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Recent Progress in the Development of Biosensors for Chemicals and Pesticides Detection

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ABSTRACT Chemicals and pesticides contamination in the food, drinking water, and environment ecosystem have become one of the most serious problems for human public health in the world due to their large amount used and wide application in the agriculture industry. Therefore, the detection and analysis of contamination in the food and drinking water by using techniques that are simple and suitable for fast screening are important. This review gives an overview of the last trends and recent advances biosensors for chemicals and pesticides detection based on electrochemical, optical and mechanical transducers strategies. Furthermore, the biosensors are classified according to their immobilized biorecognition elements including aptamer, antibodies, enzymes, and molecularly imprinted polymers. The implementation of nanomaterials such as graphene, carbon nanotubes, and metals nanoparticles are also emphasized and discussed in this review, these nanomaterials provides remarkable features to the biosensors such highly sensitive and accurate which allowing efficient pesticides detection. In addition to highlighting and summarizing various novel sensors, this review also provided some drawbacks, challenging, prospects as well as the current efforts to enhanced optical sensors.

INDEX TERMS Biosensors, chemical detection, electrochemical transducer, mechanical transducer, optical transducer, pesticides detection.

I. INTRODUCTION

In the last three decades, the detection of hazardous chemicals and pesticides has been attracting both industrial and academia attention. Pesticides are hazardous chemicals often found in water, soil, fruit, vegetables and other agricultural products. These pesticides may exist in huge amount and harmful levels which considered as environmental pollution and environmental hazardous threat, even a few amounts of contamination can cause serious effects on human health. Pesticides are commonly used to prevent and control the pets and weeds for boosting crop productivity in recent agricultural activities [1]. Although, the use of the pesticides increase the food productivity, however, the presence of the pesticides residues in the food, water and environment cause

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serious food contamination which create a potential hazard to human health and severely breakdown the ecosystem [2]. In addition, the organophosphorus pesticides (OP) such as malathion, paraoxon, parathion, diazinon, and dichlorvos are the most extensively used in modern agriculture due to their low cost and their high effectiveness against the insects on rice, cotton, and vegetables [3]–[8]. However, pesticides have severe effects on human health include dizziness, nausea, difficulty breathing, numbness, decreased coordination, slow heartbeat, and headache [9]–[11].

Therefore, the organophosphorus pesticides pollution has attracted more researcher concern and become one of the most critical challenges. Thus, the analysis and monitoring of the (OP) pesticides residue in the food and water must be continuously carried out on-situ and in real time to ensure food quality and to protect the human from possible dangerous hazards [12]. Pesticides detection and

analysis have been carried out using current analytical methods including mass spectrometry (MS), high-performance liquid chromatograph (HPLS), and gas chromatograph (GC) [1], [13]. Although these techniques have demonstrated powerful trace analysis with high sensitively and excellent reproducibility, but there are some drawbacks including time consuming, sophisticated equipment and long sample preparation process which are defense the on-situ and real time detection [14]. Thus, in recent years, alternative ways for the detection of the pesticide has been illustrated such as Capacitive-based sensors [15]-[18], field effect transistor (FET) based sensors [19], [20] Micro-Electro-Mechanical systems (MEMS) [21], Quartz Crystal Microbalance (QCM) [8], [22], [23] and Film Bulk Acoustic Resonator (FBAR) [24], [25]. In this review, we investigate and discuss the current techniques used for chemicals and pesticides detection, taking into account the use of recognitions elements, including the enzymes, antibodies, aptamers, and molecular imprinted polymers.

II. PESTICIDES

Pesticide sensor is basically a chemical sensor that transforms chemical information, such as the concentration of a specific pesticide or chemical element into an analytically, readable and useful signal. The chemical information is induced by the chemical reaction between the biorecognition element such as aptamer, antibody, and polymer with the pesticide target. These types of chemical sensors are called biosensors, in which a biochemical reaction is the source of the analytical signal. For the past years, there are extensive efforts have been contributed to develop pesticides biosensors for monitoring the pesticide residue in the drinking water and food.

Pesticides are chemicals widely used in modern agriculture to sway a various types of agricultural insects that usually damage crops as well as they used to enhance the yields productivity [26]. Although pesticides are directly sprayed to the plants, but only 1% of the applied pesticide is successfully reached the pests or insects and the other amount of pesticides are stick to the vegetables and fruits and remain on it [27]. The remained amount of pesticides in the food has become one of the most alarming challenges due to their harmful consequences to human health [1]. Pesticides also have been used for non-agricultural applications such as insects' control in the atmosphere environment, grass management, and pets care in the accommodation, and industrial vegetation control. Therefore, it will also leave harmful residues into the environment such as the agricultural soil, drinking water, and food [28]. Thus, the detection of pesticides residues considers as a challenge for food and water safety management, and environment protection.

Additionally, pesticides have been classified into two different groups, the chemical pesticides and biopesticides [5]. The chemical pesticides are synthesized chemicals that directly kill the insects, where the biopesticides are obtained naturally from natural sources such as oil, animals, and bacteria [29]. The chemical pesticides are classified into five different types depending on their application, there are insecticides, herbicides, and fungicides, rodenticide, and nematicides. However, the chemical pesticides are the most common used in the food agricultural especially the insecticides pesticides. The insecticides pesticides are divided into four major families, namely as organophosphorus, carbamates, organochlorines, and pyrethroids [29].

Furthermore, the OPs pesticides are one of the most extensively pesticides used nowadays in agricultural and household application [1]. The OPs are among the most hazardous and toxic pesticides as well as their residues in the surrounding environment can cause long term effect in the human health. However, the OPs are preferable over organochlorine (OC) pesticides due to less toxicity and compared with other pesticides [30]. Hexaethyl tetra phosphate (HETP) was the first Ops discovered in 1942, which used as an insecticide in agricultural application [31]. Currently, various types of OPs are used as insecticides including malathion, parathion, diazinon, dichlorvos, terbufos, methyl parathion, and phosmet [6], [32].

However, the widespread application of pesticides has resulted in the serious contamination in food and drinking water which lead to serious human health problem. Therefore, in order to control and detect the hazardous pesticides, a sensitive and rapid detection method is required urgently [33]. In this review, the recent progress in the development of chemicals and pesticides detection methods are illustrated and investigated.

III. CLASSIFICATION OF BIOSENSORS FOR CHEMICALS AND PESTICIDES DETECTION

Currently, there are several types of biosensors for chemicals and pesticides detection methods such as electrochemical [6], [34], [35], optical [36], [37] and mechanical detection method. The electrochemical detection methods are including the screen-printed electrodes [38], [39], Field Effect Transistor (FET) [40]-[42] and capacitive-based method [43]. In the other hand, the optical detection methods are including, optical-MEMS [28], [44], colorimetry [26], surface-enhanced Raman scattering method [45], Surface Plasmon Resonance (SPR) [46], chemiluminescent [47], [48], and fluorescent [8], [36]. Furthermore, the mechanical detection methods are including the mass sensitive detection by microcantilever deflection [7], [28], [49], bulk acoustic waves such as Film Bulk Acoustic Resonator (FBAR) [5], [24], [50], [51] and Quartz crystal Microbalance (QCM) method [22], [52]. Fig.1 shows the classification of some of the current available detection methods.

Furthermore, there are different aspects of the pesticide's sensors such as the biorecognition materials which are aptamer, antibodies, and enzymes and the routine of the chemical reaction between the pesticide's residues and the sensing materials is an affinity biosensor. Affinity biosensors are usually divided into two categories which are the labelled and the label-free biosensor [53], [54]. In the labelled biosensors, labels are usually applied as an easy tool to confirm the interaction and binding that occur between the probe



FIGURE 1. Classifaction of the pesticides sensors.

and the target. This process is performed by labelled the target molecules with fluorescence markers such as quantum dots, radioactive species, magnetic beads, or active enzymes [55]–[58].

Although, the labelled interaction is suitable for simple, accurate and quick bioreaction analysis, but this technique is characterized by several disadvantages [5]. For instance, the labelling process may cause disturbance during the probe and the target molecules interaction, and it is known that the labelling technique is costly, required extra materials, and it is considered a long-running process due to the requirement of installing a sophisticated additional instrument to measure the fluorescence signals, moreover, this hinders the miniaturization of the system [18]. Therefore, the attraction of the label-free technique is that the analyte will be directly detected with no or a few sample preparations. Furthermore, the label-free interaction must have strong specific binding between the probe and the target. It is therefore important to have a sensitive transducer with capability of measuring the changes occurring during the interaction [59].

Furthermore, Enzymatic biosensors are one the most popular tools have been used during the last few decades as they demonstrated some unique properties [1], [60], [61]. These enzyme-based biosensor for pesticides residue detection has shown very sensitive measurement range which able to detect 10^{-10} M [1], but they need loner incubation time and they show poor specificity due to the short lifetime of the enzymes and due to the interference from many other substances such as heavy metals and other type of pesticides, etc. Furthermore, the enzyme-linked immunosorbent assay (ELISA) method is highly sensitive and has demonstrated good specificity, however, it requires labelling of the molecules, which is difficult for small molecules such as the pesticides residue

however, the OPs are small molecules in the level of hundreds of Daltons, thus the labelling process might affect detection sensitivity [5], [62].

Moreover, antibody-based immunoassay schemes have been used for pesticides detection, but, the antibody preparation for small molecules is complex and difficult [63], therefore, researchers have developed alternative bio-recognition elements such as aptamers to overcome the drawbacks of the enzyme and antibodies [28], [45], [64]–[66]. In the following section, those types of biosensors are systematically elaborated, and their advantages and drawbacks are presented [66]–[71].

IV. ELECTROCHEMICAL-BASED BIOSENSORS FOR CHEMICALS AND PESTICIDES DETECTION

Electrochemical biosensors have been demonstrated to be useful tools for chemicals and pesticide residue detection [57], [73], [74]. The electrochemical techniques are often preferred over other analytical techniques due to their remarkable properties including the low cost, easy to operate, their potential to be portable as well as their fast response. The electrochemical biosensors are classified by the signal being measured which are impedance, current, and potential, therefore, the sensors are characterized as impedimetric, amperometric, and potentiometric sensor [15], [75], [76]. Recently, the Electrochemical impedance spectroscopy (EIS) technique has been used extensively for the pesticide's residue detection due to their unique features including fast response, simple preparation, highly sensitivity and specificity. In addition, the electrochemical impedance spectroscopy has been classified into two main techniques which are Faradic EIS and non-Faradic EIS [77], [78]. More details will be disused in the following sections.

A. CAPACITIVE-BASED BIOSENSORS FOR CHEMICALS AND PESTICIDES DETECTION

The growing interest in the handhold or personalized devices for the chemicals and pesticides detection sparking the need for remarkable devices with low cost, fast response, and portable capabilities that can facilitate the daily life and produce easily and accurately result. To this direction, researchers are investigated new ideas to avoid the traditional techniques through miniaturized and developing the current systems. Capacitive devices addressed the requirements and have the perspective to be used as portable device [79]. Furthermore, the development of new technologies such as the microelectronics fabrication facilities and micromachining equipment's attracting the researcher's interest in the development of the microsystems and MEMS devices and their application. In addition, the capacitive biosensors have the feasibility of cost reduction and the possibility to put and integrate the sensor components including the transducer and the signal-processing electronic circuit on a common substrate [80].

The term "capacitive biosensor" is usually refereed to a subcategory of an electrochemical biosensor which is called electrochemical impedance spectroscopy (EIS) based biosensor, where the capacitance changes are measured. Principally, the EIS based biosensors are operating in both Faradaic and non-Faradaic modes [18]. In Faradic impedance mode, a redox couple is utilized, and the reaction occur due to the charge transfer through the electron traveling to/from the electrode surface [81]. Alternatively, in the non-faradaic mode, the changing currents are dominant and capacitive changes occurring due to the charge distribution, surface dielectric, or local conductance [82]. Furthermore, the non-faradaic approaches have the advantages comparing with the faradaic, due to non-faradaic reaction does not require pre-addition of redox probes to the analytical solution [18]. However, the sensitivity of the non-faradaic sensor is less compared with the redox probe sensors.

To best of our knowledge, one of the first article and appearance of what is known today as capacitive based-sensor for liquid using capacitive label-free technique was on the 1986 when Helen Berney has introduced the development of a new type of biosensor named as capacitive affinity sensor, where the dielectric properties changes at an electrode surface or between the electrodes were monitored [83]. A biorecognition reaction in the solution have been obtained between the analyte and the layer that immobilized on the surface of the electrodes, this reaction could be monitoring directly without the need for indicators or labels [83]. For instance, an aptamer-based capacitive biosensor can be constructed by immobilizing a specific pesticide aptamer in the thin layers on an electrode or between two electrodes and measuring changes in the dielectric properties when the aptamer binding with the pesticide target [16], [43].

In particular, the capacitive biosensor can be interdigitated or electrode-solution interface [83]. It has been demonstrated in the literature that the utilization of the interdigitated microelectrodes IDEs has additional advantages including easy fabrication process, flexibility in the sensor size, low power consumption, fast reaction kinetics, high sensitivity, labelfree, and have the ability of the IDEs to be integrated with readout circuits [18], [30], [84]–[89].

Madianos et al. [84], [90] have developed a label free biosensor for highly selective detection of acetamiprid and atrazine pesticides using Faradic EIS technique and utilizing two-dimensional platinum nanoparticle films and specific aptamer for the pesticides. They have compared the result of the impedimetric biosensor using bare interdigitated electrode without applying any nanoparticles and the result of the IDEs with the two-dimensional platinum nanoparticle films, the biosensor with the nanoparticles has demonstrated remarkably improved performance for atrazine detection with detection limit of 40 pM. The improved interdigitated electrode biosensor faradic EIS based aptasensor shown higher sensitivity and selectivity in the detection of atrazine and acetamiprid pesticides residues in real samples, but this kind of biosensor needs addition of a redox-active species, which made the biosensor bulky system and could not be integrated to small chips to meet the requirement of the portable biosensor.

Marrakchil et al. [91] have developed a sensitive, label-free immunosensor for atrazine pesticide detection using interdigitated gold microelectrode. The immunosensor was based on antibody physisorption as immobilization technique. This immobilization technique was proposed as a cost-effective gold-functionalization strategy alternative to SAM-based strategy. The antibody-atrazine interaction was measured in dynamic range from 10 to 150 ng/mL and the limited detection of the atrazine in PBS buffer was 10 ng/mL. Other researcher Thanh et al. [41], have enhanced graphene interdigitated ion selective field effect transistor (ISFET) with capability of fast in-situ tracing of carbaryl pesticides. The biorecognition was based on the enzymatic inhibition of carbaryl towards urease. The urease enzyme was immobilized on the interdigitated electrode using glutaraldehyde vapor as cross-linking agent. The ISFET biosensor was demonstrated high sensitivity to the carbaryl as low as $10^{-8} \mu \text{gmL}^{-1}$.

In addition, Cao *et al.* [92], have synthesized an electrochemical immunosensor based on interdigitated array microelectrodes (IDAMs) for sensitive, specific and rapid detection of chlorpyrifos pesticides. The interaction between the chlorpyrifos pesticide target and the anti-chlorpyrifos monoclonal antibodies on the gold microelectrodes surface induced an impedance change in the IDAMs surface. The electrochemical impedance spectroscopy was used to detect chlorpyrifos pesticide through measuring the impedance changing. The impedance change was found to be proportional to the chlorpyrifos concentrations in the range of 10^0-10^5 ng/mL and the limit of detection was found to be 0.014 ng/mL. Although, this device has demonstrated high selectivity and selectivity, but the reaction is based on the redox [Fe(CN)₆]^{3-/4-} probe which is defend the portability of the device.

Moreover, Fan et al. [93] have prepared highly sensitive and selective aptamer-based biosensor for acetamiprid pesticide detection based on electrochemical impedance spectroscopy. Gold nanoparticles were electrodeposited on the bare gold electrode surface for improving the sensitivity of the aptasensor. The modified gold electrode by gold nanoparticles was used as a platform for acetamiprid pesticides specific aptamer immobilization. The formation of acetamiprid-aptamer complex on the gold nanoparticles-deposited electrode surface resulted in an increase of the electron transfer resistance. Therefore, the biosensor has demonstrated that when the concentration of the acetamiprid has been modified the resistance changed. Thus, the change of the resistance strongly depends on the acetamiprid pesticides concentration, which is applied for quantification process. The biosensor has shown wide linear range from 5 to 600 nM with a low limit of detection of 1 nM [93]. The capability of the developed aptasensor for determining acetamiprid in the real samples, wastewater and tomatoes have been successfully evaluated. The effective area of the modified aptasensor with gold nanoparticles has been clearly demonstrated approximately 4-fold higher than that of the bare gold electrode.

Valera et al. [63], [94], [95], have created label-free impedimetric immunosensor using interdigitated microelectrodes for atrazine detection. The immunosensor operation principles is based on two coplanar non-passivated interdigitated metallic microelectrodes and the differential measurement of the impedance frequency spectrum, and the recognition layer is deposited on the top of the interdigitated electrode. The developed sensor is operated without redox electrode and the sensor shows a limit of detection of 8.34 \pm 1.37 μ gL⁻¹ which is lower than the Maximum Residue Level (MRL) indicated by European union to be 100 μ gL⁻¹ [63]. In another research, they have developed a conductimetric immunosensor based on interdigitated microelectrode to detect residual amounts of atrazine pesticide in a complex matrix, such as red wine. This immunosensor has been developed with specific antibodies labelled with gold Nanoparticles. The main advantage of the developed sensor is related to the use of simple and inexpensive DC measurements for the detection process. The conductive measurement for the detection process were performed at room temperature and at different sweep bias and in a Faraday cage [94]. The conductivity measurements were carried out after the incubation of the antibodies labelled with the gold nanoparticles. The inclusion of the gold nanoparticles has introduced new structure, where the gold nanoparticles acts as new small fingers, reducing the gap of the interdigitated microelectrodes and increase the electric filed between them. Furthermore, the atrazine pesticide level in the solution were quantified by impedance measurement in wide frequency range and the fitting of the Nyquist plots of impedance spectra to the equivalent circuit that correctly represents the system [95]. Therefore, the atrazine pesticide concentration could be related to the difference in the resistance of the solution of the system. By using this technique, they have claimed that the limit of the detection has been found to be $50 \ \mu g \ kg^{-1}$.

Furthermore, Facure et al. [15] have developed an electronic tongue based on graphene hybrid nanocomposites for trace levels of organophosphate pesticides using impedance spectroscopy measurement. The developed sensor was fabricated using interdigitated electrodes consisted of four sensing units deposited by graphene hybrid nanomaterials for enhancing the sensitivity of the device using the drop casting process. The nanocomposites were prepared by reduction process of graphene oxide in the present of conducting polymers and gold nanoparticles. The sensor was characterized by measure the changes in the electrical resistance for each sensing unit having pesticide samples, the output of the sensor revealing that the system was able to discriminate the pesticides at nanomole concentration. The prepared and deposited nanomaterials have successfully provided sensing units with high specific surface area and high sensitivity for the malathion and other types of pesticides samples and the system shown capability to detect the pesticides with low concentration down to 0.1 nML^{-1} . This system is based on non-faradaic impedance spectroscopy measurements which performed using a fixed potential at sweep range of frequency and it is not necessary to use a reference electrode.

B. FIELD-EFFECT TRANSISTOR-BASED BIOSENSORS FOR CHEMICALS AND PESTICIDES DETECTION

The field-effect transistor biosensors (Bio-FETs) for pesticides and biomedical applications have experienced a huge development in both FET characteristics and the bio-receptor structures modification [96], [97]. This section initially provides the recent progress in the Bio-FETs biosensors for pesticides detection by analyzing and summarized remarkable conducted studies.

Biosensor has been introduced by Clark in 1962 [98], since that time, the biosensors have been widely used in diverse applications such as pesticides detection [33], food analysis [53], cancer diagnosis [99], and biomedical application [96], [100], etc. Bio-FETs are one of the various kinds of biosensors which consisted of integration between bio-receptors and ion-sensitive field-effect transistor (ISFET). These integrations provided unique features for the Bio-FETs such as easy fabrication and fast response. Furthermore, since the invention of the ISFET in 1970 by Bergveld [101], there have intensive development and evaluated the FET transducers in various biosensor applications through the implementation of nanomaterials [20], [102]. The operation principle of the FETs biosensors is depending on the charge carriers of the substrate materials [103], [104]. Therefore, there are usually two different kinds of FETs, the n-type FET biosensor with electrons as the main charge carriers and p-type with holes as the charge carriers [105]. In more details, for n-types FETs systems, the sensing elements that have been immobilized on the sensing channels will show more conductance if the probes detect positively

charged molecules due to the accumulation of the charge carriers on the sensing channels. On the other hand, the p-type system, the binding between the sensing elements with positive charges results in conductance decline due to a reduction of the charge carriers (holes), however, the conductance raises when the sensing elements detected negative charges due to the hole accumulation [100], [106].

The functionality of the FETs biosensors have been enhanced through applied nanomaterials such as graphene, carbon nanotubes, and metals oxides [102], [107], [108]. The use of graphene and graphene-related nanomaterials in FETs have presented switchable charge-carrier mobility through their interaction with molecules [106]. Biosensors based on nanomaterials field-effect transistors have gained much attention as a cutting-edge approach in the biosensor application due to their attractive features such as their excellent performance in aqueous solution, real-time and fast response, high sensitivity and operated at very low voltage [107], [109], [110].

Fenoy et al. [111] have presented a new strategy of Acetylcholinesterase (AchE) immobilization on graphene field-effect transistors for acetylcholine detection. The demonstrated method is based on electrosynthesis of amino polymer layer on graphene channel substrate. The polymer film presented an excellent electrostatic charge and exhibited a remarkable improvement in the pH sensitivity from (40.8 to 56.3 μ A/pH unit). The graphene FETs shown a shift in Dirac point to more negative values due to conductivity changes induced by the enzyme-catalyzed hydrolysis process. These fabricated biosensor devices showed lower limited of detection of 2.3 μ M with range of monitoring Ach from 5 μ M to 1000 μ M in a flow configuration. The presented biosensor devices demonstrated very low RSD of 2.6%, which revealing good devices reproducibility. Furthermore, the biosensor demonstrated a high selectivity, long-term response and a fast response time with average time of 130s.

Islam et al. [112] have effectively fabricated microfluidic biosensor based on graphene field effect transistor for chlorpyrifos pesticide detection in real samples. The biosensor was fabricated using Si/SiO2 substrate and introduced a single layer graphene nanomaterial which exhibited remarkable sensitivity performance towards pesticide detection. The graphene sensing layer was successfully modified by immobilized anti-chlorpyrifos antibodies. The modified electrode was characterized using FTIR, SEM and UV-Vis spectra technique. The developed graphene FET biosensor demonstrated highly stability, sensitivity, and specificity for chlorpyrifos pesticide detection. The fabricated graphene FET biosensor detection ability was reported by measuring the changes in electrostatic potential. The FET presented an excellent response for chlorpyrifos pesticide detection with limited of detection up to 1.8 fM in spiked samples with linear range of 1 fM to 1μ M.

Thanh *et al.* [41] have successfully prepared graphene films using low-pressure chemical vapor deposition (LPCVD) method on polycrystalline copper foil.

The graphene films were utilized on interdigitated ion selective field effect transistors (ISFETs) to enhance the sensitivity of the fabricated sensor for carbaryl pesticide detection. The reported biosensor was based on enzyme biorecognition through enzymatic inhibition of carbaryl towards urease. The response of the biosensor was observed based on the activities of the enzymatic reaction, where weak current response was obtained from the weaker enzymatic activity of urease with carbaryl. Furthermore, the reported ISFET biosensor demonstrated high sensitivity towards carbaryl pesticide with low concentration detection of 10-8 μ gmL-1. The unique prepared graphene films were characterized using RAMAN, AFM, FESEM and UV-Vis spectra. The graphene films shown strong functionalized hydroxyl groups which formed a strong binding reaction with the amide groups possess in both carbaryl and natural substrate of urease.

Table 1 shows the summery of electrochemical biosensors devices for chemicals and pesticides detect including the current change-based biosensors, resistance change-based biosensors, resistance change-based biosensors, impedance change-based biosensors, and the capacitance change-based biosensors. The table also presented the nanomaterials that have been used to enhance the biosensors performance and the biorecognition elements that have utilized in the biosensors.

V. OPTICAL BIOSENSORS FOR CHEMICALS AND PESTICIDES DETECTION

Optical biosensor methods have been extensively applied for pesticides contaminants detection in food, water and environment because of their excellent merits including easy preparation, lower cost of the materials, and clear observation of the result [48], [77], [125]. However, the quantification of the pesticides requires complex equipment's and professional workers to perform the processes [126].

Miliutina et al. [127] have designed a novel framework for detection and on-line monitoring of organophosphorus pesticides in water and soil samples using a functionalized plasmon active optical fiber. The optical fiber was functionalized using a metal organic to introduce high affinity surface towards the target pesticides Multimode optical fiber was used as naked substrate and a thin gold layers were deposited on its surface, which had affected the absorption band of the plasmon. The designed metalorganic framework successfully afforded the detection of pesticides and distinguished their concentration based on the plasmon absorption band shift. The presented framework layers were characterized and confirmed using XRD, Raman, and XRD measurements. The pesticides detected by the framework were compared and checked using Raman spectroscopy and ellipsometry, which shown a good agreement and corresponding between the spectroscopy and the shift in the designed optical framework refractive index.

Cakir and Baysal [128] have reported sensor chip nanofilms for surface plasmon resonator devices utilizing molecular imprinting method. This study investigates the

Method type	Principle of detection	Material used	Pesticide target	Bio- recognition	Sample	limit of Detection	Year	References
Electrochemical	Current change	Au-NPs	Imidacloprid	Antibody	Tap water Tomato	22 pM	2020	[113]
Electrochemical	Resistance change	CNT, ZnO	Atrazine	Antibody	PBS	21.61 KΩ/µg/mL	2020	[114]
Electrochemical	Current change	Chitosan, Au- NPs, MWCNT	Paraoxon	enzyme	Spinach	0.03 µg/L	2019	[115]
Electrochemical	Impedance change	Platinum nanoparticles	Acetamiprid Atrazine	Aptamer	Water	10 pM	2018	[84][90]
Electrochemical	Resistance change	rGO, Au-NPs	Malathion, Cadusafos	N/A	Tap water	0.1 nM/L	2017	[15]
Electrochemical	Capacitance change	N/A	Bisphenol A	Aptamer	Canned food	152.93 aM	2017	[116]
Electrochemical	Capacitance change	N/A	Pathogen	DNA	N/A	1.5 aM	2017	[80]
Electrochemical	Resistance change	MWCNT	Tetracycline	Aptamer	Milk	10 ⁻⁹ M	2017	[117]
Electrochemical	Impedance change	Chitosan	Carbaryl	enzyme	N/A	1 ng/mL	2017	[118]
Electrochemical	Impedance change	N/A	Chlorpyrifos	Antibody	N/A	0.014 ng/mL	2015	[92]
Electrochemical	Impedance change	Au/MWCNT- rGONR	Acetamiprid	Aptamer	Water	1.7*10 ⁻¹⁴ M	2015	[119]
Electrochemical	Impedance change	N/A	Carbofuran	Antibody	N/A	N/A	2014	[120]
Electrochemical	Impedance change	N/A	Carbendazim	Aptamer	Tap water	0.9 ng/mL	2014	[121][122]
Electrochemical	Impedance change	Au-NPs	Acetamiprid	Aptamer	Tomatoes	1 nM	2013	[93]
Electrochemical	Impedance change	N/A	Atrazine	Antibody	Water	10 ng/mL	2011	[91]
Electrochemical	Impedance change	Au-NPs	atrazine	Antibody	Red wine	50µg kg ⁻¹	2010	[94][95]
Electrochemical	Impedance change	N/A	Atrazine	Antibody	Red wine	0.19 μg L ⁻¹	2008	[123]
Electrochemical	Resistance change	N/A	Atrazine	Antibody	Wine grapes	8.3 μg L ⁻¹	2007	[63]
FET	Current change	Graphene	Acetylcholine	enzyme	Spiked urine	2.3µM	2020	[111]
FET	Resistance change	Graphene	Chlorpyrifos	Antibody	Spiked samples	1.8fM	2019	[112]
FET	Current change	Graphene	Carbaryl	Enzyme	N/A	10 ⁻⁸ μg/mL	2018	[41]
FET	Current change	CNT	Atrazine	Antibody	Water	0.001 ng/mL	2015	[124]

TABLE 1. Summery	of e	lectrochemical	biosensors	for	pesticides	detect.
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N/A= no data available.

affinity and kinetic of pesticides binding with the SPR sensor. The study implemented by investigated the binding of the pesticides that imprinted and nonimprinted with the SPR sensor. In addition, the selectivity of the pesticide imprinted nanofilms was compared with the selectivity of the nonimprinted nanofilms, the SPR sensors analysis has showed that the imprinted nanofilms demonstrated more selectivity and sensitivity than the nonimprinted nanofilms. Furthermore, the capability of the SPR for pesticides detection was validated for qualitative and quantitative analysis by using exact masses of pesticides molecular and fragmentation ions and determined by liquid chromatography ion trap time of flight mass (LC/MS-IT-TOF) spectroscopy. The analysis exhibited that the limited detection of the dimethoate and carbofuran were found to be 16.92 ng/L and 20.47 ng/L in the spectroscopy technique and 8.37 ng /L, 7.11 ng/L when utilizing the SPR sensor system respectively. The results of the SPR presented a remarkable accuracy, good recovery features, with recovery percentage between 90 and 95 for both pesticides, higher sensitivity, excellent selectivity, and reduced detection limits compared to the liquid chromatography spectroscopy.

Bala *et al.* [32] have presented a novel sensing strategy for malathion pesticide detection using the colorimetric sensing technique, employing unmodified gold nanoparticles, aptamer and polyelectrolyte polydiallydimethylammonium (PDDA). This technique is based on the specific malathion aptamer protecting the surface of the gold nanoparticles from aggregation in the solution containing NaCl [77]. However, when the malathion pesticide present in the solution, the aptamer turn into new structure to form aptamer/malathion complex, consequently the gold nanoparticles go through salt-induced aggregation, changing the color of the solution from red to blue revealing that the malathion pesticides present in the solution, and the solution color will not change if there is no malathion pesticide present in the solution [32]. This type of biosensor is straightforward and can be completed in a few minutes. This method was linear in the concentration range of 0.5-1000 pM with limit of detection of 0.06 pM and this assay has successfully recognized malathion pesticide in the present of other substance, therefore, it has the potential to be used for the rapid screening of malathion pesticide process [32]. However, the colorimetric sensing process is required complex equipment to recognize the color changing and quantify the color intensity with related to the pesticide quantification, thus, this is defending the capability of the sensor to be used as portable device for in-situ process [27].

Table 2 presented the summery of the optical biosensor for pesticides detection including the wavelength

Method type	Principle	Material	Pesticide	Bio-	Sample	limit of	Year	Referenc
	of	used	target	recogniti		Detection		es
	detection			on				
SPR	Wavelengt	Gold layer	Fenitrothion,	N/A	Water,	N/A	2020	[127]
	h change		Paraoxon		soil			
SPR	Reflectivity	N/A	Dimethoate,	Molecular	Water	8.37 ng/L	2019	[128]
	change		Carbofuran	imprinted		7.11 ng/L		
Fluorescence	Intensity	polymer	Malathion	Aptamer	Water	4 pM	2018	[62]
	change							
SERS	Intensity	Silver	Malathion	Aptamer	Tape	N/A	2018	[45]
	change	nanoparticle			water			
Colorimetric Color	Color		Malathion	Aptamer	N/A	0.06 pM	2016	[132][37]
	change	Au-NPS						

 TABLE 2. Summery of optical biosensor for pesticides detection.

N/A = no data available.

changes-based biosensor which utilized the surface plasmon resonance technology, reflectivity changes-based biosensor also used the surface plasmon resonance technology, intensity change-based biosensor utilized fluorescence and SERS technology, and colorimetric based biosensor. Furthermore, in the optical biosensors, the researchers always applied metals nanoparticles such as silver nanoparticles, gold nanoparticles, and some types of polymers as demonstrated in table 2.

The optical-based biosensors for chemicals and pesticides detection are sometimes preferable over the conventional analytical techniques due to their advantages including the high sensitivity, specificity, selectivity, small size, real-time and label-free detection of many chemicals, biological, and pesticides substance. However, the optical biosensors required specific material with advanced structure, electrical and optical properties for the chemicals and pesticides detection and required sophisticated equipment's for the device characterization. Therefore, the optical biosensors are still need extra development to be capable for the portable diagnosis application.

VI. MECHANICAL BASED BIOSENSORS FOR CHEMICALS AND PESTICIDES DETECTION

Micro-electro-mechanical systems (MEMS) resonant sensors have been shown their ability and excellent performance in the micro-weighing and mass sensors [27], [77], their application including DNA hybridization and immunosensor development [131]. Piezoelectric MEMS resonator sensors can be used as sensitive, selective and label-free sensors for biological and chemical detection in real time [25].

Currently, there are various types of label free MEMS such as, micro-cantilevers devices for sensing and actuations processes using electrostatic, piezoelectric, optical, and electromechanical methods, thin film piezoelectric MEMS resonant mass sensors, and quartz-crystal-microbalance (QCM) [25]. The QCM is a piezoelectric resonant sensor device, QCM is one of the most extensively utilized mass-sensing method for chemical and biological species detection. The reported QCM sensors are operated by a considerably high resonance frequency about 5-20 MHz [22]. In addition, the thin film piezoelectric resonant sensors are similar to the QCM in the way of their operation, where generating acoustic waves and measuring the variation in the surface of the sensor [50], [131], [132].

Furthermore, in the last decade, there are several types of MEMS actuators and sensors have been developed for the chemical and biological detection in aqueous and liquid environment. In the actuations section, there are MEMS sensors developed with electrothermal, electrostatic, and capacitive excitation method. However, by comparing the electrostatic to the electrothermal excitation at a certain frequency in air and DI water, they found that the electrostatic actuation increased by 60-70 times in water due to the material permittivity and the thermal conductivity in the thermal actuation [133], [134].

Al-ghamdi et al. [133] have successfully design and fabricated a novel electrostatic MEMS actuator with capacitive sensor for mercury acetate detection in deionized water environment. The sensor utilized polymeric sensing material to observe the mercury acetate dissolved in the water. The sensor is based on the mass change measurement and the response was successfully detected through the frequency shift measurement. In addition, Mukundan and Pruitt [135] have presented an electrostatic comb-drive actuator operated in high conductive solution. The operated frequency of the actuators was found to be range 1-10 MHz in ionic and biological cell environment. They have demonstrated different designs to overcome the attenuation due to losses in the parasitic impedance. The electric double layer phenomena have been investigated and the response of the fabricated device has been measured using planar force mechanism.

In the other hand, Tao *et al.* [136] have developed and demonstrated in-plane-mode resonant cantilever sensor for real time detection of chemical and biological in liquid environment. They have designed and developed the

Method and mode	Bio recognition	Target	Frequency	Quality factor	LOD	Reference
Electrostatic actuation- capacitive sensing MEMS	Polymer	Mercury acetate	32-39 MHz	N/A	N/A	[133]
Electrostatic actuation- capacitive sensing MEMS	N/A	Cell	1-10 MHz	N/A	N/A	[135]
Electrothermal actuation Piezoresistive sensing	biotin	E. Coli , Hg ²⁺ ions	N/A	2096 in air, 249 in water	100 ppb	[136]
FBAR Shear mode with ZnO film	Enzyme	Chlorpyrifos pesticide	1.47 GHz	411 in air, 298 in liquid	$4.1 \times 10^{-11} M$	[24]
FBAR Shear mode with AIN film	Antibody	CEA protein	1.2 GHz	170	2045.89 Hz cm ² ng ⁻¹	[137]
FBAR mode with AlN film	Aptamer	Tumor marker Mucin	575 MHz	N/A	818.6 Hz nM ⁻¹ .	[138]

TABLE 3. Summary of the pesticides detection methods using MEMS.

N/A = no data available.

cantilever with electrothermal excitation mode and piezoresistive frequency read out. Furthermore, they have illustrated that the in-plane-mode can decrease the liquid drag force, comparing to the out of-plane resonance cantilever. The device shows Q-factor of 249 in water with cantilever connected with a phase-lock-loop interface circuit, and Q-factor of 2096 in air. However, some other researchers suggested that the electrothermal actuation mode is not perform well comparing with the electrostatic actuation mode [133].

Furthermore, Chen *et al.* [24] have presented a shear mode film bulk acoustic resonator (FBAR) with ZnO film for the pesticide detection operated with 1.47 GHz and Q-factor 411 in air and 298 in liquid solution. The illustrated detection principle is based on enzymatic reaction between the enzyme and the pesticide which effect the mass loading on the surface of the resonator. The pesticide sensing by FBAR is similar to the quartz crystal microbalance (QCM) where the specific enzyme immobilized on the surface of the device and once the target binds to the immobilized enzyme receptor, the frequency of the natural resonance will be decreased due to the increasing in the mass after the binding successfully performed.

Zheng *et al.* [137] have reported a shear mode film buck acoustic resonator operated with resonant frequency near 1.2 GHz for carcinoembryonic antigens (CEA) detection in liquid environment. The device was fabricated and integrated with a polydimethylsiloxane (PDMS) microchannel. They have obtained that the frequency shift of the sensor was proportionately increase with the concentration of the target. Furthermore, the Q-factor of the device was 170 and the sensitivity of the sensor was calculated to be approximately 2045.89 Hz cm² ng⁻¹. These kind of devices shows great application potential for the mass loading biosensors in the liquid media. Furthermore, thin film acoustic resonators with AIN have been developed by Guo *et al.* [138] for biological detection. The device operated with a resonant frequency of 575 MHz and utilized aptamer as biorecognition materials for tumor marker mucin 1. The device shows sensitivity about 818.6 Hz nM⁻¹ and good linear relationship between the frequency shift and concentrations of MUC1 ranging from 30 to 500 nM, with limited detection of 500 nM. However, the Q-factor of the device is not calculated in the published paper.

In addition, Cervera, et al. [22] have enhanced a highfundamental-frequency QCM for quantification of carbaryl pesticides chemical residues in honey for food safety requirement. The device is based on piezoelectric sensor with operated frequency of 100 MHz and biorecognition element of antibody immunoassay. The detection principle of the device is depending on the transducer which converts the bio-recognition events from the surface of the device into a measurable electrical signal in term of electrical phase. The shift of the electrical phase can be used as quantified method for the pesticide's concentration detection. The QCM device has demonstrated its ability to determine the carbaryl in honey with limit of detection of 17 ug/L without any sample pretreatment. However, the QCM devices are showing some disadvantages in detection small amount of pesticides and their structure is easy to fraction and broken [52]. From the various researches that have been implemented, this section can be concluded by, the suitable actuation mode for the chemical and biological detection sensors is the electrostatic and piezoelectric actuation modes, in the other hand the electrothermal actuation mode is characterized by some researchers to be less effective [133]. Furthermore, the sensing read out mode, it is concluded that the most recommended mode is the capacitive mode. However, there are some challenges

in the actuation mode for liquid environment such as the formation of the electric double layers around the electrodes which merged in the fluids creates effect that impedes the electrostatic actuation [139]. Another challenge is electrolysis, the disassociation of hydrogen and oxygen atoms due to voltage difference between the actuation electrode [134]. Furthermore, the squeeze-film damping, added mass, and the motion of the structure in the fluid are other types of challenges need to overcome in the future researches [15], [64], [71]–[75]. These types of challenges are addressed and still under development and they might overcome by a unique design.

VII. CONCLUSION AND FUTURE PROSPECT

This review describes various detection and analytical strategies such as electrochemical, optical and mechanical methods, which have developed using enzymes, antibodies, aptamer, and molecularly imprinted polymers for chemicals and pesticides detection to ensure food safety. The electrochemical biosensors have shown significant improvement during the last decade and they provide a powerful analytical tool for chemicals and pesticides determination with simple, rapid, selective, sensitive, and inexpensive features. In addition, this review has also highlighted some drawbacks of the electrochemical biosensors especially in the process of converting the biosensors to be used as portable devices. While remarkable progress has been made towards improving the sensitivity of the detection through the utilization of nanomaterials, there are also opportunities to enhance the reusability and portability of the devices.

Furthermore, researchers have developed the optical biosensors and there have been tremendous progressed in enhancing their capabilities to monitoring the chemicals and pesticides in the food industries. Some of the latest advances strategies has been described, however, the optical biosensors are still facing difficulties due to the complex and huge equipment required for the detection process which is not desired for the portable and on-site monitoring of chemicals and pesticides. On the other hand, MEMS based biosensors for biological, chemicals and pesticides detection have illustrated with some drawbacks which are still needed to overcome. Therefore, the future endeavors should directly focus on the addressed obstacles to improve the devices performance and current demands such as on-site monitoring of the dangerous chemicals for enhancing environment and ecosystem life.

Overall, the prospect of the in-situ and portable biosensors as instruments for chemicals and pesticides detection seems significant and powerful tools and should attract more researchers to this area of research. Furthermore, the in-sit, portable and cost-effective analytical method for chemicals and pesticides detection is expected to be the dominant tools in the instrumentation field.

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