9

Review Article

Peshang Khdir Omer, Eman Ibraheem Abdulkareem, Rebaz Anwar Omer* and Rzgar Faruq Rashid

A review of organometallic compounds as versatile sensors in environmental, medical, and industrial applications

https://doi.org/10.1515/revic-2024-0055 Received July 7, 2024; accepted August 1, 2024; published online August 28, 2024

Abstract: Sensing technology is gaining attention and continuously advancing, making it a recommended element of individualized healthcare management. This is due to the powers exhibited by organometallic compounds, which are further enhanced by the field of bioengineering. Organometallic compounds have a wide range of biological activity and find uses in industrial and material science fields. Their unique ability to specifically target and overcome constraints faced by traditional counterparts makes them potential contenders for sensor technology. These compounds are highly sensitive to changes in their environment, allowing them to be utilized as sensors for detecting various chemicals or conditions. Additionally, the versatility of organometallic compounds enables their integration into different sensor platforms, making them suitable for environmental monitoring, medical diagnostics, and industrial quality control. This article provides a comprehensive summary of recent advancements in the design and synthesis of organometallic compounds, with a specific emphasis on their potential use as sensors. It also discusses the changes made to the structure, the processes used for functionalization, the incorporation of microfluidics, and the resulting impact on the materials' sensing capabilities. These biologically derived methods align with sustainability goals and enhance the affordability, applicability, and effectiveness of sensing.

Peshang Khdir Omer, Department of Physics, College of Science, University of Riparian, Sulaymaniyah, Iraq

Eman Ibraheem Abdulkareem, Department of Chemistry, Faculty of Science & Health, Koya University, Koya, KOY45, Kurdistan Region, Iraq **Rzgar Faruq Rashid**, Department of Medical Laboratory Science, College of Science, Knowledge University, Erbil, 44001, Iraq

Keywords: sensing technology; organometallic compounds; biological activity; sensors; microfluidics

1 Introduction

In the past few years, researchers have shown a notable surge in their attention towards organometallic elements, that are distinguished by the existence of a minimum of a single bond among a carbon atom with a metal. ^{1,2} This heightened attention towards these drugs can be ascribed to its unique chemical composition and biological characteristics. For a substance to be categorized as organometallic, there is necessary for there to exist at least a single covalent connection between a metal and a carbon atom, whereby the carbon atom is a constituent of an organic molecular group. ³ The different uses of organometallic compounds has greatly broadened the scope of chemistry. Catalysts are used in lab and commercial settings to speed up processes without being utilized up. Furthermore, they function as intermediaries in different procedures. ⁴

Organometallic substances are becoming increasingly favourable options for the production of sensors due to their distinctive characteristics.⁵ The use of them as sensors has greatly enhanced the detection and tracking of dangerous gases in factories, enabled evaluation of the atmospheric environments,⁶ and helped in the prevention of fires and explosions accidents. The existing scientific review widely recognizes the importance of their uses, as demonstrated by a multitude of reviews, books with research papers produced in this past few years. However, it is clear that there are current shortcomings when it comes of having the capacity to choose, maintain stability, and other elements related to the progress of delicate substances. Therefore, the investigation and progress of innovative high-performance sensors have significant practical importance and usefulness.⁷

Chemical alarms are typically produced after being detected by chemical detectors. Sensors that use chemicals are able to be mostly fall into two types: electrochemical sensors and photochemical detectors. Various recognizing uses, such as continuous tracking, conserving energy, alarm

^{*}Corresponding author: Rebaz Anwar Omer, Department of Chemistry, Faculty of Science & Health, Koya University, Koya, KOY45, Kurdistan Region, Iraq, E-mail: rebaz.anwar@koyauniversity.org. https://orcid.org/0000-0002-3774-6071

systems, contamination monitoring, asset identification, analysis of processes, meteorological observations, distant evaluation, manufacturing automation, culinary maintenance, manufacturing, telemetry, which and healthcare, are all examples of instances in where chemical detectors are utilized extensively. Chemical sensors share parallels with the gustatory and olfactory senses that are present in human beings. Furthermore, Ammonia (NH₃), CO, H₂, and methylbenzene are substances that these sensors can detect, even if human organs aren't very good at it. Chemical sensors are instruments that can identify chemical substances. Chemical data including pressure, concentration, and particle activity are transformed into an electrical impulse via these devices. 9,10 The generation of either quantitative or qualitative information on individual chemicals is made possible by this signal's existence, with the capacity to accurately analyses both the timing and location aspects. The process of identifying and describing chemical substances presents several complex challenges, requiring the use of chemical sensors to evaluate their distinct features. The identification of the sensing capabilities of a molecular unit relies on the chemical composition and reaction of that molecule. It is possible for the amount or proportion of the item or compound that is being analysed to have an effect on the sensitivity as well as the upper limit of detecting.¹¹

In recent times, scientists have demonstrated an intense desire to utilizing compounds that are organometallics as biological sensors in medical care settings to enhance diagnosis of medical problems and monitoring of patients. 12,13 The term "biosensor" refers to very sophisticated analytical machinery that integrates a biological detecting component. 14,15 This type of technology may be utilized for a wide variety of purposes, such as evaluation, study of drugs, monitoring, protection, and security of the natural world, biomedicine, food manufacturing and safety, and monitoring of the environment. A primary biosensor, which was developed in 1962 by Lyons and Clark, was intended to be used for the purpose of determining the amount of glucose present in biological samples. Electrochemical detection was the method that was applied by this biosensor apparatus, employing a glucose oxidase electrode that was immobilized oxygen or hydrogen peroxide can be detected using this method. 16 Since then, there have been notable progressions in techniques and uses involving biosensors, employing innovative approaches that integrate nanotechnology, bioelectronics, and electrochemistry. Technical procedures that are utilized in biosensors are derived from detecting methods that are either label-based or label-free. 17 The efficacy of mainly utilizes label-based sensing depends on the distinguishing attributes chemical compounds that are used for the goal of identifying targets. While generally reliable,

these kinds of biosensors frequently call for the incorporation of a specialized component of the detection system which is manufactured using an adsorbed protein of interest. On the other hand, the label-free method allows for the identification of molecules of interest which are neither labelled or difficult to mark.¹⁸

In the years that have passed, there have been an increasing tendency for multidisciplinary cooperation, which involves putting up the disciplines of the field of biotechnology biological engineering, electrical and electronics engineering, and others in order to build label-free biosensors. 19 There have been numerous uses for these label-free biological sensors in the fields of both environmental research and healthcare, and they have been shown to be extremely successful in a variety of detecting procedures. The introduction of the glucometer, utilizing glucose sugar oxidase-based biosensors, marks a significant breakthrough pertaining to the field of electrochemical biosensor techniques.²⁰ The biosensors for glucose are highly favoured in the medical field, especially in hospitals and diagnostic clinics, because they play a crucial role in enabling regular evaluation in patients' levels of glucose in their blood with diabetes. However, biosensors for glucose often face challenges due to unstable enzyme activity or lack of uniformity, which requires further calibration. These cited restrictions led to the creation of several biomolecules with unique electrochemical properties. As a result, this made it easier to investigate and recognize biosensors that measure glucose that have become more efficient.²¹

Taking this into consideration, organometallic compounds are now recognized as potentially useful options for the construction of biosensors. Because of their distinctive characteristics, they are well-suited for overcoming certain constraints faced by conventional biosensors. When creating biosensors with electrochemical activity, it is usual to modify the outermost layer of metal and carbon-based electrodes using biomaterials such as DNA, antibodies, or enzymes. In order to generate output signals, biosensors make use of biomaterials that are located on the surface of the electrode, often through the process of either binding or catalytic reactions. The creation of biosensors with electrochemical activity to assess the amount of reactive oxygen species and antioxidants present in the body is an important modern advance.^{22,23}

The aim of this review is to highlight the potential of organometallic compounds in advancing sensor technology for individualized healthcare and other fields. It focuses on the unique properties of these compounds, including their biological activity and sensitivity to environmental changes, which make them suitable for use in drug development, diagnosis, and various sensing applications. The article also

covers recent advancements in the design, synthesis, and functionalization of organometallic compounds, emphasizing their integration into sensor platforms for diverse applications like environmental monitoring, medical diagnostics, and industrial quality control. Additionally, it discusses how these methods align with sustainability goals and improve the affordability and effectiveness of sensing technologies.

2 Literature review

This review provides a thorough analysis of the evolving properties of organometallic materials, with a specific emphasis on their application as biological sensors and their potential impact on medicine.

2.1 Principle of organometallic complexes

The term "organo-" is used to describe the fundamental concepts of organometallic substances and includes all compounds that include a link among M–C in an organyl group (such as organoplatinum complexes). Aside from the traditional metals found in the s, d, and f block elements, the p-block metalloid components like selenium, arsenic, silicon, and are boron believed to generate compounds that are organometallics.²⁴

There are some organometallic biosensor compounds as illustrated in Figure 1.

- a) Inorganic, organic, or polymeric insoluble substrate found within the sample under investigation.
- b) A chemically attachment of indicator by electrical or covalent bonds, or it is absorbed, physically adsorbed, dispersed, or immobilized to the substrate. The chemical engages in a process that can be reversed with the

organometallic substances, leading to the formation of a reaction product that displays unique emissions, refraction, or absorption within the wavelength range of 150–15,000 nm. Some instances, the N-[2-(4-hydroxy benzyl) phenyl] derivatives of triphenylmethane are among the indications that fall within this category and 1,10-phenanthroline.

c) An optical detector measures the absorption, reflection, or emissions of a modified support at a certain wavelength and transforms it into the quantity of organometallics present in the solution being monitored. The methodology for quantifying amount of organometallic elements present in the sample by the utilization of an internet-connected sensors in negative charged in nature polymeric reactions has been elucidated.²⁵

2.2 Preparation techniques that are commonly used

A brief overview of the procedure for the preparation of 4,4',4" – Tris [trans-Pt (PEt₃)₂I(ethynyl phenyl)] ammine Figure 2 was reported by Ghosh et al. The procedure involves synthesizing Tri[p-ethynyl phenyl] amine and subsequently combining it with trans-diiodo bis (triethyl phosphine) platinum in a Schlenk Container with a circular bottom and a capacity of 100 mL under a N₂ atmosphere. Subsequently, 25 mL of toluene that has been dried and degassed, together with 10 mL of diethyl amine that has also been dried, were introduced. Introduce 25 mg of CuI into the solution following continuous agitation for approximately several minutes at temperature of the surrounding environment. After being left at room temperature for 16 h, a minor quantity of diethyl ammonium iodide precipitates in the mixture. The solvent used was removed under vacuum,

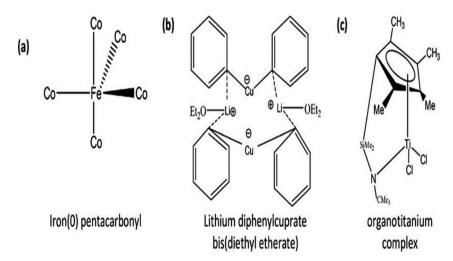


Figure 1: Organometallic complex examples.²⁵

$$\begin{array}{c} B_{\Gamma_2} \\ AcOH \\ \end{array} \begin{array}{c} B_{\Gamma_2} \\ AcOH \\ \end{array} \begin{array}{c} Me_3SiC \equiv CH \\ NEt_3, Pd\text{-catalyst} \\ \end{array} \begin{array}{c} Na_2CO_3 \\ MeOH \\ \end{array} \begin{array}{c} MeOH \\ \end{array} \\ PEt_3 \\ Et_3P \\ PEt_3 \\ \end{array} \begin{array}{c} PEt_3 \\ PEt_3 \\ PEt_3 \\ \end{array} \begin{array}{c} Na_2CO_3 \\ PEt_3 \\ PEt_3 \\ \end{array} \begin{array}{c} Na_2CO_3 \\ PEt_3 \\ PEt_3 \\ \end{array} \begin{array}{c} Pet_3 \\ Pet_3 \\ Pet_3 \\ Pet_3 \\ \end{array} \begin{array}{c} Pet_3 \\ Pet_3 \\ Pet_3 \\ Pet_3 \\ \end{array} \begin{array}{c} Pet_3 \\ Pet_3 \\ Pet_3 \\ Pet_3 \\ Pet_3 \\ \end{array} \begin{array}{c} Pet_3 \\ \end{array} \begin{array}{c} Pet_3 \\ Pet_4 \\ Pet_5 \\ Pet_$$

Figure 2: (4, 4′,4″ – Tris[trans-Pt (PEt₃)2I (ethynyl phenyl)] amine) preparation scheme.²⁶

resulting in the remnant. The column chromatography procedure was then performed on silica gel using a solvent mixture of hexane or benzene to extract the desired product. The yellow waste was isolated, followed by the end result was created having an output of 64 % (2:1). In order to obtain the nitrated result (M), the iodide derivatives are treated with silver nitrate. M (12 mg, 0.006 mmol) and L (2.86 mg, 0.009 mmol) solutions were both dissolved in methanol and acetone, respectively. were combined and subjected to overnight cooking in a bath of oil heated to 50 °C. The addition of ether resulted in a yield of 96 % for the product.²⁶

2.3 Potential biosensing applications

A biosensor is created by combining an electrical, optical, or piezoelectric actuator in conjunction with a biological sensor, which may include an antibody, enzyme, cell, microorganism, or dsDNA. The biosensors provide a practical approach for screening and monitoring algal toxins, in addition to instrumental analytic techniques.²⁷ Diverse categories of biosensors have been created to detect algal toxins and evaluate the risks linked to toxin poisoning. These biosensors employ several

concepts like piezoelectric, fluorescence polarization, electrochemiluminescence (ECL), surface plasmon resonance (SPR), and electrochemical are some of the techniques that are included. The bio-responsive component comprises a variety of elements, such as microorganisms and biological (molecules and structures). There are three primary components that make up biological sensors: such as biological elements that detects and generates signals in response to the analytic agent, a signal the transducer, and an apparatus for reading. Since its introduction by Clark and Lyons in 1962, the use of biological sensors has been increasing.

A broad range of applications for biosensors could be found in a variety of disciplines, including healthcare, agriculture, the environment, and food production, among others. In addition, they are applied for the identification of infections in products such as poultry, fresh meat, and vegetables. In the beginning, the primary focus of early investigations in the field of wearable sensors was on the monitoring of important physiological indicators and the assessment of physical activity. Monitoring equipment have diverse applications in various fields like fitness, sports, medicine, consumer products, and entertainment. Moreover, gadgets that are employed to track for signs of

falls in the elderly community.³¹ Wearable technology is being utilized to measure essential physiological indicators for medical tracking, including high blood pressure, blood sugar levels, ECG readings, heartbeat, perspiration production, temperature of the body, saturation of oxygen in the blood, breathing rate, and capnography. Furthermore, biological sensors are currently utilized for the swift detection and evaluation toxins produced by algae found in seafood, marine algae, and samples taken from freshwater. The main challenge in the actual application of it is the biosensors that lack of comprehensive understanding of identification processes and the behaviours of dangerous macromolecules at detecting connections, although progress in transducer systems.³²

2.3.1 Dopamine's function in the biosensor system

In addition to being an important neurotransmitter, dopamine also performs critical roles throughout the cardiac and nervous systems. Thus, higher quantities of dopaminergic serve as a sign of cardiotoxicity, characterized by symptoms such as rapid heart rate, high blood pressure, and inadequate cardiac function. On the other hand, it is well-established that reduced dopamine amounts in the brain are a contributing factor in the development of a number of neurological diseases and disorders, such as Alzheimer's illness, parkinsonism, schizophrenia, and stress-and depression-related disorders.³³ Furthermore, biosensors made of electrochemical substances exhibit prompt and highly sensitive responsiveness, allowing for immediate

monitoring, and can be effectively reduced in size for insertion into living cells. However, there are still a few unresolved problems that need to be addressed. At first, it is crucial for biosensors to demonstrate an increased degree of responsiveness in the given concentration ranges. In the case of an unaffected person, this range normally falls among a value of 0.01-1 µM. On the other hand, those who are affected by Parkinson's illness requires detecting skills that lie in the nanomolar interval.³⁴ Furthermore, it is noted in Figure 3 it is in order for the biosensors to efficiently separate dopamine from its pollutants, such as uric acid or ascorbic acid, it is vital for them to possess a sufficient level of selectivity. This is because it is essential for the biological sensors to be able to distinguish between the two substances. These interfering compounds experience inside the same voltage range as dopamine, oxidation taking place. The complicated architecture of biological matrices, such as blood or serum for humans, presents a substantial obstacle in analysing authentic samples with the dopamine biosensor, mostly due to its selectivity. This matrix includes not just common substances that can interact, such as uric acid or ascorbic acid, also many neurotransmitters in the body and molecules. To identify dopamine in real material using electrochemical methods, it is usually necessary to include extra steps as part of the procedure for preparing samples to reduce the impact of the matrix impact.³⁵ Centrifugal force is an essential step that must be done before diluting and analysing blood specimens. In contrast, urine samples only need to be diluted before examination. Specialized substances can be used to reduce the influence of the matrix by removing the desired substance or interfering substances. Furthermore,

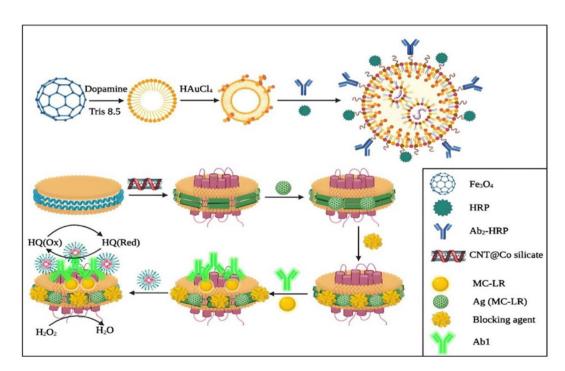


Figure 3: Using dopamine for proceeding of biosensor.⁵

while analysing specimens from biology like cerebrally additional fluid, the number of obtainable specimens is extremely restricted. Therefore, it is crucial to use cautious attention while handling them. Using miniaturized Microelectrodes designed for the purpose of conducting real-time analysis within living organisms is considered advantageous for these types of specimens.36

2.3.2 Amperometry glucose sensors

There has been a considerable improvement in the treatment of patients who have diabetic as a result of the employment of amperometry glucose sensors, and continuing research is studying potential uses of these sensors in the regulation of insulin dosage. However, there are situations where the precision of current sensors is not ideal, which can be caused by variables including calibration inaccuracy, sensor deviation, or delay. Inaccuracies can pose considerable issues in a closedloop glycaemic control system. In order to measure the movement of electrical current that takes place between electrodes throughout the process of a redox process, amperometry biological sensors are utilized.³⁷ It is commonly acknowledged that among amperometry biosensor systems, the glucose sensor (GOs) has been investigated the most. In this mechanism, GOs catalyses between glucose and the relationship between and oxygen, leading to the production of a substance known as H₂O₂. Conventional method of illustrating the signal is graphing the current of electricity (estimated in amps) against the amount of glucose. This relationship is a result of a reduction-oxidation reaction involving at the working electrode either a mediator or H₂O₂ molecule. The majority of biosensors that use amperometry that use conducting polymers (CPs) are classified as third-generation biosensors. In these biosensors, on the surface of the transducer, both the enzyme and the mediator are directly connected to one another. Consequently, recognition of indication does not depend on the mediation of chemical waste materials or the dispersion of chemical waste materials being present.³⁸

Amperometric biological sensors are employed to measure the current or voltage produced by the chemical interaction of electrically charged substances on the transducer's interface. This is accomplished by administering a persistent voltage or current, contingent upon the particular measurements being carried out. The change in electrical current is exactly proportional to the amount present of the individual item being studied. The amperometry biological sensors make use of a working electrode (WE), which is typically constructed of expensive elements such as gold, titanium, and nickel, or materials like carbon coated with bioreceptor components or indium tin oxide. In order to perform its function, an amperometric sensor measures the

amount of electric current that is produced when a voltage is applied. This current is produced as a result of the enzymatic conversion or protein absorption that takes place at the electrode's outermost laver. Through the detection of an analyte's current reaction at a particular potential, amperometric detectors are utilized for the purpose of determining the concentration of an analyte. MET makes it possible to detect levels of glucose in blood vessels at low potentials while simultaneously improving both sensitivity and specificity.^{39,40} The process of signals creation takes place on the electrode's surface, as depicted in Figure 4. Substrate facilitates the involvement of the enzyme in the oxidationreduction process, while MET deoxidizes and replenishes it. The catalysis flow is produced by the transport of mediators between the enzyme and the electrode molecule, as a result of the oxidation-reduction cycling between reduced and oxidized states. Potential application of mediator for the sensitive determination of glucose in the bloodstream with low limits of detection.41

The voltage that is applied throughout the process of electron migration of the analytes is what keeps the process moving forward, and the current being measured indicates the concentration of the substance being studied. The present state is regulated by the law of Faraday that affected by a dynamic response which generates situations within the environment that are stable through its presence. When measuring the amount of the electroactive species, it is absolutely necessary to differentiate between capacitive currents and faradaic currents. A technique known as chronoamperometry used to study the relationship between current and time while the potential remains constant. Enzymatic processes and their inhibition by certain toxins, like okadaic acid (OA), are used in several amperometric sensors. This method usually depends on inhibiting poisons that particularly target the immobilized protein phosphatase, PP2A.42 The method measures the changes in quantification of enzyme activity using the measurement of the current produced by the relevant enzymatic substrates. Employing electrochemical enzyme sensors ensures great sensitivity in the detection of OA. A study was conducted to create a customized composite film via electro polymerization, which consisted of poly-o-aminophenol-carbon nanotube (PoAP-CNT). While the PP2A enzyme was being immobilized on a screen-printed carbon electrode (SPCE), the composite film was utilized as a substrate. The construction of a portable electrical enzyme sensing for OA detecting was accomplished by utilizing this method, which resulted in the limit of detection that was significantly lower compared to that provided by the colourimetric PP2A inhibition assay. 43 This is illustrated in Figure 5.

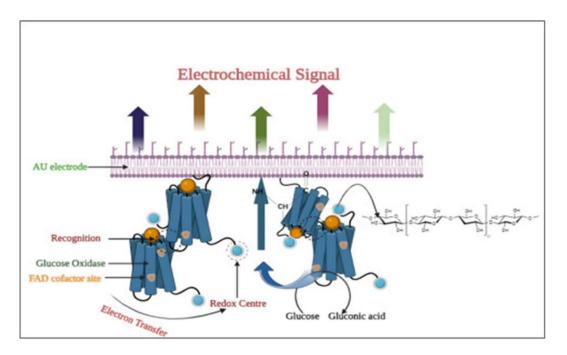


Figure 4: The amperometric glucose biosensor generates glucose signals through a specific process.⁵

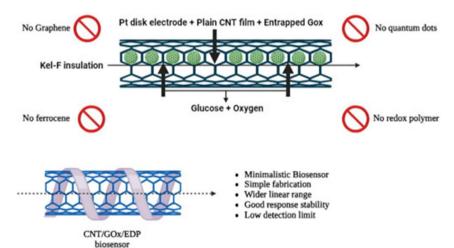


Figure 5: The carbon nanotube biosensors that are used for the labelling of electrochemical enzymes are disposable.⁵

2.3.3 Optical biosensing application

In recent years, there has been notable advancement in the area both optical and electronic technology. As a result, there has been a surge in research and development activities focused on optic and fibre optic biomedical devices. Recently, newly founded healthcare businesses, established leaders in the field of medical devices, and universities have shown a high degree of interest and made substantial efforts to investigate optical innovations for different diagnostics and sensor purposes. Such uses involve a variety of sensors that utilize both biochemical and biophysical concepts.

Optical bio-physical sensors are utilized for evaluating various physiological parameters such as temperature of the body, the blood motion, and pressure in the brain.⁴⁴ Conversely, the diagnosis of cancer, the identification of blood molecules, and the monitoring of blood nutrients are all examples of possible applications for optical biochemical sensors. When it comes to optical biomedical sensors, fibre optic probes are an appropriate choice to remotely monitor physiological data inside the human body. Fibreoptic probes have numerous favourable attributes, making them extremely valuable in diverse applications. Significantly, these probes demonstrate substantial capacity for miniaturization, allowing them to be used in tiny

systems. Furthermore, fibre optic probes show exceptional biocompatibility, especially when it comes to the visible and near-IR wavelength range. Additionally, using radiation as an interface allows for rapid data transfer, improving efficiency for testing purposes. A concise description of current study activities in the field of biological optical sensors will be included in this part and will be presented here. These include the study of a variety of processes, including interferometry, infrared absorption and scattering, among others. 45

2.4 Microbial electrochemical sensors

Microbial electrochemical detectors are a type of microbial electrochemical technology (MET) that can identify pulses using either anodes or cathodic electrically charged microorganisms and/or biofilms. These METs stand for bio electrochemical devices (BES), in which microorganisms operate as biological catalysts to enhance intended processes. 46

External electron transfer (EET) pathways are very important for the operation of microbial electrochemical technology (MET), especially when it comes to bioremediation. Electron transfer between microorganisms and electrodes, where both microorganisms and electrodes serve as cathodes and anodes, can occur via two distinct approaches. The primary mode involves immediate management of the transfer; involves the formation of an interaction between the outermost layer of the electrode and a biofilm that is both electrically conductive and alive. A further aspect of the alternative method is the use of an indirect transfer mechanism supported by soluble redox shuttles. In the field of wastewater treatment, the use of direct electrolysis technologies (EET) is a used technique. This technology makes use of microbial electrolysis cells, it is commonly considered advantageous and was found to lead to increased current density and increased Coulomb efficiency, when examining the pros and cons of bioremediation versus direct organic waste treatment, it is important to think about whether indirect EET might have some advantages. These behaviours are mostly attributed to the prevalence of redox mediators in subsurface environments, which include, among others, sulphur, iron, and humic acid species. A recent study found that placing an anode in the right place can indirectly speed up the oxidation process of petroleum hydrocarbons in marine sediments. The findings of this study support this hypothesis. Included in this discussion is an illustration of a study that provided evidence. The elimination of toxic sulfide molecules is the way by which this improvement is performed. This improvement is accomplished by increasing the metabolic rate of sulphate-reducing bacteria, which is encouraged by it. The capacity of the oxidation reduction

mediator to move and travel is one of the most significant aspects of indirect electrochemical electron transfer. This ability results in a wider range of action for the electrode, which is one of the most important aspects at all. The biologically active zone in the subsurface extends as a result of this alteration, which is the effect that this has on the planet.⁵

2.4.1 Pathogen detection sensors

The electrochemical detection of microorganisms has the ability to rapidly detect and monitor infections and bacterial infectious illnesses. The detection systems have the ability to rapidly, accurately, and effectively detect pathogenic microorganisms, cell metabolites, signalling chemicals, and hormones. Microbial electrochemical detectors are capable of detecting glucose and L-lactate, which are chemicals involved in cellular signalling. The detectors employ Gluconobacter oxidants and Hansenula polymorpha. Microbial electrochemical sensors are utilized in clinical pathogen identification applications to detect electrochemically active pathogenic bacteria in samples that are clinically significant. ⁴⁷ The aforementioned designs do not have any organic catalysts present on the surface of the electrode by creating redox-active mediators as secondary metabolites, pathogenic bacteria seen in clinical specimens perform the function of catalysts. The presence of the particular pathogen under investigation is the only condition under which these mediators provide a signal that can be detected. Scientists have developed microbial electrochemical detectors using arrays. Such sensors can efficiently and rapidly identify the aggressive disease of humans Pseudomonas aeruginosa. Redox-active phenazine metabolites are generated and monitored for recognition throughout infections. Microbial electrochemical sensors possess the capability to swiftly and economically identify infections in both environmental monitoring and medical diagnostics, while also being highly adaptable. Several microbial electrochemical sensing platforms have been created for pathogen detection. However, only a few have extensively investigated analytical figures of merit such as response times and linear dynamic ranges, and have conducted tests on the sensors in complicated biological contexts. Other detrimental microorganisms present in samples may impede the effectiveness of microbial electrochemical sensors employed for pathogen detection. Subsequent investigations in this domain could gain advantages through the utilization of wearable and self-sustaining microbiological electrochemical sensors.48

2.4.2 Toxicity monitoring sensors

Toxic biosensors have been developed through the use of antibiotics, heavy metals, and pesticides to alter the metabolic processes of electroactive bacteria. Presently, researchers are focussing on improving the sensitivity of these gadgets through investigating alternative operating options, such as continuous or transient operations, while also striving to make them smaller in size. There were studies on the presence of electrically charged bacteria that can withstand high amounts of certain heavy metals, such as Cr, Cd, and Ni. Microorganisms have been utilized in this process. In the development of stress detectors, offering the benefits of cost-effectiveness and portability. 49 The experimental results clearly showed that it is possible to restore the electrical impulse as long as the number of elements remains under a specified limit. Developing portable devices that are capable of functioning independently and do not require an external power source has been the subject of a great amount of attention and effort in recent years. Furthermore, it is of the utmost importance to admit that the microbial electrochemical sensors that were utilized for the purpose of toxicity assessment did not display substantial levels of selectivity. This is something that should be acknowledged. Nevertheless, the impact of a wide variety of hazardous compounds on the response of these sensors makes it possible to take precautionary steps and identify potentially dangerous situations in a timely way. The use of full photosynthetic bacteria and chloroplasts that have been isolated has recently been exploited by researchers in order to develop herbicide biosensors that are able to function through using solar power. 50 At the regulatory levels established by the United States Environmental Protection Agency, the biosensor that was discussed before is able to detect the quantities of pesticides that are regularly used. Anodic microbial electrochemical sensors for toxicity monitoring have the stated goal of increasing the detection limits of pollutants. This is in contrast to biosensors, which primarily focus on increasing the linearity range of their range of detection. The World Health Organization (WHO) has established a standard for water quality, and the detection levels of these toxicity biosensors continue to exceed that standard.⁵¹ MET-based sensors, which are utilized for the treatment of wastewater, have been subjected to previous research that has investigated the impacts of a number of biocides, as well as the presence of heavy metal ions, including Agb, Hg2b, Pb2b, and Cu2b. It was determined through the course of the research that the biocides were not having any impact whatsoever on the responses that the biofilm was exhibiting at the time. The electrocatalytic performance of the biotechnology is evaluated based on these current responses, which are used as a measurement standard. The results of the study suggest that microbial fuel cells have the potential to be utilized in the field of wastewater treatment. This conclusion is based on the implications of the investigation. As a further point of interest, the findings indicate that biofilms that are electrically charged and originate from wastewater might not be suitable for use as sensor components in microbial toxicity sensors. In this regard, the results demonstrate. 52 Evaluated the sensor' performance in complex biological contexts by measuring analytical parameters such as both linear dynamic ranges and reaction times are used. Efficacy of microbial electrochemical detectors in identifying pathogens could be impeded by the presence of detrimental microorganisms in the specimens. Subsequent investigations in this domain could gain advantages from the utilization of wearable and selfsustaining microbial electrochemical detectors.⁴⁸

2.5 Application of MF technology to sensors and biosensors

The field of microfluidics (MF) is concerned with the development and implementation of technological solutions that make it possible to exert control over fluids on a microscopic level.⁵³ The technology serves an essential part in the advancement of bioassay-based chemical sensors, particularly in areas such as immune assays, amplifying DNA, cell division, and evaluation. Microfluidic systems an easy approach for managing several aspects of the cellular microenvironment, including orientation in space, providing a practical method for controlling. In MF systems, the creation of cellular arrays is being done by the utilization of one-step cell patterning. This is being done in order to improve diagnostic applications. In the realm of nanotechnology, techniques such as lab-on-a-chip (LOC) and microfluidics (MF) are included. Recently, there has been a growing use of these methods to examine biological processes, specifically in the context of studying cells. It is likely that technologies such as MF or LOC have the possibility of not only making it easier to examine individual cells but also providing a platform for the development of cells. They could do both of these things. In addition to this, these technologies are able to effectively integrate and automate the process of manipulating cells in conjunction with detecting methods.⁵⁴ For the objective of isolating mesenchymal stem cells that were obtained from amniotic fluid, the MF has been successfully employed throughout the process. The stem cells have been identified through the utilization of size-based selection criteria and by the modification of the flow velocity of the specimen in order to assess their capability of passing through a variety of MF channels that are distinguished by their variable sizes. The earlier work revealed an initial efficiency of the separation of mesenchymal stem cells after separation at 82.8 %. Nevertheless, by iterative cycling, the degree of separation was notably enhanced to 97.1 %. MF devices have been increasingly utilized in the areas of cancer diagnostics, respiratory illness identification, and heart attack monitoring.⁵⁵

2.5.1 The diagnosis of cancer

Cancer, a multifaceted illness that may develop in many bodily parts, is universally acknowledged as a widespread and extremely deadly worldwide medical problem. The need of rapidly detecting malignancy is undeniable. 56,57 Right now, many methods such as PET scanner, MRI, and CT scan are utilized for the identification and determination of the extent of tumours that are cancerous. The chemotherapy medications used for the treatment of cancers often cause several side effects. The simultaneous accomplishment of therapeutic and diagnostic outcomes is made possible through the incorporation of nanoparticles with imaging or locating agents into the system. One of the multifunctional systems that are utilized for this particular application is consisting of theragnostic nanoparticles. For the purpose of identifying and describing cancer biomarkers, MF systems are utilized. These biomarkers include circulating tumour cells (CTCs), circulating tumour DNA (ctDNA), exosomes, non-coding RNA (ncRNA), and a variety of biological metabolites and proteins. In addition, the evaluation of biomarkers in small volumes of liquid samples acquired from people who have cancer on a regular basis is an essential component in the process of developing individualized therapy. The use of antibodies that were immobilized on CTC chips allowed for the precise separation of CTCs from blood. CTCs, which mostly express epithelial cell adhesion molecules, were isolated from blood. The debulking, inertial concentrating, and isolation steps of the CTC-iChip system were incorporated into the system in order to improve it.⁵⁸ Ganesh et al. developed a new microfluidic (MF) device using Electrodes made of zinc oxide and pH sensors were utilized in order to differentiate between circulating tumour cells (CTCs). Oscillating flow, acoustic waves, cluster-chip, and Dean vortex flow are examples of MF technologies that have the potential to successfully separate CTCs from blood without the need for labelling. It is essential to highlight the utilization of these technologies. Furthermore, a range of techniques including immunoaffinity, he isolation of exosomes has been accomplished through the utilization of a dielectrophoretic system, a nano membrane filter, lateral displacement, and acoustic fluid. Microfluidic (MF) devices provide valuable tools for studying and addressing related to cancer processes, examples of such processes include apoptosis, resistance to therapy, metastasis, and invasion. Through the utilization of nano-scale porous silicate particles that were loaded with doxorubicin, Han et al. developed a system that is responsive to both redox and pH signals. Specifically, the purpose of the study was to evaluate the management of nanoscale porous silicate particles in the context of breast cancer treatment. Researchers conducted

an independent study where they developed a medication method of administration using polymer nanoparticles that contained paclitaxel and lonidamine. These nanoparticles were specifically designed to target the EGFR receptor. The purpose of this method is to efficiently address drugresistant breast cancer cells by employing a combined therapy strategy. In the research carried out by Baghbani and colleagues, a result of the usage of ultrasound in conjunction with doxorubicin-loaded alginate-stabilized perfluorohexane nanodroplets, it was discovered that the tumours in mice that were afflicted with breast cancer were reduced considerably.^{5,59}

2.5.2 Detection of cardiovascular diseases

Inadequate health of the heart and blood vessels can lead to cardiovascular diseases (CVDs), which include coronary artery disease (CAD), stroke, and hypertension. These disorders have a significant influence on the rates of premature death around the globe. The accurate identification of cardiovascular disease (CVD) has a crucial role in decreasing mortality rates. Currently, when the health of the heart and blood vessels is impaired, CVDs such as stroke, hypertension, and CAD can develop. These disorders have a significant influence on the rates of premature death around the world. 60 Nevertheless, it is crucial to improve the precision, specificity, and sensitivity of current methods of diagnosis to develop effective diagnostic systems for the early detection of cardiovascular diseases.⁶¹ Beck et al. developed a sensor device using microfluidics (MF) to check for variations in the levels of NT-proBNP. Silver nanoparticles (AgNPs) were modified so that they could function as a labelling agent, which allowed this to be performed. In order to accomplish this objective, the application of flow injection analysis was employed to detect AgNPs that had been changed by antibodies. This facilitated the incorporation of laminar flow assay and electrochemical analysis. The developed biosensor allows precise identification of NT-proBNP using an insignificant volume collected from the finger prick. This renders the biosensor appropriate for utilization in a residential environment and facilitates its user-friendly operation. 62 In their research, Yin et al. introduced a magnetic field (MF) platform having a unique snail-shaped structure. The objective of this platform was to identify certain biomarkers, including myoglobin, cardiac troponin I, and creatine kinase-MB, for the goal of diagnosing an acute myocardial infarction. In this study, a microfluidic chip (MF chip) was developed. The device utilized a chemiluminescence detector and included a reaction layer at its core, which contained particular antibodies. 63

3 Conclusions

This study offers a thorough examination of the application of metals as sensors and emphasizes significant investigations into novel medical substances. The investigation of organometallic compounds is a research issue that is both fruitful and currently undergoing rapid advancement in a variety of rehabilitative fields. For the purpose of monitoring complexes and keeping track of intermediates and species in solution, both chemical and biological methods are utilized. Utilizing detection and characterisation techniques greatly enhances the identification and structural investigation of the resulting solid complex. Our understanding of the structural and molecular alterations that are related with the utilization of metallic sensors is being greatly improved by both preclinical and clinical research. The capacity of organometallic compounds to function as sensors is the primary reason for their significance in the domains of chemistry, electrochemistry, and biology. With applications in the quickly developing domains of bioanalytical and medicinal sciences, this flexibility in molecular biology provides tremendous promise and many benefits. Microfluidics (MF) has lately proven outstanding success in treating COVID-19, even surpassing their established application in the detection of cardiovascular illness and cancer. This breakthrough comes in addition to the other benefits that MF offers in the identification of diseases. With the help of a mass transfer or reaction kinetics approach, it is possible to manipulate the control of the signal in sensing characteristics. Whether the limiting step is mass transfer or reaction kinetics, it is essential to be aware that the performance of the device can vary greatly depending on which one is selected.

Research ethics: Not applicable.

Author contributions: The authors have accepted responsibility for the entire content of this manuscript and approved its submission.

Competing interests: The authors state no conflict of interest.

Research funding: None declared. Data availability: Not applicable.

References

- 1. Fagnou, K.; Lautens, M. Rhodium-Catalyzed Carbon-Carbon Bond Forming Reactions of Organometallic Compounds. Chem. Rev. 2003, 103, 169-196.
- 2. Marks, T. J. Introduction to the "Recent Advances in f-Element Organometallic Chemistry" Special Issue of Organometallics. Organometallics 2013, 32, 1133-1136.

- 3. Tyagi, M. K.; Nishad, G. R.; Verma, D. K.; Guo, L.; Berdimurodov, E. Classification of Organometallic Compounds. In: Organometallic Compounds: Synthesis, Reactions, and Applications, 2023; pp 47-70.
- 4. Elschenbroich, C. Organometallics; John Wiley & Sons: USA, 2006.
- 5. Mishra, D. P.; Acharya, B.; Tripathy, S.; Barik, B.; Sahu, P. K. An Overview of the Biosensing Potential of Organometallic Compounds. Chem. Phys. Impact 2023, 100326; https://doi.org/10.1016/j.chphi.2023.100326.
- 6. Bastani, K.; Rao, P. K.; Kong, Z. An Online Sparse Estimation-Based Classification Approach for Real-Time Monitoring in Advanced Manufacturing Processes from Heterogeneous Sensor Data. IIE Trans. **2016**, 48:579-598.
- 7. Vigneshvar, S.; Sudhakumari, C.; Senthilkumaran, B.; Prakash, H. Recent Advances in Biosensor Technology for Potential Applications-An Overview. Front. Bioeng. Biotechnol. 2016, 411; https://doi.org/10. 3389/fbioe.2016.00011.
- 8. Fracchiolla, N. S.; Artuso, S.; Cortelezzi, A. Biosensors in Clinical Practice: Focus on Oncohematology. Sensors 2013, 13, 6423-6447.
- 9. Dornelles Mello, L.; Kisner, A.; Oliveira Fonseca Goulart, M.; Tatsuo Kubota, L. Biosensors for Antioxidant Evaluation in Biological Systems. Comb. Chem. High Throughput Screen. 2013, 16, 109-120.
- 10. McDonagh, C.; Burke, C. S.; MacCraith, B. D. Optical Chemical Sensors. Chem. Rev. 2008, 108, 400-422.
- 11. Frost, M. C.; Meyerhoff, M. E. Real-Time Monitoring of Critical Care Analytes in the Bloodstream with Chemical Sensors: Progress and Challenges. Annu. Rev. Anal. Chem. 2015, 8, 171-192.
- 12. Patra, M.; Gasser, G. Organometallic Compounds: An Opportunity for Chemical Biology? Chembiochem 2012, 13, 1232-1252.
- 13. Peng, K.; Zheng, Y.; Xia, W.; Mao, Z.-W. Organometallic Anti-tumor Agents: Targeting from Biomolecules to Dynamic Bioprocesses. Chem. Soc. Rev. 2023, 52, 2790-2832.
- 14. Palchetti, I.; Mascini, M. Biosensor Technology: a Brief History. In Sensors and Microsystems: AISEM 2009 Proceedings; Springer: USA, 2009; pp 15-23.
- 15. Purohit, B.; Vernekar, P. R.; Shetti, N. P.; Chandra, P. Biosensor Nanoengineering: Design, Operation, and Implementation for Biomolecular Analysis. Sensors Int. 2020, 1100040; https://doi.org/10. 1016/j.sintl.2020.100040.
- 16. Jamal, A.; Rahman, M. M.; Khan, S. B.; Faisal, M.; Akhtar, K.; Rub, M. A.; Asiri, A. M.; Al-Youbi, A. O. Cobalt Doped Antimony Oxide Nano-Particles Based Chemical Sensor and Photo-Catalyst for Environmental Pollutants. Appl. Surf. Sci. 2012, 261, 52-58.
- 17. Bhattacharjee, S.; Gokalgandhi, B.; Singh, A. Industrial Automation and Sensing Using ZigBee. Int. J. Comput. Appl. 2014, 105, 37-40.
- 18. Agriopoulou, S.; Stamatelopoulou, E.; Skiada, V.; Varzakas, T. Nanobiotechnology in Food Preservation and Molecular Perspective. In: Nanotechnology-Enhanced Food Packaging, 2022; pp 327–359.
- 19. Gaba, S.; Chauhan, N.; Chandra, R.; Jain, U. Future Advances of Artificial Biosensor Technology in Biomedical Applications. Talanta Open 2024, 9, 100301.
- 20. Kitamura, A.; Torii, K.; Uneyama, H.; Niijima, A. Role Played by Afferent Signals from Olfactory, Gustatory and Gastrointestinal Sensors in Regulation of Autonomic Nerve Activity. Biol. Pharm. Bull. 2010, 33, 1778-1782.
- 21. Seekaew, Y.; Pon-On, W.; Wongchoosuk, C. Ultrahigh Selective Room-Temperature Ammonia Gas Sensor Based on Tin-Titanium Dioxide/ Reduced Graphene/Carbon Nanotube Nanocomposites by the Solvothermal Method. ACS Omega 2019, 4, 16916–16924.
- 22. Debus, B.; Parastar, H.; Harrington, P.; Kirsanov, D. Deep Learning in Analytical Chemistry. TrAC, Trends Anal. Chem. 2021, *145*, 116459.

- 23. Loock, H.-P.; Wentzell, P. D. Detection Limits of Chemical Sensors: Applications and Misapplications. Sensor. Actuator. B Chem. 2012, 173, 157-163.
- 24. Cortes-Clerget, M.; Yu, J.; Kincaid, J. R.; Walde, P.; Gallou, F.; Lipshutz, B. H. Water as the Reaction Medium in Organic Chemistry: From Our Worst Enemy to Our Best Friend. Chem. Sci. 2021, 12, 4237-4266.
- 25. Brown, W. H.; Iverson, B. L.; Anslyn, E.; Foote, C. S. Organic Chemistry; Cengage Learning: India, 2022.
- 26. Ghosh, S.; Mukherjee, P. S. Self-Assembly of a Nanoscopic Prism via a New Organometallic Pt3 Acceptor and its Fluorescent Detection of Nitroaromatics. Organometallics 2008, 27, 316-319.
- 27. Nayak, M.; Kotian, A.; Marathe, S.; Chakravortty, D. Detection of Microorganisms Using Biosensors - A Smarter Way Towards Detection Techniques. Biosens. Bioelectron. 2009, 25, 661-667.
- 28. Rahman, M. S.; Abdulrazak, L. F. Utilization of a Phosphorene-Graphene/TMDC Heterostructure in a Surface Plasmon Resonance-Based Fiber Optic Biosensor. Photon. Nanostruct: Fundam. Appl. 2019, *35*, 100711.
- 29. Newman, J. D.; Setford, S. J. Enzymatic Biosensors. Mol. Biotechnol. 2006, 32, 249-268.
- 30. Chen, S.; Qi, J.; Fan, S.; Qiao, Z.; Yeo, J. C.; Lim, C. T. Flexible Wearable Sensors for Cardiovascular Health Monitoring. Adv. Healthcare Mater. 2021, 102100116; https://doi.org/10.1002/adhm.202100116.
- 31. Salayma, M.; Al-Dubai, A.; Romdhani, I.; Nasser, Y. Wireless Body Area Network (WBAN) a Survey on Reliability, Fault Tolerance, and Technologies Coexistence. ACM Comput. Surv. 2017, 50, 1-38.
- 32. Khor, S. M.; Choi, J.; Won, P.; Ko, S. H. Challenges and Strategies in Developing an Enzymatic Wearable Sweat Glucose Biosensor as a Practical Point-Of-Care Monitoring Tool for Type II Diabetes. Nanomaterials 2022, 12, 221.
- 33. Liu, X.; Liu, J. Biosensors and Sensors for Dopamine Detection. View **2021**, 2, 20200102.
- 34. Decarli, N. O.; Zapp, E.; de Souza, B. S.; Santana, E. R.; Winiarski, J. P.; Vieira, I. C. Biosensor Based on Laccase-Halloysite Nanotube and Imidazolium Zwitterionic Surfactant for Dopamine Determination. Biochem. Eng. J. 2022, 186, 108565.
- 35. Sangubotla, R.; Kim, J. Fiber-Optic Biosensor Based on the Laccase Immobilization on Silica-Functionalized Fluorescent Carbon Dots for the Detection of Dopamine and Multi-Color Imaging Applications in Neuroblastoma Cells. Mater. Sci. Eng. C 2021, 122, 111916.
- 36. Fu, C.; Sun, Y.; Huang, C.; Wang, F.; Li, N.; Zhang, L.; Ge, S.; Yu, J. Ultrasensitive Sandwich-Like Electrochemical Biosensor Based on Core-Shell Pt@ CeO2 as Signal Tags and Double Molecular Recognition for Cerebral Dopamine Detection. Talanta 2021, 223, 121719.
- 37. Ward, W. K.; Wood, M. D.; Troupe, J. E. Understanding Spontaneous Output Fluctuations of an Amperometric Glucose Sensor: Effect of Inhalation Anesthesia and Use of a Nonenzyme Containing Electrode. Am. Soc. Artif. Intern. Organs J. 2000, 46, 540-546.
- 38. Andriukonis, E.; Celiesiute-Germaniene, R.; Ramanavicius, S.; Viter, R.; Ramanavicius, A. From Microorganism-Based Amperometric Biosensors Towards Microbial Fuel Cells. Sensors 2021, 21, 2442.
- 39. Cetinkaya, A.; Kaya, S. I.; Ozkan, S. A. A Collection of the Best Practice Examples of Electroanalytical Applications in Education: From Polarography to Sensors. J. Solid State Electrochem. 2023, 1–27; https:// doi.org/10.1007/s10008-023-05637-0.
- 40. Dimcheva, N. Nanostructures of Noble Metals as Functional Materials in Biosensors. Curr. Opin. Electrochem. 2020, 19, 35-41.
- 41. Nikitina, V. N.; Daboss, E. V.; Vokhmyanina, D. V.; Solovyev, I. D.; Andreev, E. A.; Komkova, M. A.; Karyakin, A. A. The Widest Linear Range of Glucose Test Strips Based on Various Mediators and Membranes for

- Whole Blood Analysis. J. Electroanal. Chem. 2023, 938117445; https:// doi.org/10.1016/j.jelechem.2023.117445.
- 42. Ren, Y.-S.; Li, H.-L.; Piao, X.-H.; Yang, Z.-Y.; Wang, S.-M.; Ge, Y.-W. Drug Affinity Responsive Target Stability (DARTS) Accelerated Small Molecules Target Discovery: Principles and Application. Biochem. Pharmacol. 2021, 194, 114798.
- 43. Díez-Pascual, A. M.; Cruz, D. L.; Redondo, A. L. Advanced Carbon-Based Polymeric Nanocomposites for Forensic Analysis. Polymers 2022, 14, 3598.
- 44. Kaur, B.; Kumar, S.; Kaushik, B. K. Recent Advancements in Optical Biosensors for Cancer Detection. Biosens. Bioelectron. 2022, 197, 113805.
- 45. Roriz, P.; Silva, S.; Frazão, O.; Novais, S. Optical Fiber Temperature Sensors and Their Biomedical Applications. Sensors 2020, 20, 2113.
- 46. Santoro, C.; Arbizzani, C.; Erable, B.; Ieropoulos, I. Microbial Fuel Cells: From Fundamentals to Applications. A Review. J. Power Sources 2017, 356, 225-244.
- 47. Dizaji, A. N.; Ali, Z.; Ghorbanpoor, H.; Ozturk, Y.; Akcakoca, I.; Avci, H.; Guzel, F. D. Electrochemical-Based "antibiotsensor" for the Whole-Cell Detection of the Vancomycin-Susceptible Bacteria. Talanta 2021, 234, 122695.
- 48. Yu, J.; Yang, M.; Li, Z.; Liu, C.; Wei, Y.; Zhang, C.; Man, B.; Lei, F. Hierarchical Particle-In-Quasicavity Architecture for Ultratrace In Situ Raman Sensing and its Application in Real-Time Monitoring of Toxic Pollutants. Anal. Chem. 2020, 92, 14754-14761.
- 49. Salek Maghsoudi, A.; Hassani, S.; Mirnia, K.; Abdollahi, M. Recent Advances in Nanotechnology-Based Biosensors Development for Detection of Arsenic, Lead, Mercury, and Cadmium. Int. J. Nanomed. 2021, 803-832; https://doi.org/10.2147/ijn.s294417.
- 50. Naik, S. S.; Lee, S. J.; Theerthagiri, J.; Yu, Y.; Choi, M. Y. Rapid and Highly Selective Electrochemical Sensor Based on ZnS/Au-Decorated F-Multi-Walled Carbon Nanotube Nanocomposites Produced via Pulsed Laser Technique for Detection of Toxic Nitro Compounds. J. Hazard Mater. 2021, 418, 126269.
- 51. Venkatesan, M.; Veeramuthu, L.; Liang, F.-C.; Chen, W.-C.; Cho, C.-J.; Chen, C.-W.; Chen, J.-Y.; Yan, Y.; Chang, S.-H.; Kuo, C.-C. Evolution of Electrospun Nanofibers Fluorescent and Colorimetric Sensors for Environmental Toxicants, pH. Temperature, and Cancer Cells-A Review with Insights on Applications. Chem. Eng. J. 2020, 397, 125431.
- 52. Mahajan, S.; Jagtap, S. Metal-Oxide Semiconductors for Carbon Monoxide (CO) Gas Sensing: A Review. Appl. Mater. Today 2020, 18,
- 53. Özbey, A.; Karimzadehkhouei, M.; Akgönül, S.; Gozuacik, D.; Koşar, A. Inertial Focusing of Microparticles in Curvilinear Microchannels. Sci. Rep. 2016, 638809; https://doi.org/10.1038/srep38809.
- 54. Hung, L.-H.; Teh, S.-Y.; Jester, J.; Lee, A. P. PLGA Micro/nanosphere Synthesis by Droplet Microfluidic Solvent Evaporation and Extraction Approaches. Lab Chip 2010, 10, 1820-1825.
- 55. Gharib, G.; Bütün, İ.; Muganlı, Z.; Kozalak, G.; Namlı, İ.; Sarraf, S. S.; Ahmadi, V. E.; Toyran, E.; Van Wijnen, A. J.; Koşar, A. Biomedical Applications of Microfluidic Devices: A Review. Biosensors 2022, 12,
- 56. Koparir, P.; Parlak, A. E.; Karatepe, A.; Omar, R. A. Elucidation of Potential Anticancer, Antioxidant and Antimicrobial Properties of Some New Triazole Compounds Bearing Pyridine-4-Yl Moiety and Cyclobutane Ring. Arab. J. Chem. 2022, 15, 103957.
- 57. Swain, S.; Kumar Sahu, P.; Beg, S.; Manohar Babu, S. Nanoparticles for Cancer Targeting: Current and Future Directions. Curr. Drug Deliv. 2016,
- 58. Ozkumur, E.; Shah, A. M.; Ciciliano, J. C.; Emmink, B. L.; Miyamoto, D. T.; Brachtel, E.; Yu, M.; Chen, P.-I.; Morgan, B.; Trautwein, J.; Kimura, A.; Sengupta, S.; Stott, S. L.; Karabacak, N. M.; Barber, T. A.; Walsh, J. R.;

- Smith, K.; Spuhler, P. S.; Sullivan, J. P.; Lee, R. J.; Ting, D. T.; Luo, X.; Shaw, A. T.; Bardia, A.; Sequist, L. V.; Louis, D. N.; Maheswaran, S.; Kapur, R.; Haber, D. A.; Toner, M. Inertial Focusing for Tumor Antigen–Dependent and-Independent Sorting of Rare Circulating Tumor Cells. Sci. Transl. Med. 2013, 5, 179ra47.
- 59. Park, E. S.; Jin, C.; Guo, Q.; Ang, R. R.; Duffy, S. P.; Matthews, K.; Azad, A.; Abdi, H.; Todenhöfer, T.; Bazov, J.; Chi, K. N.; Black, P. C.; Ma, H. Continuous Flow Deformability-based Separation of Circulating Tumor Cells Using Microfluidic Ratchets. Small 2016, 12:1909-1919.
- 60. Sinha, A.; Tai, T.-Y.; Li, K.-H.; Gopinathan, P.; Chung, Y.-D.; Sarangadharan, I.; Ma, H.-P.; Huang, P.-C.; Shiesh, S.-C.; Wang, Y.-L.; Lee, G. B. An Integrated Microfluidic System with Field-Effect-Transistor

- Sensor Arrays for Detecting Multiple Cardiovascular Biomarkers from Clinical Samples. Biosens. Bioelectron. 2019, 129, 155-163.
- 61. Cheng, H.-L.; Fu, C.-Y.; Kuo, W.-C.; Chen, Y.-W.; Chen, Y.-S.; Lee, Y.-M.; Li, K.-H.; Chen, C.; Ma, H.-P.; Huang, P.-C.; Wang, Y. L.; Lee, G. B. Detecting miRNA Biomarkers from Extracellular Vesicles for Cardiovascular Disease with a Microfluidic System. Lab Chip 2018, 18, 2917-2925.
- 62. Beck, F.; Horn, C.; Baeumner, A. J. Dry-Reagent Microfluidic Biosensor for Simple Detection of NT-proBNP via Ag Nanoparticles. Anal. Chim. Acta 2022, 1191, 339375.
- 63. Yin, B.; Wan, X.; Qian, C.; Sohan, A. M. F.; Wang, S.; Zhou, T. Point-Ofcare Testing for Multiple Cardiac Markers Based on a Snail-Shaped Microfluidic Chip. Front. Chem. 2021, 9, 741058.