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AN OVERVIEW OF NANOSENSORS AND THEIR POTENTIAL APPLICATIONS : PERSPECTIVES AND PROSPECTS

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Abstract: **Advancements in nanomaterials and enhancement in fabrication techniques have made it possible for nanosensors and nanotechnology to reach a wide spectrum of applications. This review briefs the broader aspects of physical, chemical, optical, and biological sensors and their fabrication methods. The types of nanosensors mentioned in the article are used to detect specific characteristics over several applications varying from biological and chemical to automotive and aerospace industries. This study provides an overview of present nanosensor technologies, and it also gives the reader an idea of what the future beholds for this crucial segment of nanotechnology. The study also provides an overview of the findings achieved in the use-specific detections that vary from existing processes.**

Keywords: **Microelectro mechanical Systems (MEMS), Nanoelectro mechanical systems (NEMS), Surface-enhanced Raman Spectroscopy (SERS), Covid-19, Internet of Nano Things (IoNT)**

I. INTRODUCTION

Sensors are devices that monitor and convert physical impact changes into signals that can be detected or measured. This physical value is first acquired by the sensor, transforming it to the desired signal for optimization [1]. Nanotechnology concepts were initially introduced. Richard Feynman, Nobel Laureate in Physics, in December 1959. One of the most significant advancements today is nanotechnology, which advances materials at the nanoscale [2]. Nanotechnology and nanoscale materials are relatively new and innovative fields of study. Nanoparticle's small size and unique optical, catalytic, mechanical, and magnetic properties, which are not present in bulk materials, allow the development of innovative devices and their nearly unprecedented applications [3]. Nanomaterial advancements, along with concurrently developing microelectro mechanical systems (MEMS)/ nanoelectro mechanical systems (NEMS) technology, have resulted in dramatic improvements in all sorts of sensors., field development, including cost and speed of research, nanoscale size, low sample volume requirement [4]. Nanotechnology has developed one of the most exciting cutting-edge fields. Nanomaterials in mechanical, biomedical, IT sector, environmental, etc., monitoring applications have been facilitated by a wide range of size and morphology, chemical compositions with appropriate surface properties, and other factors [5]. Nanosensors have become increasingly important in enhancing the quality of health, environmental and quality control, and other applications worldwide. This is because nanotechnologies have provided highly exciting inputs that have allowed nano-sensors to obtain unparalleled levels of quality parameters [6]. The use of a wide variety of nanomaterials (metal-based, polymers, carbon allotropes composites) in the form of nanotubes, nanoparticles, nanowires, and nanorods has significantly improved detection for the desired application. Nanomaterial's unique configurable and flexible characteristics, such as optical, electrical properties, and improved shock bearing capacity, allow a wide range of ultra-sensitive reactions and detection mechanisms (via measuring properties such as electrical, thermal, piezoelectric, and optical). These nanomaterials' fascinating properties that appear in the nanoscale range make it easier to combine nanomaterials to create desired nano-inspired sensors for a wide range of applications [7]. These nanosensors can be classified into optical sensors, physical sensors, chemical sensors, and biosensors, which include well-known and widely used applications, have benefited from nanomaterials [2]. The key contributions of this paper are as follows: Various types of nano-sensors, Fabrication techniques and Applications of nano-sensors.

II. TYPES OF NANOSENSORS

The nanosensors are being used in various works in different fields; thus, studying these types becomes vital. In this section, different types and categories of nanosensors are discussed in detail.

2.1. Optical Nanosensors

Sensors with at least one nanoscale dimension were created to make quantitative measurements in the intracellular environment. These are also having various types.

2.1.1. Surface-enhanced Raman Spectroscopy (SERS) Nanosensors

Because of its high sensitivity and spectrum selectivity, surface-enhanced Raman Spectroscopy (SERS) is a practical approach for detecting and analyzing organic dyes. This phenomenon is when the Raman signal intensity of molecules is amplified as the metal surface absorbs them. Titanium oxide (TiO_2), a semiconductor nanomaterial, has shown promising results as a photo catalyst due to its properties of non-toxicity and photo stability. Nanoparticles of noble metals had been introduced to TiO_2 to improve its characteristics. The advantage of this enhancement is that it becomes easier to detect and remove absorbed molecules in situ on a single material [8].

2.1.2. Electrical signal transduction

Piezoresistive nanowires are used efficiently for the motion readout of static and resonant MEMS sensors. The unit for measurement of radiation dose is Gray (Gy). It equals absorbing one joule of radiation energy per kilograms of matter. The pressure sensors working efficiently in the severe environment have shown good resistance to gamma radiation until tens of Kilo Gray (KGy). In these sensors, the remaining gamma radiation sensitivity is determined by the sections of the piezo resistor and the nature and amount of the do pant. A small part of the piezo resistor is neutralized by high dopants concentration in MEMS and NEMS nano gauges. P. Janioud et al. found that suspended silicon nano gauges bridge-based MEMS holds suitable for applications requiring a high resilience gamma radiation by proving that ^{60}Co γ radiation with a radiation dose-dependent on the coefficient of resistance, radiation impacts on resistivity is indeed very mild. 16.5 ppm/KGy, reduced by using a half Wheatstone bridge and the differential mode [9].

2.1.3. Up conversion optical transduction

Up conversion nanoparticles (UCNPs) consist of inorganic crystalline structures like $NaGdF_4$, $LiLuF_4$, $NaYF_4$, and dopant lanthanide ions such as Tm, Ho, and Er unique energy levels and generate distinctive emission peaks. In a non - linear anti-Stokes optical mechanism, such nanoparticles can transform low-frequency near-infrared light (NIR) to shorter wavelength emissions visible or UV. Because of its qualities of non-harmful NIR excitation and negligible auto-fluorescence backgrounds, UCNPs are frequently employed in optical imaging, controlled drug delivery, and photodynamic treatment. They are also used in bioassays due to the excited state lifespan decline. [10]. When lower energy photons stimulate a material through multiphoton processes, photons with higher energy levels are released. This is known as photon-up conversion. Materials based on $NaYF_4^-$ doped with Yb^{3+} and Er^{3+} or Tm^{3+} have been recognized as one of the most efficient photon up converting materials. Photon up converting materials can help in achieving a high signal-to-noise ratio. Single-stranded nucleic acids and proteins can be detected by sandwich assay format or direct labeling [11].

2.2. Biological Nanosensors:

Biosensors monitor the analytes in the biological system consisting of the receptor that recognizes the biological activity taking place, and the signal transduction element is responsible for converting the analyte received into reading or output. The optimal qualities for a nanosensors being utilized in vivo and vitro applications include stability, physiological range of the sensor, excellent selectivity against interference, minimal disruption of normal biological activities, and high biocompatibility [12].

2.2.1. Quantum Dot based Fluorescent Nanosensors

Compared to the single fluorescent dye molecule, a single quantum dot consists of tens of thousands of individual atoms with delocalized chemical bonding, which enhances its tolerance against photon-induced damage. Therefore, they have been utilized for signal reporting with excellent photo stability. The physical dimensions of QDs are close to the exciton of the Bohr radius. These consist of electrons and hole carriers, leading to an increase in the band-gap energy that results in splitting the continuous energy bands at discrete levels, which forms an intermediate between molecules and bulk materials. They are used for sensing pH, Ca^{2+}, and K^+ in vitro applications [12]. Figure 1 shows super-resolution image of Quantum Dots.

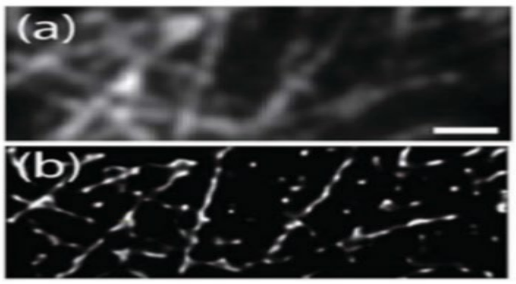

Fig 1. Super-resolution image of Quantum Dots [12].

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2.2.2. Carbon Nano Tube (CNT) as Biosensors

Carbon-based nanostructures are known for their unique and enhanced properties, and they comprise high sensitivity as they are used in immobilized enzymes keeping high biological activity. They have a fast response time and can quickly mediate fast electron transfer kinetics promoting electron transfer reactions. These biosensors have a low potential for redox reactions and less surface degradation, making them highly stable and lasting longer. When an enzyme electrode is submerged in the test solution, the CNT-based biosensors meet the requirements of amperometry-based electrochemical biosensors, which convert chemical signals to electrical signals. CNT can also be applied to optical, piezoresistive, and calorimetric nanosensors [13].High-resolution TEM image (inset) of the CNT can be seen in figure 2.

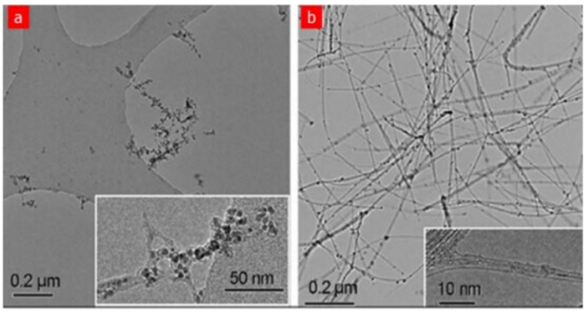

Fig 2. High-resolution TEM image (inset) of the CNT [13].

2.2.3. Biocompatible Nanosensors

The fluorescence diagnosis signal transduction is required because rare earth-doped up conversion nanoparticles (UCNPs) provide a unique wavelength upconverting capacity and excellent detection sensitivity; they may be employed in bio-detection. Q. Chen et al. studied the concentration of the dopant ions, Gd3þ ions at different doping levels were introduced to induce the phase transformation of $NaYF_4^-$ based nanoparticles at the temperature that range from 240℃ to 310℃ at a reaction time of 60 minutes. By performing this experiment, the fluorescence spectra with a wavelength ranging from 500nm to 900nm were recorded at room temperatures with 652nm and 806nm tagged as a characteristic peak for Aflatoxin B1 (AFB1) and Deoxynivalenol (DON), respectively. This helped in assembling a highly efficient nanoprobe for up conversion of nanoparticles for simultaneously sensing the multi-toxins [14]. Figure 4 shows TEM image of the $NaYF_4$; Tm^{3+} and Yb^{3+}nanoparticles.

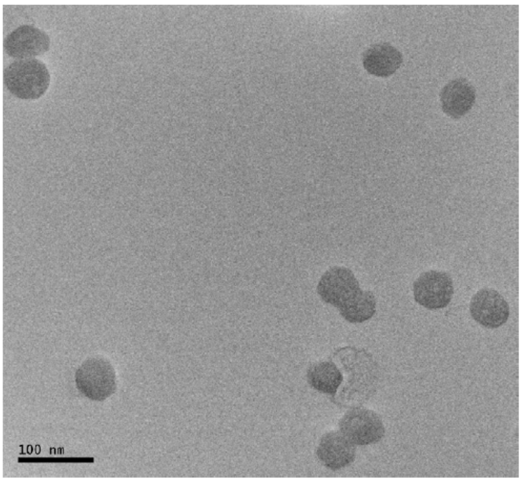

Fig 3. TEM image of the $NaYF_4$; Tm^{3+} and Yb^{3+}nanoparticles.[14].

2.3. Chemical Nanosensors

Chemical nanosensors are made up of sensitive cantilevers and electronics that can sense individual biological or chemical molecules.

2.3.1. Fluorescence-Based Nanosensors

Compared to fluorescent organic dyes, fluorescent nanoparticles such as quantum dots (QDs), gold nanoclusters, carbon-dots, and up conversion nanoparticles also worked as probes for sensor applications because they have a restrictive, turntable, and symmetric band with good sensitivity and photo stability. In addition, due to their biocompatibility, these particles are simple to make [4].

2.3.2. Calorimetric Sensors

The cumulative oscillation of electrons located on the surface of nanoparticles, known as localized surface plasmon resonances (LSPR), is exceptionally responsive to fluctuations in refractive or dielectric indices. Nanoparticles are often used for sensing applications as a result of their plasmonic characteristics. Due to plasmon coupling, the plasmonic characteristics of metal nanoparticles are dependent on the interparticle distance, and the aggregation of these particles may be detected as a change in the colloidal solution [4].

Carbon dot-based optical nano sensors are used for detection of metal contaminants of water. Lead is a contaminant that has adverse effects on human health. This contamination of water takes place due to the industrial processes, mining and burning of fossil fuels. Selective sensing of Pb^{2+} by a fluorescence quenching effect, the detection limit was calculated to be 12.7 nM which showed good recovery rate in real water samples [15]. The existing detection limit of Hg^{2+} is 0.23 nM hence fluorescent carbon nanoparticles and rhodamine mixture was used to

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prepare a sensor. Rhodamine nano hybrid demonstrated cell-permeability and dual emission nature such as blue and red emission [16]. Metal nanoclusters, semi conducting quantum dots and metal organic frameworks are the existing fluorescent probes for detection ofFe^{3+}. A selective sensing of theFe^{3+} with a detection limit of 0.25 µM is reached when carbon dots-based iron synthesized from black tea by the use of hydrothermal method [17]. To sense the Fe^{3+} in human serum samples a study using synthesized nitrogen-doped carbon dots with high quantum yield was carried which had a detection range of 140 nM and 100-2000 µM [18]. As(III) analysis is performed by synthesizing fluorescent gold clusters (AuCs) with a dipeptide L-cysteinyl-L-cysteine ligand [19]. A later study used a sensor that can be reused by the removal of As(III) on GSH-carbon dots which consisted LOD of 32pM [20].

III. FABRICATION TECHNIQUES FOR NANO SENSORS

Nanosensors are utilized in various applications; thus, understanding the various manufacturing processes is essential. The most frequent materials used to make nano-sensor components are carbon nanotubes and graphene, a carbon-based nanomaterial. The optical and electrical characteristics of graphene, based on the 2-D plasmonic platform, make it ideal for this application[21].

3.1. Top-Down Approach

In a top-down approach, the components of the nanosensors are manufactured using more extensive and externally controlled tools from a microscale perspective [22]. Popular top-down methods utilized for the fabrication of nanoscale components on a scale below 100nm [23] are Microcontact Printing [24], Imprint Lithography [25], Direct-Write Dip-Pen Nanolithography [26]. Despite technological and physical constraints, nanoscale components can be manufactured with atomic precision using top-down approach manufacturing methods, thanks to the continuous evolution of classical lithography manufacturing techniques [27]. For example, using a combined Transmission Electron Microscope-Scanning Tunnelling Microscope technology, graphene nanoribbons are often used in field-effect transistors or graphene-based nanosensors nano-antennas may be quickly produced from bulk graphene (SEM-TEM) [28]. The Bio-Hybrid Approach entails the use of bioactive compounds in the construction and assembly of integrated nanodevices. Biosensors, nano actuators, and biological data storage elements present in live organisms can be utilized in designed or synthetic nanodevices [29].

3.2. Bottom-Up Approach

The Bottom-Up approach for the manufacturing of nano-sensor components focuses on having complex nano-sensors built using smaller components [22]. Molecular manufacturing is described as the assembly of the nano-devices molecule by a molecule that serves the purpose and the definition of the bottom-up approach manufacturing [30]. In 2007, IBM Corp. developed the state-of-the-art self-assembly method applied to the manufacturing and assembly of nano-sensor components. In this method, the strands of DNA produced are organized and integrated on materials that are compatible with current semiconductor production equipment. The DNA-generated strands are used to create small circuit boards for assembling carbon-based nanotubes, nanoparticles, nanowires, and nanoribbons [30].

3.3. Bio-Hybrid Approach

The Bio-Hybrid Approach entails the use of biological components in the construction and assembly of integrated nanodevices. Biosensors, nanoactuators, and biological data storage elements found in live organisms can be utilized in designed or synthetic nanodevices [29]. For biologically based nanodevices, ATP batteries that imitate mitochondrial activity might be utilized as an alternative energy source. The capacity to recycle or re-engineer biological structures present in live creatures will benefit biomedical applications, allowing molecular communications technology[22]. Figure 4 summarizes approaches for the fabrication techniques of nanosensors.

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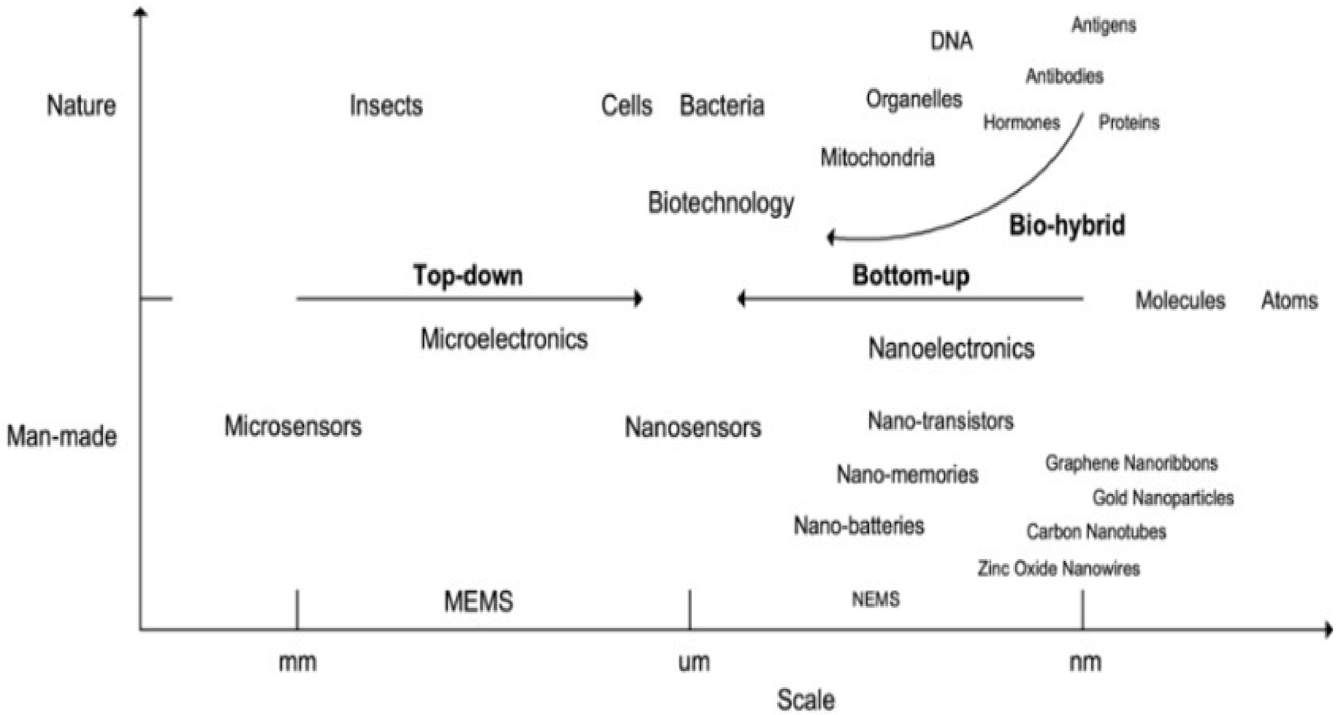

Fig 4. Approaches for the fabrication techniques of nanosensors [22].

IV. APPLICATION

Nanosensors are getting popular nowadays because their size is minimal compared to other sensors present in the market. The process of installation is straightforward, and these are widely used in many fields. In this paper, we tried to cover some different fields where nanosensors are widely used.

4.1. For detection of Covid-19

COVID-19 is a viral infection that can spread rapidly if preventative measures are not taken; hence the detection of the COVID-19 virus becomes very important otherwise. If an infected person roams here and there without knowing, as the routine testing procedure takes almost two to three days in this time duration, that person can unintentionally spread the virus, so its early detection can help reduce this. Proper medication can be done on time, which can save many people's lives in the future [31]. The conventional COVID-19 test involves molecular techniques, serological immunoassays, and chest CT imaging; however, these techniques involve limitations and experts to review the reports. Nanomaterials combined with nanoparticles have aided in the advancement of POC-based immunosensors. Nanomaterials of various shapes and sizes are used as substrates for biorecognition elements immobilizations (BREs), which benefit solid bulk substrates. Chandra et al. (Chandra, 2020) developed an impedimetric immunosensor that could detect the COVID-19 virus. With the suitable electrical property, graphene Oxide (GO) was used to develop a high-performance biosensing device providing analytical outcomes. The diagnostic agent was an anti-RNA-dependent RNA polymerase (RsRp)/ Helicase (H) gene of SARS-Cov-2, which has no cross-reaction with human corona viruses or other viruses. In addition, an electrochemical nanoprobe was designed for the fast detection of chemical analytes contained in human blood. This nanoprobe had high conductivity surfaces like gold-sputtered nano-hierarchical 3D dendrite and multi-walled carbon nanotube (MWCNT) integrated dendrite and other chemicals nanomaterials to accommodate BREs and specific sensing of protein targets of COVID-19. Both of these sensors had data accusation of electrical signals linked to a smartphone interface through an attached module. The module would be the input where the saliva sample is placed and displayed on the smartphone screen, which does not require expertise to operate [32]. Figure 5 shows different implementations of nanosensors (graphene).

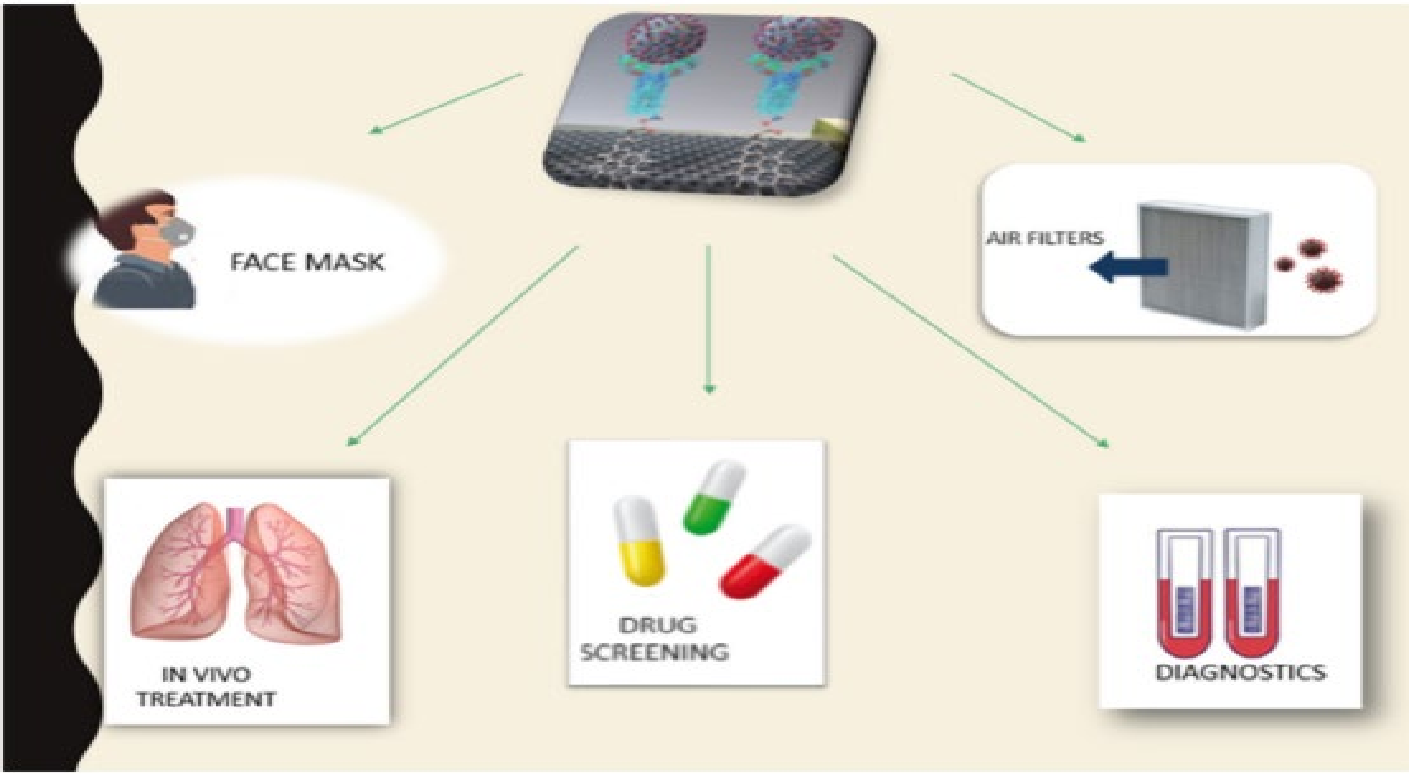

Fig 5. Different implementations of nanosensors (graphene) [31].

4.2. Detection of Air pollution

Air pollution is the major problem in every major city, as NO_2 is the major pollutant and it is harmful to live organisms, so its detection is essential. Isabel Sayago et al. studied that electro-spun tin oxide nanofibers (NFs)can also be used to detect air pollution in the electronic nose, as it detects the NO_2 even at low concentrations at low temperatures. These sensors are cost-friendly as the manufacturing cost is meager, and they can detect NO_2 even at 0.1 to 0.5 ppmv and temperatures ranging from 25 to 200°C [33].

4.3. Internet of Nano Things (IoNT)

The Internet of Things (IoT) has formed extensive networks of various objects and devices that have directly or indirectly affected human lives. Nanotechnology has brought further improvements in these networks using molecular nanosensors and electromagnetic (EM) nanoparticles. The enhancement was possible as the nanodevices that are nanoscale networks connect a multitude of sensors and devices and process the information for better understanding and management of data across various domains. This nanoscale network is called the Internet of Nano-Things (IoNT). In IoNT the nanodevices override the organic communications in the biological environment or utilize biomolecules (nucleotides, amino acids, peptides) for communication. These nanodevices also use electromagnetic (EM) communication that includes antennas, EM transceivers, and processors of nanoscale, which is more conventional than molecular communication. This data collection is possible due to the sensor network architectures and routing technology that favors the IoNT algorithm design. The nanodevices on the human body catch various electrocardiographic signals and real-time data regarding pathogens and allergens, resulting in better diagnosis of the patient or individual's health conditions. Besides tracking real-time data, nanosensors are attached at various sites and places to check and monitor the bacterial level and presence of viruses at particular instances [34].

4.4. Automobile tire

Anand Nayar et al. proposed a Carbon-Nanotube-TFT-based pressure nanosensors to determine the vehicle's accurate tire pressure. This demonstrates the potential for creating low-cost technology for pressure detection in uneven ground, which might eventually find its way into the automobile industry. Paired with an additional material thickness sensor, it is possible also to integrate a tire tread wear monitoring system which can be used for an integrated smart-tire system that can transmit data to the user wirelessly from the pressure chamber to the device using a Bluetooth transmitter, also combining the benefits from the Internet of Nano-Things (IoNT) [35].

4.5. Damping and Vibration

Ali Naderi et al. mentioned that axial-flexural vibrations coupling has been a common phenomenon in mass nanosensors. The Generalized Differential Quadrature Method (GDQM) and Generalized Integral Quadrature Method (GDQM) have been used to attain the vibration characteristics of the nanosensors. It is essential to obtain natural frequencies of comparable mass values. It is necessary to investigate the coupling effects that play a role in the vibration behavior of mass nanosensors since this information may enhance the precision of nanosensors[36].

4.6. Medical Application

For biological regulation of enzymes in cells of the human body, copper ions (Cu^{2+}) play a vital role. These help in the transfer of electrons of physiological processes. As a result, this may lead to different biological and health issues if these ions are in excess or even inadequate in the human body cells. The excessive content of these ions has toxic results as it adversely affects the kidneys and other organs of the body. In contrast, scarcity of these cupric ions leads to neurological diseases like Alzheimer's, Wilson's disease, etc., and hinders intracellular enzyme activity. To understand and verify these in the human body. Saipeng Huang et al. used a fluorescent nanosensors (nanoprobe) and detected the number of copper ions in the cells incorporating carbon quantum dots (CDs) along with the ammonium group. Carbon dots were used as they possess optical and electronic properties and better biocompatibility, and water solubility. For experimentation, amino group ions were used at different stages and temperatures, leading to the formation of $(NH_2)^-$ CDs. The UV absorption spectra at 201 nm gave a redshift of 30 nm once the cupric ions were added, resulting in the capture of the co ions. This demonstrated the optical character of $(NH_2)^-$ CDs. Followed by this was the emission and excitation of the spectrum at 360 nm and 455 nm, respectively, with the absence and presence of 100 Cu^{2+}. The stable optical properties of the $(NH_2)^-$ CDs were seen when the excitation wavelength was confirmed at 360 nm, which was verified by keeping the emission wavelength of $(NH_2)^-$ CDs constant at 455 nm and excitation wavelength ranging from 320 nm to 420 nm (a strong blue emission was recorded in between 340 nm to 360 nm). The fluorescence intensity in the absence of the cupric ions in initial stages and quenched fluorescence intensity with the presence of copper ions in the following stages were dependent on the pH values, which indicates that in $(NH_2)^-$ CDs solution, pH value is a crucial element that affects the sensing system in the solution. The use of the solution consisted of properties like photo stability, strong sensitivity, high selectivity, rapid fluorescence response, neglected interference, good cell permeability, and low cytotoxicity. This experiment showed the linear relationship of fluorescence and cupric ion concentrations from 0.005 μm to 600 μm [37].

V. CONCLUSION

The interest in nanosensors has gained importance over the years due to the rise in a wide range of potential applications. This paper highlighted some different kinds of nanosensors that may be used in different fields. The significant types which were discussed were optical, biological, and chemical nanosensors. Three fabrication techniques discussed were top-down, bottom-up, and bio-hybrid approaches. As outlined in this review, nanosensors are applied in medical and biological applications and detection during the Covid-19 crisis. It has several applications in automobiles for dampening vibration, understanding tire dynamics, and in the field of IoT known as the Internet of Nano-Things (IoNT). With progression in nanotechnology, the following years may witness changes like enhanced reliability and better affordability, which would be possible with a rise in production volumes and scaling of nanosensors in specific domains. This will enable the shift of applications from controlled to harsh environments. Nanocomposites and specific biomarkers used in packaging detect microorganisms, toxic substances in vivo and vitro environments, and food conditions show potential as the edibility of the sensors is increased.

VI. FUTURE SCOPE

The nanosensors are very small in size and are replacing the conventional sensors in many fields, which give the nanosensors the enormous potential to be researched in different fields such as –

- Use of nanosensors in the defense sector to detect guided and non-guided missiles so that they could be countered,
- Some nanosensors can be injected into military personnel while going on a mission to detect their real-time location; by this, they can be found easily if they go missing.
- Some nanosensors can be aviation industries for an advanced navigation system, and much more future applications might be there.

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