Chapter 6 Application of Nanomaterial-Based Biosensors for Healthcare Diagnostics

Arpan Deyasi, Arighna Basak, and Angsuman Sarkar

Abstract Diagnoses of multifactorial diseases are always difficult owing to lack of proper sensors which can not only detect the low level concentration molecularly imprinted polymers and peptides, but also able to generate electrically measurable signal from biochemical interactions. Nanomaterial-based biosensors are the most accepted and trusted tools in this regard, which serves both the purpose with comparatively lower cost, reliable, and transportable. These sensors are mostly built on wide variety of nanomaterials, including quantum dot, carbon nanotube, grapheme, magnetic nanomaterials, nanofibres, optical nanoresonators and a few imprinted structures. These novel aspects of applications make a new insight of material science research directed towards biological tiny sensor elements, particularly detection of those elements which are not possible by any other physically realisable detecting elements. Applications of nanobiosensors hover around from environment protection by detecting pesticides, water contaminants, etc. to determination of drug residue in food and drinking water. In present day, they are utilised in forensic science, thanks to the possibility of making intra-cellular detection. Laser base sensors at submicron level are capable of detecting organism inside living cells. The final target is to obviously develop lab-on-a-chip, which will make revolution in present medical care facility, and should be affordable to all financial class of people.

A. Deyasi (\boxtimes)

Department of Electronics and Communication Engineering, RCC Institute of Information Technology, Kolkata 700015, India e-mail: deyasi_arpan@yahoo.co.in

A. Basak

A. Sarkar

Department of Electronics and Communication Engineering, Brainware University, Barasat 700125, India

Department of Electronics and Communication Engineering, Kalyani Govt Engineering College, Kalyani 741235, India

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6.1 Introduction

Rapid identification of any infectious illness while it is still in its early stages is critical for public health and efficient clinical results. A disease's early and correct diagnosis is crucial to a successful medical treatment. The process of illness diagnosis entails determining the nature and origin of the condition, as well as analysing the patient's antiquity and pertinent test statistics [\[1](#page-12-0)]. Health analysis must be rapid, precise, and exact, through as a couple of 'false findings' as achievable. Identification techniques that are very highly sensitive and specific assist in the initial analysis of diseases and give an improved forecast. Medical identification technology has a significant influence on overall population health care, and hence, progress in this area is one of applied science's most important goals [[2\]](#page-12-1).

In modern years, much bioengineering research has focussed on producing fast, accurate, movable, and affordable investigative equipment which may be used by patients to observe their own health. For diagnosis, a variety of assays and methods are available, including biosensing element, immunoassay, medical imaging and genetic-based testing. Enzyme-linked immunosorbent assay (ELISA), polymerase chain reaction (PCR)-based genetic tests and discolouration substance for bacterial and viral illnesses such as Gram and Giemsa stains are among the most extensively used symptomatic substances [\[3](#page-12-2)]. Traditional diagnostic procedures have limitations, including low sensitivity, low specificity, and a long decision-making time. The use of nanotechnology in the development of diagnostic tools has proven revolutionary due to the enhanced sensitivity, specificity, and utility of the equipment [[4,](#page-12-3) [5\]](#page-12-4). Biomarker sensing is typically related to expensive prices, extended wait times, and the use of sophisticated automated analysers in centralised laboratories. Nanostructured materials are promise in the development of improved diagnostics because they are cost-efficient, quicker, and more long-lasting. They might also be utilised to eliminate the need for time-consuming laboratory diagnostics and promote pointof-care identification. Nanotechnology, in conjunction with genomics, proteomics, and molecular machine systems, can aid in the development of onsite medical diagnostics that are effective, dependable, and fast. By making it simpler to create novel materials for medical diagnostic equipment, nanotechnology has transformed these modalities.

Lung cancer, ischaemic heart illness, cirrhosis of liver, and other infective diseases stay among the world's top sources of mortality [\[6](#page-12-5)]. A lack of early diagnosis thwarts effective and affordable treatments. Because of its user-friendly, cost-effective, trustworthy, and rapid sensing platforms, biosensors have gained appeal in the field of healthcare diagnostics [[7\]](#page-12-6). In compared to traditional detection techniques such as spectroscopy or chromatography, biosensing technology provides a lot of advantages. These advantages include the removal of the requirement for highly trained operators, faster response times, mobility, and increased sensitivity [[8\]](#page-13-0). With the aid of new biosensors, the detection period of diseases like anthrax has been lowered from 2–3 days to 5 min [[9\]](#page-13-1).

Nanomaterials are distinct as resources through at tiniest one dimension of 1– 100 nm [\[10](#page-13-2)]. The mainstream of their element particles or molecules are positioned on the outward of the constituents because of tiny size, resulting in a striking difference in their important physicochemical belongings when associated to the substance of the same materials. The quantum properties originating from intermittent performance due to the quantum detention of delocalised electrons are another reason generating substantial variations in the properties of nanomaterials. Because there are supplementary elements on the outward of these nanoparticles than in the bulk, they have low energy and hence an inferior melting point. However, the physiognomies of these elements are determined by their form. Nanorods, on behalf of example, can have quite dissimilar physiognomies than nanospheres of the identical material [[7\]](#page-12-6). Chemical reactivity is enhanced by around 1000-fold as a result of the increased surface area per unit mass [\[11](#page-13-3)]. Quantum dots, for example, are synthetic nanostructures that take use of quantum phenomena in nanoparticles. They work as artificial atoms since their electrical performance is extremely adjacent to the tiny particles or individual atoms, because the three-dimensional detention of electrons at the Nanoscale region creates a quantised energy scale. Nanoparticles have magnetic moments as well, owed to numerous unpaired electron turns from hundreds of particles, and exhibit their greatest performance at 10–29 nm diameters due to super magnetism, making them useful as dissimilarity agents in magnetic resonance imaging (MRI) $[10-13]$ $[10-13]$. Nanomaterials can be classified in a variety of ways as a result of all of these features. Based on their chemical makeup, nanomaterials may be categorised into three categories: (1) nanomaterials made of carbon allotropes, (2) inorganic nanoparticles, such as Au, Ag, and $SiO₂$, and (3) organic nanomaterials, such as polymeric nanomaterials. Various nanomaterials used as biosensors are schematically represented in Fig. [6.1](#page-3-0).

Design of nanobiosensor is the trend of research in twenty-first century, which, in turn, critically depends on the development of novel materials and devices in lower dimension. Precisely, identification and detection of physical/living analytes is a very sensitive process, and, therefore, requires sophisticated instruments where reduced dimensional devices play pivotal role in determining weaker signals in near accurate form. Several synthesised nanodevices like semiconductor nanowire, carbon nanotube, quantum dot, nanowire field-effect transistor (FET) have already established their value in evaluating signals from living cells, virus, DNA, biomarker, etc. [[1\]](#page-12-0). Due to its large surface-to-volume ratio, quantisation effect and tunable (subject to external excitation) discrete eigenstates, effective determination of living microorganisms is possible which are obviously in the equivalent dimension of artificial nanostructures [\[14](#page-13-5)]. In this present chapter, nanodevices based on inorganic materials are analysed, and corresponding sensing applications are mentioned. The work is a comprehensive review in this specific domain with a keen focus on recent developments as well as research trends in nanobiosensors.

Fig. 6.1 Various types of nanomaterials used in biosensors

6.2 Application of Carbon Allotrope-Based Nano Biosensors

Carbon-based nanomaterials have received a lot of interest in the medical technology field in recent years. Carbon-based nanomaterials are extremely esteemed owed to the existence of a range of carbon-based nanomaterials like fullerenes, graphite, diamonds, and lonsdaleite, by way of more advanced forms like nanohorns, graphene, and nanotubes which are illustrated in Fig. [6.2](#page-4-0) [\[15](#page-13-6)]. Each of these allotropes has distinct properties that have led to their distributed use in a mixture of biological applications, including cancer therapy, drug delivery, etc. in addition to bioimaging, biosensing, and other medical diagnostics [\[16,](#page-13-7) [17\]](#page-13-8). Carbon-based nanomaterials have an unequalled mix of electrical, optical, and mechanical physiognomies, resulting in diminished sensors through excellent enactment and reduced power consumption. These nanomaterials are tractable and thermally constant in environment, through high electron mobilities and a high strength-to-weight ratio [\[18](#page-13-9)]. Such biosensor materials can detect a wide range of chemicals that have uses in healthcare diagnostics and illness POC analysis [\[19](#page-13-10)]. Fullerenes, [[20–](#page-13-11)[24\]](#page-13-12) nanotubes (CNT) [[25](#page-13-13)[–30](#page-14-0)], films of graphene and its derivatives $[31–34]$ $[31–34]$ $[31–34]$, quantum dots $[35–38]$ $[35–38]$ $[35–38]$ $[35–38]$, and nanodiamonds [[39–](#page-14-5)[44\]](#page-14-6) are carbon allotrope-based nanomaterials that have played a significant part in recent biosensor developments. In the case of local exposure, such sensors provide improved three-dimensional resolution, as well as real-time and label-free non-devastating detection.

Nanodiamond

Fig. 6.2 Various crystalline allotropes of carbon

6.2.1 Carbon Nanotubes

CNTs are regarded as promising building blocks for biosensors because of their increased aspect ratio, large surface area, amazing optical and electrical physiognomies, excellent thermal and chemical robustness, and great mechanical strength [[15\]](#page-13-6). Due to their higher sensitivity, lower background, decent SNR ratio, comprehensive preoccupation range, label-free disclosure, and real-time observing, CNTs provide biosensors as an advantage [\[19](#page-13-10)]. They act as scaffolding for the immobilisation of biomolecules, which improves signal transduction and identification [\[45](#page-14-7)]. Carbon nanotubes' semiconducting characteristic allows them to be used as tiny field-effect transistors (FETs) [\[29](#page-13-14)]. They might be used to construct top-of-the-line nanoscale electrodes due to their enhanced excellent conductivity along their length. CNTs' adjustable near-infrared emission, which reveals local dielectric function alterations while being resistant to photobleaching, is particularly interesting. They are also perfect for optical biosensing since they have a high luminous intensity and good luminous properties. [[46–](#page-14-8)[51\]](#page-15-0). CNTs have a density that is a sixth that of steel yet are 100 times powerful, making them suitable for use in piezoresistive sensors [[52–](#page-15-1)[55\]](#page-15-2). It's also feasible to make calorimetric sensors that trust on modification in

nanotube size induced by temperature changes [\[15](#page-13-6), [56](#page-15-3)]. Various crystalline allotropes of carbon are shown in Fig. [6.2.](#page-4-0)

Several CNT-based biosensors for glycaemic indicators in diabetes mellitus must be developed. Hatada et al. developed a label-free chemiresistor-based affinity sensor for haemoglobin A1c (HbA1c) and a bacterial periplasmic protein (SocA) using single-walled carbon nanotubes (SWCNTs). Continuously, proteolytic hydrolysis method, HbA1c, produces fructosyl valine (FV), which the sensor can detect in an absorption variety of 1.2–1909 nM. Comba et al. used a CNT (CNT-muc) nanocompound halted on a platinum outward to create a long-lasting enzymatic biosensor for glucose. CNT's high surface area aided in the restriction of the GOx enzyme. Using chronoamperometry, the CNT-based sensor was capable to sense glucose in the variety of 0.002–3.2 mM, through a LOD of 3 M. Another research [[57\]](#page-15-4) used MWCNT scaffolds with cobalt functionalised MoS2 to obviate the need for the GOx. This scaffold has a low detection limit and may be used to detect glucose over a additive concentration range of 0.2–16.2 mM. (80 nM). Aryal and Jeong introduced a thermally reduced graphene oxide–MWCNT (TRGO-MWCNT) nanocomposite adapted with ambient plasma and -cyclodextrin for uric acid (UA) perception (CD) [[58\]](#page-15-5). This sensor had a LOD of 0.06 M and could produce linear responses in the range of 10–300 M. Bollella et al. exploited the electron exchange capabilities of MWCNT and poly(methylene blue) (pMBexcellent) to develop a second-generation Au-based sensor for incessant lactate detection in epidermal interstitial fluids. After immobilising lactate oxidase (LOx) on the sensor, lactate disclosure between 10 and 200 M was possible with a degraded sensing limit (2.4 M). Shen et al. improved a label-free immunosensor for lucrative POC perception using SWCNT [\[30](#page-14-0)]. They employed non-covalent assembling communications using SWCNT and PCA to create a water-based ink capable of immobilising human serum albumin (HSA) antibodies. The SWCNT-based ink could detect 0.015–9.43 nM HSA while consuming a 1 pM LOD. Huang et al. developed an immune chromatographic test that allowed visual detection of rabbit immunoglobulin G using IgG antibodies (Ab1) powerless on MWCNT attracted with Fe3O4 (MMWCNT) (IgG) [[51\]](#page-15-0). Visual detection in blood had a detection limit of 10 ng mL⁻¹ and a linear dynamic range of 10–200 ng mL⁻¹. Other CNT-based nanoparticle (AuNP) nanocomposite through exposure of antibody (dAb) coating by way of a reporter probe was used to make another visual immune chromatographic biosensor accomplished of discovering carcinoembryogenic antigen (CEA), used as a biomarker for lung cancer [\[46](#page-14-8)]. The cotton threadbased approach allowed a straight information via the naked eye with a genuine response in the range of 10–500 ng mL⁻¹ and a LOD of 2.36 ng mL^{-1.} Meng et al. described a similar optical biosensor for human ferritin antigen (HFA) that employed MWCNT to achieve a linear concentration range of 100 to 5000 ng mL^{-1} with a LOD of 50 ng mL^{-1}. CNT-based surface plasmon resonance (SPR) optical sensors have also been reported. Pathak and Gupta developed a polypyrrole (PPy) MIP on carboxylated multiwalled carbon nanotubes (CMWCNT) with a permselective nafion membrane for the detection of dopamine (DA).

Biosensors made of carbon nanotubes are widely used to detect cancer and neurological diseases. For example, prostate-specific antigen (PSA), a chemiresistivebased CMWCNT biosensor was industrialised [[59\]](#page-15-6). Anti-P-gp-SWCNT film twisted on a SiO2–Si layer was used in another CNT-based detector for the disclosure of P-glycoprotein (P-gp) for leukaemia biomarker.

6.2.2 Graphene

Graphene is a new form of carbon element composed of $sp²$ hybridised carbon molecule configured in a hexagonal arrangement. At ambient temperature, the electrons in graphene give it unique characteristics including ambipolar like electric field properties, higher quantum hall effects and thermal conductivity. It has a twodimensional artefact, which results in a large surface area and high porosity. As a result, graphene may adsorb a variety of gases, including methane, hydrogen, and carbon dioxide [\[7](#page-12-6)]. The number of layers and the stacking sequence of graphene can be denatured to alter its properties. It is extremely translucent, with a high modulus of elasticity and a good resistance to fracture. Furthermore, graphene is capable of physisorption interactions with a variety of biomolecules, making it an excellent option for biosensors [\[15](#page-13-6)]. Graphene derivatives, such as graphene oxide (GO), can exhibit fascinating properties such as fluorescence. GO, RGO, and graphene quantum dots are the most frequent graphene derivatives utilised in biosensing (GQDs) [\[60](#page-15-7)– [62\]](#page-15-8). Cysteine [\[63](#page-15-9)–[66\]](#page-15-10), glycaemic biomarkers [[67](#page-15-11)], cholesterol [[68\]](#page-15-12), neurotransmitters [[69,](#page-16-0) [70\]](#page-16-1), H2O2 [[71\]](#page-16-2), cancer cells [\[72\]](#page-16-3), nucleic acids [\[73](#page-16-4)], pharmaceutical medicines [\[36\]](#page-14-9), and pathogenic microorganisms [\[61](#page-15-13)[–63\]](#page-15-9) may all be detected using graphene-based biosensors. Graphene has been used to create a plethora of optical and electrochemical biosensors for the detection of different amino acids. Graphenebased biosensors serve an important role in the identification of incurable and lethal diseases such as diabetes and various forms of cancer. Jaberi et al. discovered and built an RGO–Au nanostructure-based electrochemical nanogenosensor for HbA1c exposure on a flexible and inexpensive graphite sheet (GS) conductor [[73\]](#page-16-4). HbA1c levels can be altered by a variety of illnesses, including haemolytic anaemia and sickle cell anaemia etc., production it an inaccurate biomarker for diabetes mellitus diagnosis. Apiwat et al. elucidated this problem by replacing glycated HAS (GHSA) for HbA1c biomarker [[74\]](#page-16-5).

6.2.3 Nanodiamonds

Nanodiamonds (NDs) are the only carbon allotrope-based nanomaterials that include sp3 hybridised carbon centres, as opposed to the other carbon allotrope-based nanomaterials previously described. To individual's resultant by their higher exact area, which may approach 400 m² g⁻¹ [\[75](#page-16-6)], NDs exhibit excellent features of diamond, like comprehensive band gap electrical performance, chemical motionlessness, thermal conductivity, and exceptional mechanical things. Microdiamonds can be ground at high-pressure, high-temperature (HPHT) settings or carbonaceous explosives can be detonated to produce them (DND). After easy functionalisation through amines, thiol group halides, etc., they can connect covalently or non-covalently by bioparticles. HPHT diamonds have a lot of nitrogen impurities, which can be converted into vacancy-related colour epicentres, resulting in fluorescent nanodiamonds (FND). FNDs can be used as effective biosensing, bioimaging probes, and contrast agents due to the photophysical properties of the vacancy centres [\[76](#page-16-7)[–78](#page-16-8)].

For the reason that of their glowing countryside and capacity to identify a variety of metal ions, NDs have been extensively engaged in biosensing. For the finding of Hg2 + ions, Shellaiah and colleagues produced photoluminescent cysteamine (CYA)-modified nanodiamonds [\[79](#page-16-9), [80](#page-16-10)]. CYA has free thiol groups that can trap mercury ions and forms amide bonds with NDs. Heavy metal ions can also be quantified using NDs doped with nitrogen. Pb^{2+} and Cd^{2+} were detected concurrently using one-dimensional nitrogen-doped nanodiamond nanorods (N-DNR) for an electrochemical sensor.

NDs have been used to detect a variety of therapeutically relevant substances, containing neurotransmitters, medicines, and poisons, in addition to biomarkers for chronic diseases like diabetes [\[81](#page-16-11)]. Dai et al. electrophoretically dropped NDs on a boron-doped diamond (BDD) conductor and then enhanced it with Ni nanosheets for enzyme-free glucose sensing [[82\]](#page-16-12).

6.3 Applications of Inorganic Nanomaterial-Based Biosensors

At the nanoscale, transitional metals and noble metals have remarkable characteristics. Unique quantum effects and optical characteristics result from the extra superficial particles combined through moderately occupied last but one or prepenultimate orbitals. They can not only be utilised to make excellent alloys, but they can also be similarly combined through other organic and carbon-based materials to create nanocomposites with a variety of diverse properties or totally new ones [\[7](#page-12-6)]. Anisotropies in inorganic nanomaterials might include triangular, round, and nanohole. Bimetallic alloys, core–shell architectures, nanotubes, and nanowires are only a few examples. Each of these nanomaterials can improve the biocompatibility and transduction characteristics of biosensors by utilising appealing interface and surface features. They can operate as immobilisation platforms, boost refractive index modification, catalyse interactions between substrates and chemiluminescents, magnify mass changes, and accelerate electron transfer [[83](#page-16-13)[–91](#page-17-0)]. Aside from immobilisation, such nanoparticle platforms might serve as electron wires in electrochemical sensors, translating biomolecular physicochemical changes into quantifiable signals.

Aside from their massive surface area, many inorganic nanomaterials, such as $Fe₃O₄$, have a magnetic nature and may be easily controlled by an external magnetic field, allowing for minor abstraction and buffer replacement. They similarly give a higher SNR ratio in biological examples [\[92–](#page-17-1)[95\]](#page-17-2). They may be used to homogenise, trap, enrich, transport, and label analytes, which is very useful in POC testing. Microfluidic fraternisation, which is critical in lab-on-chip biosensing, may be accomplished using them. The majority of magnetic nanoparticles (MNPs) are made up of an amagnetic core made up of pure elements (such as Co and Fe), alloys (such as FePt), or iron oxides (such as maghemite -Fe₂O₃ or Fe₃O₄). This core is often coated with inorganic [[96\]](#page-17-3) or polymeric [\[97](#page-17-4)] molecules that act as biofunctionalisation sites. By embedding numerous MNPs in a non-magnetic matrix, superparamagnetic behaviour may be created [[7,](#page-12-6) [92\]](#page-17-1).

Biosensor development has recently focused on innovative inorganic structures like nanowires, nanocages, and nanoshells. Nanoshells are a new class of nanomaterials with high plasmon importance, consisting of a dielectric silica core surrounded in a highly conducting, ultrathin layer of silver or gold. This allows resources to be precisely wangled to equal the wavelength for specific usage, such as near-infrared (NIR) zones where optimal light penetration over tissue is required [[7,](#page-12-6) [98\]](#page-17-5). Surfaceenhanced Raman spectroscopy (SERS) is being investigated as a viable platform for in vivo exposure on nanoshell substrates [[99–](#page-17-6)[101\]](#page-17-7). Nanocages are heavy nanostructures with absorbent walls, often composed of decent metals [\[69](#page-16-0), [102\]](#page-17-8). They have a lot of promise for biofunctionalisation and biomolecule immobilisation because of their large surface area. They have uncommon electrical and thermal physiognomies. Noble metal nanowires have SPR-like physiognomies which can be adjusted depending on their thickness [\[103](#page-17-9)[–105](#page-17-10)]. Like nanoneedles, nanowire arrays may penetrate cellular lipid bilayers, allowing for cytosensing and other medical identification applications. Silicon oxide NW can be utilised as a substance for structure immobilisation in FET biosensors [[7,](#page-12-6) [104](#page-17-11)]. Inorganic nanoparticles have been utilised in healthcare diagnostics in a number of ways. We will concentrate on the most widely used nanomaterials, like magnetic nanoparticles, quantum dots, and nanostructures like nanoshells, nanowires, and nanocages, in this study.

6.3.1 Nanowires

Nanowires (NW) are a type of mono-dimensional nanoparticle that comprises nanotubes, nanobelts, and nanorods, among others. NWs are at least 1000 times their diameter in length. NWs may be made from semiconducting materials like Si, InP, and GaN, as well as dielectric materials like $TiO₂$ and $SiO₂$ [[37,](#page-14-10) [106](#page-18-0)]. The LSPR characteristics of noble metal NWs are thickness dependant. Because of its conductive characteristics, $SiO₂$ NWs are frequently used in FET biosensors and have a lot of potential in healthcare biosensing. The use of NWs as substrates on behalf of receptor control to allow requisite with different bioparticles leads in sensitive perception, fast analysis, and the possibility of shrinking [[104\]](#page-17-11). Nuzaihan and coworkers

Silicon Nanowire

Silver Nanowire

TiO₂ Nanowire

Fig. 6.3 Various types of nanowires

recently disclosed a silicon nanowire (SiNW)-based microfluidic electrical sensor for sensitive detection of the dengue virus (DENV) DNA oligomer [[107\]](#page-18-1). On a silicon wafer, the SiNW was created using a top-down method. Surface alteration, DNA immobilisation, and DNA hybridisation were then used to functionalise the SiNW. The sensor was able to reach a LOD of 2.0 fM because to its esoteric molecular gate control technique. Kim et al. developed a silicon nanowire FET biosensor with a honeycomb nanowire (HCSiNW) design for ultrasensitive detection of cTnI. [[108\]](#page-18-2). The Debye effect gave the gadget excellent sensitivity and selectivity. cTnI antibodies were immobilised on the surface of the HCSiNW. Vertically oriented platinum nanowires had a greater density of AuNPs than a 2D planar modification. The nanowires boosted the electron compactness on the electrode surface, which improved the signal-to-noise ratio. Figure [6.3](#page-9-0) depicts several nanowires utilised in sensor applications.

6.3.2 Nanowire-Based Sensors

The major research carried in the field of nanobiosensors deals with nanowirebased devices. Due to its extremely small power consumption and larger stable time

period, detection of biomolecules and chemical species [[109\]](#page-18-3) become advantageous. Working principle of these sensors critically depends on the fabrication methods, and electrical properties, as briefly outlined in the previous subsection. However, there are ample opportunities for its development for detecting subnanometric organisms with major fabrication challenges. Owing to large increase of surface-to-volume ratio compared to bulk counterpart, these sensors found in drug discovery and DNA detection. Carbon nanotube-based sensors are of special category for ultra-sensitive biomolecule detection [\[110\]](#page-18-4). It has another advantage if higher oscillator strength and extremely low thermal noise [\[111](#page-18-5)], which facilitates minute detection. This is the special type of one-dimensional nanostructure which is able to detect present of species electrically [\[112](#page-18-6)]. This type of detection also helps to detect label-free biosensors. Owing to higher sensitivity and scalability, these nanobiosensors have been appreciated from practical stand-points.

6.3.3 Quantum Dots

The traditional inorganic QD is a bimetallic substance centre via a shell region, such as chalcogenide. Despite the fact that the thickness of QDs is smaller than the Bohr radius of the electron-hole, quantum confinement effects dominate, resulting in distinct visual properties. Stokes shifts generated by NIR or UV electromagnetic radiation during eager electron relaxation to holes provide stronger photoluminescence than organic dyes. Proteins [\[113](#page-18-7), [114\]](#page-18-8), infections [[107\]](#page-18-1), lung cancer biomarkers [[115\]](#page-18-9), and nucleic acids [\[116](#page-18-10), [117\]](#page-18-11) are among the substances that have been detected using QDs. Nonetheless, the toxicity of cadmium, a frequent component in quantum dots, in addition to the propensity of defensive coatings to degrade in vivo are preventing broad in vivo usage of quantum dots [[118\]](#page-18-12). Using QDs on a microfluidic device, a wide range of target molecules may be identified efficiently. A sensor like this was recently utilised to identify and subtype three influenza viruses $(H_1N_1, H_3N_2,$ and H_9N_2) [[119\]](#page-18-13). Streptavidin-coated quantum dots (Str-QDs) with immobilised biotinylated DNA served as fluorescent imaging labels, while capture probes were DNA-immobilised super paramagnetic beads (SMB). The sensor worked by using nucleic acid hybridisation on a microfluidic device with a regulated micromagnetic ground.

Another research on protein recognition found that metal oxide nanoparticles of $Eu₂O₃$ and CuO, in addition to decent metal nanoparticles of silver and gold, can destroy the fluorescence of CdSe QD [[113](#page-18-7)]. The fluorescence movement of QDs was reinstated with the addition of analyte, since analyte–QD communications released QDs from the nanoparticle–QD complex. The fluorescence intensity was also enhanced by the communications between the proteins and the QDs. A combination of QD fluorescence with immunomagnetic separation (IMS) has been shown to provide favourable results in pathogen identification [\[107](#page-18-1)]. Magnetic nanoparticles with gold shells and biotinylated *E. coli* antibodies were used as detention probes for *E. coli*, while chit-coated CdTeQds were used as reporter probes in a sarnie

immunoassay. IMS was used to eliminate the bacteria from the sensing elucidation before moving on to fluorescence investigation.

6.3.4 Quantum Dot-Based Sensors

Quantum dot-based nanobiosensors make their mark for selective identification of diagnosis. Owing to their tunable optical properties, i.e. emission/absorption spectrum, biosensors made by semiconductor QD already exhibit superior sensitivity and also photo-chemical property [[120\]](#page-18-14). For selection of specific DNA, protein, enzyme, mRNA, etc., quantum dot-based nanobiosensors are already proved their salient features as reported already in various literatures [[121\]](#page-18-15). For antibiotic detection, quantum dot-based biosensors are researched [[122\]](#page-18-16) and proved efficient. Material parameters in this respect play a great role in determining the sensitivity of the sensor. Carbon quantum dots are used for early stage cancer biomarkers [\[123](#page-18-17)] compared to semiconductor QDs. It has the additional feature of better water solubility which is exhibited as the biocompatibility.

6.3.5 NWFET-Based Sensors

Nanowire field-effect-based transistors have been centre of attraction in last few years owing to possibility of making ultra-sensitive sensors for detecting mostly label-free specimens. Junctions are sometimes made of Schottky types in order to make to safe during operation [\[124](#page-18-18)] where devices are made on silicon-on-insulator wafers. Investigations at cellular levels are now become possible because of these sensors, thanks to the surface functionalisation and other transistor properties [\[125](#page-18-19)]. For different subcellular structural diagnosis, these sensors are proved as extremely useful, precisely because of their lower noise generation. Very recently, it is reported that grapheme FET can detect SARS-CoV-2 [\[126](#page-19-0)] in less time which may usher a new direction of Covid-19 treatment.

6.3.6 Magnetic Nanoparticles

Superparamagnetic nanoparticles include $Fe₂O₃$, $Fe₃O₄$, FePt, and a variety of other related nanoparticles. These particles can have a wide variety of sizes, ranging from 10 to 1000 nm, depending on their production method. MNPs are commonly used as either transducers or tags in biomolecule conjugation. MNP biosensors have applications in a variety of fields, including food science, medical diagnostics, and environmental research [[127\]](#page-19-1). Before MNPs may be employed in healthcare biosensing, three prerequisites must be met: (1) to manage their mobility in blood without the

need for highly intense magnetic fields, MNPs must retain a greater intensity magnetisation. allowing MNPs to transfer close to the beleaguered tissue; (2) MNPs should be biocompatible and non-toxic; (3) MNPs should be between 10 and 50 nm in size to avoid combination or precipitation due to gravitational forces and to confirm colloidal constancy, especially in water at pH 7.0, resulting in a large superficial zone for a precise volume of the material [\[128](#page-19-2), [129](#page-19-3)].

The use of MNPs in cancer detection at an early stage has shown great promise. Pal et al., for example, used monoclonal antibodies (mAbs) to multiplex MNPs for detecting ovarian cancer biomarkers (cancer antigen 125 (CA-125), Apo-lipoprotein A1 (ApoA1), and 2-microglobulin (2-M)) [\[130](#page-19-4)]. Polyclonal antibodies were used to create a sandwich test (pAbs). With the aid of magnetic force, the sandwiched elements were then detached from the sensing position. Simultaneously, the fluorescence change was monitored in real time against a standard concentration. Pathogens are frequently identified using MNPs.

6.4 Conclusion

Several nanomaterials and corresponding sensors are investigated some of which are highlighted in this chapter based on their spectra of application as well as their acceptance among scientific community. Properties of these sensors are critically depended on their electronic and optical properties, and therefore, material aspect is also taken care into consideration while making a detailed review. A comprehensive literature search is carried out on major nanobiosensors, and most favoured outcome from application stand-point is reported.

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