai et al. 2015; Bala et al. 2018; M. Liu et al. 2019a; Qi et al. 2016), enzymes (Chronopoulou et al. 2019; Kestwal et al. 2015; H. Li et al. 2018b; Wei et al. 2017; Xue et al. 2016), molecularly imprinted polymers (Feng et al. 2017; Saylan et al. 2017; Ye et al. 2018), and antibodies (Lin et al. 2018; Ouyang et al. 2018b; Shu et al. 2017) for pesticide sensing (Table 6.2). Optical sensors provide a number of advantages such as rapid detection, easy protocols, simple operation, high sensitivity, on-site detection, broad linearity range, and cost-effectiveness (Pang et al. 2016). On the basis of recognition element and signal output design, optical sensors for pesticide detection can be classified into the following categories: colorimetric, fluorescence, chemiluminescence, photoluminescence, and surface-enhanced Raman scattering (SERS). The technique and recent examples of each of these broad categories have been discussed in detail.

Table 6.2 List of optical sensors developed for the detection of pesticides

S. no.	Pesticide	Category	Sample	Technique	Time	LOD	References
1	Carbaryl	Carbamate	Apple and tomato	SERS	60 min	4.51 ppm	Liu et al. (2013)
2	Chlorpyrifos	Organophosphate	Water and apple	SERS	15 min	35 ppt	Kim et al. (2015)
3	Acephate	Organophosphate	Urine	SERS	NM	19 ppb	Clauson et al. (2015)
4	Deltamethrin	Pyrethroid	Tea leaf and apple	SERS	30 min	0.02 ppm	Hou et al. (2015)
5	Thiabendazole	Benzimidazole	Apple	SERS	10 min	0.1 ppm	He et al. (2014)
6	Thiram	Dithiocarbamate	Apple, pear, and grape	SERS	10 min	4.63 ng/cm^2	K. Wang et al. (2017c)
7	Thiram	Dithiocarbamate	Apple	SERS	30 min	0.03 ppm	Jiao et al. (2019)
8	12 pesticides	Different types	NM	SERS	20 min	10 ppm	Mu et al. (2018)
9	Thiram and thiabendazole	Dithiocarbamate and benzimidazole	Apple and cabbage	SERS	NM	0.1 ppm and 1 ppm	Chen et al. (2019)
10	Thiram	Dithiocarbamate	Apple	SERS	30 min	10^{-10} M	Zhu et al. (2018)
11	Thiram and ferbam	Dithiocarbamate	Water	SERS	NM	0.46 nM and 0.49 nM	Lee et al. (2018)
12	Tetramethylthiuram disulfide and thiabendazole	Thiuram disulfide and benzimidazole	Apple, pear, cucumber, and spinach	SERS	10 min	228.8 ng/cm^2	Jiang et al. (2018)
13	Chlorpyrifos and carbaryl	Organophosphate and carbamate	Water and medicine	Chemiluminescence	10 min	0.033 ng/mL	Ouyang et al. (2018a)
14	Tributyltin	Organotin	Water	Photoluminescence	80 min	12.78 ppb	Zor et al. (2015)
15	Carbaryl	Carbamate	Water	Colorimetry and fluorescence	40 min	0.23 µg/L	Qiu et al. (2018)
16	Terbuthylazine and dimethoate	Chlorotriazine and organophosphate	Water, green tea, and apple juice	Ultraviolet-visible	10 min	0.02 µM and 6.2 nM	Chen et al. (2018)

(continued)

Table 6.2 (continued)

S. no.	Pesticide	Category	Sample	Technique	Time	LOD	References
17	Monocrotophos and dimethoate	Organophosphate	Soft drink	Ultraviolet-visible	30 min	2.51 ppb and 1.5 ppb	Palanivelu and Chidambaram (2019)
18	2,4-Dichlorophenoxyacetic acid	Organochlorine	Bean sprouts	Fluorescence	20 min	90 nM	Zhang et al. (2018)
19	Azinphos-methyl	Organophosphate	Water	Photoluminescence	80 min	0.67 µM/212 ppb	Singha et al. (2019)
20	Dichlorvos	Organophosphate	Tap water	Photoluminescence	60 min	0.172 ppm/0.778 µM	Sahub et al. (2018)
21	Thiacloprid	Neonicotinoid	Water	Photoluminescence	5 h	0.03 mg/L	Liu et al. (2018)
22	Parathion methyl and fenpropathrin	Organophosphate and pyrethroid	Medicine	Colorimetric and chemiluminescence	15 min	0.17 ng/mL and 0.10 ng/mL	Ouyang et al. (2018b)
23	Paraoxon	Organophosphate	Carrot and peach	Colorimetric	60 min	4 ng/mL	Han and Wang, (2018)
24	Paraoxon-ethyl	Organophosphate	River water	Colorimetric	60 min	25 µg/L	Hua et al. (2018)
25	Chlorpyrifos	Organophosphate	Apple, pear, green pepper, and tomato	Fluorescence	NM	89 nM	X. Y. Xu et al. (2018b)
26	Dimethoate	Organophosphate	Water	Fluorescence	15 min	0.14 µM	Wang et al. (2016)
27	Imidaclothiz	Neonicotinoid	Water, soil, pear, rice, apple, tomato, pak choi, and cabbage	Fluorescence	60 min	2.1 ng/mL	M. Wang et al. (2017b)
28	Acetamipirid	Neonicotinoid	Water	Fluorescence	40 min	3.2 nM	Hu et al. (2016)
29	Parathion methyl, monocrotophos, and dimethoate	Organophosphates	Apple, capsicum, and cucumber	Fluorescence		0.67, 23, and 67 ng/L	Long et al. (2015)

LOD limit of detection, *SERS* surface-enhanced Raman spectroscopy, *UV* ultraviolet, *NM* not mentioned, *ppm* parts per million, *ppb* parts per billion, *ppt* parts per trillion

6.2.1 Colorimetric Sensing Technique

In colorimetric sensing, the change in the color of the reaction, upon interaction of recognition element and target, indicates the presence of the analyte molecule. This change can be visible to the naked eye, making them a potent candidate for point-of-care diagnostics, and can be quantitized spectrophotometrically. Based on the type of recognition element employed, the colorimetric (CL) sensing techniques can be aptamer-based, antibody-based, enzyme-based, or others (Tram et al. 2016).

Among different categories of nanomaterials employed for colorimetric sensing strategy, gold nanoparticles have emerged as appealing nanomaterial for the development of point-of-care sensors for pesticide detection. Recently, a colorimetric aptasensor using gold nanoparticles for the detection of malathion pesticide has been reported (Abnous et al. 2018). Gold nanoparticles (GNPs) tend to form aggregates in the presence of salts, and surface modification of gold nanoparticles with aptamers or antibodies can prevent this aggregation formation (Fig. 6.2). When these aptamer-functionalized gold nanoparticles (GNPs) are exposed to the target containing samples, the aptamer leaves the surface of gold nanoparticles (GNPs) and renders them to aggregation in the presence of salt. This aggregation changes the color of the solution from red to blue and is visible to the naked eye and can be quantitated by measuring the absorbance at 650 nm. The assay was able to detect malathion in the range of 5 pM–10 nM within just 35 min with detection limit of up to 1 pM. The assay also showed good specificity toward malathion over other pesticides, viz., atrazine, fenthion, parathion, phorate, chlorsulfuron, diuron, and permethrin. The assay was also tested to check the presence of malathion in spiked serum samples, and 90% recovery was reported.

In another study conducted by Palanivelu and Chidambaram, an enzyme-based colorimetric sensor was developed for the detection of organophosphorus pesticides, viz., monocrotophos and dimethoate (Palanivelu and Chidambaram 2019).

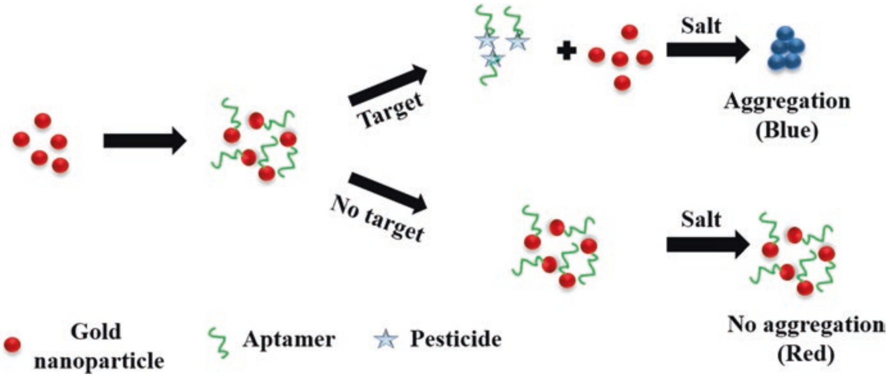

Fig. 6.2 Schematic showing colorimetric sensing of pesticide using gold nanoparticles: Aptamer prevents the aggregation of gold nanoparticles in the presence of salt. In the presence of target analyte, aptamer leaves the surface of gold nanoparticles and renders them for aggregation which can be detected spectrophotometrically

Acetylcholinesterase was immobilized in mesoporous silica nanoparticles, and the degradation in enzyme activity in the presence of organophosphorus pesticides was measured spectrophotometrically. The organophosphorus pesticide binds to the acetylcholinesterase and hinders its activity. For the colorimetric assay, a chromophoric substrate 5,5′-dithiobis-(2-nitrobenzoic acid) was used to monitor the inhibition in enzyme activity in the presence of pesticides. The method was also verified with the electrochemical technique by cyclic voltammetry. The limit of detection of 2.51 ppb and 1.5 ppb was reported for monocrotophos and dimethoate, respectively.

6.2.2 Fluorescence Sensing Technique

The fluorescence-based sensor provides easy and fast detection with very high sensitivity toward the target species. Different types of materials have been employed for the fluorescent sensing such as fluorescent dyes (Liang et al. 2014; Strianese et al. 2009), metal nanoparticles (Dou et al. 2015; Li et al. 2013; Zhang et al. 2018), carbon nanomaterials (J. Li et al. 2018a; Sharma et al. 2018; Wei et al. 2012, 2018), rare earth materials (Shen and Yan 2015; Xu and Yan 2016), and semiconductor materials (Amjadi and Jalili 2017; Lu et al. 2017). In the fluorescence sensor, the binding of event can be observed by the naked eye or can be easily measured by fluorimeter (Yan et al. 2018).

Lin et al. have reported an aptamer-based fluorescent sensor for the detection of acetamiprid pesticide (Lin et al. 2016). The study involved Mn-doped ZnS (ZnS:Mn) quantum dots (QDs) as beacon and multi-walled carbon nanotubes (MWCNTs) as quencher (due to their strong π- π stacking interactions with double-bond groups). The acetamiprid-specific aptamer was conjugated with ZnS:Mn quantum dots (Fig. 6.3). In the absence of pesticide, the fluorescence resonance

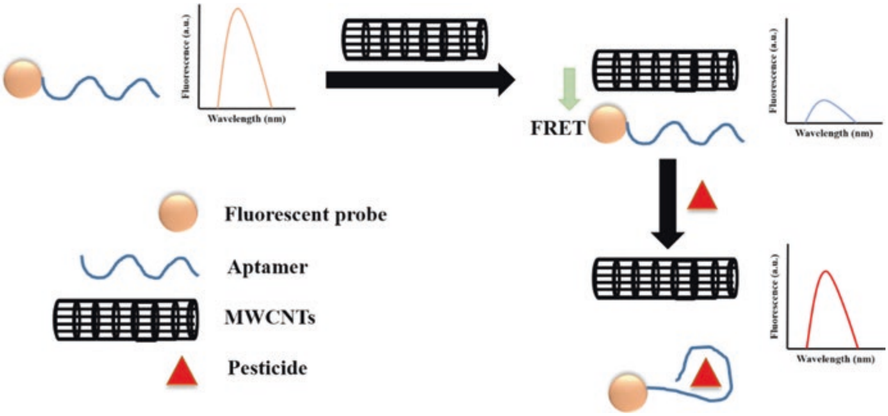

Fig. 6.3 Detection of the pesticide using fluorescence-based sensor: The fluorescence of probe gets quenched in the presence of multi-walled carbon nanotubes (MWCNTs). In the presence of analyte, due to structural changes, the probe gets away from the multi-walled carbon nanotubes and increases in fluorescence observed which is directly proportional to the concentration of the analyte

energy transfer (FRET) between ZnS:Mn quantum dots and MWCNTs turns off the fluorescence of the quantum dots. When the pesticide is present, the aptamer-bound ZnS:Mn quantum dots get separated from multi-walled carbon nanotubes (MWCNTs), and the fluorescence gets turned on. The lowest detection limit of acetamiprid using this method is 0.7 nM. The sensor showed high selectivity toward acetamiprid compared to other pesticides having similar structure. The performance of the sensor was also tested in river water and cabbage leaf samples, and 90% recovery was achieved.

Long et al. have developed $NaYF_4$:Yb,Er upconversion nanoparticles (UCNPs) and acetylcholinesterase-based fluorescence assay for the detection of organophosphorus pesticides, namely, parathion methyl, monocrotophos, and dimethoate (Long et al. 2015). This assay is based on the FRET between upconversion nanoparticles (UCNPs) and gold nanoparticles (GNPs). The GNPs significantly quench the fluorescence of upconversion nanoparticles (UCNPs), while organophosphates inhibit the AChE enzyme. Acetylthiocholine is a substrate of AChE and hydrolyzes into thiocholine. When the AChE is active, thiocholine is generated which forms electrostatic interactions (gold-thiol) with AuNPs. These interactions resulted in disintegration of gold nanoparticles (GNPs) from upconversion nanoparticles (UCNPs) and aggregation of gold nanoparticles (GNPs). In the presence of organophosphate pesticides, the activity of AChE is inhibited and no thiocholine is formed, and gold nanoparticles (GNPs) keep quenching the fluorescence of upconversion nanoparticles (UCNPs). The decrease in fluorescence indicates the increase in the amount of pesticide. The detection limit for parathion methyl, monocrotophos, and dimethoate was reported to be 0.67, 23, and 67 ng/L, respectively. The assay was also tested for parathion methyl in apple, capsicum, and cucumber samples with recovery above 95%.

6.2.3 Chemiluminescence Sensing Technique

Chemiluminescence detection techniques have advantages like low detection limit, high sensitivity, wide linearity range, and simple operation (Qi et al. 2016; Zeng et al. 2013; Zong et al. 2013). But, unlike other optical techniques like fluorescence and UV-visible spectroscopy, the wavelength is not considered, and signal intensity is the only parameter in chemiluminescence detection. Therefore, to discriminate the signal of different probes is very difficult (Shu et al. 2017). He et al. have employed the metal-organic gels (MOGs) for the detection of pesticides (He et al. 2018). They have synthesized iron-based metal-organic gel (MOG) nanosheet hybrids with gold nanoparticles (GNPs) and exploited their peroxidase activity. These hybrids have enhanced peroxidase-like activity and synergistically increased chemiluminescence activity because of fast generation of $OH^{\bullet}$, $O_2^{\bullet-}$, and $^1O_2$. The hybrid structures were utilized for the detection of organophosphorus pesticide, viz., ethoprophos by enzyme-based inhibition chemiluminescence sensing. Acetylcholinesterase (AChE) enzyme hydrolyzes acetylcholine to choline which can directly react with oxygen to form H_2O_2. Ethoprophos inhibits the acetylcholinesterase activity and in turn reduces the generation of H_2O_2. This decrease in H_2O_2

can be monitored by chemiluminescence. With this sensor, they were able to detect the pesticide up to 1 nM concentration. The sensor was also tested to determine the concentration of the pesticide in spiked river and tap water samples. The recovery of the pesticide in the samples was in the range of 95.5–106.5%.

Shu et al. have developed a multiplexed immunochromatographic test strip (ITS) based on a time-resolved chemiluminescence strategy for the detection of two pesticides (Shu et al. 2017). They have developed a unique bifunctional antibody by hybrid hybridoma method for the detection of parathion methyl and imidacloprid. Horseradish peroxidase and alkaline phosphatase were employed as the chemiluminescent probes for the labelling of the haptens of parathion methyl and imidacloprid, respectively. Since both probes have different kinetic properties of chemiluminescence, the pesticides could be identified in distinct time frames. Using this technique, they were able to detect up to 0.058 ng mL^{-1} of pesticide in just 22 min. The sensor was also tested in the spiked medicine samples.

6.2.4 Photoluminescence Sensing Technique

Photoluminescence utilizes quantum dots as fluorophores, and they provide multiple advantages over organic fluorophores like small bandwidth, and the fluorescence is size-dependent when excited with a specific wavelength (Huang et al. 2008). Photoluminescent sensors are highly sensitive and can be easily integrated with smartphones for real-time detection (Dou et al. 2015; Zarei 2017). Zor et al. have reported a photoluminescence biosensor for the detection of tributyltin pesticide (Zor et al. 2015). Tributyltin is an organotin compound used as an antifouling agent on the bottom of ships, boats, docks, etc. to inhibit the growth of marine organisms. Its leaching in the sea water results in toxicity to many marine species. Zor et al. have used a composite material – magnetic silica beads/graphene quantum dots/molecularly imprinted polypyrrole (mSGP) – for capturing, concentration, and detection of the tributyltin. Molecularly imprinted polypyrrole captures the analyte, magnetic silica beads concentrate it, and graphene quantum dots act as an optical transducer. The photoluminescence of the graphene quantum dots gets quenched upon the binding of analyte, i.e., tributyltin. This decrease in the photoluminescence is directly proportional to the concentration of tributyltin which can be detected in the range of 10 ppb–10 ppm.

An enzyme-based sensor has been developed for the detection of dichlorvos – an organophosphorus pesticide (Sahub et al. 2018). They have developed a sensor based on graphene quantum dots (GQDs), acetylcholinesterase (AChE), and choline oxidase (CHOx) where graphene quantum dots (GQDs) were utilized as photoluminescent molecules. AChE quenches the luminescence of graphene quantum dots (GQDs). But when pesticide is present in the sample, it binds to the AChE and prevents quenching which results in concentration-dependent increase in photoluminescence. This change can be easily monitored for the detection of dichlorvos in the sample, and performance of the sensor does not get affected by the presence of different metal ions. The detection limit of this sensor for the dichlorvos was 0.172 ppm (0.778 μM).

6.2.5 *Surface-Enhanced Raman Scattering Sensing Technique*

Raman scattering is the inelastic scattering of photons where the frequency of scattered photon is not the same as the incident photon. This Raman scattering is observed only in Raman-active molecules. The scattering gets accentuated in the presence of gold and silver nanoparticles, and the phenomena are known as surface-enhanced Raman scattering (SERS). Jiao et al. have developed a simple and rapid surface-enhanced Raman scattering (SERS) sensor for the detection of thiram pesticide (Jiao et al. 2019). They have fabricated worm-shaped gold and silver bimetallic nanochains by laser-assisted technique. Firstly, the gold nanotwins were synthesized by pulsed laser ablation having ample hydroxyl (-OH) groups on the surface. Then, $AgNO_3$ solution was added for the reduction of Ag by hydroxyl groups to compose bimetallic AuAg nanochains. These nanochains showed high surface-enhanced Raman scattering (SERS) activity as compared to monometallic gold nanoparticles because of intermetallic synergies within two metals. The sensor is able to detect 10^{-7} M (0.03 ppm) on apple surface and also depicted excellent linearity in the range of 10^{-3}–10^{-7} M.

A smartphone-based Raman sensor has been reported for the detection of 12 different pesticides (Mu et al. 2018). They have developed a surface-enhanced Raman scattering (SERS) system conjugated with smartphone for rapid detection of pesticide for application as point-of-care sensor. The signal-to-noise ratio was minimized by the use of high numerical aperture lenses and direct spatial coupling technology. The optical system was ameliorated by substituting the ordinary planar reflective grating with volume phase hologram (VPH) grating. The system was fabricated with an attachment to focus the laser on the sample. They were able to detect 12 different pesticides up to a limit of 10 ppm.

Furthermore, Liu et al. have reported the detection of carbaryl, phosmet, and azinphos-methyl and phosmet pesticides in various samples using commercially available surface-enhanced Raman scattering (SERS) substrates – Q-SERS (Nanova, Columbia, MO, USA) and KlariteTM (Renishaw Diagnostics, Glasgow, UK) (Liu et al. 2013). Similar substrates have also been used for pesticide detection in other studies (Fan et al. 2014).

6.3 Electrochemical Sensors

Recently, electrochemical sensors have gained attention because they overcome the limitation of other techniques like no sample pretreatment requirement, no expensive instrumentation, and ease of operation and have several advantages such as speed, sensitivity, and simple protocol. A number of antibody-based (Bhardwaj et al. 2016; Talan et al. 2018), enzyme-based (Arduini et al. 2019; Zhang et al. 2014), molecularly imprinted polymer-based (Gui et al. 2018; Motaharian et al. 2016; Zamora-Gálvez et al. 2017; Zhang et al. 2017), and aptamer-based (Fig. 6.4) (Madianos et al. 2018b; G. Xu et al. 2018a) electrochemical sensor have been developed (Table 6.3).

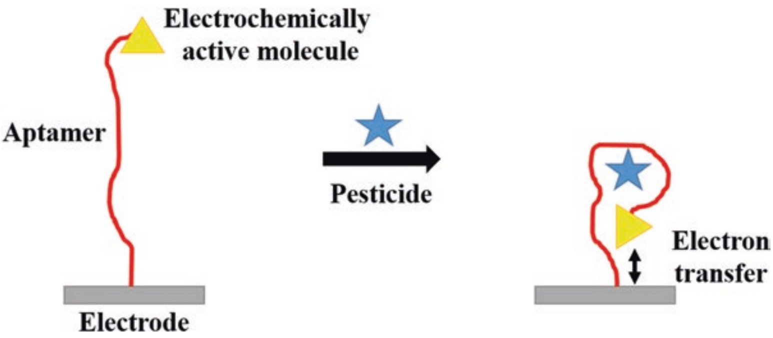

Fig. 6.4 Electrochemical sensing of pesticide with aptamer as probe: The binding of analyte to the aptamer induces a structural change leading to the change in the position of electrochemically active probe. This alters the electron transfer and is monitored by measuring the current

6.3.1 Amperometric Sensing Technique

Amperometric biosensor measures the change in current in response to an event with respective time or potential of the electrode. Kumar et al. have reported an interesting biosensor based on flower-like gadolinium molybdate (Gd_2MoO_6; GdM) for the detection of fenitrothion pesticide (Kumar et al. 2018). The flower-like GdM were prepared by sol-gel method and immobilized by drop coating on mirror-polished glassy carbon electrode. The detection of the fenitrothion was performed by cyclic voltammetry with detection limit of 5 nM with good recoveries of pesticide in both soil and water samples. In addition, the photocatalytic degradation of the fenitrothion pesticide has also been reported where GdM photocatalyst was able to degrade about 99% of fenitrothion under ultraviolet light.

Recently, Fan et al. have developed a label-free amperometric sensor for the detection of atrazine pesticide in less than 2 h (Fan et al. 2019). The study involved the use of nickel hexacyanoferrate nanoparticles immobilized on reduced graphene oxide for aptamer-based detection. Gold nanoparticles were electrochemically deposited to improve conductivity and for immobilization of aptamer. The binding of atrazine to the aptamer inhibits the electron transfer resulting in the decrease in electrochemical signal which was monitored by differential pulse voltammetry, and detection limit of up to 0.1 pM was achieved. The performance of the biosensor was tested in the presence of various interferents such as simazine, propanil, malathion, 2,4-dichlorophenoxyacetic acid, p-nitrochlorobenzene, 2,2-binaphthol, and bisphenol A. The current changes discerned in the presence of these interfering moieties were less than 10%. The sensor was also used to test the presence of pesticide in lake water and river water samples with above 97% recovery.

Table 6.3 List of electrochemical sensors developed for the detection of pesticides

S. No.	Pesticide	Category	Sample	Technique	Time	LOD	References
1	Fenitrothion	Organophosphate	Soil and water	DPV	80 min	5 nM	Kumar et al. (2018)
2	Carbendazim, chlorpyrifos, DDT, dinocap, ethion	Benzimidazole, organophosphate, organochlorine, phenol, organophosphate	Potato	CV	30 min	2 ppb; 60 b	Borah et al. (2018)
3	Chlorpyrifos	Organophosphate	Apple and celery cabbages	DPV	40 min	70 pg/mL	G. Xu et al. (2018a)
4	Fenitrothion	Organophosphate	Grapes and cranberry	DPV	30 min	0.15 nM	Govindasamy et al. (2018)
5	Malathion, chlorpyrifos, and parathion methyl	Organophosphate	Cabbage	DPV	NM	0.01 pM, 0.1 pM, and 0.01 pM	Ma et al. (2018b)
6	Cypermethrin	Pyrethroid	Water	DPV	NM	0.1 ppm	Nurdin et al. (2019)
7	Chlorpyrifos	Organophosphate	Water	Photoelectrochemical enzymatic fuel cell	20 min	0.012 ng/mL	Gai et al. (2018)
8	Omethoate	Organophosphate	Cabbage and cucumber	DPV	30 min	1.7×10^{-12} M	Ma et al. (2018a)
9	Paraoxon	Organophosphate	Apple and pak choi	CV	30 min	0.013 μg/L	Zhao et al. (2018)
10	Parathion methyl	Organophosphate	Ground water	DPV	15 min	1.21 ppb	Nie et al. (2017)
11	2,4-dichlorophenoxyacetic acid and atrazine	Organochlorine and triazine	River water	CV	15 min	50 ppb	Arduini et al. (2019)
12	Fenitrothion	Organophosphate	Tap water	CV	50 min	19.6 nM	Bolat et al. (2018)
13	Parathion methyl	Organophosphate	Soil and tap water	DPV	NM	0.3 nM	X. Liu et al. (2019b)

(continued)

Table 6.3 (continued)

S. No.	Pesticide	Category	Sample	Technique	Time	LOD	References
14	Chlorpyrifos	Organophosphate	Apple, cabbage, and pomegranate	CV	30 min	10 fM	Talan et al. (2018)
15	Acetamiprid and atrazine	Neonicotinoid and triazine	Water	EIS	60 min	0.6×10^{-11} M and 0.4×10^{-10} M	Madianos et al. (2018a)
16	Lindane	Organochlorine	Water, grape, orange, tomato, and cabbage	LSV	NM	100 pM	Anirudhan and Alexander (2015)
17	Glyphosate	Organophosphate	Water	Potentiometric	30 min	0.5 ppm	Vaghela et al. (2018)

LOD limit of detection, *DPV* differential pulse voltammetry, *CV* cyclic voltammetry, *EIS* electrochemical impedance spectroscopy, *NM* not mentioned, *ppm* parts per million, *ppb* parts per billion

6.3.2 *Impedimetric Sensing Technique*

Impedimetric biosensors measure the change in impedance of the system in response to a binding event. A capacitive sensor has been developed for the detection of parathion methyl pesticide (Li et al. 2012). The sensor is based on molecularly imprinted polymer (MIP) and electrochemical polymerization technique. Firstly, gold nanoparticles (GNPs) were electrochemically deposited to increase the surface area of the glassy carbon electrode. Then, MIP film of polyquercetin (pQu)-polyresorcinol (pRe) was deposited on the surface of electrode using cyclic voltammetry. After that, dodecanethiol was used to fill the defects on the surface layer. The cavities of parathion methyl were created by washing with ethanol acidic solution. The measurements were done using electrochemical impedance spectroscopy (EIS). The sensor was tested on different water samples, and fruit surfaces with a detection limit of 0.34 nM were achieved. This sensor was also capable of detecting the pesticide on the fruit samples after 72 h of spraying.

Madianos et al. have developed an electrochemical impedimetric biosensor for the detection of acetamiprid and atrazine pesticides (Madianos et al. 2018b). The sensor was fabricated by depositing platinum nanoparticles on interdigitated electrodes to form platinum nanowires which act as bridges. Aptamers for specific detection of pesticide were immobilized on the platinum nanoparticles for the label-free sensing. The binding of the pesticide with the aptamer hinders the electron transport, and hence increase in impedance was observed. This increase in impedance is proportional to the pesticide concentration. The limit of detection for acetamiprid and atrazine was reported to be 1 pM and 10 pM, respectively. The performance of the sensor was also tested in tap and bottled water samples.

6.3.3 *Potentiometric Sensing Technique*

In a potentiometric biosensor, difference in potential of electrodes is measured. A urease-based potentiometric biosensor has been reported for the detection of glyphosate herbicide (Vaghela et al. 2018). The sensor is based on the inhibition of urease activity by glyphosate, and this activity was monitored potentiometrically. The urease enzyme was entrapped in agarose-guar gum membrane along with gold nanoparticles. Gold nanoparticles were used to enhance the electrochemical response and to minimize the insulating effect of protein shell. The urease enzyme catalyzes urea and produces ammonium ions which are directly proportional to the urease activity. Two-electrode setup has been used for the sensing of ammonium ions by ammonium ion-selective electrode with Ag/AgCl as reference electrode. An extra op-amp inverter has also been used in the setup to amplify the potential difference ten times between the electrodes. A detection limit of 0.5 ppm was achieved, and good stability of the sensor has been reported up to 180 days. The specificity of the sensor was also good toward glyphosate as compared to dichlorvos, dimethoate, 2,4-dichlorophenol, and paraquat dichloride.

Anirudhan and Alexander have developed a molecularly imprinted polymer-based potentiometric biosensor for the detection of an organochlorine pesticide, lindane (Anirudhan and Alexander 2015). Firstly, they have synthesized the multi-walled carbon nanotube-based molecularly imprinted polymer for the lindane with methacrylic acid as monomer and ethylene glycol dimethacrylate as cross-linker. For the electrochemical detection, a two-electrode system with copper as working and calomel as reference electrode was used, and linear sweep voltammetry was performed. The detection limit of the sensor was found to be 100 pM. The reusability of the sensor was also shown for up to nine cycles after washing with methanol/acetic acid (9:1) when electrodes were stored in methanol at 4 °C when not in use. The sensor shows very good selectivity for lindane as compared to chlorpyrifos, 2,4-dichlorophenoxyacetic acid, dichlorodiphenyltrichloroethane, 2,4,5-trichlorophenoxyacetic acid, and β-hexachlorocyclohexane. The sensor was also tested to detect the spiked sea water, tap water, grapes, orange, tomato, and cabbage samples, and above 95% recovery was obtained.

6.4 Conclusion and Future Perspectives

While the use of pesticides in agricultural setup has sustained the growing food demand worldwide, its unfavorable effects on humans as well as other creatures can be seen in the form of diseases and disorders. Pesticide detection has gained much importance due to the increase in the number of cases of severe toxicity and ill effects caused even by trace amount of pesticides present in the environment. Older technologies in pesticide detection such as gas chromatography, high-performance liquid chromatography (HPLC), and gas chromatography-mass spectroscopy (GC-MS) which require complex sample preparation protocol, skilled personnels, and specialized instruments are now being replaced and dominated by newer methods such as optical sensors and electrochemical sensors, reducing the cost and time for sample preparation, and can provide on-site detection of pesticide. Because of the small size, portability, and ease of use, biosensors have emerged as the most useful inventions of this century, benefitting mankind with its wide commercial applicability. Thus, biosensor technology has a big role to play in pesticide detection as it carries several advantages such as simpler protocols, ultrasensitive detection, and faster response. The upcoming and evolving nanomaterial- and nanocomposite-based biosensing technique has a lot to offer in terms of unique optical, mechanical, electrical, and magnetic properties along with the continuous improvement in synthesizing and controlling material at the nanoscale. At this scale, the sensitivity and specificity of pesticide detection can be increased multifold enabling detection even at femto level.

In addition, commercialization of these biosensing technologies and innovation in instrumentation are needed in order to utilize these methods on daily basis with time and cost-effectiveness. Further advancement in these biosensor techniques can be made possible by integrating different methods together, thus overcoming the limitation caused by one technique with the other one. An example of such integration can be seen where gold nanoparticle (GNP)-based colorimetric methods were combined with surface-enhanced Raman scattering (SERS) to get enhanced Raman signal. Such integration can lead to increased sensitivity, high precision, and broadened applications in pesticide detection. Also, point-of-care (POC) detection calls for much cheaper, portable, and handy biosensing technology with much stable recognition element or substrate, which can stay useful and active even at environmental conditions for in-field analysis. Also, future endeavors should be in the development of technologies with reduced complexity that can be used by non-expert personnels easily. Hence, pesticide detection by biosensor technology is a promising domain, and we might expect few effective products for mass application in the near future.

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Chapter 7
Development of Optical Sensor Strips for Point-of-Care Testing for Pesticide

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Abstract Disposable or point-of-care sensors are a promising tool for low-cost and rapid sensing of analytes including pesticides. They find important applications in pesticide-contaminated food, agro-products, and water quality monitoring. This chapter highlights the implication and significance of pesticide residue identification in foodstuffs and overviews the most frequently engaged analytical techniques, and finally their benefits and limitations are discussed. Disposable strip-based biosensors have their intrinsic advantages and some disadvantages, but their cost-effectiveness and portability have turned them as a potential possibility for point-of-care (POC) testing of various pesticides. The fabrication of robust, low-cost, reliable, and sensitive sensors with the aid of both simple naked eye-based and portable readout-based detectors is the driving factor in this sensor's technology area. The pending limitations can be overcome by adapting new specific recognition elements and better signal generative particles or systems. The integration of these devices with card readers or smartphones can make them more user-friendly and will provide more accurate quantitative information.

The development of LFAs and paper sensors with multiplexing capabilities will further add to their practical utility. In the future, it is expected that LFAs and portable user-friendly sensors will be made available to the general public for POC testing of complex parameters, e.g., dengue, chikungunya, typhoid, etc. These tools have immense significance toward the screening of food and water samples for pollutants like pesticides, heavy metals, pathogens, etc. In overall, future successes and adoption of LFA paper sensors in a wide range of environmental monitoring application call for the realization of more stable devices capable of handling multiple analytes with high sensitivity without sacrificing the simplicity and cost advantages. The possibilities of future research and development in the field of colorimetric-/fluorescence-based assays are deliberated.

Keywords Aptamer · Pesticide · Immunoassay · Nanosensors · Rapid detection · Organophosphates · Gas chromatography · Antibody · Biosensors · Immunochromatographic assay · Point-of-care

Abbreviations

2,4,5-T	2,4,5-Trichlorophenoxyacetic acid
2,4-D	2-(2,4-Dichlorophenoxy)acetic acid
AChE	Acetylcholinesterase enzyme
AMP	p-(Aminomethyl)phenyl
ASE	Accelerated solvent extraction
ATChI	Acetylthiocholine iodide
BC	Before Christ year
BSA	Bovine serum albumin
C	Control
CE	Capillary electrophoresis
CLC	Capillary liquid chromatography
CNS	Central nervous system
CPE	Cloud point extraction
c-SWCNTs	Carboxyl-functionalized single walled-carbon nanotubes
DDT	Dichlorodiphenyltrichloroethane
DNA	Deoxyribonucleic acid
DPV	Differential pulse voltammetry
dSPE	Dispersive solid-phase extraction
DTNB	5,5′-Dithiobis(2-nitrobenzoic) acid
ECD	Electron capture detectors
ELCD	Electrolytic conductivity detectors
EPA	Environmental Protection Agency
EU	European Union
FAM	Carboxyfluorescein
FAO	Agriculture Organization of United Nations
FAO/WHO	World Health Organization
FID	Flame ionization detectors
FPD	Flame photometric detectors
GC	Gas chromatography
GCE	Glassy carbon electrode
GCxGC	Comprehensive two-dimensional gas chromatography
GNPs	Colloidal gold nanoparticles
GO	Graphene oxide
GUP	General use pesticides
hCG	Human chorionic gonadotropin
HILIC	Hydrophilic interaction liquid chromatography
HIV	Human immunodeficiency virus
HPLC	High-performance liquid chromatography
IAA	Indole acetic acid
IFE	Inner-filter effect
LC x LC	Two-dimensional liquid chromatography
LC	Liquid chromatography

LD 50	Lethal dose
LFA	Lateral flow immunoassay
LFIA	Lateral flow immunochromatographic assay
LOD	Limit of detection
LOQ	Limit of quantification
LP-GC	Low-pressure gas chromatography
LPME	Liquid-phase microextraction
MAE	Microwave-assisted extraction
MB	Methylene blue
MCPA	2-(4-Chloro-2-methylphenoxy)acetic acid
MIP	Molecularly imprinted polymers
μLC	Micro-liquid chromatography
MRLs	Maximum residue limits
MS	Mass spectrophotometers
MW	Microwave
nano-LC	Nanoliquid chromatography
NC	Nitrocellulose
NHS	N-Hydroxysuccinimide
NIST	National Institute of Standards and Technology
NPD	Nitrogen-phosphorus detectors
OPH	Organophosphate hydrolase
PAHs	Polyaromatic hydrocarbons
PCR	Polymerase chain reaction
PID	Photoionization detectors
PM	Protamine molecules
POC	Point-of-care
POP	Persistent organic pollutant
PTV	Programmed temperature vaporization
QuEChERS	Quick, easy, cheap, effective, rugged, and safe
RF-QDs	Ratiometric fluorescent quantum dots
RNA	Ribonucleic acid
RPLC	Reversed-phase liquid chromatography
SBSE	Stir bar sorptive extraction
SELEX	Systematic evolution of ligands by exponential enrichment
SERS	Surface-enhanced Raman scattering
SPE	Solid-phase extraction
SPME	Solid-phase microextraction
SPR	Surface plasmon resonance
ssDNA	Single-stranded DNA
T	Test
TCD	Thermal conductivity detectors
TLC	Thin-layer chromatography
UHPLC	Ultrahigh-performance liquid chromatography

7.1 Introduction

Global food production and security is one of the major challenges of the twenty-first century. The global food demand to supply ratio is continuously increasing with growing population of the world. In this view, food security against various biotic and abiotic factors attracts particular emphasis (van Dijk and Meijerink 2014). Consequently, several scientific and technological interventions have positively affected global food production, collection and storage, and distribution systems (Cole et al. 2018).

In recent times, loss of food due to pests has emerged as one of the biggest threat for global food security. The loss due to pests is estimated to be in the range of 20–40% of the total annual yield and varied for different food types. For example, in case of seed cotton, the loss could be potentially as high as 80% of the total annual yield (Oerke 2006; Cerda et al. 2017). These pests range from small insects to large rodents, weeds, and even pathogenic bacteria, fungi, or viruses. They negatively impact the total yield by affecting food quantity and quality at pre- and post-harvest stages. Consequently, pest control regime has equally attracted significant emphasis alongside food production.

Some of the earliest pest control in the recorded history dates back to 2500–1500 BC when ancient Chinese and Sumerian civilizations used natural sulfur and plant extracts to control insects and fungi. Other inorganic chemicals such as copper, arsenic, mercury, and Bordeaux mixture have been also used during the late 1880s to early 1900s as an effective insecticide. Pyrethrins, extracted from flowers of genus *Chrysanthemum* (*Pyrethrum*), were also used as effective insecticides (Flint and van den Bosch 1981; Casida 2010). It was in 1939, when Paul Hermann Müller discovered the insecticidal activity of organochlorines (particularly dichlorodiphenyltrichloroethane (DDT)), a new era of synthetic pesticides for pest control in agriculture was commenced. For his discovery, Müller was awarded the Nobel Prize in Physiology or Medicine. The chlorinated hydrocarbons like DDT and lindane made significant impact during world war and were very effective in controlling vectors of diseases such as malaria, typhus, and yellow fever. The broad-spectrum activity of DDT in controlling various agricultural pests and vector-borne diseases fuelled tremendous research activity toward development of synthetic chemicals targeting different classes of pests (Berry-Caban 2011). These synthetic chemicals were collectively called as pesticides. Fuelled with the success of DDT, several different types of chemical pesticides were developed during throughout the 1940s–1960s with unrestricted use. These pesticides targeted different classes of pests such as insects, weeds, herbs, rodents, etc. and were used unrestrictedly. However, after three decades of unrestricted use, negative impact of DDT on human health and environment was realized which ultimately led to its prohibition for agricultural use in 1972 by the US Environmental Protection Agency (EPA). Other countries also followed the suite and completely prohibited the use of DDT for agricultural use by the 1980s barring some developing nations. The most destructive impact of DDT and other pesticides on human health was their bioaccumulation and biomagnification through food chain. The bioaccumulation of DDT produces hepatic, cutaneous, and nervous disorders in humans. It also exhibits teratogenic effects and negatively impacts the human reproductive health (Beard 2006).

Consequently, monitoring of pesticide residues in foodstuffs gained significant attention in the last few decades. In fact, residual pesticides are frequently found in the foodstuffs, and therefore their maximum permissible quantity in the food is strictly governed by various statutory bodies around the world. However, due to the complex nature and different chemical properties of food matrix, detection of residual pesticides is quite challenging. Several sophisticated analytical techniques have emerged for analysis of pesticide residues in food, but many of them suffer from significant limitations such as higher cost of analysis, bulkiness, sophisticated operations, and exhaustive sample preparation methods. In this context, disposable, low-cost, and point-of-care detection methods with considerable sensitivity and specificity are at focal point of current research and development. Recently, several optical detection methods have been employed for sensitive and selective detection of pesticide residues in foodstuffs. An optical signal such as fluorescence emission, absorption, and polarization is inherently selective in nature and does not get affected by conditions such as humidity, temperature, buffer solution, inorganic contaminants, etc. and is excellent for developing robust detection platform. Continued development in excitation and collection optics also enables ultrasensitive detection of analyte suitable for pesticide residue analysis.

This chapter aims to provide an overview of current strategies employed in development of optical detection platforms for pesticide residues in foodstuffs. Brief introduction to synthetic pesticide classification and their health risk and recent development in sample preparation and analytical techniques for trace residue detection has been also briefly discussed.

7.2 Classification of Pesticides

There are several ways synthetic pesticides can be classified based on the target pest against which they are effective like insecticides, miticides, herbicides, nematicides, fungicides, molluscicides, rodenticides, and many more. However, this type of classification does not indicate their toxicity profile especially against human beings and the environment.

The World Health Organization (WHO) adopted more inclusive classification method based on their health risk (hazard) (IPCS 2009). In this method, the pesticides are ranked according to their toxicity into four different groups from extremely hazardous to slightly hazardous pesticides (Table 7.1). The toxicity of pesticide is estimated from its lethal dose (LD 50) value in rats through oral and dermal administration.

A more comprehensive method of pesticide classification was adopted jointly by the Food and Agriculture Organization of United Nations (FAO) and World Health

Table 7.1 Classification of pesticides based on their hazard (IPCS 2009)

WHO class	Definition	Lethal dose (LD 50) (mg kg^{-1} body weight for rats)	
		Oral	Dermal
Ia	Extremely hazardous	Less than 5	Less than 50
Ib	Highly hazardous	5–50	50–200
II	Moderately hazardous	50–2000	200–2000
III	Slightly hazardous	More than 2000	More than 2000
U	Unlikely to produce acute hazard	5000 or above	

Organization (WHO) to describe a pesticide highly hazardous if it has one or more of the following characteristics (WHO 2009):

- Exhibits acute toxicity (classes Ia and Ib)
- Carcinogenicity
- Mutagenicity
- Reproductive toxicity
- Evidence of severe or irreversible adverse effects on human health
- Listed under persistent organic pollutants (POPs) (web-link: http://chm.pops.int/)
- Listed under substances that deplete the ozone layer (web-link: http://ozone.unep.org)
- Listed under Rotterdam Convention for hazardous pesticides and industrial chemicals in trade (web-link: http://www.pic.int/)

Synthetic pesticides can also be classified based on their general chemical structure.

7.2.1 *Organochlorines*

Organochlorine pesticides are a group of chlorinated organic compounds which are water insoluble, resist biodegradation, and are highly persistent in the environment. They tend to bioaccumulate in fatty tissues in human (Jayaraj et al. 2016). A well-known example of this class is dichlorodiphenyltrichloroethane (DDT) (Turusov et al. 2002). Organochlorine pesticides constitute a large number of pesticides among all the other pesticides used worldwide. They were introduced to mainly eradicate disease vectors of malaria, dengue, and typhus. The low cost and ability to control large spectrum of pests led to their extensive usage, mainly in developing countries. However, due to their persistent nature in the environment and health hazard associated with their bioaccumulation and biomagnification in humans, many pesticides are now banned in most of the developed nations.

Humans are exposed to organochlorines mainly via ingestion route due to consumption of contaminated food. On exposure, organochlorines attack the central nervous system (CNS) causing dysfunction in nerve conduction by altering electrophysiology of the neurons (Keifer and Firestone 2007). The acute toxicity of pesticide is characterized by seizures and respiratory arrest leading to death. The chronic exposures of pesticides also have marked an effect on human health. These compounds tend to accumulate in fat tissues and are difficult to metabolize. They are also considered as potent carcinogen in humans. Perhaps the most dangerous aspect of organochlorines is their ability to cross blood-placenta barrier and produce teratogenicity, i.e., ability to produce congenital malformation (birth defects) in neonates (Kalliora et al. 2018).

7.2.2 Organophosphates

Organophosphate pesticides are the organic esters of phosphoric acid and constitute one of the most widely utilized classes of insecticides globally. A classic example of organophosphate pesticides is parathion. These pesticides are generally utilized for elimination of agriculture, home, garden, and veterinary pests. In contrast to organochlorine pesticides, an organophosphate pesticide easily gets degraded via hydrolysis through exposure to light, moisture, and soil. However, organophosphates do produce acute and subacute toxic effect due to exposure through ingestion, dermal, or inhalation route.

On exposure, the organophosphate pesticide also directly acts on nerve conduction by irreversibly inactivating the enzyme acetylcholinesterase (AChE) through phosphorylation (Kwong 2002). The enzyme degrades the neurotransmitter molecule acetylcholine after the passage of nerve stimulus between two neuronal junctions (i.e., cholinergic synapses). However, its inactivation by the pesticides leads to overaccumulation of acetylcholine, resulting into overstimulation of the nerve conduction and nervous system dysfunction. The acute symptom ranges from loss of reflexes, convulsions, dizziness, and nausea to involuntary muscle contractions, twitching, and respiratory failure leading to death depending on the level and route of exposure. Fastest symptom appears after inhalation causing respiratory problems.

The organophosphate pesticides also possess strong mutagenicity due to their capability of alkylating the deoxyribonucleic acid (DNA) nitrogenous bases with alkyl groups (mostly methyl and ethyl groups) (Wild 1975; Wooder and Wright 1981). They also prime nitrogenous bases with nucleophilic groups making them susceptible to react with electrophiles, thus increasing the incidences of cancer and other genetic disorders in agricultural farmers (Lerro et al. 2015).

7.2.3 Carbamates

Carbamate pesticides are derivatives of carbamic acid (NH_2COOH), and the active component in these pesticides is carbamate esters. The first carbamate pesticide was introduced into market in 1956 as carbaryl. Carbamates are utilized commonly in households, agriculture farmlands, and garden as insecticides, herbicides, fungicides, and nematicides. Carbamates exert their effect by inactivating the enzyme acetylcholinesterase through carbamylation in the similar fashion as organophosphate pesticides do (Miller 1982; Kiran Dip Gill et al. 2011). However, carbamates act much faster, and inactivation takes place through covalent attachment. Humans are exposed to carbamates through oral, dermal, or inhalation route. The symptoms of exposure are similar to that of organophosphate pesticides but last for shorter duration as the enzyme inhibition is reversible and carbamates easily get metabolized (Tang et al. 2006).

7.2.4 Pyrethroids

Pyrethroid (and pyrethrin) pesticides are natural organic compounds originally extracted from flowers of pyrethrums (*Chrysanthemum coccineum* and *C. cinerariaefolium*) and are commonly utilized for their insecticidal properties (Casida 1980). The functional group responsible for their activity is ketoholic esters derived from chrysanthemic and pyrethroic acids which act on the central nervous system causing paralysis of the organism. Unlike other organophosphate, organochlorine, and carbamate pesticides, pyrethroids have selective toxicity toward insect nervous systems than in mammal (Croft and Whalon 1982). This could be attributed to their lower dermal absorption and efficient hepatic metabolism in mammals. Pyrethroids exert their toxic effect by elongating the opening time of voltage-sensitive sodium ion channels in neurons and causing neuronal hyper-excitation (Soderlund 2012).

Although pyrethroids are considerably safer as compared with other pesticides, however, acute toxicity does occur if exposed to high level of concentrated pyrethroids. The main route of exposure is through inhalation or ingestion, while dermal toxicity is very rare. The symptom ranges from mild paresthesia, nausea, dizziness, and anorexia to more severe seizures, coma, pulmonary edema, and even death depending on the amount and route of exposure.

7.2.5 Phenylamides

Phenylamides are highly active class of fungicides primarily used against fungal plant pathogens such as members of orders Peronosporales, Sclerosporales, and Pythiales (Gisi and Sierotzki 2015). These pathogens cause downy mildew, root rot, and late blight diseases in various cash crops like onions, peas, avocados, potatoes, tomatoes, and grapes. They actively penetrate into plant tissues and are transported toward the root and shoot, an apical region which is the most affected part by the disease. Phenylamides block the nucleic acid synthesis in target pathogens by affecting the RNA polymerase I enzyme activity (Yang et al. 2011). They also affect the mitosis and cell division in pathogens. Although effective against many fungal pathogens, excessive use of phenylamides encourages development of resistance in target pathogens through gene mutations (Cooke 1992). Exact molecular mechanism of resistance development has not been understood yet. It is therefore highly recommended to use phenylamides in concurrence with resistance management guidelines.

7.2.6 Benzoic Acid

Benzoic acid and its derivatives such as dicamba, dichlobenil, chlorambin, bromoxynil, ioxynil, and naptalam are used as potent herbicides to kill target weeds in crops. For example, dicamba is one of the most consumed benzoic acid herbicides which selectively kills broadleaf weeds in corn crops. Dicamba mimics natural plant hormone auxins and causes abnormal growth of the target weed by affecting cell divisions (Christoffoleti et al. 2015). It is absorbed through the soil and is systematically distributed within the plant including new leaves. Dicamba has been also reported to inhibit the enzyme acetylcholine esterase similar to organochlorine and organophosphate pesticides and thus produce neurotoxic effect (Potter et al. 1993). It also inhibits several enzymes in the liver involved in detoxification and excretion of foreign chemicals (Espandiari et al. 1998).

Dicamba is relatively a safer herbicide (moderately hazardous) with oral lethal dose 50 (LD 50) of 1700 mg kg^{-1} in rats. Acute exposures in humans have been found to induce allergic reactions like skin rash, shortness of breath, swollen glands, and other symptoms like vomiting, nausea, and loss of voice (Moon and Chun 2014). However, a study found out that farmers exposed to dicamba were more susceptible to develop non-Hodgkin's cancer after two decades of exposure (McDuffie et al. 2001).

7.2.7 Phthalimide

Phthalimide pesticides are the second most important group of organic fungicides after phenylamides. Phthalimide fungicides include pesticides such as captan and folpet which are one of the most consumed fungicides worldwide (Gordon 2010). These pesticides are applied in different varieties of crops including fruits, nuts, and ornamental plants. The fungicidal activity of the pesticides stems from their pH-dependent reactivity. Under alkaline pH, both pesticides are hydrolyzed to release their active component, trichloromethylthio functional group, $SCCl_3$ or also called as thiophosgene (Chen et al. 2011). Thiophosgene is a highly reactive volatile compound which rapidly reacts with other functional groups such as amines, amides, imides, and alcohols. It also hydrolyzes to produce hydrogen sulfide, carbonyl sulfide, and hydrochloric acid.

In general, both folpet and captan are considered safe for humans at normal exposure levels and are categorized as "general use pesticides (GUP)" (Bernard and Gordon 2000). Acute toxicity to higher levels may cause moderate irritation of the skin, respiratory tract, and eyes. However, long-term genotoxicity of captan and folpet is a cause of concern (Arce et al. 2010; Berthet et al. 2012).

7.2.8 Dipyrids

Dipyrid pesticides include two widely utilized herbicides: paraquat and diquat. Both of them are categorized as synthetic, nonselective, contact herbicides and have strong redox (reduction-oxidation) property (Akhavein and Linscott 1968). Due to their strong redox property, both pesticides produce superoxide anion on reaction molecular oxygen. The oxygen radical then causes cell death via oxidative stress.

Humans are exposed to paraquat and diquat mainly through ingestion route. The acute toxicity of paraquat has been reported to cause extreme reactions in human with lethal dose 50 (LD 50) as little as 3–5 mg kg^{-1}. The affected organs from paraquat toxicity include the gastrointestinal tract (GI tract), liver, kidney, heart, and lungs (Fortenberry et al. 2016). A severe and often life-threatening manifestation of the pesticide toxicity occurs in lungs wherein oxidative damage due to the pesticide induces pulmonary edema and progressive fibrosis resulting into death (Dinis-Oliveira et al. 2008). Dermal absorption of paraquat is lower, but exposure may still cause contact dermatitis, erythema, blistering, and abrasion damages (Gawarammana and Buckley 2011). Diquat toxicity on the other hand has a marked effect on the central nervous system (CNS) causing brain stem infarction particularly involving the pons (Saeed et al. 2001). The exact mechanism of neurotoxicity of diquat has not been established yet.

7.2.9 Phenoxyalkonates

Phenoxyalkanoic acid pesticides are commonly used herbicides that selectively kill broadleaf weeds (Kennepohl et al. 2010). These pesticides mimic the natural plant hormone indole acetic acid (IAA) and selectively induce rapid, uncontrolled growth in broadleaf weeds while having no effect on monocotyledonous crops (like wheat, corn, etc.). The uncontrolled growth causes weeds to outgrow their nutrient supply and thus eventual death. Several pesticides of this class are hugely popular as household herbicides including mecoprop, 2-(2,4-dichlorophenoxy)acetic acid (2,4-D), 2-(4-chloro-2-methylphenoxy)acetic acid (MCPA), and 2,4,5-trichlorophenoxyacetic acid (2,4,5-T). The 2,4,5-T herbicide is now discontinued in many countries due to contamination with dioxin pollutants (Neuberger et al. 1999). Although soil microflora are able to degrade these herbicides, their excessive use causes groundwater pollution through leaching and is now a big concern (Paszko et al. 2016). The toxicological studies of these herbicides have found them safe for humans at normal exposure level. Acute exposure may produce symptoms ranging from severe eye irritation to slurred speech, twitching, jerking, low blood pressure, and unconsciousness (Islam et al. 2018).

7.2.10 Triazines

Triazines are also herbicidal pesticides and include common herbicides such as propazine, atrazine, chlorazine, desmetryne, etc. For example, atrazine was one of the most utilized herbicides in the United States for corn crops (Pike et al. 2008). A unique member of this class is cyromazine which is actually an insect growth regulator which affects insect molting and pupation (Van De Wouw et al. 2006). Triazines are among the oldest herbicides with their herbicidal properties discovered back in the 1950s. Application of triazines is often combined with other herbicides to widen the weed control spectrum. In general, triazines are heterocyclic aromatic in nature and block electron transport in photosynthesis (Trebst 2008).

Among the various classes of pesticides, triazines are least toxic of all. Acute toxicity arises only after large quantity of pesticide is ingested, and symptoms could include moderate irritations to the eyes, skin, and respiratory tract. The LD 50 of atrazine in rats is around 1800 mg kg^{-1}, thus categorized as slight to moderately toxic for humans (Bray et al. 2008).

7.2.11 Heavy Metal Pesticides

Several heavy metal salts and organometallic compounds based on heavy metal have found their use as pesticides for controlling a variety of pests (Galal-Gorchev 1991; Gimeno-García et al. 1996; Bencko and Yan Li Foong 2017). These pesticides include inorganic salts or organometallic compounds of different heavy metals like arsenic, mercury, cadmium, lead, sulfur, zinc, tin, copper, etc. Some examples of heavy metal pesticides includes Paris green (copper acetoarsenite), Scheele's green (copper arsenite), cacodylic acid (contains arsenic), trifentin acetate (contains tin), ziram (contains iron), etc. Although metal-based pesticides show broad control spectrum for pest, their non-biodegradability, environmental persistence, soil and water pollution, and bioaccumulations into higher organism through food chain are a serious cause of concern. The toxicology of such pesticides is similar to that of heavy metal exposure and has been discussed in details elsewhere (Tchounwou et al. 2012).

7.3 Determination of Pesticide Residues

Pesticides are used worldwide for controlling different kinds of pests and for different types of crops. Natural degradation of pesticides is often very slow and depends on various factors such as climatic conditions, soil microflora, and inherent chemical or thermal stability of the pesticide itself (Kah et al. 2007). Several pesticides are inherently very stable (chemically) and are therefore difficult to degrade naturally. They are classified as "persistent organic pollutants (POPs)" (Jayaraj et al. 2016). Inadvertently, many of these pesticide residues therefore end up into the consumer foods and therefore pose a great risk to public health. The situation is further aggravated by excessive use of pesticides by agricultural farmers especially in developing countries due to poor awareness. These excess pesticides cause significant air, water, and soil pollution and threaten to disturb the ecological balance of the region (Wasim et al. 2009). Furthermore, these pesticides enter into food chain and tend to bioaccumulate in higher organisms including humans and have long-term toxic effect (Katagi 2010). The teratogenic toxicity of pesticide DDT is a grim reminder of this (Longnecker et al. 1997). Considering the consumer (humans and livestock) safety and environmental sustainability, quantitative estimation of pesticide residues in foodstuffs is of paramount importance. To address this issue, various statutory bodies around the world such as Codex Alimentarius Commission, WHO, FAO, and European Union (EU), as well as national governments in various countries, have set a maximum limit of pesticide residues called "maximum residue limits (MRLs)" in foodstuffs to minimize consumer exposure (Despina Tsipi 2015; Economou 2015; WHO 2018). These limits set a legal level of pesticide concentration allowed in foodstuffs for consumption and trade. Generally, set concentration limits vary with the type of pesticide and end consumers (adults vs. children).

The complex matrix of food and trace level of pesticide residues pose a daunting challenge in accurate quantification of pesticide residues. Consequently, it becomes essential to extract or pre-concentrate pesticide residues in a suitable matrix for further analysis. Although there are several other factors which significantly affect the quantitative estimation of pesticide residues in foodstuffs, such as the method of sampling, storage and transport conditions of samples, time period of analysis, internal standard for validation, and more, we have limited our discussion to different methods of sample preparation and subsequent analytical techniques utilized in determination of pesticide residues (Lehotay and Cook 2015).

7.4 Sample Preparation for Pesticide Residue Analysis

Sample preparation is considered as the most significant and rate-limiting step in analysis of pesticide residues. It is a multistep process involving crude methods of grounding, crushing, blending, and homogenizing samples as well as sophisticated chemical extraction and enrichment methods. The primary objective of sample preparation step is to extract, enrich, and purify pesticide residues from complex chemical food matrix into a simple or suitable one, so that an accurate determination of pesticide residue could be possible through subsequent analytical technique. If incorrectly done, this step has the highest possibility to introduce contaminant or experimental errors, thereby significantly altering the analysis (Yolci Omeroglu et al. 2015). Therefore, whenever possible, sample preparation should be avoided, and the residues should be directly analyzed through various analytical techniques. However, practically, almost in every instance, sample preparation has become essential due to complex nature of food matrix. Several chemical extraction methods have been reported over the years which are generally based on either solvent-based extraction or sorption-based extraction (Zhang et al. 2012). Some important extraction methods used in analysis of pesticide residues are briefly discussed here.

7.4.1 "Quick, Easy, Cheap, Effective, Rugged, and Safe" Extraction Method

This extraction method also called as "QuEChERS" was first introduced by Anastassiades and coworkers and is considered as a breakthrough in sample preparation method for pesticide residue analysis (Anastassiades et al. 2003). It has seen a phenomenal increase in its applicability worldwide (González-Curbelo et al. 2015). The extraction approach includes extraction of the analyte from a thoroughly homogenized sample into a suitable solvent system (such as acetonitrile), followed by salt-out partitioning of water using magnesium sulfate ($MgSO_4$) salts and finally cleaning up of residual matrix components by dispersive solid-phase extraction (dSPE). The residual pesticide analyte remains in the extract. The general nature and adaptability of the method have been utilized to extract several different kinds of analytes including pharmaceuticals, mycotoxin, and polyaromatic hydrocarbons (PAHs) apart from pesticide residues (Cvetkovic et al. 2016; Jettanajit and Nhujak 2016). The extraction method is also relatively cheaper, rugged, and more safer and has been shown to be compatible for extraction of pesticide residues from different kinds of food matrices such as primary agricultural products, eggs, baby foods, fish, and even milk (Lehotay 2011; Jeong et al. 2012; Garcia and Gotah 2017). It has been also found suitable for extraction of pesticide degradation products from food matrix.

7.4.2 Accelerated Solvent Extraction

Accelerated solvent extraction (ASE) is a type of solvent-based extraction technique designed to accelerate the extraction process through application of high-pressure solvent at elevated temperature. Sample is generally kept in a specialized sample holder along with inert sorbent material such as diatomaceous earth and then subjected to a closed solvent flow-through system. The high temperature and pressure allow greater extraction efficiency in terms of recovery of residues as well as shorter time duration due to higher solvent penetration (Gan et al. 1999). Another advantage of the method is that very small quantity of solvent (~ 10 times less) is required for the extraction process which is particularly relevant for environmental sustainability (Giergielewicz-Możajska et al. 2001). However, it lacks selectivity due to which many contaminants are co-extracted with the target residue; thus, a subsequent cleanup process is necessary. In some cases, unwanted analyte dilution due to repeated cycles of extraction is encountered.

7.4.3 Supercritical Fluid Extraction

Supercritical fluids are generally highly compressed gases which combine the gaseous and liquid properties in an intriguing manner. It can effuse through a solid material like a gas, whereas simultaneously can also dissolve analytes like a liquid. Supercritical fluids were recently introduced as extraction medium for residual pesticides from food matrices (Valverde-García et al. 1996; Motohashi et al. 2000). Supercritical carbon dioxide (CO_2) fluid has been used as an extraction medium in almost all of the studies due to its easy preparation (critical point 30.9 °C, 73.8 bars), low cost, chemical inertness, and low toxicity (Wu and Han 2013). It is an excellent solvent for extraction of nonpolar organic molecules including pesticides and other high molecular weight organic compounds (Berglöf et al. 1999). For the extraction of polar molecules, CO_2 solvent is often mixed with solvent modifiers or cosolvents such as water, methanol, acetone, or chloroform. Due to high pressure and gaseous properties, supercritical CO_2 can penetrate into sample and improve extraction properties. However, it also co-extracts high quantity of fatty contaminants from the samples which requires additional cleanup procedures before analytical determination.

7.4.4 Liquid-Phase Microextraction

Liquid-phase microextraction (LPME) is also a type of solvent-based extraction process wherein a very small volume of organic solvent (usually in microliters) is utilized for extraction of residual pesticides from an aqueous matrix (Lambropoulou and Albanis 2007). The extremely small volume of receiving solvent allows very high enrichment of target analyte. The extraction method has been utilized in the different approaches.

Single-Drop Microextraction

In this approach, a single droplet (microliter volume) of extraction solvent is exposed to liquid sample containing pesticide residues via a tip of a microsyringe. The tip could be placed inside the aqueous medium or in the headspace of a closed container for extraction. Once the extraction is complete, the extraction solvent is drawn back into the microsyringe and then processed further. Determination of pesticide residues in tea, juice, and wine using this approach has been reported previously (Jin et al. 2012).

Dispersive Liquid-Liquid Microextraction

This approach uses a three-solvent system consisting of an extraction solvent (organic, water immiscible), a dispersive solvent (organic and water miscible), and an aqueous sample containing residual pesticide. The extraction and dispersive solvent are rapidly mixed into the aqueous sample containing residual pesticides, resulting into formation of cloudy dispersions of small micro-droplets for extraction. The extraction solvent is then separated from the aqueous sample and analyzed for residual pesticides. This extraction method has several advantages such as small volume of organic solvent; easy operations; rapid, efficient, and low-cost approach; and high recovery and enrichment factor and could be directly linked with subsequent analyzer. It has been utilized for extraction of pesticides from tea, wine, and honey. Combinatorial approach with other extraction procedures has been reported to produce excellent recoveries of pesticide residues (Zgoła-Grześkowiak and Grześkowiak 2011).

Hollow-Fiber Liquid-Phase Microextraction

This method utilizes a sealed, porous polypropylene tube of very small diameter and connected to a syringe at one end, while the other end is filled with extraction solvent (organic). The tube is then immersed into an aqueous solvent containing residual pesticide which is allowed to migrate from aqueous phase to organic phase through tube walls. After a predetermined extraction time, the extraction solvent is drawn back into the syringe. In a slightly different configuration, three-phase extraction is carried out using another acceptor solvent inside the lumen of the tube. The analytes migrate into the acceptor phase via intermediary organic solvent (Alsharif et al. 2016). Due to simplicity and adaptability of HF-LPME, several different types of pesticide residues including organosulfurs, organochlorines, organophosphates, fungicides, and carbamates have been extracted from different types of food matrices (Shen and Lee 2002; Cai et al. 2016).

Solid-Phase Extraction

Unlike solvent-phase extraction this method described above, solid-phase extraction is based on sorption of pesticide residues on a solid matrix or adsorbent which could then be eluted into a suitable solvent system. Although it suffers from long extraction times, they provide highly selective and highly enriched pesticide concentrates for subsequent analysis. Furthermore, the method is highly versatile due to available selection choices for sorbent matrix and elution sample (Berrueta et al. 1995). It could be utilized for several different purposes such as pesticide isolation, solvent exchange, and purification or enrichment of pesticide residues and derivatization of analyte molecules (Deger et al. 2000; Zwir-Ferenc and Biziuk 2006; Cazorla-Reyes et al. 2011). Generally, SPE is carried out using packed columns of sorbent matrix, which after some preconditioning could selectively bind to analyte pesticides. The interfering compounds are removed by successive washing and elution steps, and finally the bound pesticide molecules are eluted in selected buffer or solvent systems (Poole 2002). The recent advances in this method are directed toward development of novel microextraction processes or sorbent materials to achieve higher recoveries in short durations from ever-complex food matrices. Several different sorbent matrices have been developed for selective SPE such as molecularly imprinted polymers (MIPs) (Olcer et al. 2017), restricted access materials (RAMs) (Boos and Fleischer 2001), immunoaffinity sorbents (IASs) (Delaunay et al. 2000), carbon nanotubes (Latrous El Atrache 2016), and custom-made sorbents for specific applications (Zhao et al. 2011a).

Matrix Solid-Phase Dispersion

Unlike SPE method which requires liquid sample for extraction, this technique is developed for extraction and cleanup of residual pesticides from viscous, solid, and semisolid (gel) samples. It also combines the homogenization, disruption, extraction, and cleanup processes into one single process. It involves blending and homogenization of solid food samples (e.g., cereals) with an inert absorbent material (C_{18}, C_8, silica, diatomaceous earth aluminum sulfate, etc.) and small quantity of extraction solvent (Tsochatzis et al. 2010). The food matrix is completely disrupted and dispersed as very fine particles allowing higher surface area for simultaneous cleanup and extraction. Simultaneous sample preparation and extraction also minimize the operational cost and analysis duration.

Solid-Phase Microextraction

The solid-phase microextraction (SPME) was introduced as a solvent-free extraction technique in which residual pesticide is bound by liquid extractant (usually polymer) or solid-phase sorbent supported on an inert matrix by simple exposure in a liquid medium or at the headspace of the closed container. Sufficient extraction time is kept for the residual analyte to equilibrate in between sample and extraction medium. The concentration of the final extracted residue is dependent on its distribution coefficient. The extracted residues can then be desorbed through heating and directly fed into gas chromatography (GC) or eluted in a solvent for liquid chromatography (LC) techniques. The efficiency of the method is dependent on several factors such as mode of extraction, the sample-extractant chemistry, pH, ionic strength and organic content of sample, temperature, and duration of extraction procedure and desorption conditions. These factors are needed to be optimized for target residue and type of sample. However, this method benefits from miniaturization, automation of device, versatility, and easy connectivity with downstream chromatographic techniques. Advances in novel sorbent materials and extraction phases are being continuously made to ensure highly efficient extraction process (Beltran et al. 2000).

Stir Bar Sorptive Extraction

The stir bar sorptive extraction (SBSE) is a modified variation of solid-phase microextraction method, wherein a magnetic stir bar is coated with the sorbent material for extraction of analyte residue from the liquid sample (Giordano et al. 2009). The incubation time is generally longer to allow complete extraction, after which, the analyte is desorbed either thermally for GC analysis or in organic solvent for LC analysis. The principal difference between solid-phase and stir bar sorptive extraction is the larger amount (50–200 times more) of extraction phase used in stir bar extraction which allows higher recoveries, better reproducibility, and higher enrichment (Li et al. 2012). The focus of current developments in SBSE is toward novel sorbent materials particularly for extraction of polar analytes or for a selective analyte (e.g., MIPs) (Rykowska and Wasiak 2013).

Microwave-Assisted Extraction

Microwave-assisted extraction (MAE) was introduced in 1986 and has been used for extraction of organic pollutants and pesticides for a variety of matrices (Ganzler et al. 1986). Instead of conventional heating, microwave heating is utilized for extracting residual analytes into organic solvent. The polarity of the sample analytes and organic solvent plays an important role in extraction efficiency. For example, n-heptane produced highest efficiency in extraction of organochlorine and pyrethroid pesticides from Chinese teas (Ji et al. 2007). Alternatively, solvents compatible with downstream chromatographic separations such as hexane, acetone, dichloromethane, and ethyl acetate are also utilized for microwave extraction of pesticide residues (Chen et al. 2007). Other important factors include extraction temperature and time. In general, higher temperature and shorter duration favor more efficient extraction; however, excessive heat should be avoided to prevent pesticide degradation (Singh et al. 2007). Microwave extraction offers higher extraction efficiency, automation, and simultaneous extraction of multiple analytes. However, co-extraction of food matrices during MAE required additional cleanup.

Ultrasound-Assisted Extraction

This another rapid extraction process is assisted by ultrasound waves. The ultrasonic waves produce microbubbles through acoustic cavitation which disrupts the cell walls and facilitates solvent penetration of the food samples. Better solvent penetration and heating effect of ultrasonic wave yield higher extraction efficiency. Similar to microwave extraction, the extraction efficiency using ultrasound depends on extraction time, polarity of solvent, and temperature (Ramos et al. 2008; Fontana et al. 2010). The ultrasound is preferred over microwaves for extraction of thermolabile pesticide residues (Rezaei and Hosseini 2011). Other advantages of ultrasound-assisted extraction include lower solvent consumption, shorter extraction time, and cleaner and cheaper operations.

Cloud Point Extraction

Cloud point extraction (CPE) or micelle-mediated extraction (MME) was introduced as an extraction technique to minimize the consumption of organic solvents (Tani et al. 1997). In this method, nonionic surfactant molecules are utilized to extract organic pesticide residues through micelle formation. After a critical concentration, these surfactant molecules self-assemble into spherical micelles at its cloud point temperature with hydrophobic interiors. Pesticide residues being organic in nature, partition themselves into these micelles. The micelle formation is indicated by cloudy appearance of the solution. When allowed to settle, these micelles coalesce to form a separate phase containing concentrated pesticide residue which is then isolated and diluted with small quantity of organic solvents. Several different nonionic surfactants have been reported for pesticide residue analysis including polyethylene glycol (MW6000), Triton X-114, Triton X-100, Tween 20, etc. having different cloud point temperature and extraction efficiencies (Quina and Hinze 1999; Zhang 2011; Zhao et al. 2011b). Other critical factors for cloud point extraction include pH, temperature, and ionic strength of the aqueous phase (Santalad et al. 2012; Tan et al. 2013). Advantages of this method include significantly reduced requirement of organic solvents, simple operations, and single-step extraction as well as enrichment.

7.5 Analytical Techniques for Determination of Pesticide Residues

The complex matrix of food samples containing several interfering agents necessitates sample preparation stage wherein residual pesticide is extracted, purified, and enriched for their detection through various downstream analytical techniques (Rather et al. 2017). Due to the very low concentration of pesticide residues and stringent MRL conditions, accurate estimation of the residual pesticide is of absolute necessity. Furthermore, real samples often contain multiple pesticide residues at different concentrations. Consequently, sophisticated analytical methods which could provide high sensitivity and selectivity for residual pesticide of interest are usually employed for analysis (Grimalt and Dehouck 2016). Due to the presence of multiple pesticide residues and complex interfering agents from food matrices, separation techniques are employed to separate individual residues followed by their detections (Cowburn and Stockley 2005; Gerage et al. 2017).

Almost exclusively two types of chromatographic separations, gas chromatography (GC) and liquid chromatography (LC), are employed for residual pesticide analysis in food samples. These separation techniques are further linked in tandem with various detectors or mass spectrophotometers (MS) for estimation of pesticide residues (Stachniuk and Fornal 2016). Some other techniques, such as thin-layer chromatography (TLC) and capillary electrophoresis (CE), are also employed in pesticide residue analysis which have been reviewed elsewhere (Chang et al. 2016; Sherma 2017).

7.5.1 Gas Chromatography

Gas chromatography (GC) technique was pioneered by Martin and Synge during the 1940s and is still a preferred choice of analysis for determination of residual pesticides in food samples (EL-Saeid and Selim 2013; Hernández et al. 2013). Particularly for nonpolar, semipolar, volatile, or semi-volatile and thermally stable pesticides, gas chromatography is still preferred over liquid chromatography method due to its higher resolution. Higher resolution is also suitable for analysis of samples containing multiple pesticide residues. Cost and time of analysis are one of the significant factors which drive the choice of analytical methods for pesticide residue detection. Conventional gas chromatography systems required significant amount of time and resources for analysis. However, developments in various aspects of the system including instrumentation and data processing during the last few decades helped evolving several faster, more efficient, and cost-effective variants of the technique (Dömötörová and Matisová 2008). For example, a fast gas chromatography system can analyze a sample within 20–40 min run time with higher efficiency than the conventional systems. Very fast and ultrafast gas chromatography systems having analysis time within seconds and sub-seconds, respectively, have been also developed recently (Donato et al. 2007). Several strategies were adopted in the instrumentation of the chromatography systems for achieving faster analysis time (Korytár et al. 2002). Utilization of narrow-bore columns (reduced internal diameter) was found to increase the efficiency of the chromatographic separation and reduces analysis time (Klee and Blumberg 2002; Dömötörová et al. 2006). Narrow-bore columns also improved the average linear velocity of carrier gas which when combined with other techniques such as column shortening, thinner stationary phase, high heating rates, and optimized carrier flow rate resulted into higher efficiency. In general, 5% phenyl 95% polydimethylsiloxane stationary phase column with a bore diameter of 0.25 mm and length of 20–30 m is used in gas chromatography. Significant improvements were also made in the sample injections system (Shim et al. 2015). The earlier split or splitless gas chromatography injectors suffered from large sample volume requirement or reduced sample loading capacity. The sealed heating of analytes to generate vapors in these injectors was also a potential source of error due to sample degradation and discrimination. Subsequently, programmed temperature vaporization (PTV) mode is developed in which sample is vaporized in a controlled manner such that matrix components and co-extracted compounds are expelled from the split valve or are trapped in the line. These injectors also allow introduction of large sample volumes into the column which significantly increases the resolution and improves limit of quantification (LOQ) (Korenková et al. 2004). Another approach to increase the analysis time is to use a relatively short wide-bore analytical column under vacuum conditions and directly connected to an MS detector. Usually an intermittent restriction column of smaller bore size is used between the inlet and the analytical column. The low pressure in the column significantly increases the carrier gas flow rate and improves analysis time by 3–5-fold. Another benefit of low-pressure gas chromatography (LP-GC) is lowering of elution temperature which is suitable for thermally labile pesticide residues (Ravindra et al. 2008; Sapozhnikova 2014). However, one downside of the technique is the loss of separation quality resulting in wider peaks.

Comprehensive two-dimensional gas chromatography (GCxGC) has emerged as another powerful technique to achieve better separation and higher resolution in significantly lower analysis time. In this approach, two analytical columns with different separation mechanisms are linked in series through a modulator. The function of the modulator is to efficiently transfer (reinject) the effluent of one column into another as narrow consecutive chromatographic band. The separation in the second column is rapidly achieved depending on the nature and length of the stationary phase. Ideally, separation in the second column should be completed before the next injection step (Dallüge et al. 2003).

After the chromatographic separation in gas chromatography column, individual pesticide residues are identified and quantitated in the detector system which is often coupled in tandem with the chromatographic column. Several compatible detector systems are utilized with gas chromatography, among which mass spectrometers (MS) are extensively utilized for multi-residue analysis (Botitsi et al. 2011; Utture 2015). In MS detectors, pesticide residues are first ionized, and a mass spectrum of ionized fragments is generated using different mass filters. The mass spectrum is then compared with in-built standard pesticide libraries for identification and quantification of the residues through automated analysis. Standard mass spectral library of pesticides and peak identification software are available in the National Institute of Standards and Technology (NIST) and are usually provided with commercial GC analyzers. Detailed description of working of mass spectrometers including ionization methods, various mass filters, and detectors for identification and quantification of pesticide residues from food matrices has been reviewed previously (Botitsi et al. 2011). Other detectors for analysis of pesticide residues eluting from the GC column include flame ionization detectors (FID) (Maier-Bode and Riedmann 1975), nitrogen-phosphorus detectors (NPD) (Fenoll et al. 2005), electron capture detectors (ECD) (An and Shin 2011), thermal conductivity detectors (TCD) (Beckman and Bevenue 1962), flame photometric detectors (FPD) (Zhao et al. 2014), photoionization detectors (PID) (Soo et al. 2018), and electrolytic conductivity detectors (ELCD) (Coulson 1965). The choice of detector for GC depends on several factors such as cost, analysis time, residue type, and required sensitivity. For analysis of samples contaminated with multiple residues, MS are so far the best detectors as it can identify several pesticides at one go. On the other hand, detectors such as NPD can selectively identify nitrogen- and phosphorous-containing pesticides given that matrix effect has been minimized through proper sample preparation (Łozowicka 2013).

7.5.2 Liquid Chromatography

Liquid chromatography is another sophisticated analytical technique which uses organic (reverse phase) or aqueous (normal phase) medium as the mobile phase. In contrast to gas chromatography, liquid chromatography is more suitable for detection and analysis of more polar, thermally instable, and nonvolatile pesticide residues (Kuster et al. 2009; Stachniuk et al. 2017). For example, pesticides such as carbamates, benzoylurea insecticides, and benzimidazole fungicides are more polar and are therefore suitable for analysis by liquid chromatography (Chamkasem 2018). Liquid chromatography gives more degree of freedom in separation techniques due to diverse choice of organic and aqueous medium as mobile phase. Several mechanisms of separation could be employed in this system including polarity and ionic charge on the pesticide residues (Gennaro et al. 1996; Stachniuk and Fornal 2016). Apart from pesticide residues themselves, liquid chromatography is also able to analyze and detect pesticide metabolites and degradation products (Radford et al. 2014). To decrease the analysis time for analysis of multiple pesticide residues, sample preparation steps such as QuEChERS have been employed before liquid chromatography (Zheng et al. 2018). Recently, it is also coupled with high-resolution MS for rapid, multi-residue analysis (Gómez-Ramos et al. 2013). However, it should be kept in mind that sample preparation step must efficiently enrich all the potential pesticide residues. While using MS detectors for analysis, care must be taken that ionization, detection, and mass analyzer are compatible for all the potential pesticide residues (Helen et al. 2015).

Another significant development in the column is to use much finer (< 2 μm) stationary phase particles as compared with 3–5 μm diameter particles used in conventional high-performance liquid chromatography (HPLC). The reduction in particles size increases the chromatographic resolution by several folds due to narrow and concentrated sample band. The linear velocity of the mobile phase also increases with decreased particle size providing rapid analysis. Such LC systems having particle size of stationary size lower than 2 microns are collectively called as ultrahigh-performance liquid chromatography (UHPLC) or simply ultraperformance LC (UPLC) and are recently being preferred for multi-residue analysis (Petrie et al. 2016; Tong et al. 2016). Using a narrow-bore, short analytical columns with high mobile phase flow rate also contributes to rapid analysis. In this direction, monolithic liquid chromatography columns have emerged as viable alternative. These columns are constructed from organic polymers through in situ polymerization of the monomers. Depending on the type of monomer, the monolithic column could be uncharged and hydrophobic in nature to allow efficient reversed-phase interaction. Due to their small size and wide pores, monolithic columns allow efficient separation. One of the major advantages of monolithic columns is that they can withstand very high flow rate of up to 10 mL min^{-1} without generating significant back pressures. This significantly reduces the analysis time (Tanaka et al. 2001; Díaz-Bao et al. 2015).

Recent advancement in the instrumentation has made possible to fabricate narrow-bore columns of different diameters such as 0.5–1.0 mm used in micro-LC (μLC), 100–500 μm diameter column in capillary LC (CLC), and less than 100 μm diameter column in nanoliquid LC (nano-LC) (Guiochon and Colin 1984; Asensio-Ramos et al. 2017). In nano-LC, flow rate of nanolitresmin^{-1} could be achieved which provides excellent sensitivity. Such narrow-bore analytical columns also allow fabrication of miniaturized chromatographic systems with high resolution. Another development in LC columns is the use of fused silica particles as stationary phase (Ali et al. 2009). The narrow size distribution and high particle density of fused silica allow homogeneous, efficient packing of the chromatographic column. The chromatographic resolution obtained with these particles is comparable to that obtained with sub-2 μm particles but at significantly lower back pressures.

Similar to GCxGC, multidimensional LC also contributes to rapid analysis time (Dugo et al. 2008; Cacciola et al. 2017). For example, two-dimensional LC x LC system combining hydrophilic interaction liquid chromatography (HILIC) and reversed-phase liquid chromatography (RPLC) has been recently reported which is capable of detecting 300 pesticides (Kittlaus et al. 2013). The HILIC separation system is used for separating polar compounds by utilizing a polar stationary phase and organic-aqueous solvent mix as mobile phase. The water in the mobile phase is used as strong eluting agent. As compared with traditional RPLC, it provides much better separation and subsequent detection of polar residues in MS (van Nuijs et al. 2011).

7.6 Modern Optical Sensing Strategies

Recent modern optical sensor offers a facile, quick, and inexpensive approach for sensitive and specific detection of pesticide based on lateral flow immunoassay (LFA), colorimetric assay, fluorescence, surface-enhanced Raman scattering (SERS), and chemiluminescence strategy signal variations. Mostly, these sensors have recognition component that can interact specially with preferred target analyte (pesticide) and transducer component that is used for signaling the requisite result. Enzyme, antibody, molecularly imprinted polymers, aptamer, and affibody are used as recognition elements in the modern sensing approaches; these modern sensing techniques magnet scientific community to advance analytical narration of sensor (Yan et al. 2018).

7.7 Lateral Flow Immunochromatographic Assay

Dipstick test or lateral flow assay (LFA) is a paper-based support system for the detection and quantification of target analytes in multifarious mixtures, where the sample having target molecules is employed on a test device and the results are demonstrated within 5–30 min. Economical and ease of production of this paper-based substrate has ensued in the escalation of its applications to various fields of food industry, beverages, and biomedical application wherein prompt tests are essential (Yan et al. 2018).

Lateral flow or dipstick test strips technology, also familiar as lateral flow immunochromatographic assay (LFIA), is a paper-based immune recognition assay conjoining the principles of thin-layer chromatography. This lateral flow machinery exploits specific immunoreactions (antigen-antibody interaction) along lateral flow inside porous paper strips. This strips technology is economical, fast, easy to perform, and an affordable point-of-care diagnostic tool and nowadays widely applied in the detection of a variety of molecules such as toxins, pesticides, pollutant, microorganisms, and hormones. Colloidal gold, silver, selenium, carbon nanoparticles, color latex beds, quantum dot (Verheijen et al. 1998; Liu et al. 2011), etc. are widely exploited as labels of antibody to sense the presence of desired molecules. In comparison with sophisticated instrumental examination, LFA is a simple, rapid, and low-priced technique suitable for medical diagnosis, on-site testing, point-of-care testing, and detection of various environmental and agricultural pollutants as well (Zhou et al. 2004; Delmulle et al. 2005; Molinelli et al. 2008; Blažková et al. 2009; Liu et al. 2011). Colloidal gold nanoparticles (GNPs) are extensively used by scientific community due to their bright color and physiochemical stability. In the LFAs either competitive or sandwich-type immunoassays, the GNPs conjugated antibody flow along a paper matrix together with the target analyte compelled by capillary force. Ultimately GNP-conjugated antibody accumulates or assembles upon immune recognition at a defined area pre-treated by an antibody or antigen. As a consequence of immunoreaction, qualitative or semiquantitative detection of various target molecules is thus recognized by an optical reader either by naked eyes or using the assistance of optical density analysis.

7.7.1 Principle of Lateral Flow Immunoassay

A simple principle works behind the LFA technique. To describe, a liquid sample having the analyte of interest moves with the assistance of capillary action through various zones of polymeric or paper strips, on which molecules that can specifically capture the analyte are pre-adhered. A classical lateral flow test strip (Fig. 7.1) comprises of overlapping membranes that are fixed on a backing card for better stability and handling. As shown in Fig. 7.1, the sample is applied on the adsorbent sample pad at one end of the test strip that is infused with buffer salts and surfactants that make the sample suitable for interaction with the detection platform system. The sample pad of LFA takes care that the analyte of interest present in the sample will be able to bind to the capture reagents of conjugates as well as on the membrane. The applied sample travels through the conjugate release matrix (pad), which holds recognition receptor such as antibodies or affibody that is specific to the target analyte. Antibodies are conjugated to some colored or fluorescent particles – usually colloidal gold and latex beds or microspheres. The sample is applied on the sample pad of the strips, together with the GNP-conjugated antibody bound to the target analyte, and travels along the strip into the detection area. The detection zone of LFA is constituted by a porous membrane (nitrocellulose membrane) with specific bio-receptor or components (generally antibodies, aptamer, or antigens) immobilized in the test lines usually known as capture bio-receptor. The role of capture bio-receptor is to respond with the analyte bound to the conjugated antibody. Recognition of the analyte presents in the sample consequences in an appropriate response on the test line, whereas a response on the control line points toward the proper liquid flow through the strip. The color readout, denoted by the lines appearing with different intensities, can be evaluated by the naked eye or via a devoted

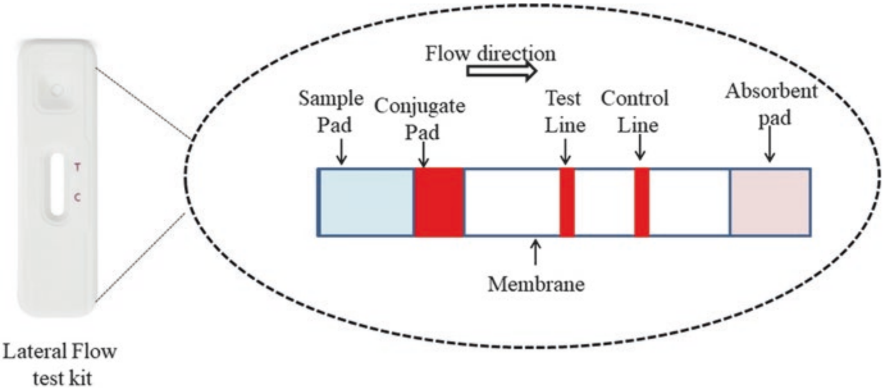

Fig. 7.1 Schematic illustration of a lateral flow immunoassay test strip. Lateral flow machinery exploits specific immunoreactions (antigen-antibody interaction) along lateral flow inside a porous paper strips. Typically lateral flow assay (LFA) is generally constituted of the following components: sample pad, conjugate matrix pad, bio-receptor immobilized (antibodies or affibody) membrane, and adsorbent pad

colorimetry or optical reader. In recent century, there has been increasing demand for rapid point-of-care diagnostic test for multiple analytes concomitantly under the same conditions. And multiple diagnostic assays with multiple test lines of antibodies specific to different target analytes can be immobilized in an array setup (Xu et al. 2014; Yen et al. 2015). Likewise, multiple test lines with the same antibody immobilized on LFA test strips can be used for semiquantitative assays, and this assay is commonly known as “ladder bars” assay. The principle that works behind this assay is based on the stepwise capture of color nanoparticle conjugate-antigen complexes by the immobilized antibody on each successive line. Subsequently, the number of lines seeming on the test strip is directly proportional to the concentration of the analyte (Leung et al. 2008; Fung et al. 2009; Fang et al. 2011; Koczula and Gallotta 2016). An absorbent pad is attached at the end of the strip to maintain movement of the liquid flows across the device because of the capillary force of the strip material. On the other hand, the absorbent pad is use to prevent backflow of the liquid and wick the excess reagents.

Two formats of the LFIA can be distinguished: direct and competitive. A direct test is used for larger analytes such as the protein p24 antigen practiced in the human immunodeficiency virus (HIV) test (Workman et al. 2009) and on the other example human chorionic gonadotropin (hCG) having multiple antigenic sites used in pregnancy tests (Butler et al. 2001). The hCG-based pregnancy tests are an example of a sandwich-based assay, where the target analyte is immobilized between two paired antibodies raised against two different antigenic sites. In the direct lateral flow immunoassay test, the presence of the test line indicates a positive result, and the absence of the test line indicates a negative result. However, the occurrence of the control line directs the legitimacy of the assay, and the control line usually contains species-specific anti-immunoglobulin antibodies, specific for the antibody in the defined conjugate. In the competitive tests, small analytes having single antigenic site are used, which cannot bind to two antibodies concurrently. In this assay, the analyte blocks the binding sites on the antibodies on the test line, inhibiting their interactions with the colored conjugate receptor. Therefore, a positive result is showed by the absence of signaling the test line, whereas the control line should be noticeable independently of the test result.

7.7.2 Magnetic Particle Aggregate-Based Lateral Flow Immunochromatographic Assay

Typical lateral flow immunochromatographic assay (LFIA) strip comprises of five different modules: a sample pad where a sample solution applies, a conjugate pad loaded with the particle-labeled antibody, a nitrocellulose membrane used as the chromatography matrix, an absorbent pad serving as the liquid sink, and a backing card for supporting all the parts. In general, on the nitrocellulose membrane, goat anti-rabbit antibodies were immobilized as the control line (C-line), whereas a band of coating antigen, paraoxon methyl hapten-OVA, was drawn as the test line (T-line).

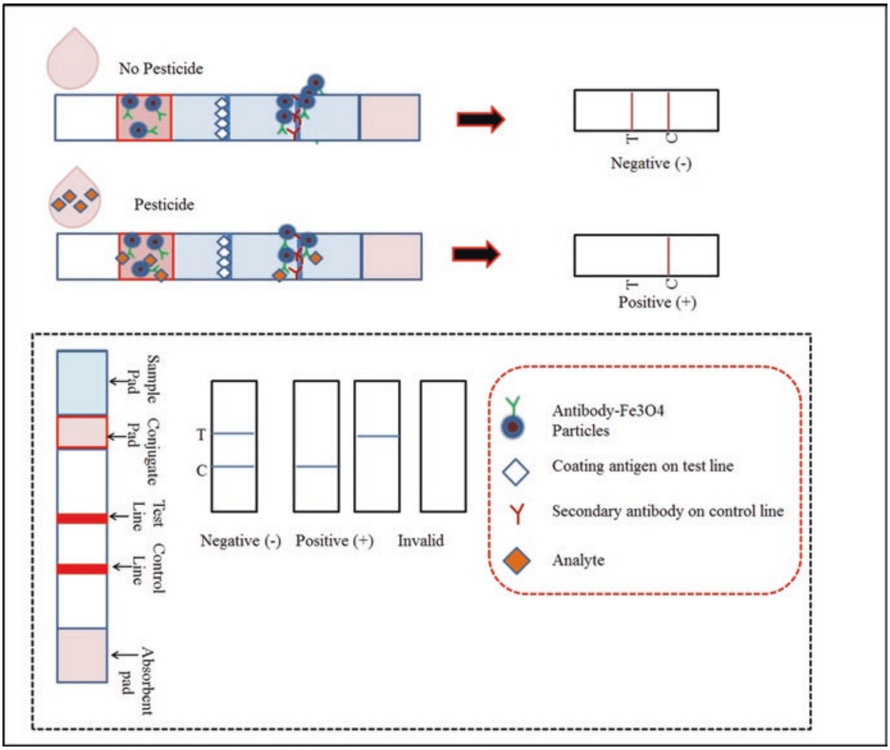

Fig. 7.2 Nanoparticle particle aggregate-based lateral flow immunochromatograpic assay (LFIA). Immunochromatographic assay is based on competitive inhibition, in which a pesticide-protein-carrier conjugate competes with the free Ag present in the sample. In this assay the nitrocellulose membrane immobilized with analyte at test line and secondary antibody on control line

Initially, conjugate pad was immobilized with 2 μL solution of the prepared particle-antibody conjugate. Afterward the abovementioned lateral flow components were dehydrated appropriately. Finally, the lateral flow components were assembled with the overlaps between the sample pad and conjugate pad. To ensure the solution is migrating properly through the strip during the detection for that 2 mm distance should kept between the conjugate pad and the nitrocellulose membrane (Fig. 7.2) (Liu et al. 2011).

Magnetic Fe_3O_4 particles were prepared by cross-linking iron nanoparticles having surface carbonyl groups with poly-L-lysine aggregates. Functionalized magnetic nanoparticles were coupling with antiparaoxon methyl polyclonal antibody, and the resultant particle aggregate-based probes were used in a LFIA of pesticide residue of paraoxon methyl (Fig. 7.2). Quantitative results on the signal amplification effect of Fe_3O_4 nanoparticles by the controlled aggregation were extracted via relative optical density analysis. By this technique, detection limit of paraoxon methyl was found to be 1.7 ng/mL by using the particle aggregates under optimized conditions.

7.7.3 Antibody-Based Electrochemical Sensor

One of the most common pesticides imidacloprid is used as insecticide, for pest control and seed treatment, globally. Imidacloprid has been described as toxic and potential carcinogenic pesticide. The hazardous nature of imidacloprid makes its regular monitoring of great relevance specially in the field of agriculture and environment; consequently, there is an urgent need to develop sensitive and rapid test technique for in-field analysis. In this direction, the scientific community has developed an electrochemical-based competitive immunoassay using specific monoclonal antibodies for the sensitive and fast determination of imidacloprid (Fig. 7.3). The optimized electrochemical biosensor demonstrated a worthy reproducibility and logarithmic response in the range 50–10,000 pM of imidacloprid. By this method, an estimated limit of detection (LOD) has found to be 24 pM, and it was below the maximum levels as permissible by the regulatory authority. Standard analytical techniques such as high-performance liquid chromatography, mass spectrometry, and enzyme-linked immunosorbent assay analysis were also executed for the evaluation of developed biosensor. Where the electro-immuo-biosensor revealed

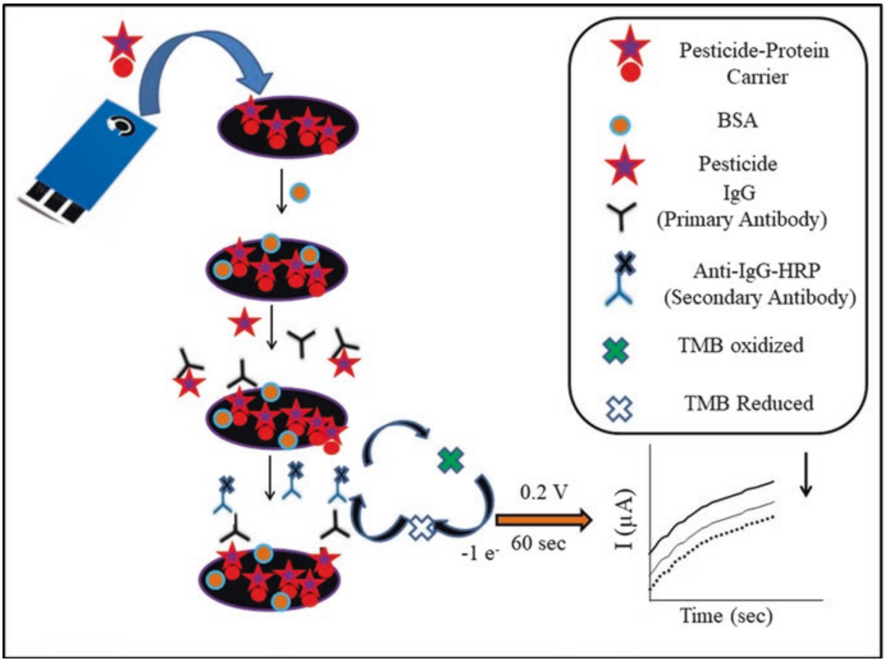

Fig. 7.3 Principle of enzyme-labeled electrochemical immunosensor for the detection of pesticide. The electrochemical immunoassay is based on competitive inhibition, in which a pesticide-protein-carrier conjugate competes with the free Ag present in the sample concentration of pesticide to be monitored which is correlated with the amount of labeled antibody to the corresponding ligand coated on the electrode surface

wide range of linear response along with lower detection limit. The abovementioned features ensure that the developed electrochemical sensor is as an effective, valuable, and applicable method for the infield determination of imidacloprid (DOI: 10.1039/x0xx00000x).

7.8 Enzyme-Based Sensors for the Determination of Pesticides

Several enzyme-based biosensors have been developed using different nanomaterials for the detection of pesticide. The nanomaterials used in the enzyme-based sensors are able to increase the signal amplification, along with sensitivity and specificity for analyte. The most commonly used enzymes in the biosensors for the detection of pesticides are acetylcholinesterase (AChE), organophosphate hydrolase (OPH), and laccase. The principle behind the enzyme-based biosensors reduction of the catalytic activity of enzymes in the presence of pesticides, which act as inhibitors for the enzymes, so this basic mechanism is used for detection of pesticides (Fig. 7.4).

For instance, the substrate acetylcholine is converted into acetic acid and choline in the presence of water by enzyme AChE. Scientific investigators have been using this reaction method to develop AChE-based biosensors for the determination and identification of pesticides in different samples. Several standard methods such as conductometry, optical, piezoelectric, amperometric, and colorimetry have been used in enzyme-based biosensors for the recognition and determination of reaction end products, primarily choline. The response intensity observed from the result indicates the presence of pesticide in the sample.

7.8.1 Paper Sensor Based on the Enzyme

Enzyme-activated paper biosensor was developed for the detection of acetylcholinesterase (AChE) inhibitors including organophosphate and carbamate pesticides. A colorimetric assay based on the Ellman principle, the assay strip is composed of a paper support (1 × 10 cm), onto which glutaraldehyde with AChE, a cross-linking biopolymer chitosan gel, was immobilized. In this assay, 5,5′-dithiobis(2-nitrobenzoic) acid (DTNB) and acetylthiocholine iodide (ATChI) are used as outside reagents. Bioactive paper biosensor assay protocol involves introducing the sample to sensing area through dipping of a paper in the pesticide-containing solution. After incubation with sample, the paper is placed into acetylthiocholine iodide solution to induce enzyme-catalyzed hydrolysis of the substrate and yield a yellow color product, and the yellow color intensity indicates the levels of the AChE inhibitors in sample (Fig. 7.5). This enzyme-based biosensor is capable of detecting

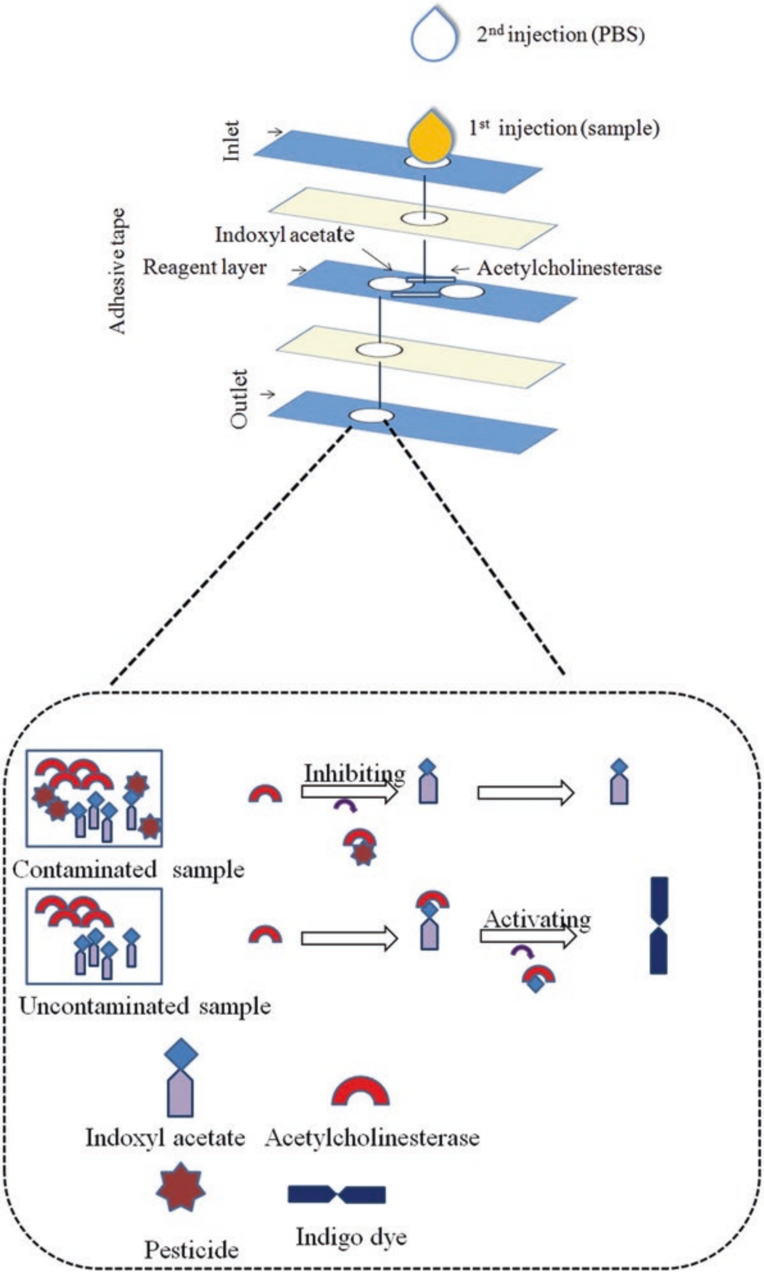

Fig. 7.4 Enzyme immobilized paper-based analytic device for the pesticide detection. The principle behind the enzyme-based biosensors, reduction of the catalytic activity of enzymes in the presence of pesticides, which act as inhibitors for the enzymes, so this basic mechanism is used for detection of pesticides

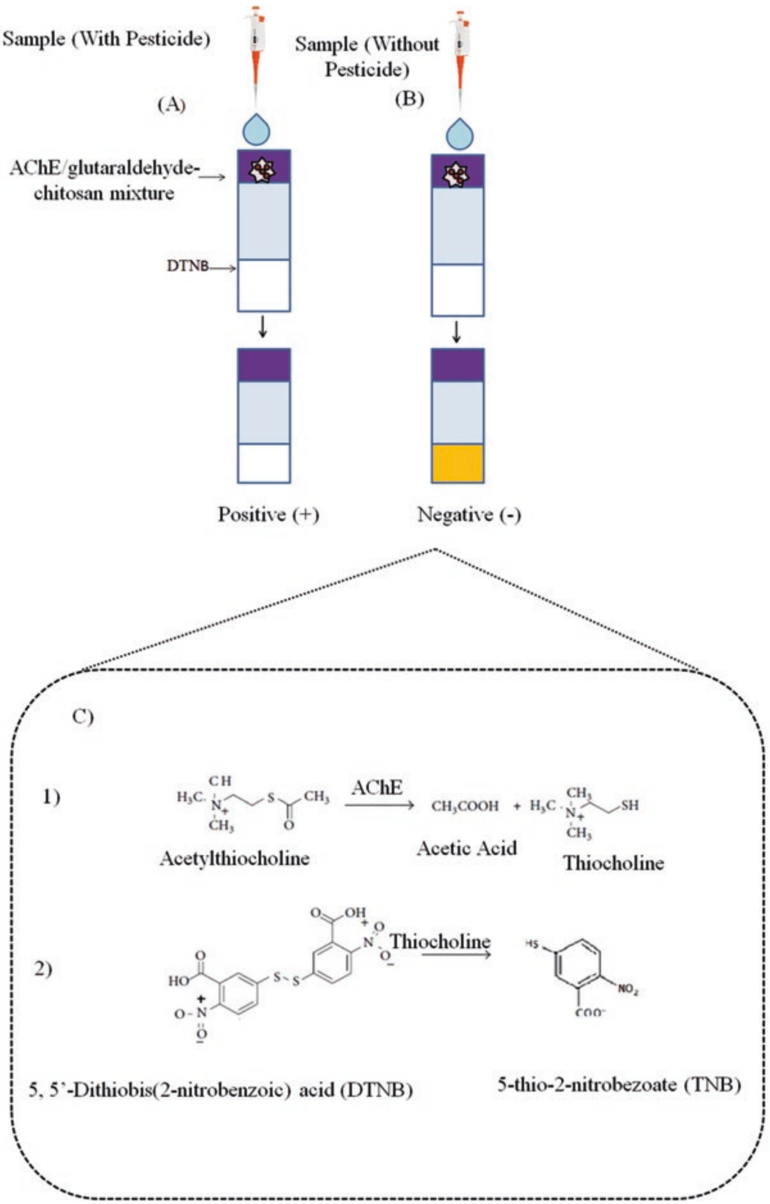

Fig. 7.5 Principle of enzyme-activated paper biosensor for the pesticide detection. The assay strip is composed of a paper support, onto which AChE was immobilized. In this assay, 5, 5′-dithiobis(2-nitrobenzoic) acid (DTNB) and acetylthiocholine iodide (ATChI) are used as outside reagents. Introducing the sample to sensing area through dipping of a paper in the pesticide-containing solution. After incubation with sample, the paper is placed into acetylthiocholine iodide solution to induce enzyme-catalyzed hydrolysis of the substrate and yield a yellow color product, and the yellow color intensity indicates the levels of the AChE inhibitors in sample

organophosphate and carbamate pesticides with worthy detection limits (methomyl = 6.16×10^{-4} mM and profenofos = 0.27 mM). Results obtained from paper-based biosensor are quick, sensitive, specific, economical, portable, disposable, and user-friendly (Badawy and El-Aswad 2014).

Contamination of soil, water, and agriculture field by pesticides is an ever-increasing problem, associated with field of human health care and environment management. Globally, extensive research has been done in the field of pesticide detection methods, with an aim to make the detection system more convenient, fast, economical, and easy to use. Several rapid detection strategies for pesticide have been developed; among them paper-based assay is persuasive for real-time pesticide sensing due to its exceptional advantages including disposability; portable, on-site use; and low price. A layer of three sheets of patterned paper-based colorimetric biosensor for chlorpyrifos has been developed. In this colorimetric assay, the blue color is produced via the reaction between two molecules, acetylcholinesterase and indoxyl acetate, and this reaction is inhibited by the presence of pesticide molecules in the sample solutions. In the optimized conditions, the estimated detection of limit (LOD) has found to be 8.60 ppm for pesticide by this method within 5 min. For water quality monitoring and food analysis, the paper-based device is to be used as a first-screening analytic device (Kim et al. 2018).

7.9 Nucleic Acid-Based Techniques for Pesticide Analysis

7.9.1 Aptamers

Aptamers are synthetic oligonucleotide biomolecules, typically single-stranded DNA and ribonucleic acid (RNA) that can bind to specific targeted molecules with high affinity and specificity. Aptamers have been extensively used in both basic and clinical research purposes, exclusively as a therapeutic and diagnostic agent. Aptamers have tremendous conformational change capability upon target analyte binding; this unique character makes them the most suitable and fit candidate to design on-site portable bio-devices for analytical applications (Sekhon et al. 2018).

Single-stranded DNA (ssDNA) or RNA nucleic acid aptamers recognize a wide range of target molecules with high affinity and specificity and have remarkable applications as therapeutic and diagnostic agent (Sekhon et al. 2018). Aptamers have the ability to accurately bind a large variety of small molecules including amino acids, metal ions, small peptides, proteins, viruses, organic molecules, and biological cells (Wang et al. 2011). Like antibodies, aptamers have a great potential as analytical tools for detection owing to their capacity to form expanded three-dimensional structure and shape (Sekhon et al. 2017). In the field of environmental monitoring, aptamers have generated a huge interest, having higher sensitivity and selectivity in comparison to antibodies. Aptamers can be produced in the large scale by in vitro system, and modification of aptamers with various functional groups can be incorporated into biosensing platforms (Sekhon et al. 2018).

7.9.2 Chemical Synthesis of Aptamer

Aptamer performance can be improved by chemical modification with functional groups, and this chemical modification enables the aptamer to immobilize on suitable substrate and ease the ability for bio-conjugation (Ruscito and DeRosa 2016). Aptamer-based biosensing platform for pesticide detection has not been evolved enough, fairly due to the complex process of aptamer generation and selection. Generally, SELEX (systematic evolution of ligands by exponential enrichment) method is adopted for the generation of aptamer against a variety of small molecule. The main challenge during the selection of aptamer is the partitioning of bound and unbound sequences; particularly, small size target molecule complicates the separation process. To overcome the problems of immobilization of small molecules with the solid matrix, firstly the targeted N-fluoroacetyl glycine pesticide was conjugated with bovine serum albumin (BSA) protein by N-hydroxysuccinimide (NHS) chemistry (Cao et al. 2016). In the recent approach, graphene oxide (GO) has been used for generating aptamers for small-molecule pesticides during SELEX. By this modified GO-SELEX approach, high-affinity aptamers for three different analytes without immobilizing the targets have been successfully generated (Nguyen et al. 2014). In vitro SELEX method has been performed to get high affinity and specificity of aptamers. The most critical asset of SELEX process is efficient partitioning between target binding and non-binding oligonucleotides (Gopinath 2007). DNA aptamers produced against various pesticides are selected from an immobilized random ssDNA library comprising of 10^{14}–10^{15} nucleotides. In this perspective, the ssDNAs binding to the targeted pesticides are eluted from the immobilized ssDNA library after each round of polymerase chain reaction (PCR) and enriched the aptamer as the selection round progresses. Selection of specific aptamer is determined by output to input ratio of fluorescence intensity of the eluted solution, and ratio is absolutely associated with the number of selection rounds. ssDNAs obtained from optimal round selection process are cloned into suitable cloning vector, and bacterial colonies are recognized and picked for DNA sequencing. The top DNA aptamer sequence with the highest homogeneity is selected for further characterization.

7.9.3 Aptasensors for Pesticide Detection

At the current time, biosensor is representing a rapidly expanding field that has noticeably contributed to the reduction and robust detection of environmental pollutants, mostly environmental monitoring of organic pollutant, potentially noxious elements, pesticides, and pathogenic microbes. Several conventional analytical methods are available for environmental monitoring such as chromatographic techniques, mass spectroscopy, etc., which require expensive reagents and laborious sample enrichment and need a skilled person (Lang et al. 2016; Hassani et al. 2017). Therefore, there is an imperative necessity to develop cutting-edge, highly sensitive, and inexpensive sensing devices to detect pollutants and noxious elements, which

Table 7.2 Different aptamer-based sensing platforms for the detection of pesticides

Sensor	Detection	Detection system	Limit	References
Colorimetric	Omethoate	ssDNA-wrapped AuNP aptamer-based nanoprobes	0.1 μmol L^{-1}	Wang et al. (2016)
SPR	Profenofos	Surface plasmon resonance (SPR) sensor	3.6 × 10^{-4}μg mL^{-1}	Dong et al. (2012)
	Profenofos	Fiber-optic SPR-based sensor	2.5 × 10^{-6} μg L^{-1}	Shrivastav et al. (2016)
Electrochemical	Chlorpyrifos	Electrochemical aptasensor based on CuO NFs and c-SWCNTs	70 pg mL^{-1}	Xu et al. (2018)
	Profenofos	Photoelectrochemical (PEC) sensor	1 nM	Shi et al. (2012)
Fluorescence	Isocarbophos	Aptamer-based Fluorescence assay	11.4 μM for isocarbophos	Li et al. (2016)
	Profenofos		14.0 μM for profenofos	

are accountable for causing injurious effects to the ecosystems and human health. In the case of accidental release of pesticides, the current available methods are insufficient and ineffective for in situ monitoring of pesticide. In this context, urgently environmental monitoring biosensors are needed that are fast, miniaturized, portable, and easy to operate (Arduini et al. 2013; Zhang et al. 2014b; Guo et al. 2017). Aptamer-based biosensor has been successfully developed and applied in the field of food safety for the investigation of unwanted elements such as antibiotics, biological toxins, heavy metals, etc. These aforesaid aptasensors are worked with the combination of nanomaterials, electrochemistry, and fluorescence technology (Duan et al. 2011; Chen et al. 2012; Jiang et al. 2014; Lu et al. 2015; Luan et al. 2016). Several numbers of small-molecule-binding aptamer have also been reported along with selectivity and specificity (Majerfeld et al. 2005), to develop various aptamer-based biosensor systems (Lee et al. 2010). These aptasensors are widely divided into various platforms such as colorimetric aptasensor, electrochemical aptasensors, fluorescence aptasensor, microcantilever array aptasensor, and surface plasmon resonance (SPR). However, these sensors have been used for pesticide residual analysis. Aptasensor is rapid screening method for the observing of pesticides and this is simple in operation, inexpensive to detect with high specificity and selectivity. The potential for applying modified aptamers to pesticide detection is still developing (Table 7.2).

7.9.4 Colorimetric Aptasensor

Colorimetric biosensors seem to be promising alternatives over traditional techniques for small analyte detection. Aptasensor caring several unique properties such as simplicity, rapidity, and cost-effectiveness. In the field of biosensor research,

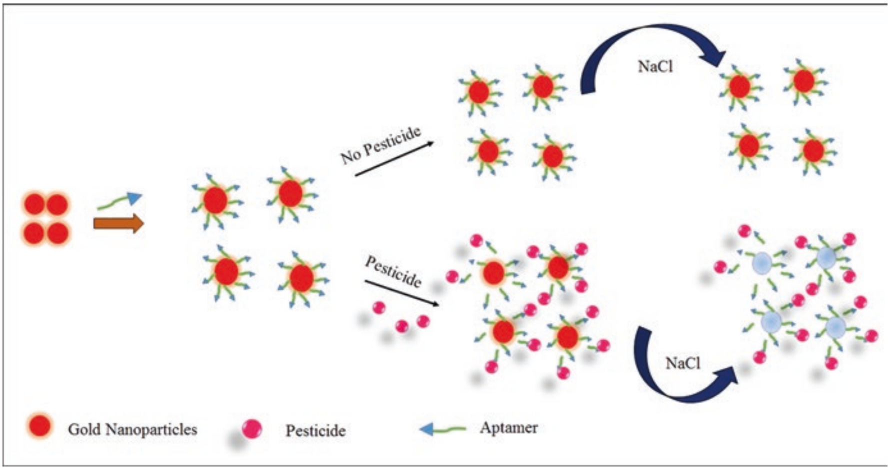

Fig. 7.6 Gold nanoparticle-conjugated aptamer-based colorimetric assay for the detection of pesticide. In the presence of pesticide, gold nanoparticle-conjugated aptamers apart from gold nanoparticles and nanoparticles aggregate when sodium chloride solution is added in the reaction tubes. In the absence of pesticide, nanoparticle does not aggregate in the presence of sodium chloride solution

gold nanoparticles (GNPs) were the most established and trusted nanoparticles due to their distinct physical and chemical attributes, serving as excellent nanoparticles for the chemical or biological sensors. Gold nanoparticles are experienced an ideal optical indicator for signaling analyte recognition events, because of their different states of gold nanoparticles, to make ensuing in distinct color changes. In the recent time, aptamer-based biosensors (aptasensors) have practiced and gained significant attention to overcome the lack of specificity of the colorimetric sensors. Gold nanoparticles conjugated aptamer established colorimetric assay for the detection of pesticide exhibited high selectivity, subsequent disconnection of aptamer molecules from gold nanoparticle. This gold nanoparticle-based colorimetric aptasensor demonstrated a good linearity, which using the pesticide-binding aptamer and target-induced color changes in the gold nanoparticles (Fig. 7.6).

7.9.5 Fluorescence Aptasensor

A number of research reports have employed aptamer-based biosensor for the detection of organophosphorus pesticides with fluorescence approaches (Weerathunge et al. 2014; Zhang et al. 2014a; Dou et al. 2015). The fluorescence-based sensing of analyte has been broadly applied via fluorescent-labeled baroreceptor with high sensitivity. A fluorescence method based on the specific recognition of aptamer was evaluated for detection of organophosphorus pesticides such as isocarbophos and profenofos, and this fluorescence-based detection method combined aptamers with

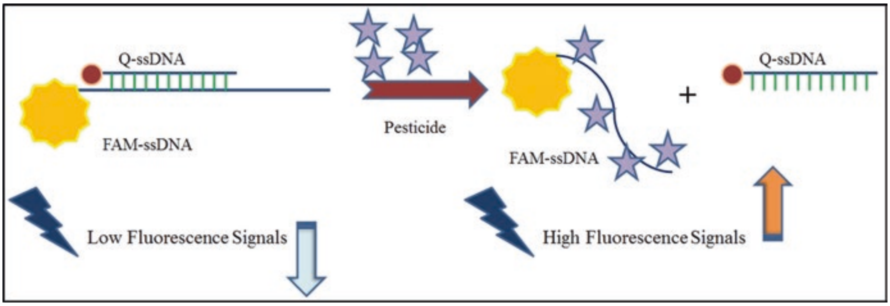

Fig. 7.7 Quencher-based molecular beacon probe for fast screening tests for pesticide detection. In this technique, carboxyfluorescein (FAM) fluorophore was labeled at the 5′-end of the aptamer, and its complementary sequence is tagged with the quencher DABCYL at the 3′-end. Fluorophore-tagged aptamer and its complementary sequence hybridize to form a double-stranded structure. As a consequence of hybridization reaction, fluorescence resonance energy transfer occurs as the fluorophore is close to the quencher, resulting in weak signal intensity as the fluorescence is quenched. In the presence of pesticide, double standard aptamers separated from each other and consequence of this reaction fluorescence signal enhance

highly sensitive fluorescence detection method. In this method, carboxyfluorescein (FAM) fluorophore was labeled at the 5′-end of the aptamer, and its complementary sequence is tagged with the quencher DABCYL at the 3′-end. In this experiment, fluorophore-tagged aptamer and its complementary sequence hybridize to form a double-stranded structure. As a consequence of hybridization reaction, fluorescence resonance energy transfer occurs as the fluorophore is close to the quencher, resulting in weak signal intensity as the fluorescence is quenched. Though target molecules (isocarbophos and profenofos) specifically recognize and with binds by aptamer, then aptamer dissociates from the complementary sequence, leading to the recovery of fluorescence and hence increasing the intensity signal (Fig. 7.7). This quencher-based molecular beacon probe method was low cost and appropriate for fast screening tests for pesticide detection, as well as the specificity and sensitivity for target molecules such as isocarbophos and profenofos (Sekhon et al. 2018; Li et al. 2016).

7.9.6 Surface Plasmon Resonance Sensor

Surface plasmon resonance (SPR) is an optical analytical technique that induces plasmons via generation of electromagnetic waves. This optical technique stimulated the resonant conduction electrons by the interface between negative and positive materials stirred by incident light. The above optical analytical technique also allows the detection of mass rise on the surface of metal substrates. SPR-based chemosensor or biosensor is usually known as a label-free detection technique for analyte; this technique is rapid, highly sensitive, and highly selective. SPR based chemosensor or biosensors usually known as a label-free detection technique for analyate, this technique is rapid, highly sensitive and highly selective. In another sensing platform, molecularly imprinted polymer (MIP)-based SPR sensor has been developed, and it is used to detect profenofos in pesticide-spiked samples (Dong et al. 2012). Molecularly imprinted polymer (MIP)-based SPR sensor has displayed high sensitivity and selectivity and good stability, and its detection limit was found to be in the range of 0.001–0.1 μg mL^{-1}. However in another similar study, SPR and molecular imprinting techniques along with optical fiber technology has been reported for the detection of profenofos (Shrivastav et al. 2016). In the field of biosensing, molecular imprinting is modern techniques, and it forms three-dimensional binding pockets with identical complementary shape and size of the specific template molecule. The binding of template molecule with molecularly imprinted polymer (MIP) layer is recognized by SPR technique through change in the dielectric nature of the sensing polymer surface.

7.9.7 Aptamer-Based Electrochemical Sensors

Aptamer-based electrochemical sensing mechanism is shown in Fig. 7.9. In this sensing method, bare glassy carbon electrode (GCE) was loaded with an adhesive agent (Nafion) (McGovern et al. 2003). Then, an adhesive-loaded electrode was modified with two different nanocomposites comprising of copper oxide (CuO) nanoflowers and carboxyl-functionalized single-walled carbon nanotubes (c-SWCNTs). However, the surface area of the electrode is increased with the help of CuO-SWCNT nanocomposite, and coating on the electrode enhances the electron transfer. And c-SWCNTs were liable for immobilizing the aminated probes and directly involved in the hybridization between aptamers and aminated probes. The 3′ distal end of aptamer was complementary with amino-modified capture probe, and its 5′ distal was labeled with an amino group at its 5′ distal terminus. Carboxyl-functionalized SWCNTs were immobilized with p-(aminomethyl)phenyl (AMP) by covalent bonding, between the carboxyl group on c-SWCNTs and its amino group. In another study, the electrode surface was immobilized with a specific aptamer, which was used to detect chlorpyrifos pesticide (Dai et al. 2012). In the above study, to monitor the DNA hybridization event, differential pulse voltammetry (DPV) of methylene blue was adopted. In this experiment, methylene blue was used as a redox indicator for DNA hybridization, and it can able to bind with single-stranded DNA or double-stranded DNA chains in a non-covalent manner (Kelley et al. 1999; Gorodetsky et al. 2008). The specific recognition of methylene blue with unbound guanine base of nucleic acid was key reactions of the methylene blue with nucleic acid chain (Erdem et al. 2001), the intercalation into double-stranded DNA base pairs and the electrostatic adsorption (Tani et al. 2001; Castaño-Álvarez et al. 2007). By adding chlorpyrifos pesticide on the working electrode, aptamer-chlorpyrifos complex structure was formed, decreasing the amount of methylene blue bound to guanine bases in the aptamer domain. Subsequently, the aptamer was enacted to dissociate from semi-duplex, resulting in the escape of methylene blue from the

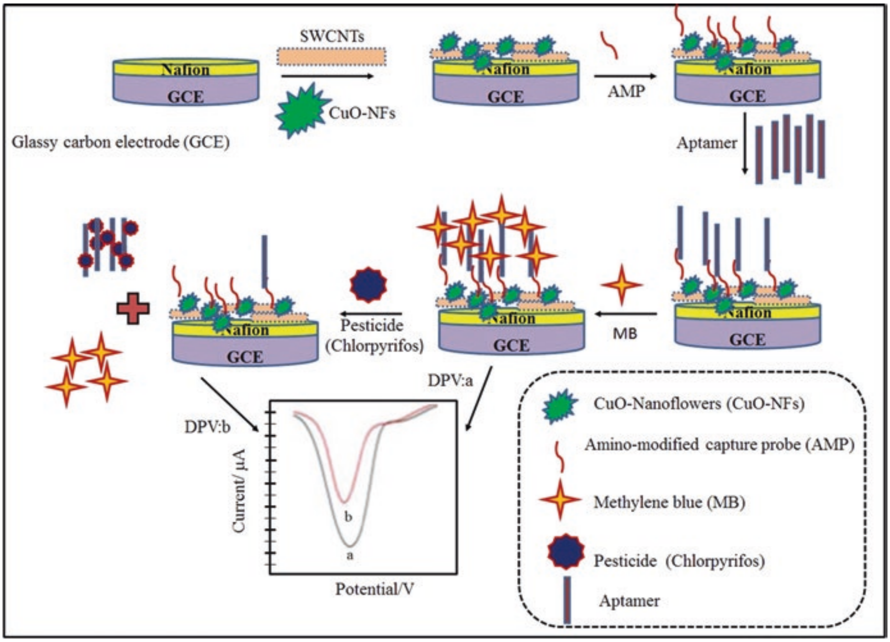

Fig. 7.8 Graphic sketch of the aptamer-based electrochemical biosensor for selective detection of pesticide. Electrode surface was immobilized with specific aptamer, which was used to detect chlorpyrifos pesticide. To monitor the DNA hybridization event, differential pulse voltammetry (DPV) of methylene blue was implemented. Methylene blue was used as a redox indicator for DNA hybridization, and it can able to bind with single-stranded DNA or double-stranded DNA chains in a non-covalent manner. The specific recognition of methylene blue with unbound guanine base of nucleic acid was a key reaction of the methylene blue with nucleic acid chain, the intercalation into double-stranded DNA base pairs, and the electrostatic adsorption. Change of DPV signal can be used to quantify chlorpyrifos

sensing surface of the electrode. Thus, when chlorpyrifos concentration was increased, the DPV peak current of methylene blue decreases. Therefore, the change of DPV signal can be used to quantify chlorpyrifos (Fig. 7.8). It is well-known that nucleic acids can be denatured by urea, so this biosensor can be simply rejuvenated by dipping in urea solution and also be recombined with the aptamer; in this way the biosensor can achieve repeated detection of chlorpyrifos (Xu et al. 2018).

7.10 Inner-Filter Effect-Based Sensor for the Detection of Pesticide

The inner-filter effect (IFE)-based sensing platform has been developed for the detection of pesticide; IFE has been developed between gold nanoparticles (AuNPs) and ratiometric fluorescent quantum dots (RF-QDs). This inner-filter effect has

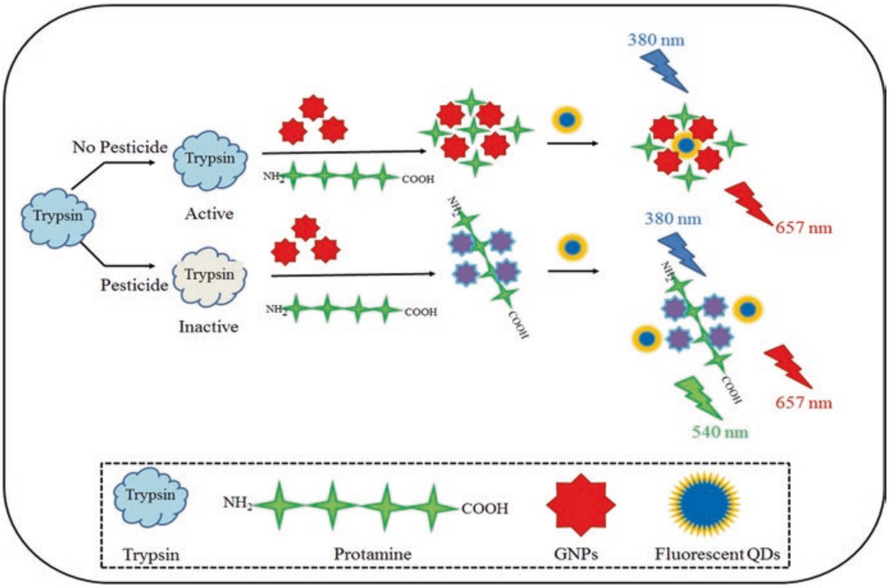

Fig. 7.9 Principle of inner-filter effect-based sensor for the detection of organophosphorus pesticide using gold nanoparticles on fluorescent quantum dots (QDs). In this sensing technique, two differently colored CdTe QDs have been used for the development of ratiometric-QDs by hybridization, in which in the silica sphere red emissive QDs were entrapped to act as the reference signal and the green emissive QDs were covalently attached on the silica surface serving as the response signal. Fluorescence of QDs could be effectively turned on by using protamine molecules (PM), due to their strong electrostatic attraction that exists between the protamine and AuNPs. The chemical nature of protamine is a protein; it can easily be hydrolyzed by a trypsin enzyme, leading to fluorescence quenching. In this assay, the activity of trypsin could be inhibited via parathion methyl, and then the fluorescence could be recovered again.

been used for the sensitive detection of organophosphorus pesticides. In this sensing technique, two differently colored CdTe QDs have been used for the development of RF-QDs by hybridization, in which in the silica sphere red emissive QDs were entrapped to act as the reference signal and the green emissive QDs were covalently attached on the silica surface serving as the response signal. In this assay, AuNPs were used as quencher molecules, and it quenched the fluorescence of RF-QDs by gold nanoparticles based on IFE. Fluorescence of QDs could be effectively turned on by using protamine molecules (PM), due to their strong electrostatic attraction that exists between the protamine and AuNPs. The chemical nature of protamine is a protein, and it can easily be hydrolyzed by a trypsin enzyme, leading to fluorescence quenching. In this assay, the activity of trypsin could be inhibited via parathion methyl, and then the fluorescence could be recovered again. The inhibition efficiency of PM to trypsin activity was estimated by measuring the fluorescence of RF-QDs. In the optimized conditions, the detection limit was found to be 0.018 ng mL^{-1} by this method. The detection strategy is shown in Fig. 7.9.

7.11 Advantages of Biosensors

The design and applications of various types of biosensors and chemical sensors have been discussed which are widely used for the quantitative and quantitative assessment of various types of pesticides. Different varieties of strip-based diagnostic or detection tools are available both on research level and commercial scales. Generally, the strip-based sensors (including lateral flow assays and screen-printed electrode-based sensor) function on the principle of color or fluorescence change in the presence of the target analytes. The sensitivity and specificity of the tools are provided with a judicious selection of dyes or nanoparticles/enzyme alongside the biorecognition molecules, e.g., antibodies, aptamers, and nucleic acids. In comparison to bulky and laboratory-based methods, the lateral flow assays (LFAs) are rapid, simple, and low cost and do not require specialized trained persons to operate. Thus, they are categorized as point-of-care testing tools. Time to be spent in testing and waiting for the results is reduced from hours to minutes. With improvement in several component qualities, it has become possible to design LFAs with added features of multiplexed analysis and accurate assessment of color intensities to provide high sensitivities. In overall, future successes and adoption of strip-based sensors in a wide range of environmental monitoring application call for the realization of more stable devices capable of handling multiple analytes with high sensitivity without sacrificing the simplicity and cost advantages.

7.12 Conclusion

Disposable strip-based biosensors have their intrinsic advantages and some disadvantages, but their cost-effectiveness and portability have turned them as a potential possibility for "point-of-care" (POC) testing of various pesticides. The fabrication of robust, low-cost, reliable, and sensitive sensors with the aid of both simple naked eye-based and portable readout-based detectors is the driving factor in this sensor's technology area. The pending limitations can be overcome by adapting new specific recognition elements and better signal generative particles or systems. The integration of these devices with card readers or smartphones can make them more user-friendly and will provide more accurate quantitative information. The development of LFAs and paper sensors with multiplexing capabilities will further add to their practical utility. In the future, it is expected that LFAs and portable user-friendly sensors will be made available to the general public for POC testing of complex parameters, e.g., dengue, chikungunya, typhoid, etc. These tools have immense significance toward the screening of food and water samples for pollutants like pesticides, heavy metals, pathogens, etc. In overall, future successes and adoption of LFAs paper sensors in a wide range of environmental monitoring application call for the realization of more stable devices capable of handling multiple analytes with high sensitivity without sacrificing the simplicity and cost advantages.

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Chapter 8
Metal and Ion Detection Using Electrochemical and Wireless Sensor

Rajnish Kaur, Aanchal, and Varun A. Chhabra

Contents

Abstract Heavy metal ions are mostly found in water bodies through fertilizers and industrial as well as domestic waste which shows adverse effect on human health and environment. Their detection in environment and food is mandatory as they are toxic and non-biodegradable. There is an urgent need of effective guidelines for the detection of toxic heavy metal ions like lead, cadmium, chromium, mercury, arsenic, etc. Exposure of these materials will result in severe complications in the future. Excessive damage can be done by these metal ions as these can get accumulated in the body and food chain. Various sources of contamination include municipal wastewater, industrial wastewater, mining wastes, etc. Cadmium is one of the most toxic elements, and its detection is done by carbon nanotubes, graphene, metal nanoparticles, etc. The basic principle of working of electrochemical sensors and three-electrode setup has been discussed in detail. Fabrication of various organic as well as inorganic materials on electrode surface for sensing toxic heavy metal ions has been explained.

Cost-effective methods for determination of traces of these metal ions have been discussed on the basis of electrochemical sensors. These sensors include various sensory materials such as inorganic, organic as well as biomaterials and wireless sensors

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which include basic inductive capacitor (LC) sensors. Different electrochemical analysis techniques are stated like cyclic voltammetry, linear sweep anodic stripping voltammetry, square wave anodic stripping voltammetry, etc. Unique properties of metal nanoparticles, quantum dots, graphene, carbon nanotubes, polymers, enzymes, etc. have been highlighted for detection of heavy metal ions. Detection limits obtained by fabricating different materials on electrodes and their composites have been mentioned for different traces of toxic metal ions. In this article, the performance analysis of different metal ion detections has been done on the basis of inorganic nanomaterials, organic materials, biomaterials and wireless sensors. It is observed that in case of inorganic nanomaterials, the detection limit achieved varied from 0.04 μg L^{-1} to 500 μg L^{-1}. In case of organic material, the detection limit for metal ion detection is from 0.3 μg L^{-1} to 13 μg L^{-1}, but in case of biomaterials, it is around 5×10^{-10} M to 2.5×10^{-8} M. And in case of wireless sensors, the detection sensitivity is around 50 μM to 500 μM. So, it can be concluded that inorganic nanomaterials have the best sensitivity followed by organic materials and then biomaterials and wireless sensors.

Keywords Metal ions · Detection limit · Electrochemical · Wireless sensing

8.1 Introduction

Toxic heavy metal ions that are mostly found in water bodies through fertilizers are the major environmental pollutants with an adverse effect on humans as well as animals (Cui et al. 2015). These heavy metal ions have potential to cause severe damage to the liver, brain, kidneys, lungs, etc. (Tu et al. 2004). The main sources of production for these toxic materials are industries, fertilizers, pesticides and household wastes (Baruah and Dutta 2009; Tuzen et al. 2006). As heavy metal ions are non-biodegradable, it is mandatory to detect these toxic materials for their treatment accordingly. Electrochemical sensing of heavy metal ions is one of the methods that grabs attention in the past few years (Aragay and Merkoçi 2012). In this sensing technique, there is a three-electrode system, namely, reference electrode (RE), counter electrode (CE) and working electrode (WE) (Hanrahan et al. 2004). Various parameters like current, potential, capacitance, electrochemical impedance, etc. have been measured as a response to the presence of heavy metal ions (Price 2019). Detection signals are noted and various techniques are used for electrochemical sensing like potentiostatic (controlled-potential) technique, galvanostatic (controlled-current) technique, impedance measurement or electrochemiluminescence (using quantum dots) (Luo et al. 2006). Current or potential can be controlled using either galvanostatic or potentiostatic measurement techniques. Aqueous solution containing heavy metal ions acts as electrolyte (Cui et al. 2014). There are two types of electrochemical setup, namely, (1) two-electrode cell arrangement and (2) three-electrode cell arrangement. In two-electrode cell arrangement, half reactions take place at the working electrode (WE), and cell potential is measured through the reference electrode (RE). Excitation signal is provided by

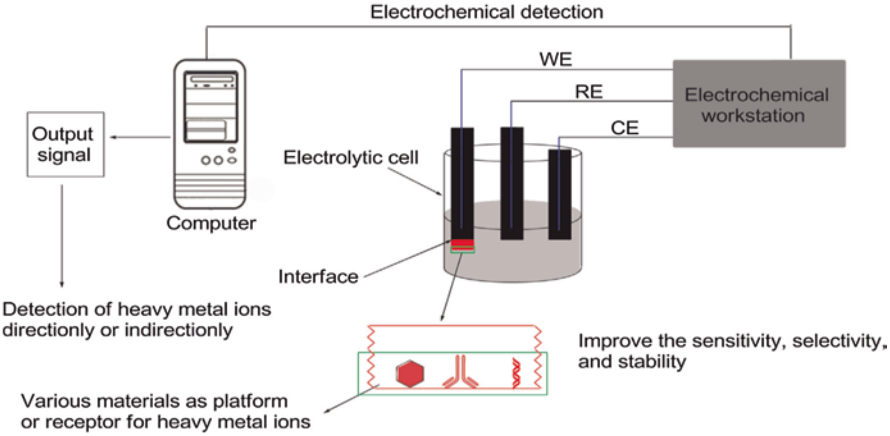

Fig. 8.1 General principle of electrochemical sensing of heavy metal ions. Three-electrode system, namely, reference electrode (RE), counter electrode (CE) and working electrode (WE), is dipped in an electrolyte solution, forming an electrolytic cell (Cui et al. 2015). (Copyrights 2015, with permission from Elsevier)

external power supply. In three-electrode cell arrangement, a new electrode named counter electrode (CE) is introduced, and current is passed between the working and counter electrode. The sections of counter and working electrodes are separated by glass separators. Excitation signals to electrode setup are provided by electrochemical workstation which are embedded with inbuilt power source. Then this electrochemical workstation is connected to a computer in which required software platform is provided which analyse the data received from the experiment (Malik et al. 2019). The general principle of electrochemical sensor is illustrated in Fig. 8.1.

Recent advances in nanomaterials and biomaterials due to their unique physical, chemical and mechanical properties have led to their extensive applications in sensing based on electrochemistry (Luo et al. 2006; Zhang and Fang 2010). By fabricating these materials on the electrode surface, sensing electrodes can be formed for selective detection of heavy metal ions (Chey et al. 2012). Here we will discuss various inorganic, organic as well as biomaterials for selective sensing of heavy metal ions (Sánchez et al. 2010).

8.2 Metal and Ion Detection Using Electrochemical Sensors

8.2.1 Inorganic Nanomaterials

Materials having two or more dimensions with size in the range of 1–100 nm, prepared with inorganic elements, are known as inorganic nanomaterials (West and Halas 2003). Due to their unique electrochemical, optical, magnetic and catalytic properties as well as large surface-area-to-volume ratio, they are commonly used in electrochemical detection of heavy metal ions (Manikandan et al. 2018). Various inorganic nanomaterials include metal, metal oxide, quantum dots, carbon nanotubes and graphene-based nanomaterials (Lu et al. 2018).

Metal Nanoparticles

Metal nanoparticles exhibit various properties like large surface-area-to-volume ratio and electrochemical and optical properties which make them suitable for selective sensing of heavy metal ions (Chen et al. 2013; Kumar et al. 2017). Mercury is a widely used metal nanomaterial in the fabrication of electrode for sensing applications (Nagles et al. 2012). As mercury is difficult to handle because of its toxicity issue, which is a major environmental issue, its usage as electrode material is banned. Instead of mercury, other less toxic metal nanoparticles such as bismuth-coated carbon electrode are used which also show attractive voltammetry performances (Sopha et al. 2014). Using these nanoparticles, different heavy metal ions like cadmium (Cd), lead (Pb), and zinc (Zn) etc. have been detected, and a detection limit of 0.3 μg L^{-1} was obtained for lead (Wang et al. 2000). Such mercury-free electrodes are environmental friendly. Nanocomposite of reduced graphene oxide (rGO) and bismuth (Bi) as an electrode material provides a better choice for trace analysis of heavy metal ions like Cd^{2+}, Pb^{2+}, Zn^{2+} and Cu^{2+} (Prakash 2012; Stozhko et al. 2008). The detection limits by rGO/Bi nanocomposite electrode at different deposition potentials for Cd^{2+}, Pb^{2+}, Zn^{2+} and Cu^{2+} were 2.8, 0.55, 17 and 26 μg L^{-1}, respectively (Sahoo et al. 2013). Other than bismuth, antimony nanoparticle-modified boron-doped diamond electrode has been used for electroanalytical determination of Pb^{2+} and Cd^{2+} by linear sweep anodic stripping voltammetry over the range of 50–500 μg L^{-1} (McGaw and Swain 2006; Toghill et al. 2009).

Another widely used metal nanoparticle for sensing mechanism is gold (Au) nanoparticle. Gold nanoelectrode ensembles (GNEEs) grown by colloidal chemical approach on three-dimensional silicate network are used for electrochemical detection of As, Hg and Cu heavy metal ions (Forsberg et al. 1975; Kumar Jena and Retna Raj 2008). Square wave anodic stripping voltammetry (SWASV) has been used for detection. GNEE electrode shows linear response for As and Hg of up to 15 μg L^{-1} (Kumar Jena and Retna Raj 2008). GNEE electrode exhibits superior analytical performance than existing electrodes. For highly sensitive and selective sensing of Hg, Au nanoparticles/graphene was constructed as electrode (Aragay et al. 2011; Szunerits et al. 2017). The nanocomposite thus facilitates electron transfer processes which further provide selective sensing of Hg. The detection limit calculated was as low as 0.000006 μg L^{-1} which is below the guideline value from the World Health Organization (WHO) (Ding et al. 2014). This advanced nanocomposite electrode was also beneficial for direct detection of Hg in river water specimens (Chey et al. 2012; Ding et al. 2014).

Screen printing electrode (SPE) is also one of the mature techniques which has been widely used for the production of sensors with extremely low cost and for sensitive detection of heavy metal ions (Niu et al. 2013). Gold nanoparticles deposited on disposable screen printing electrodes were developed for enhanced voltammetric detection of Cr (Cathum et al. 2002; Liu et al. 2007). The detection limit of Cr obtained is 5 μg L^{-1} (Liu et al. 2007). On the other hand, Au nanoparticle-modified SPE provides fast and simple detection of trace amounts of Cr (Desmond et al. 1998).

Quantum Dots

Quantum dots are semiconductors that possess many varied properties depending upon their material and structure (Stampfer et al. 2008). Optical properties of quantum dots can be tuned according to their size, i.e. particles can absorb or emit specific wavelengths of light by controlling their size (Jin and Maduraiveeran 2018; Madhura et al. 2019). Its applications in electrochemiluminescent sensing are of great interest. Graphene quantum dots (GQDs) show various applications due to their extraordinary physiochemical properties (Ananthanarayanan et al. 2014). GQDs/gold nanoparticle composite is used for electrochemical detection of heavy metal ions like Hg^{2+} and Cu^{2+} (Li et al. 2013; Ting et al. 2015). It shows ultralow detection limit, i.e. 0.02 nM for $Hg^{2+}$and 0.05 nM for Cu^{2+} (Ting et al. 2015). Fabrication and characterization of SnO_2 quantum dots for sensitive and selective electrochemical sensing of cadmium ion were also studied for sensing of cadmium ions (Ruparelia et al. 2008). The fabricated SnO_2 quantum dot electrode exhibited a low detection limit of 500 μg L^{-1} (Bhanjana et al. 2015b). It is a cost-effective and an easy and accurate detection of cadmium ions (He et al. 1999). Mercury is one of the toxic and hazardous heavy metals that needs to be monitored (Duarte et al. 2015). Zinc oxide quantum dots based electrodes were prepared for highly selective detection of mercury by linear sweep voltammetry (LSV). The detection limit of prepared nanosensor was found to be 5 μg L^{-1} (Bhanjana et al. 2015a).

Metal Oxides

Nanostructured metal oxides possess biocompatibility and nontoxic and catalytic properties, so they can be used as effective electrochemical sensors for heavy metal ions (Solanki et al. 2011). Porous magnesium oxide (MgO) nanoflowers have been synthesized and characterized for highly selective and sensitive detection of Pb and Cd (Gao et al. 2008). It was fabricated on glassy carbon electrode and was electrochemically analysed by square wave anodic stripping voltammetry (Gao et al. 2016). The detection limits obtained for Pb and Cd are 2.1 pM and 81 pM, respectively (Wei et al. 2012). Iron oxide/graphene nanocomposite with plated bismuth was developed as an electrode for electrochemical sensing of Zn^{2+}, Cd^{2+} and Pb^{2+} (Wu et al. 2013). Synergetic effect between graphene and iron oxide nanoparticles has led to the formation of improvement in the electrode properties such as high catalytic activity towards detection of heavy metal ions (Pumera et al. 2010). Detection limits obtained by modified electrode for Zn^{2+}, Cd^{2+} and Pb^{2+} were 0.11 μg L^{-1}, 0.08 μg L^{-1} and 0.07 μg L^{-1}, respectively (Lee et al. 2016). Boehmite, i.e. aluminium oxide hydroxide (γ-AlOOH), shows high absorption capacity towards Cd(II) and Pb(II) (Granados-Correa et al. 2011; Salimi et al. 2017). As metal oxides do not possess good electrical conductivity, they are incorporated with graphite to fabricate electrode for electrochemical platform for detection of Cd(II) and Pb(II) by square wave anodic stripping voltammetry (SWASV) (Gao et al. 2012; Xu et al. 2013). The detection limits obtained for Cd(II) and Pb(II) are 4.46×10^{-11} M and 7.60×10^{-11} M, respectively, which were below the guideline value given by the World Health Organization (Gao et al. 2012).

Carbon Nanotubes (CNTs)

Carbon nanotubes exhibit excellent mechanical, chemical, electrical as well as structural properties that make them suitable for the fabrication of electrodes for detection of toxic heavy metal ions (Musameh et al. 2011). Researchers have proposed various carbon nanotube-based composites in the past few years to explore the potential applications of CNTs due to their properties such as large surface area, high electrocatalytic activity, etc. (Harris 2004). In order to monitor and detect traces of toxic metal ions like copper, lead, zinc, etc., CNT thread-based electrodes have been used (Morton et al. 2009). These type of CNT arrays consist of superlong CNTs that are used for detection of traces of Cu^{2+}, Pb^{2+}, Cd^{2+} and Zn^{2+} (Zhu et al. 2010). The detection limits obtained by these electrodes are 0.27 nM, 1.5 nM, 1.9 nM and 1.4 nM for Cu^{2+}, Pb^{2+}, Cd^{2+} and Zn^{2+}, respectively (Zhao et al. 2014). The CNT thread electrodes lead to simultaneous detection of heavy metal ions. A novel carbon nanotubes/poly(1,2-diaminobenzene) nanocomposite-based electrode was fabricated by multipulse potentiostatic electropolymerization (Gao et al. 2006). The composite thus synthesized by this method exhibits excellent electrical conductivity, high surface area and electrochemical stability (Neves et al. 2004; Wang 2005). Voltammetric determination of traces of heavy metals like Cd^{2+} and Cu^{2+} has been successfully done by the composite film-modified glassy carbon electrode with detection limits obtained as 0.25 μg L^{-1} and 0.33 μg L^{-1} for Cd^{2+} and Cu^{2+}, respectively (Gao et al. 2006). Bismuth-doped carbon nanotube electrode was fabricated by in situ plating of bismuth on screen-printed CNT electrode for detection of traces of lead, cadmium and zinc (Liu et al. 2005; Švancara et al. 2010). Bismuth, due to its environmental friendly nature, performs better during electrochemical analysis than mercury as the latter is difficult to handle because of its toxicity (Hočevar et al. 2005). Screen printing technique was used to fabricate carbon-based electrodes as it produces low-cost and sensitive electrochemical sensors (Goldberg et al. 1994). The detection limit of lead, cadmium and zinc was performed by square wave anodic stripping voltammetry techniques (Sá et al. 2015). The limit of detection obtained by Bi-/CNT-based electrode was 1.3 μg/L, 0.7 μg/L and 12 μg/L for lead, cadmium and zinc, respectively (Hwang et al. 2008). Another novel electrode was constructed by triphenylphosphine-carbon nanotube composite for simultaneous determination of Cd^{2+}, Pb^{2+} and Hg^{2+} (Zuliani and Diamond 2012). Square wave anodic stripping voltammetry was used to determine electrochemical analysis of these heavy metals

(Wang et al. 2001). Triphenylphosphine has the ability to combine with most of the transition metals as well as nanomaterials such as MWNTs to act as a suitable material in electrochemical sensor for determination of heavy metal ions. Detection limits obtained by the fabricated electrode composite were 6.0×10^{-5}, 9.2×10^{-5} and 7.4×10^{-5} μM for Pb^{2+}, Hg^{2+} and Cd^{2+}, respectively (Bagheri et al. 2013). Recently, bismuth-based electrodes have replaced mercury electrodes as mercury is toxic and unstable (Armstrong et al. 2010). Another novel composite of Hg-Bi/single-walled carbon nanotubes (SWCNTs) was fabricated on modified glassy carbon electrode (GCE) for determination of traces of heavy metals like Zn(II), Cd(II) and Pb(II). The limits of detection of Zn(II), Cd(II) and Pb(II) are lower than 2 μg/L (Ouyang et al. 2011). These heavy metals can be easily determined by modified electrode in river samples. A novel hybrid composite of multiwalled carbon nanotubes (MWCNTs) and graphene oxide (GO) sheets was studied. Due to the high hydrophilicity of GO, it exhibits excellent water solubility, and MWCNTs show excellent electrical conductivity and stability (Mani et al. 2013). The electrochemical studies for the determination of traces of Pb^{2+} and Cd^{2+} have been done by anodic stripping voltammetry (ASV). The detection limits obtained were 0.2 μg/L and 0.1 μg/L for Pb^{2+} and Cd^{2+}, respectively (Huang et al. 2014). In another research work, cysteine has been used to modify carbon nanotubes as it has very high binding constant for toxic heavy metal ions like Pb^{2+} and Cu^{2+}. The detection limits obtained for these metal ions are 8.3 nM and 20 nM, respectively (Morton et al. 2009). Figure 8.2 shows schematic illustration of voltammetric mechanisms that show formation of complex between cysteine and metal ion.

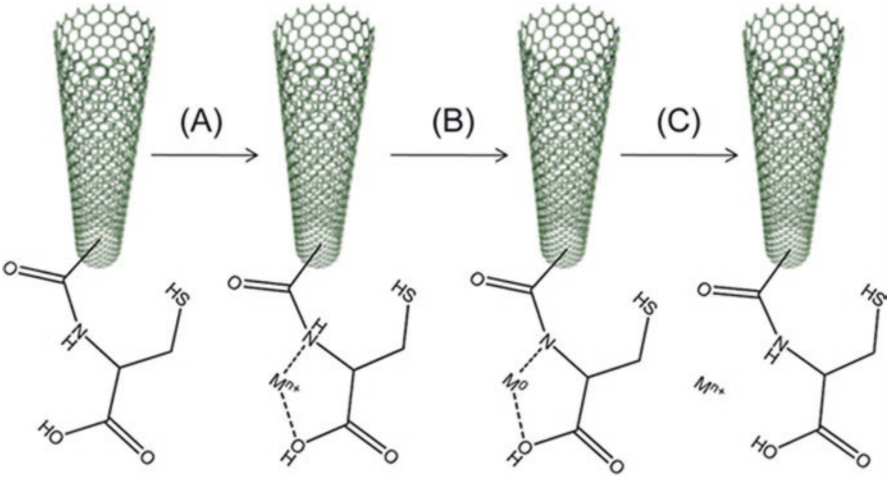

Fig. 8.2 Proposed accumulation and voltammetric mechanism of carbon nanotube-based electrode. The voltammetric mechanisms that show formation of complex between cysteine and metal ion are explained in this representation (Morton et al. 2009). (Copyrights 2009, with permission from Wiley)

Graphene

Like carbon nanotubes, graphene also possesses excellent electrical and catalytic properties, large surface area and biocompatibility which makes it suitable for fabrication of electrodes for the sensing of heavy metal ions (Xuan et al. 2016). Reduced graphene oxide (rGO) is synthesized by solvothermal method followed by the deposition of bismuth (Bi) on its surface for electrochemical detection of heavy metals like lead and cadmium. Square wave anodic stripping voltammetry (SWASV) technique was used for electrochemical analysis and detection of heavy metals. Drinking tap water has been used as test sample for evaluation, and the limits of detection obtained were 0.4 µg/L and 1.0 µg/L for lead and cadmium, respectively (Ping et al. 2014). Another bismuth film electrode plated on activated graphene was used as electrochemical sensing platform for determining traces of Zn^{2+}, Cd^{2+}, and Pb^{2+} (Lee et al. 2015). Activated graphene that has been synthesized by chemical activation of graphene oxide with potassium hydroxide (KOH) possesses excellent electrical conductivity and very high specific surface area (Zhu et al. 2011). Electrochemical measurements were performed through differential pulse anodic stripping voltammetry. Detection limits obtained through electrochemical sensing were 0.57 µg/L, 0.07 µg/L and 0.05 µg/L for Zn^{2+}, Cd^{2+} and Pb^{2+}, respectively (Lee et al. 2015). The detection limits obtained were much lower than those of the reference limit provided by the World Health Organization (WHO). Quantification of lead and cadmium in rice is a serious health concern as rice is one of the most consumed and major crops. So, in order to determine their traces in rice, graphene/ionic liquid composite-modified electrode was used in electrochemical sensing technique (Opallo and Lesniewski 2011). The electrochemical characterization to determine traces of lead and cadmium was obtained by square wave anodic stripping voltammetry. The prepared electrode exhibits various properties like large surface area, good ionic as well as electronic conductivity, etc. Detection limits obtained for cadmium and lead are 0.08 µg/L and 0.10 µg/L, respectively (Wang et al. 2014). Due to high affinity of gold (Au) towards mercury (Hg), it can be used for determination of Hg ions as it is toxic in nature and cause adverse effect on human health (Lin et al. 2015). It was incorporated with reduced graphene oxide (rGO) as it shows excellent conductivity as well as high surface area (Benvidi et al. 2015). This developed electrochemical sensor shows enormous properties and was suitable for the determination of traces of Hg. Graphene oxide was electrochemically reduced on glassy carbon electrode after which Au nanoparticles were deposited on its surface by cyclic voltammetry (Wang et al. 2016). Polyaniline (PANI) exhibits excellent electrochemical properties, good environmental stability, and nontoxic nature as an electrode material. Its composite with graphene developed an efficient electrochemical sensor for detecting traces of zinc, cadmium, and lead (Mohan et al. 2015). Although there are various electrochemical measurement techniques that provide high selectivity and sensitivity, but they are costly and have complicated processing time. So, square wave anodic stripping voltammetry has been used for electrochemical measurements and metal detection. Detection limits found by using graphene/PANI composite-based electrode were 1.0 μg/L for Zn(II) and 0.1 μg/L for both Cd(II) and Pb(II) (Ruecha et al. 2015).

8.2.2 *Organic Materials*

Small Molecules

Organic molecules containing ligands acts as electrochemical sensors for heavy metal ions due to their specific recognition of metal ions to ligands (Chen et al. 2011). The bonding or interaction between metal ions and ligands tends to form strong bonds and stable complexes. According to hard-soft, acid-base theory, soft acids tend to react faster with soft bases and vice versa (Pearson 2005). So, soft metal ions such as Hg^{2+}, Cd^{2+}, Ag^{2+}, etc. are soft acids, and they are most likely to bind with organic ligands containing sulphur. Conversely, hard metal ions like Cr^{3+} and Al^{3+} are known as hard acids, and they tend to bind with ligands containing oxygen (Parr and Pearson 1983). Gold-modified electrodes with L-cysteine act as electrochemical sensors for copper ions (Gooding et al. 2001; Yang et al. 2001). Their interaction was studied by cyclic voltammetry and chronoamperometry methods. The detection limit obtained by modified electrode for Cu^{2+} ions was below 5 μg/L (Yang et al. 2001). Another selective ligand, i.e. glutathione (GSH), has been investigated for selective determination of heavy metal ions such as cadmium ions. Cadmium ions form a stable complex with glutathione via carboxyl groups. The detection limit obtained was 5 nM (Chow et al. 2005).

Organic Polymers

Various conducting polymers include polyaniline (PANI), polypyrrole (PPy), polythiophene (PTh), etc. Incorporating these polymers with inorganic nanomaterials has led to construction of various ionic sensors. Metal organic−/polymer nanocomposite-based electrodes were also fabricated as ion sensors (Kumar et al. 2012; March et al. 2015). For example, UiO-66-NH_2/PANI was constructed as a novel electrochemical sensor material due to excellent porosity and high surface area of MOF, and excellent electrical conductivity of PANI (Boeva and Sergeyev 2014). The resultant ion sensor shows detection of traces of cadmium ions. The detection limit obtained was 0.3 μg/L for cadmium ions (Wang et al. 2017). In order to form a non-mercury electrode, it gets modified with electropolymerized thiadiazole film. To determine the traces of lead and cadmium, 2,5-dimercapto-1,3,4-thiadiazole-modified glassy carbon electrode was obtained by differential pulse anodic stripping voltammetry. The traces of toxic metals were obtained from wastewater samples, and the detection limits obtained were 0.30 and 0.05 μg/L for lead and cadmium, respectively (He et al. 2011). Another type of potentiometric sensor that is used for heavy metal ion detection is selective polymer membrane like poly(vinyl) chloride (PVC). Some ion-selective electrodes have been formed based on PVC for the determination of cobalt (Co) ions (Gupta et al. 2004). Another ion selective polymer membrane was formed to determine iron by S-methyl N-(methylcarbamoyloxy) thioacetimidate which acts as ligand in the PVC membrane electrode. It provides stable chelation with heavy metal ions. It shows good selectivity to alkali, alkaline earth and heavy metal ions (Gupta et al. 2011). Nanosized hydroxyapatite (NHAP) provides unique three-dimensional network structure so its modified glassy carbon electrode has been used for determination of lead. Electrochemical analysis was done by anodic stripping voltammetry. Nafion which is a cation-exchange membrane has been used as conductive matrix. The detection limit obtained through this ion-selective membrane-based electrode was 13 μM (Pan et al. 2009).

8.2.3 Biomaterials

Enzymes

Biosensors consist of a recognition element (enzyme, DNA, etc.), a signal-transducing (electrical, optical, or thermal) element and an amplification element. Very few enzymes are sensitive to heavy metals (Turdean 2011). The following series of reactions have been followed for biosensing using biomaterials:

$$\begin{aligned} &\mathrm{S} + \mathrm{E}_{\mathrm{ox}} \leftrightarrow [\mathrm{S} - \mathrm{E}_{\mathrm{ox}}] \rightarrow \mathrm{P} + \mathrm{E}_{\mathrm{red}} \\ &\mathrm{M}_{\mathrm{ox}} + \mathrm{E}_{\mathrm{red}} \leftrightarrow [\mathrm{M} - \mathrm{E}_{\mathrm{red}}] \rightarrow \mathrm{M}_{\mathrm{red}} + \mathrm{E}_{\mathrm{ox}} \\ &\mathrm{M}_{\mathrm{red}} \rightarrow \mathrm{M}_{\mathrm{ox}} + \mathrm{e}^{-} \end{aligned}$$

Here, S = substrate, P = product, E = enzyme and M_{ox} and M_{red} = oxidized and reduced forms of redox mediator molecules (García Sánchez et al. 2003).

Electrochemical sucrose biosensor has been developed for sensing of toxic metal ions such as Hg(II), Ag(I), Pb(II) and Cd(II). Based on this, ultramicroelectrode (UME) has been fabricated for electrochemical sensing. The electrode was modified with invertase and glucose oxidase enzymes (Brindha et al. 2018). Electrochemical analysis shows a detection limit of 5×10^{-10} M for mercury (Bagal-Kestwal et al. 2008). Due to their poor stability and reproducibility, enzyme-based electrochemical sensors have limited applications.

Amino Acids, Peptides and Proteins

Due to presence of ligands like sulphur, nitrogen and oxygen atoms which led to the metal-ligand interaction, amino acids, peptides and proteins have been recognized as biomaterials for determining traces of heavy metal ions (Shao et al. 2006). A nanocomposite sensor containing a carbon- and amino acid-based electrodes capped with gold nanoparticles was considered as a highly sensitive and selective biosensor for detection of Hg(II) (Jazayeri et al. 2018). Mercury ions interact with amino acids through metal-ligand interaction in order to form a stable complex. The detection limit obtained through electrochemical analysis was 2.3 nM which is found to be lower than reported by the Environmental Protection Agency (EPA) (Safavi and Farjami 2011). The composite formed shows high selectivity towards detection of Hg(II) obtained from wastewater. Peptides and amino acids act as recognition elements of electrochemical sensors for detection of heavy metal ions. Gly-Gly-His tripeptide modified with conducting polymer (poly(3-thiopheneacetic acid)) acts as a biosensor material for copper ion sensing (Flavel et al. 2011). Electrochemical analysis by peptide-modified electrode was carried out by square wave voltammetry. This modified electrode provides high stability and repeated use of sensor electrode. For detection of heavy metal ions, microbial sensors have also been developed. Algal sensor based on *Phormidium* sp. was developed to determine traces of lead in wastewater samples. Differential pulse stripping voltammetry has been used for electrochemical analysis. The functional groups involved in the accumulation of lead traces are carboxyl, sulphoxide and alcoholic groups. The detection limit obtained was 2.5×10^{-8} M for Pb (Yüce et al. 2010). Table 8.1 summarizes various nanomaterials used with the detection method and detection limit.

8.3 Metal and Ion Detection Using Wireless Sensors

Emergence of wireless sensors for detection of heavy metal ions has revolutionized the advancements in sensor industry. Wireless sensors are categorized as both active and passive modes (Fay et al. 2010). Passive sensors are more beneficiary than active ones as they use basic LC circuit, whereas active sensors use batteries, antennas and amplifiers that make it costly and complex (Mieyeville et al. 2012). LC sensors which consist of inductors and interdigitated electrodes (IDEs) were fabricated or screen-printed on polyethylene terephthalate (PET) substrate. Screen printing on substrate is done by silver (Ag) ink. For detection of heavy metal ions like mercury, lead, etc., palladium nanoparticles were synthesized onto electrodes (Eshkeiti et al. 2015).

Other than screen printing method, traditional photolithography techniques were also used for fabrication of LC sensors. But it has complex fabrication steps and is expensive. These sensors were fabricated using screen and gravure printing technologies (Dexia et al. 2014). It led to the detection of heavy metal ions such as cadmium sulphide (CdS) and lead sulphide (PbS). In screen printing technique, the substrate is not in direct contact to mask. The ink is applied over the screen printing plate through rubber squeeze with high pressure. The squeeze allows the ink to transfer through it onto the substrate (Lim et al. 2009). The basic principle of screen printing is illustrated in Fig. 8.3.

Table 8.1 Summary of various nanomaterial-based electrochemical detections of heavy metal ions

Sr. no.	Type of nanomaterial	Electrode substrate	Heavy metal ion detected	Electrochemical analysis method	Detection limit	References
1.	Metal nanoparticles	Bismuth-coated carbon electrode	Pb	Anodic stripping voltammetry	0.3 μg L^{-1}	Wang et al. (2000)
2.	Metal nanoparticles	Reduced graphene oxide (rGO)/ bismuth electrode	Cd^{2+}, Pb^{2+}, Zn^{2+}, Cu^{2+}	Anodic stripping voltammetry	2.8, 0.55, 17 and 26 μg L^{-1}, respectively	Sahoo et al. (2013)
3.	Metal nanoparticles	Antimony NPs/boron-doped diamond electrode	Cd^{2+}, Pb^{2+}	Linear sweep anodic stripping voltammetry	–	Toghill et al. (2009)
4.	Metal nanoparticles	Gold nanoelectrode ensembles (GNEE)	As, Hg	Square wave anodic stripping voltammetry	15 μg L^{-1}	Kumar Jena and Retna Raj (2008)
5.	Metal nanoparticles	Au NPs/graphene	Hg	Square wave anodic stripping voltammetry	0.000006 μg L^{-1}	Ding et al. (2014)
6.	Metal nanoparticles	Au NP-based screen printing electrode	Cr	Square wave anodic stripping voltammetry	5 μg L^{-1}	Liu et al. (2007)
7.	Quantum dots	Graphene quantum dot/au NPs	Hg^{2+}, Cu^{2+}	Square wave anodic stripping voltammetry	0.02 and 0.05 nm, respectively	Ting et al. (2015)
8.	Quantum dots	SnO_2 quantum dot electrode	Cd	Cyclic voltammetry	500 μg L^{-1}	Bhanjana et al. (2015b)
9.	Quantum dots	Zinc oxide quantum dot electrode	Hg	Linear sweep voltammetry	5 μg L^{-1}	Bhanjana et al. (2015a)
10.	Metal oxide	Magnesium oxide nanoflowers on glassy carbon electrode	Pb and Cd	Square wave anodic stripping voltammetry	2.1 and 81 pM	Wei et al. (2012)
11.	Metal oxide	Iron oxide/graphene with plated bismuth electrode	Zn^{2+}, Cd^{2+} and Pb^{2+}	Differential pulse anodic stripping voltammetry	0.11, 0.08 and 0.07 μg L^{-1}, respectively	Lee et al. (2016)
12.	Metal oxide	Aluminium oxide hydroxide/graphene electrode	Cd(II) and Pb(II)	Square wave anodic stripping voltammetry	4.46×10^{-11} and 7.60×10^{-11} M, respectively	Gao et al. (2012)

13.	Carbon nanotubes	CNT thread-based electrodes	Cu^{2+}, Pb^{2+}, Cd^{2+} and Zn^{2+}	Anodic stripping voltammetry	0.27, 1.5, 1.9 and 1.4 nM, respectively	Zhao et al. (2014)
14.	Carbon nanotubes	Carbon nanotubes/poly(1,2-diaminobenzene)-modified glassy electrode	Cd^{2+} and Cu^{2+}	Square wave stripping voltammetry	0.25 μg L^{-1} and 0.33 μg L^{-1}	Gao et al. (2006)
15.	Carbon nanotubes	Bismuth-/CNT-based electrode	Lead, cadmium and zinc	Square wave stripping voltammetry	1.3, 0.7 and 12 μg/L	Hwang et al. (2008)
16.	Carbon nanotubes	Triphenylphosphine/carbon nanotube electrode	Pb^{2+}, Hg^{2+} and Cd^{2+}	Square wave stripping voltammetry	6.0×10^{-5}, 9.2×10^{-5} and 7.4×10^{-5} μM	Bagheri et al. (2013)
17.	Carbon nanotubes	Hg/bi single-walled CNTs modified on glassy carbon electrode	Zn(II), Cd(II) and Pb(II)	Anodic stripping voltammetry	Lower than 2 μg/L	Ouyang et al. (2011)
18.	Carbon nanotubes	Graphene oxide (GO)/multiwalled CNTs electrode	Pb^{2+} and Cd^{2+}	Anodic stripping voltammetry	0.2 and 0.1 μg/L, respectively	Mani et al. (2013)
19.	Carbon nanotubes	Cysteine/CNT electrode	Pb^{2+} and Cu^{2+}	Anodic stripping voltammetry	8.3 and 20 nM, respectively	Morton et al. (2009)
20.	Graphene	Bismuth/reduced graphene oxide (rGO) electrode	Lead and cadmium	Square wave anodic stripping voltammetry	0.4 and 1.0 μg/L, respectively	Ping et al. (2014)
21.	Graphene	Graphene oxide/potassium hydroxide (KOH) electrode	Zn^{2+}, Cd^{2+} and Pb^{2+}	Differential pulse anodic stripping voltammetry	0.57, 0.07 and 0.05 μg/L, respectively	Lee et al. (2015)
22.	Graphene	Graphene/ionic liquid electrode	Cadmium and lead	Square wave anodic stripping voltammetry	0.08 and 0.10 μg/L, respectively	Wang et al. (2014)
23.	Graphene	Polyaniline (PANI)/graphene electrode	Zn(II), Cd(II) and Pb(II)	Square wave anodic stripping voltammetry	1.0 μg/L for Zn(II) and 0.1 μg/L for both cd(II) and Pb(II)	Ruecha et al. (2015)
24.	Small molecules	Gold-modified electrodes with L-cysteine-based electrode	Cu^{2+}	Cyclic voltammetry and chronoamperometry	5 μg/L	Yang et al. (2001)
25.	Small molecules	Glutathione (GSH)-based electrode	Cadmium	Cyclic voltammetry	5 nM	Chow et al. (2005)

(continued)

Table 8.1 (continued)

Sr. no.	Type of nanomaterial	Electrode substrate	Heavy metal ion detected	Electrochemical analysis method	Detection limit	References
26.	Organic polymers	UiO-66-NH_2/PANI electrode	Cadmium	Cyclic voltammetry	0.3 µg/L	Wang et al. (2017)
27.	Organic polymers	2,5-Dimercapto-1,3,4-thiadiazole-modified glassy carbon electrode	Lead and cadmium	Differential pulse anodic stripping voltammetry	0.30 and 0.05 µg/L, respectively	He et al. (2011)
28.	Organic polymers	Nanosized hydroxyapatite (NHAP) in PVC membrane	Lead	Anodic stripping voltammetry	13 µM	Hasret et al. (2012)
29.	Enzymes	Invertase and glucose oxidase enzyme-modified electrode	Mercury	–	5×10^{-10} M	Bagal-Kestwal et al. (2008)
30.	Enzymes	Sucrose biosensor	Hg(II), Ag(I), Pb(II) and Cd(II)	–	–	Bagal-Kestwal et al. (2008)
31.	Amino acids, peptides and proteins	Carbon and amino acid capped with Au NP-based electrode	Hg(II)	Anodic stripping voltammetry	2.3 nM	Safavi and Farjami (2011)
32.	Amino acids, peptides and proteins	Gly-Gly-His tripeptide modified with conducting polymer (poly(3-thiopheneacetic acid)) as biosensor	Cu	Square wave voltammetry	–	Flavel et al. (2011)
33.	Amino acids, peptides and proteins	Algal sensor based on *Phormidium* sp. electrode	Pb	Differential pulse anodic stripping voltammetry	2.5×10^{-8} M	Yüce et al. (2010)

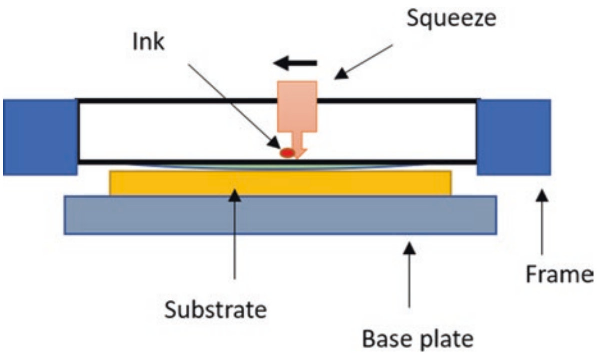

Fig. 8.3 Screen printing techniques showing the setup of substrate, base plate and frame

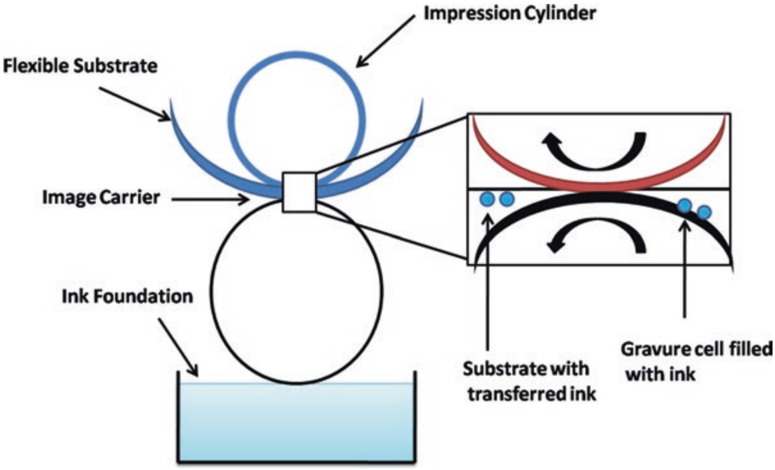

Fig. 8.4 Gravure printing setup with detection coil monitored wirelessly the frequency spectrum of printed LC sensor. (Reddy et al. 2010)

Another sensor fabrication technique used is gravure printing. It has several advantages like fast output, robustness and use of low-viscosity inks. Two types of cylinders are present in this printing technique: gravure cylinder and impression cylinder. Impression cylinder is attached to the flexible substrate and gravure cylinder is attached to the ink fountain. Gravure cylinder contains gravure cells filled with ink through which ink is transferred onto the substrate. Heavy metal ions of different concentrations are loaded onto the LC sensor by using a pipette (Reddy et al. 2010). Its basic setup is illustrated in Fig. 8.4. Detection coil monitored wirelessly the frequency spectrum of printed LC sensor. The results obtained show the potential of LC sensors to determine traces of toxic heavy metal ions.

8.4 Conclusion

This chapter presents an overview of the developments in heavy metal ion detection technology, especially centred on electrochemical methods and wireless technology. Future applications based on different properties of various organic, inorganic and biomaterials discussed here should drive the detection limit of heavy metals and ions sensors beyond the current state of the art. To move forwards, researchers from various backgrounds will need to develop strategies for further enhancement of detection limit. A range of electrochemical techniques for Pb, Cd, As, Hg, Mn and Zn detection is described and evaluated, presenting their huge potential and broad outlook. However, there are also many deficiencies of the existing technology. For example, the scope of application is still limited compared to calorimetry, as only certain types of ions can be electrochemically detected. Huge efforts have been made to design heavy metal sensors to discover different signal transduction mechanisms, resulting in optical, electrochemical, and wireless sensors with significant improvement in the sensing performance, especially detection limit and sensitivity.

In this article the performance analysis of different metal ion detection technology was made on the basis of inorganic nanomaterials, organic materials, biomaterials and wireless sensors. It was observed that in case of inorganic nanomaterials, the detection limit achieved varied from 0.04 μg L^{-1} to 500 μg L^{-1}. In case of organic material, the detection limit for metal ion detection is 0.3 μg L^{-1}–13 μg L^{-1}, but in case of biomaterials, it is around 5×10^{-10} M to 2.5×10^{-8} M. And in case of wireless sensors, the detection sensitivity is around 50 μM–500 μM. So, it can be concluded that inorganic nanomaterials have the best sensitivity followed by organic materials and then biomaterials and wireless sensors. But if we consider the cost associated with different methods, it was found that inorganic process has low-cost methods, whereas wireless sensors and organic materials have higher cost, but if biomaterials processes are considered, they have the highest cost with complex methods.

Moreover, most of the recent studies only confirmed the proof of concept for applications like heavy metal ion sensing in water samples in lab level. It is a tremendous challenge to apply these sensors to real-world samples for on-spot and accurate detection of heavy metals. Due to severe interference of additional chemical and biological species, the specificity of the sensors relies on the sample preparation before final analysis. Furthermore, sensor devices combined with a wireless detection system will be attractive for various environmental applications.

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