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New insights for integration of nano particle with microfluidic systems for sensor applications

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Abstract
A biosensor is a compact device, which utilizes biological derived recognition component, immobilized on a transducer to analyze an analyte. Nanoparticles with their unique chemical and physical properties are versatile in their applications to develop as sensors. Different nanoparticles play different roles in the sensing systems like metal and metal oxide nanoparticles. The application of Gold, Silver and Copper nanoparticles will be discussed in brief. The nanoparticles typically function as substrates for immobilization of biomolecules, as catalytic agent, electron transfer agent between electrode surface and the biomolecules, and as reactants. Microfluidic deals with manipulating very small volumes of fluids (micro and nanoliters). This miniaturized platform enhances control of flow conditions and mixing rate of fluids. The microfluidics improves the sensitivity of the analysis, and reduces the volumes of sample and reagent in the analysis. The review specifically aims at representing microfluidics-based sensors and nanoparticle based sensors. This review will also focus on probable merger of these two fields to take advantage of both the fields and this will help in pushing the boundaries of these fields further more.

Keywords Gold nanoparticles · Microfluidics · Sensor

1 Introduction

The nanotechnology deals with nano-size materials and the properties of nanomaterials have huge potential in analytical applications (Penn et al. 2003).The nano-size particles or nanoparticles are those, which have at least one dimension between 1 to 100 nm. At nano-size level particles exhibit very different chemical, physical (optical and electronic) properties from those of bulk form. The unique properties of nanoparticles are explored to develop new sensing devices with integration with new emerging technologies. The metal nanoparticles (like Copper (Cu),Silver(Ag), and Gold(Au)have excellent optical (absorbance, surface enhanced Raman spectroscopy, surface plasmon resonance), Magnetic (Abedini-Nassab et al. 2021) and electrical (Wang et al. 2001) properties. Nanoparticles size, shape and surface properties make them suitable for electro and biosensor systems (Cosnier 2014; El-Ansary and Faddah 2010; Vertelov et al. 2007). Therefore there is a strong demand for technical platforms that provide sensors with high sensitivity, selectivity and stability. Microfluidics is the study of fluid manipulation in small quantities by using tiny channels having dimensions at the microscale of tens of micrometers (Sommer et al. 2009). Microfluidics is an emerging field with diverse application in fields ranging from biology, medical diagnostic to chemistry. The advantages like portability, high accuracies and real- time detection have been pointed out in many literatures. In recent years the field of miniaturized systems of analysis based on microfluidics have exploded, the field ranges from chemical to biochemical analysis, clinical diagnostics and many other applications (Holmes and Gawad 2010; Mark et al. 2010). These applications have helped the development of the concept of lab-on-chip (LOC) devices or point of care devices. Although there is huge development in the use of microfluidic for analytical application, there are many challenges we still need to consider. The physical conditions in the microfluidic system are very different from that of conventional techniques, such as high surface tension and high surface-to-volume ratio this significantly effects the outcome (Stone and Kim 2001). The sample handling in microfluidics is not just a matter of scaling

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down; there are difficulties in adsorption, injection, mixing, and many more, which are not significant in conventional systems. The microfluidics systems are manly considered for bio sensing applications (Luka et al. 2015). Biosensor are very powerful analytical tool, due to their application ranging from food industries to medial industries (Rivet et al. 2011), from environmental protection to defense and security (Rai and Duran 2011). A biosensor is typically have a recognition element(biological recognition element like enzymes, antibodies or nucleic acids), a transducer (to immobilize the recognition elements) and a detector (which identifies the presence of specific analytes). The fusion between the properties of nanoparticles and microfluidics has led to development of low cost, efficient and portable devices for sample analysis. Therefore, there is a strong demand for technical platforms that provide sensors with high sensitivity, selectivity and stability. The integration of nanotechnology and microfluids has given rise to new forefronts in sensing and analytical applications. There are many reviews that deals with nanoparticle for sensing application (Kalantar-Zadeh and Fry 2008; Rassaei et al. 2011), and synthesis (Abedini-Nassab et al. 2021; Kulkarni and Goel 2020). This review aims to focus on new integrated field of microfluidics and nanotechnology for sensing application. With specific focus on sensors based on metallic nanoparticles like Copper (Cu), Silver(Ag), and Gold(Au).

2 Biosensors

A biosensor is a device that analyzes or detects biological and chemical substance, and generates signals, which can be analyzed to identify the analyte. This device works by integrating biological or components derived biologically in a transducer that convert the variations in mass, optical properties and conductivity into and electrical signal. The three basic components of biosensor connected in systematic order (Bhalla et al. 2016) (1) Receptor (Bio-receptor) It's a molecule that recognize the specific molecule, (2) Transducer, it convert the recognition event into a measurable signal (generally electrical), (3) Electronics, it collects the signal from the transducer and process it and gives the output The IUPAC define biosensor as self-contained integrated device, which is capable of providing specific quantitative or semi-quantitative analytical information using a biological recognition element (Thvenot et al. 1999). Biosensors are required to facilitate to play an important role analytical role in fields like, agriculture, medicine, food safety, environmental, bioprocessing, and industrial monitoring (Luong et al. 2008). Based on the biological recognition element and the transducer, the biosensor can be divided into two types.

2.1 Type of biosensor based biological recognition element

The biological sensing factor determines the selectivity and specificity of the biosensor to react to a specific target or group of analytes, thereby reducing the potential for interaction with undesirable substances (Karunakaran et al. 2015). The biological recognition elements is selected on the basis of the target of interest (e.g. for detection of bacteria or pathogens, antibodies and aptamers are suitable; whereas catalytic reactions are mediated by enzymes). Using various methods such as adsorption, covalent binding, trapment, and membrane containment, the biological recognition elements are usually immobilized. The most popular and preferred form of immobilization is covalent bonding it is highly stable and irreversible, which prevents the leakage of biological elements from the support surface (Mohamad et al. 2015). The immobilization of biological recognition elements on to the surfaces of nanomaterials (nanoparticles) has added novel and interesting dimensions for immobilization. The nanomaterial have unique physicochemical properties, which leads to improvement of biocatalysts efficiency, enhance the working and effectivity of enzymes, improves the specific surface area, reduce the loss of recognition elements thus improving reusability and reduces the cost of analysis (Sardar 2015). These properties of nanoparticle are exploited to develop new and efficient biosensors. The Fig. 1. Represent the different types of Biosensor based Biological Recognition Element.

2.1.1 Enzyme based biosensor

Enzymes are protein capable of catalytic activity at very low concentrations and they speed up the reaction rate without being consumed in the process (Robinson 2015). Enzyme biosensor combines an enzyme with a transducer that produce proportional signal to that of the concentration of the analyte. The signal is the result of catalytic activity of the enzyme on the analyte that produce change in the concentration of protons, release or uptake of gases (ammonia or oxygen), change in light (Its emission, absorption or reflectance), change in heat transmission and many other variations. These changes is detected and converted into measurable signals by the transducer, in the form of change in electrical properties like current or electrical potential, temperature, or optical properties (Coulet and Blum 1991). The advantages of using enzymes in biosensors is that they are highly selective to specific substrates (Justino et al. 2015; Songa and Okonkwo 2016). The first biosensor was glucose biosensor developed by Clark and Lyons in 1962, which utilize glucose oxidase

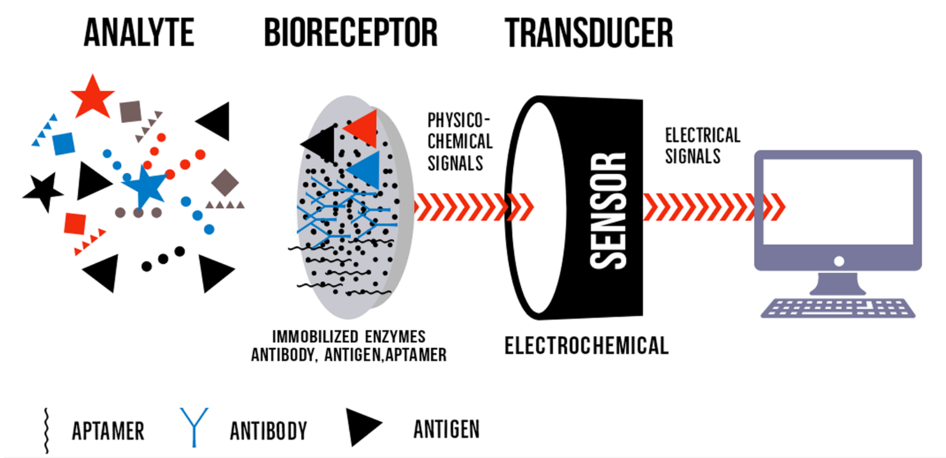

Fig. 1 Represent the different types of Biosensor based Biological Recognition Element, Enzyme, Antibody and Aptamer sensors

enzyme coupled to the electrode (Clark and Lyons 1962). The enzyme- based have recently proved to be an innovative approach in the field of disease diagnostics and research applications (Kataria et al. 2014). Table 1 Summarizes enzyme based biosensor.

2.1.2 Antibody-based biosensor

The antibody-based sensor are used for rapid detection and point of care use, with requirement of any special skill. Antibody-based biosensors or immunosensors have a wide range of applications in disease marker identification, food and environmental contaminants detection, and many more (Holford et al. 2012; Luppa et al. 2001; Ramírez et al. 2009). The development of monoclonal antibody (Mab) technology by Kohler and Milstein (1975) and recombinant technologies (Emanuel et al. 2000) have greatly helped in pushing the technology forward. In recent year the nanoparticle and paper based immunosensors have also been utilized as immobilization agent in antibody sensors, this integration significantly enhance the sensitivity and lowers the detection limits of the sensor (Akbari Nakhjavani et al. 2019; Zhu et al. 2019). The possible reason may be the increased surface area and the refraction of light in SPR based sensor(optical immunosensor) (Lee et al. 2018).

2.1.3 Aptamer-based biosensor

These sensor are based on single-stranded, short nucleotides (ssDNA or ssRNA) that interact with target molecules with weak forces like Van der Waals forces, electrostatic interactions, hydrogen bonding, the stable three-dimensional structures of these molecule helps in the interaction (Mayer 2009). These molecule were first discovered in 1990 and named aptamers, since its discovery they are used in the sensing (Rozenblum et al. 2016).

The small size, chemical stability and low cost have made aptamers an ideal element for biosensing recognition components as compared to conventional antibodies based sensors. The integration of aptamers with nanoparticles this approach have improved the performance of aptamer-based sensors. Aptamers have the potential to attach to their particular ligands with dissociation constants in the micromolar to picomolar ranges (Jayasena 1999) and can be selected for a broad variety of analytes, such as viruses, contaminants, proteins and whole cells (Rozenblum et al. 2016). Recently nanomaterials has been used to develop simple colorimetric aptamer-based sensor, this approach used the difference in folding of DNA to identify specific DNA aptamers to identify ions (Li et al. 2009; Wang et al. 2006) and proteins (Chang et al. 2013; Wei et al. 2007).

2.2 Biosensors categorized based on the type of transducers

Biosensors can be divided into many different categories depending on the type of transducer used. The transducer converts the biomolecule-analyte interaction into an optical or electrical signal (Cheng et al. 2007; Liu and Wilson 2010). The sensitivity and detection limit of the biosensor depends on both transducers and biological recognition elements. Transducers can be of following types (a) Electrochemical (These convert electrochemical reactions in electrical signals); (b) optical (These detect change in optical properties examples, including colorimetric); (c) Piezoelectric (These utilize alternating potential of crystals); (d) Magnetic (Detects change in magnetic fields) (Collings and Caruso 1997).

2.2.1 Electrochemical-based biosensors

Electrochemical biosensors offer an attractive means of analyzing the quality of a biological sample due to the direct conversion of a biological event to an electronic signal, which can be measured easily (Grieshaber et al. 2008). The

Table 1 Enzyme based sesors

	Enzyme based sensor	Sensor Application	Advantages	Disadvantages	Reference
1	**Glucose oxidase**	Electrochemical; colorimetric	Glucose specific	Reacts with oxygen; low activity	(Devasenathipathy et al. 2015; Hossain and Park 2016; Ponlakhet et al. 2016)
2	**Glucose dehydrogenase**				
a	D-glucose:ubiquinone oxidoreductase	Electrochemical; colorimetric	High activity;	Broad substrate specificity	(Guo et al. 2016; Kim et al. 2013; Liang et al. 2013)
.b	D-glucose:NAD(P)+ 1-oxidoreductase	Electrochemical	Glucose specific	Cofactor must be supplied	(Tsujimura et al. 2006; Yamaoka et al. 2008)
3	**Alcohol oxidase**	Detection of alcohol amperometrically	high operational stability (6.3% loss after 25 measurements), wide linear detection range of 10 µM-4.7 mM (R(2) = 0.9731), high sensitivity of 68.3 ± 0.35µAmM(-1) and low detection limit of 7 ± 0.027 µM for ethanol		(Chinnadayyala et al. 2015)
4	**Lactate oxidase**	electrochemical sensing platforms for the miniaturization of the lactate biosensor	limit of detection (based on 3-sigma) of 22.6 µM and exhibits a sensitivity of 3417 ± 131 µAM(-1) according to the reproducibility study		(Hernández Ibáñez et al. 2015)
5	**Cholesterol oxidase**	Amperometric biosensor to determine total cholesterol	Showed broad linear range from 0.5 mg/dL to 250 mg/dL (0.01 mM–5.83 mM) with minimum detection limit being 0.5 mg/dL (0.01 mM)		(Lata et al. 2016)

electrochemical sensor have several advantages like, easy of operations, high sensitivity, economical this have led to significant emphasis on merger of sensors and biosensors with electronic elements (Liu et al. 2015; Zhu and Shi 2018). Nanoscale materials, unique properties make them ideal for combining biological interactions with transducers that can generate electrical signal, thus helping in the development a new age bioelectronic devices with entirely new functions (Wang 2005). Nanomaterial offers an adequate microenvironment for the biological recognition elements they provide surfaces for immobilization, and helps in preserving its biochemical activity. This configuration facilitates electron transfer between immobilized biological recognition elements (proteins and antibodies) and the electrode surfaces, leading to its widespread use in the construction of electrochemical biosensors with improved analytical efficiency over other biosensor designs (Pingarrón et al. 2008).

2.2.2 Optical-based biosensors

Optical biosensor offers vital advantages in, analytical and detection techniques over the conventional analytical techniques. It allows wider application in the field of medical diagnostics to food analysis to security and defense (Damborský et al. 2016; Yoo and Lee 2016). The interaction between the target molecule and the biological recognition element cause change in the optical properties this change is measured in proportion to the concentration of the analyte (Hosseini et al. 2014). They have many benefits, making optical detection one of the biosensor field's leading methods of detection. Such benefits include low detection limit, flexibility, label-free, non-destructive, and their ability to simultaneously detect a wide range of analytes or multiple analytes with fast signal monitoring and analysis (Fan et al. 2008; Long et al. 2013). The integration of optical biosensor with microfluidic sensor technique have great potential. Optical biosensors can be easily modified and, miniaturized to be fitted in a single chip to make real time analysis possible and reusability is also possible (Chen and Wang 2020; Kuswandi et al. 2007). Many different types of biological materials, from enzymes to proteins, nucleic acids to whole cells can be recognized using optical biosensors. Optical biosensors can be of many different types based on different optical properties like colorimetric, fluorescence, chemiluminescence, electrochemiluminescence.

3 Integration of microfluidics and nanoparticles

3.1 Microfluidics

Microfluidics is the study and manipulation of minute volumes of fluid in a microchannel, and it has emerged as a technology with powerful implication in the field of biological and chemical analysis (Weng et al. 2019). There has been a steady growth in the interest and production of fluid flow devices on the microscale since the beginning of microfluidics (Whitesides 2006). Microfluidics is a multidisciplinary technology that is neither restricted nor part of an individual sector. Applications for chemical analysis in microfluidics have many merits, such as low cost, short analysis time, the ability to use very small amounts of samples and reagents, and the ability to conduct high resolution and sensitivity separations and detections, and small footprints for analytical instruments (Livak-Dahl et al. 2011). The nanoparticles, due to their very high demand in varies applications from sensing to drug delivery. There is also great demand for eco-friendly method for synthesis, which help in reduction of toxic effect on the environment. The conventional physical and chemical method of synthesis of have many drawbacks. The new green synthesis method like microbial and plant use, extract produced by these organism as reducing agent. The organism like bacteria fungi, algae, virus and plants act as Nano factories. This method produce nanoparticle in affordable and render unique microscopic structure to the nanoparticle. Significant demand and effort have recently been demonstrated in merging biosensors into lab-on-chip (LOC) technology using microfluidics systems, which add numerous advantages to biosensor technology (Luka et al. 2015). The combination of biosensors with microfluidic systems provides an optimized and miniaturized alternative to conventional repetitive laboratory methods, as samples, reagents, energy usage and waste generation are substantially reduced (Lafleur et al. 2016). The nanoparticles can also be integrated into the material used for the fabricating the microfluidic chip, a very example is conductive and magnetic nanoparticle added to the polydimethylsiloxane (PDMS) to prepare composites with conductive or magnetic properties. These composite materials can be manipulated to act as valves and actuators under external magnetic and electric fields (Jiang et al. 2014). In addition, compared to regular detection methods, microfluidic biosensors can reduce the cost and increase the limits of precision and detection sensitivity. Overall, the combination of microfluidic systems with biosensors provides a strong analytical instrument that will be an advanced step towards a home-testing solution that will help both developing and developed countries.

3.2 The functions and types of nanoparticles in biosensors

The Unique properties of nanoparticles have helped development of many applications. The optical, electric and magnetic properties of nanoparticles make them ideal materials for developing of sensors. Different types of nanoparticle i.e. metal nanoparticle, oxide nanoparticle and composite nanoparticle have been used to develop biosensors. The nanoparticles are integrated with microfluidic systems to improve the sensitivity, selectivity and stability of the sensor. The properties of nanoparticles have been already exploited in conventional nanosensors. The use of nanoparticles integrated with microfluidics have improved the detection limit, sensitivity, selectivity, portability and lowered the cost. These sensors can be classified based on their properties like (1) Fluorescent quenching, (2.) Surface-enhanced Raman spectroscopy SERS, (3.) Localized surface plasmon resonance (LSPR) (4.) Surface plasmon resonance (SPR). The various functions of nanoparticles in a sensor can be classified as: Table 2. Metal nanoparticle used in microfluidic Sensors.

3.2.1 Fluorescent quenching

The Fluorescence quenching refers to any process which reduces the intensity of fluorescence (Lakowicz and Lakowicz 1999).The metal nanoparticle (gold, silver and copper) induce efficient quenching looking at their wide application in sensing (Ghosh and Chattopadhyay 2015; Ou et al. 2019). The quenching takes place without any irreversible molecular alteration, that is, without a photochemical reaction and for quenching to occur the fluorophore and quencher must be in contact this property is important for sensor. Microfluidics system is used for droplet generation, manipulation and mixing, this improved the fluorescence for detection of Hg (II) ions with Rhodamine B quenched by gold nanoparticle (Guo et al. 2011). This integration improves the detection limit at low volume and real-time analysis of chemical reaction can be. The gold nanoparticle integrated with microfluidics were used to develop bioassay to detect specific DNA sequence, the detection is based on fluorescence quenching induced by conformational change. The gold nanoparticles was arranged in monolayer form on the walls of microfluidic chip, the DNA probes and fluorophore dye were attached this layer, this caused fluorescence quenching of fluorophores (Li et al. 2005). The method was used for the detection of the PCR product of dengue virus. The 3D origami-based chemiluminescence (CL) immunodevice, combined with the standard luminole-H_2O_2 CL method and catalyzed by Ag nanoparticles, showed excellent analytical efficiency for the simultaneous detection of (AFP, CA153, CA199, CEA) tumor markers (Ge et al. 2012). The another type of chemiluminescence is the electrochemiluminescence (ECL), the ruthenium complex/tripropylamine (TPA) show this behavior TPA acts as the acceptor of the protons this improves the ECL emission. The intercalation of Ru(phen)3 2 + into ds-DNA is the main principle was used to develop sensors using DNA-modified gold electrode (Liu et al. 2010).

3.2.2 Surface-Enhanced Raman Spectroscopy (SERS)

SERS is a molecular detection and characterization technique that relies on the enhanced Raman scattering of molecules adsorbed on or near SERS-active surfaces. It is highly sensitive and powerful technique that allows for structural detection of analytes at a very low concentration through the amplification of electromagnetic fields generated by the excitation of localized surface plasmons (Sharma et al. 2012). As the target analyte reaches or adsorbs on the surfaces (gold, silver, etc.) of metal nanoparticles, the signals can be enhanced by several orders of magnitude compared to standard Raman scattering (Sivanesan et al. 2014). The integration provides many benefits, including significate reduction in volume of analytes and reagents, improve control of parameters like flow rate, temperature control and other environmental parameters, this also reduce the cost of instrumentation and handling (Figeys and Pinto 2000; Skoog et al. 2013). The SERS micro-pattern could be easily incorporated further within microfluidic channels. Ultrasensitive *in situ* SERS monitoring from the transparent glass window was made possible by the resulting microfluidic SERS chip. This approach could be easily extended into optical microfluidic manufacturing for biochemical applications with its advantages of simplicity, versatility and cost-effectiveness (Wu et al. 2018). The SERS properties of silver is also well known, studies show silver nanoparticle (AgNPs)had a specific plasmonic resonance leading to an increase in electromagnetic enhancement, followed by SERS enhancement (Mulvihill et al. 2010). The AgNPs is used to make polymer nanocomposite to make regions of SERS sensitive area directly in the microfluidic device, this integration of microfluidic improves chromatographic efficiency of capillary electrophoresis (CE) and utilizing SERS as a means of analysis (Connatser et al. 2004). The AgNPs is used to make tunable patterned SERS-active substrate integrated with microfluidic capable of detections of Rhodamine 6G SERS spectra, which makes the cost of detection of low and inexpensive (Geng et al. 2011).

3.2.3 Colorimetric method

Colorimetric assay has proven to be an effective analytical technique due to its ease and simplicity (Jazayeri et al. 2018). The color change in colorimetry can be visually assessed even at low concentrations of the target analyte without the assistance of complex instruments. This technique is been used in combination with microfluidic system to improve the sensitivity of detection and lower its cost. A sensor based on color change of AuNPs indicating the concentration of E.coli is been developed. The Cysteine gold nanoparticles (CAuNPs) binds with E. coli through electrostatic adhesion that cause the change in plasmon absorption spectrum

Table 2 Metal nanoparticle used in microfluidic Sensors

Metal Nanoparticles	Nanoparticle Properties used for detection	Detection of	Sensor advantages	Imp Points	Year	References
Gold Nanoparticle based sensor						
	Rhodamine B quenched by gold Nanoparticle(fluorescent Quenching)	Hg (II) ion	The fluorescence intensity increased		2011	(Guo et al. 2011)
	Conformational change-induced fluorescence quenching by gold nanoparticles	DNA sequences or PCR product of dengue virus	Detection of the target genes can be performed *in situ* on the same microfluidic channel		2005	(Li et al. 2005)
	Use of droplet-based microfluidics combined with surface-enhanced Raman scattering (SERS) detection	Hg (II) ion	provides fast and sensitive detection of mercury (II) ions in water	detection limit between 100 and 500 ppt	2009	(Lim et al. 2009), (Choo et al. 2009)
	Colour change of the solution due to the existence of Hg (II) ion	Hg (II) ion				
	Fluorescent and fluorescent gold nanocluster (AuNC)-based sensor	Heavy metal mercury and the dithiocarbamate pesticide(DTC)	Rapid, in-field, detection of environmental contaminants – heavy metals and pesticides	Detection limit is between 0.6 μg L^{-1} up to at least 200 μg L^{-1} using simple fluorescence detection	2012	(Lafleur et al. 2012)
	Detection of antigen–antibody (Ag–Ab) interaction through the LSPR properties of gold nanoparticles	Sensing of bovine growth hormone also known as bovine somatotropin (bST)	Integration of microfluidics and nanoparticles Improvement of size distribution with only 8% variation	Detection limit is as low as 3.7 ng/ml (185 pM)	2013	(SadAbadi et al. 2013)
	PDMS-GNP composite microfluidic system based on the integration of a novel electrochemical immunosensor	Detection of cardiac troponin I (cTnI) and C-reactive protein (CRP)	Simultaneous detection of serum cTnI and CRP	Detection limits of 5 amol and approximately 307 amol in 30-μL samples corresponding to cTnI and CRP	2010	(Zhou et al. 2010)
	Monoclonal antibody (mAb) modified AuNPs-coated indium tin oxide (ITO) electrode was used for capturing of virions	Human Enterovirus 71 (EV71),	Dual detection by colorimetric and electrochemical immunosensor	Detection limit of 1.0 ng mL^{-1} and 0.01 ng mL^{-1}, Completed within 2 h	2018	(Hou et al. 2018)
	Polyaniline-Au nanoparticles (AuNPs) modified paper working electrode (PANI/Au-PWE)	Two tumor markers (carcinoembryonic antigen (CEA) and -fetoprotein (AFP))	The method is use paper microfluidics, it lowers the cost and lower the detection limit by 4 folds	Detection limit down to 0.5 and 0.8 pg·mL^{-1}	2014	(Li et al. 2014)

Table 2 (continued)

Metal Nanoparticles	Nanoparticle Properties used for detection	Detection of	Sensor advantages	Imp Points	Year	References
	Dual signal amplification is achieved by used primary antibody coated GNPs (Ab1-GNPs) and Co(II) catalyst, secondary antibody, luminol multifunctionalized GNPs (Co(II)-Ab2-luminol-GNPs) with chemiluminescence(CL) activity	Three Acute myocardial infarction (AMI) biomarkers i.e. heart-type fatty acid-binding protein (H-FABP), cardiac troponin I (cTnI) and copeptin were simultaneously detected	In this method (3D) microfluidic paper-analytical device (μPAD) with chemiluminescence (CL) emissions was used for the first time,for dual-signal amplification	Detection ranged from 0.1 pg/mL to 1 μg/mL, 0.5 pg/mL to 1 μg/mL and 1 pg/mL to 1 mg/mL for H-FABP, cTnI and copeptin respevtively	2020	(Li et al. 2020)
	Loop mediated isothermal amplification (LAMP) modified gold nanoparticles was used for detection of analyte	Detection of *Salmonella* spp. in food samples	Fast and accurate detection of foodborne, increased specificity in bacteria detection	Very low limit of detection (10 cfu/25 g)	2017	(Garrido-Maestu et al. 2017)
	Gold nanoparticle aggregation	Detection of E. coli O157:H7 in chicken samples			2019	(Zheng et al. 2019)
Silver Nanoparticles Based Sensor						
	Sandwich-type chemiluminescence (CL) Immunoassay system use luminuol-H2O2 CL system and catalyzed by Ag				2012	(Ge et al. 2012)
	Control of silver nanoparticles spacing for increase in surface-enhanced Raman scattering (SERS) signal intensity	Detection of (2,6-pyridinedicarboxylic acid) (DPA)	Use of Combination of, dielectrophoresis (DEP) and hydrodynamic forces to control the interparticle spacing silver nanoparticle in the microfluidic system	Detection of DPA at both ~1 and ~10 ppm concentration	2012	(Chrimes et al. 2012)
	Silver nanoparticles are modified with sodium iodide for in surface-enhanced Raman scattering (SERS) analysis	Detection methamphetamine in saliva	Microfluidic chip-based SERS platform in combination with dielectrophoresis (DEP) for highly localized trapping and release of SERS-active nanoparticles this make it reusable	500 nM methamphetamine in saliva, give positive result	2018	(Salemmilani et al. 2018)

Table 2 (continued)

Metal Nanoparticles	Nanoparticle Properties used for detection	Detection of	Sensor advantages	Imp Points	Year	References
	Surface-enhanced Raman scattering (SERS) property of *in situ* Silver colloid for analysis	Detection of azo dye, 5-(2′-methyl 3′,5′dinitro-phenylazo) quinolin-8-ol, dye is a derivative of trinitrotoluene (TNT) and a potential analyte for explosives detection	This produce a concentrated stream of colloid and thus reduce the effective volume of analysis	Detection limit of 10 fmol	2002	(Keir et al. 2002)
	Metal-polymer nanocomposites(Silver nanoparticles (AGNPs) and Polydimethylsiloxane (PDMS) for Surface-enhanced Raman scattering (SERS)				2004	(Connatser et al. 2004)
	Oligonucleotides adsorbed silver nanoparticles. (AGNPs) to enhanced Surface-enhanced Raman scattering (SERS) effect	Two different types of oligonucleotide **SRY and SPGY1**with Raman dye (Cy3 and TAMRA)	Confocal SERS detection combined with lab-on-achip technology, does not require either an immobilization or amplification for DNA analysis	SERS peaks were detectable for concentration of 10^{-11} M	2005	(Park et al. 2005)
	Microfluidic immunosensor based on silver nanoparticles (AgNPs) covered by chitosan (Cts) attached to the central channel	Epithelial cancer biomarker **EpCAM** (epithelial cell adhesion molecule)	Nanoparticles were used for anti-EpCAM monoclonal antibodies immobilization and biomarker was quantified by HRP	Detection limit is 2.7 pg mL^{-1}	2015	(Ortega et al. 2015)
	Chromatic analysis for Paper-based Analytical Device (μPAD) doped with unmodified silver nanoparticles (AgNPs)	Detection of **mercury(II)** by simple red green blue (RGB) color model		detection limit of 0.001 mg L^{-1} with very small sample volume of (2 μL)	2016,2018	(Jarujamrus et al. 2018; Meelapsom et al. 2016)
	Rapid concentration and detection of bacteria using silver nanoparticles (AgNPs) for (SERS) effect	Detection of *Saccharomyces cerevisiae*, *Escherichia coli* F-amp, and *Bacillus subtilis*	preconcentration method with SERS to rapidly concentrate and detect low bioparticle count samples	Can detect low concentration of as 10^4 colony forming units (CFU/ml)	2007	(Hou et al. 2007)

and the color change of the solution from red to blue is the method of detection (Raj et al. 2015). In the microfluidic chip the bacterial samples was first mixed simultaneously with, hydrogen peroxide, magnetic nanoparticles (MNPs) modified with antibodies and polystyrene microspheres (PSs) modified with detection antibodies and catalase enzyme this induced the color change (Zheng et al. 2019). The AuNPs coated with different chemicals like mercaptopropionic acid, mercaptosuccinic acid cysteamine, and cetyltrimethylammonium bromide, was used for colorimetric detection of microorganism with their unique color shift patter for each microbes (Li et al. 2017).

4 Conclusion

Standard approaches are costly, time consuming, and suffer from a lack of portability for defining and detecting unique targets. The biosensors are complex devices due to its interdisciplinary nature it requires knowledge of electrochemistry, electronics, material science and biochemistry. The incorporation of microfluidics and nanoparticle-based biosensors offers a versatile method to replace conventional bulky tools with a much smaller and portable device. In the recent review on biosensors, it can be noted that there is a huge amount of research going on in this field but the real test for these sensors will be in the testing of real samples, out of the controlled laboratory environment. It is anticipated that the future trajectory of biosensors and microfluidic analytical systems will be towards greater performance, convenience, cost-effectiveness, compatibility, reliability and most of all the to develop these devices as a real product that can be used by anyone.

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