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A REVIEW ON CONCEPT OF BIOSENSORS AND NANOTECHNOLOGY

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Abstract:

An integrated receptor-transducer device that can translate a biological reaction into an electrical signal is called a biosensor. Due to the numerous uses for biosensors in the last ten years, including medication delivery, environmental monitoring, water and food quality monitoring, health care and illness diagnosis, and environmental monitoring, biosensor design and development have gained significant attention from scientists and researchers.

The major obstacles to the advancement of biosensors are (i) effectively capturing bio recognition signals and converting them into electrochemical, electrical, optical, gravimetric, or acoustic signals (transduction process); (ii) improving transducer performance, meaning lowering detection limits even for the detection of individual molecules, increasing sensitivity, and reproducibility; and (iii) miniaturizing biosensing devices through the use of micro- and nanofabrication technologies. The problems can be addressed by combining zero- to three-dimensional nanomaterials with sensing technologies.

These materials have high surface-to-volume ratios, strong conductivities, shock-bearing capacities, and color tunability. The following nanomaterials (NMs) are used in the creation of nano-biosensors: carbon nanotubes (CNTs) (large surface area, high electrical and thermal conductivity), quantum dots (QDs) (color tunability), nanowires (NWs) and nanorods (NRs) (high stability and high carrier capacity). These nanoparticles can also function as transduction elements in and of themselves.

The evolution of biosensors, their types based on receptors and transducers, and contemporary methods used in biosensors using nanomaterials like NPs (such as metal oxide and noble metal NPs), NWs, NRs, CNTs, QDs, and dendrimers, as well as their recent advancement in biosensing technology with the growth of nanotechnology, are all summarized in this review.

Keywords: Biosensors, nanomaterials, nano-biosensing, gold nanoparticles, carbon nanotubes, quantum dots. Introduction

Introduction:

A biosensor is an apparatus that uses signals proportionate to the concentration of an analyte in a reaction to quantify biological or chemical responses. Applications for biosensors include illness monitoring, drug discovery, and the identification of contaminants, pathogen-causing microorganisms, and disease-indicating markers in physiological fluids (blood, urine, saliva, sweat).[Fig1]depicts a typical biosensor, which is made up of the following parts.

- **Analyte:**
  A material of interest that has to be found. For instance, in a biosensor used to identify glucose, glucose serves as an "analyte."

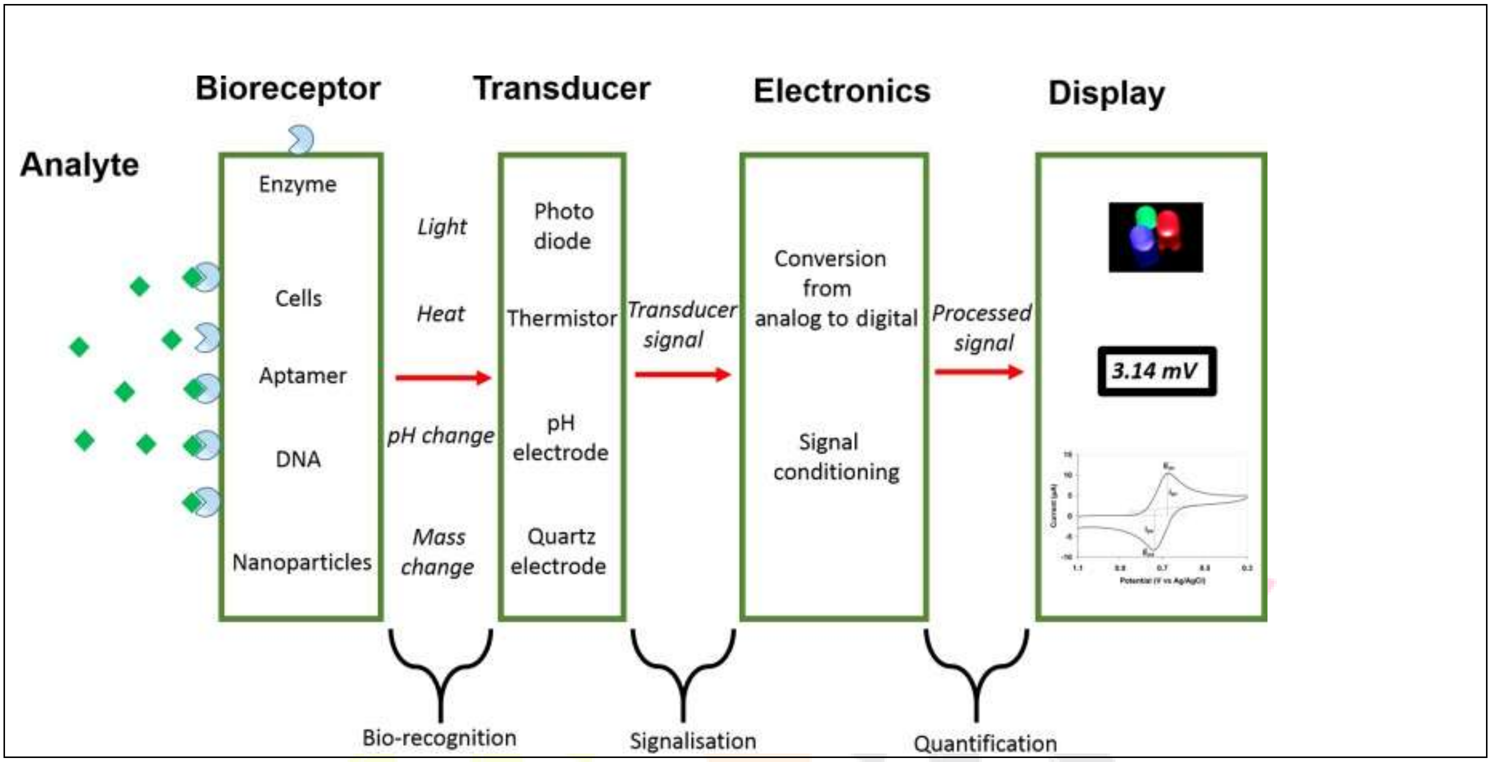
- **Bioreceptor:**
  A bioreceptor is a molecule that can identify the analyte with precision. Bioreceptors include things like enzymes, cells, aptamers, deoxyribonucleic acid (DNA), and antibodies. Bio-recognition is the process of generating a signal (such as light, heat, pH, charge or mass shift, etc.) when the bioreceptor and analyte interact.

- **Transducer:**
  An element that transforms one type of energy into another is called a transducer. The transducer's job in a biosensor is to transform the bio-recognition event into a signal that can be measured. Signalization is the term used to describe this energy conversion process. Analyte–bioreceptor interactions are typically proportionate to the optical or electrical signals produced by most transducers.

- **Electronics**:
  The electronics component of a biosensor is responsible for processing the transduced signal and getting it ready for display. It is made up of intricate electrical circuitry that carries out signal conditioning tasks like amplification and digital signal conversion from analog form. The biosensor's display device then quantifies the signals that have been processed.

- **Display:**
  A user interpretation system, such as a computer's liquid crystal display or a direct printer that produces comprehensible numbers or curves, makes up the display. This component typically comprises of a hardware and software combination that produces the biosensor's

results in an approachable way. Depending on the needs of the user, the output signal on the display may be graphic, tabular, numerical, or an image.



Schematic representation of a biosensor [Fig1]

Historical Background:

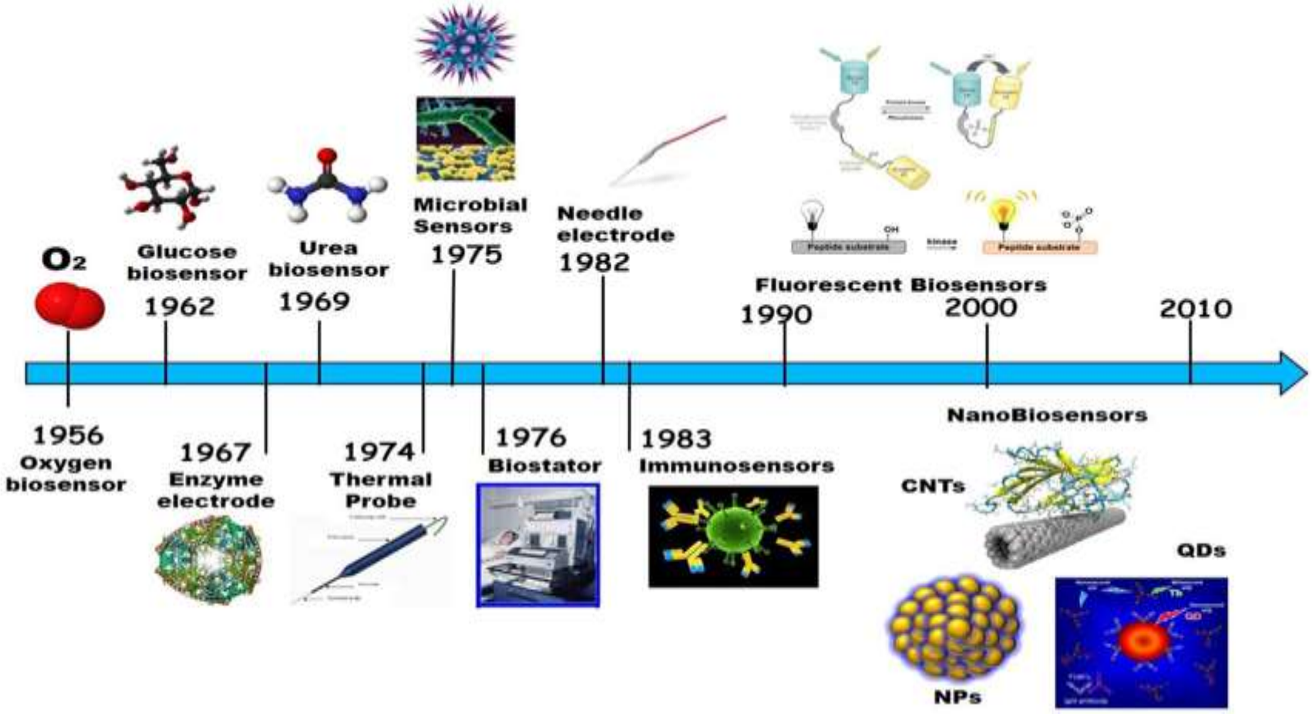
Biocatalyst (an enzyme, cell, or tissue) that can transform a biological or biochemical signal or reaction. This field of study involves a number of researchers with varying backgrounds; these include chemists, physicists, microbiologists, and, of course, electrical engineers. All of these experts are heavily involved in various aspects of the assembly of the "Biosensor" item. By taking a look back, we can also see that the idea of a biosensor has changed over the past 50 years. A biosensor is a self-contained analytical tool that reacts to the number of chemical species present in biological samples. It's obvious that this is incorrect, but it's been incredibly challenging to explain. There is no mention of the device's biological active ingredient. Therefore, a biosensor could be any type of sensor that operates on biological material, whether it is chemical (microelectrode implanted in animal tissue) or physical (thermometer).

HISTORY OF BIOSENSORS

1975: First commercial biosensor (Yellow springs Instruments glucose biosensor)
1975: First microbe-based biosensor, First immunosensor
1976: First bedside artificial pancreas (Miles)
1980: First fiber optic pH sensor for in vivo blood gases (Peterson)
1982: First fiber optic-based biosensor for glucose
1983: First surface plasmon resonance (SPR) immunosensor
1984: First mediated amperometry biosensor. Ferrocene used with glucose oxidase for glucose detection.
1987: Blood-glucose biosensor launched by Medi Sense ExacTech

We both agree that a biosensor is a device that combines a transducer and a biological sensing material, sometimes known as a molecular biological recognition element. The idea of using artificial chemical molecules to duplicate or replace biological material has recently undergone another evolution. In 1962, Professor Leland C. Clark described how "to make electrochemical sensors (pH, analytical tool made up of a transducer that can measure an electrical signal and an "enzyme transducers as membrane enclosed sandwiches" to his 1956 paper on the development of an oxygen probe. Based on this research activity, Clark expanded the range of analytes that could be measured.[2] The glucose oxidase enzyme was entrapped in a dialysis membrane and placed over an oxygen probe to demonstrate the first example. The proportionate drop in oxygen concentration was evaluated by the addition of glucose. The report that was published and used to coin the term "enzyme electrode" described the first biosensor.[3]

Subsequently, in 1967, Updike and Hicks used the same term "enzyme electrode" to refer to a device that was similar in that it allowed for the quick and quantitative measurement of glucose by immobilizing the enzyme glucose oxidase in a polyacrylamide gel on the surface of an oxygen electrode. During that time, there was a lot of activity in the electrochemical world regarding Ion Selective Electrodes (ISE) research, and it was widely accepted to expand the sensor's application to include non-ionic chemicals like glucose as well as non-electrochemical active compounds. At the time, we saw the potential to expand the research effort significantly. Unquestionably, the first groups to focus on the development of electroanalytical biosensors were those involved in the creation of ISE. An "amygdaline" sensor was created by Professor G. Rechnitz. It works by combining betaglucosidase with an Ion Selective Electrode (cyanide ISE) to produce benzaldehyde and cyanide. [4,5]



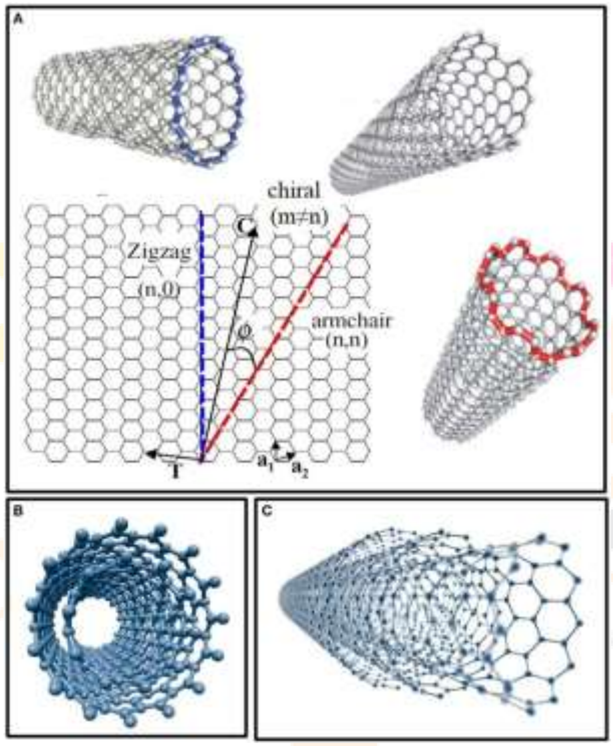
BIOSENSOR DEVELOPMENT TIMELINE [7] [Fig2]

Depiction the overview of nanomaterials used for improving biosensor technology [Table1]

Sr No	Nanomaterial used	Key Benefits
1	Carbon nanotube	Improved enzyme loading, higher aspect ratios, ability to be functionalized, and better electrical communication. [10,11,12]
2	Nanoparticles	Aid in immobilization, enable better loading of bio analyte, and also possess good catalytic properties. [13,14,15,16]
3	Quantum dots	Excellent fluorescence, quantum confinement of charge carriers, and size tunable band energy. [17,18,19]
4	Nanowires	Highly versatile, good electrical and sensing properties for bio- and chemical sensing; charge conduction is better. [20,21,22]
5	Nanorods	Good plasmonic materials which can couple sensing phenomenon well and size tunable energy regulation, can be coupled with MEMS, and induce specific field responses. [23,24,25]

Carbon nanotube

(A) Single-walled carbon nanotubes (SWNTs) structures in function of their chirality (zigzag, armchair, and chiral). (B) Model of double-walled carbon nanotubes (DWNTs). (C) Structure of multi-walled carbon nanotubes (MWNTs) made up of several concentric shells.



STRUCTURE AND MODELS OF CARBON NANOTUBES IN FUNCTION OF THEIR NUMBER OF WALLS. [Fig3]

One type of carbon is a carbon nanotube (CNT), which has a length to diameter ratio of more than 1000 and a diameter of one nanometer. The configuration of the atoms is hexagonal, much like in graphite. The cylindrical graphitic sheet, known as graphene, that makes up the structure of carbon nanotubes is assembled and rolled into a flawless cylinder with a diameter of about one nanometer. As a relatively recent member of the carbon allotropes, carbon nanotubes (CNTs) are thought to be the substance that lies between fullerenes and graphite (Tanaka et al., 1999).

Buckyballs and carbon nanotubes are both members of the fullerene structural family. A CNT is cylindrical, and whereas buckyballs are spherical, some of its ends are open, while the others are closed with complete fullerene caps. The name carbon nanotubes (CNTs) come from their size; a CNT's diameter is only a few nanometers, which is about 50,000 times smaller than the width of a human hair, and they can reach lengths of several micrometers. However, the development of commercial applications for carbon nanotubes (CNTs) has been somewhat delayed, mainly due to the high production costs of the highest quality CNTs.[26]

Carbon Nanotubes Properties and Applications[27]:-

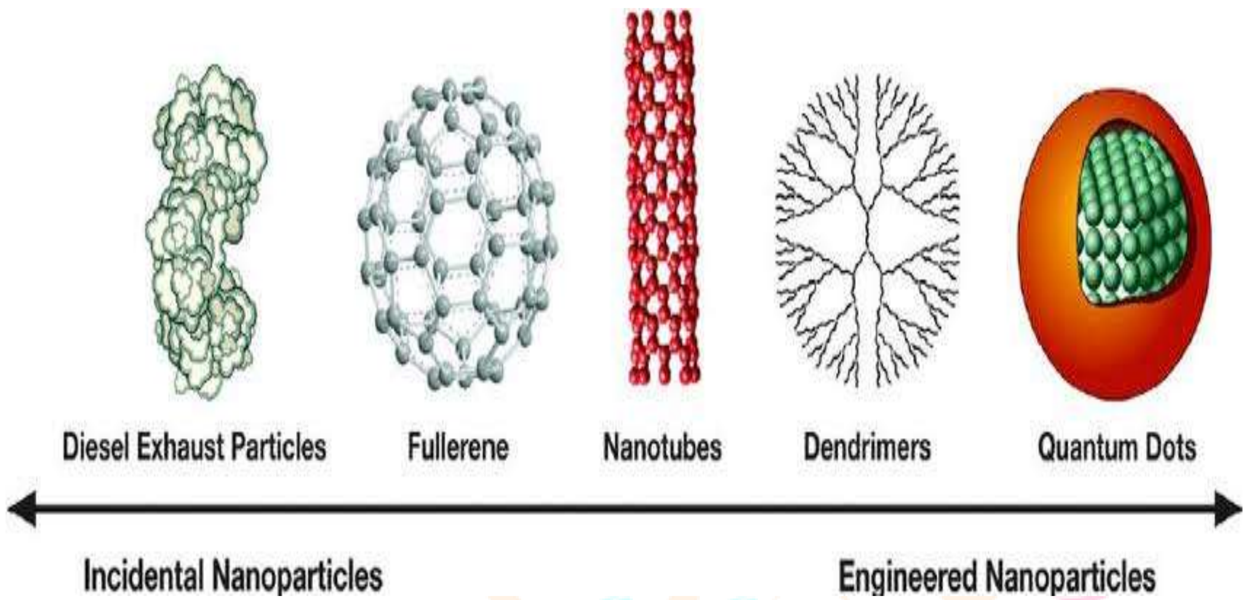
- **Carbon Nanotubes Properties:**

➢ CNTs have high thermal conductivity
➢ CNTs have high electrical conductivity
➢ CNTs aspect ratio
➢ CNTs are very elastic ~18% elongation to failure
➢ CNTs have very high tensile strength
➢ CNTs are highly flexible — can be bent considerably without damage
➢ CNTs have a low thermal expansion coefficient
➢ CNTs are good electron field emitters

- **Carbon Nanotubes Applications:**

➢ CNTs field emission
➢ CNTs thermal conductivity
➢ CNTs energy storage
➢ CNTs conductive properties
➢ CNTs conductive adhesive
➢ CNTs thermal materials
➢ Molecular electronics based on CNT's.
➢ CNTs structural applications
➢ CNTs fibers and fabrics
➢ CNTs biomedical applications

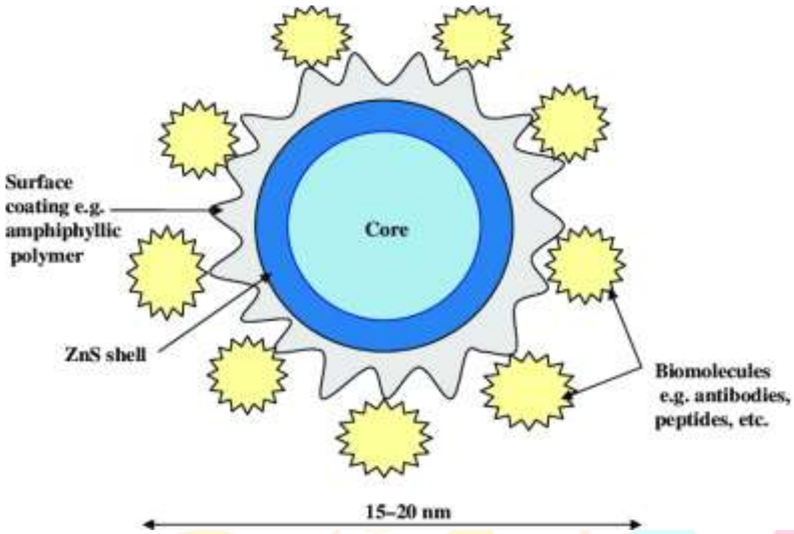
Nanoparticles:-



Nanoparticles[Fig4]

Only a limited number of labels are captured per binding event in conventional (optical) sandwich bio affinity experiments. Because of their small size, the characteristics of nanoparticles are highly impacted by the binding of target biomolecules.[28] Additionally, nanoparticles can be specifically tailored for particular bioassays. The signal from the assays is greatly increased by using nanoparticles. The need to overcome the shortcomings of organic fluorophores has motivated the application of nanoparticle-quantifying tags in optical bioassays.[29] Mirkin's team showed that DNA hybridization-induced aggregation of gold nanoparticles produces materials with extraordinary optical characteristics. Additionally, highly sensitive bioassays can be produced by semiconductor quantum dots with high fluorescence intensities. Using CdSE/AnS core-shell quantum dots coupled to streptavidin, Hahn et al. achieved highly sensitive detection of the single bacterial pathogen Escherichia coli 0157.[30]

Quantum Dots:-



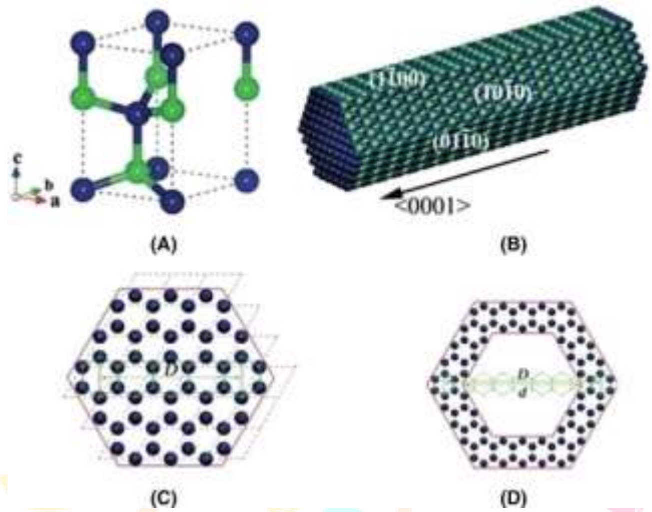
Quantum Dots[Fig5]

Typically made up of atoms from groups II–VI (e.g., CdTe, CdSe) and III–V (e.g., InP, InAs) of the periodic table, semiconductor nanocrystals, also known as quantum dots (QDs), are a type of novel fluorescent nanomaterial consisting of inorganic nuclei with organic molecules in the nanoscale range of 1–10 nm. Both form and size have an impact on their optoelectronic characteristics. Larger QDs, measuring 5–6 nm in diameter, release colors like orange and red. Shorter wavelength QDs (two to three nm) create hues like green and blue.[31][32] The precise hues differ based on the QD's particular composition. These QD cores are frequently topped with an inorganic layer to increase their quantum yield and improve the signal-to-noise ratio. The size and makeup of QDs allow them to emit a wide range of wavelengths, from visible to near-infrared (NIR) and ultraviolet (UV).[33][34] QDs' characteristics lie in the middle of those of discrete atoms or molecules and bulk semiconductors. QD surfaces cannot become more water soluble without the addition of a hydrophilic substance, such as cysteamine or mercaptopropionic acid (MPA).

In order to stop these nanoparticles from aggregating, surface conjugations with artificial polymers like polyethylene glycol (PEG) are frequently helpful.[35][36] Quantum dots (QDs) can be used to construct biosensors. Researchers may examine cellular activities at the molecular level with the use of molecular QDs, which may also aid in the detection and treatment of diseases like cancer. By conjugating antibodies to the surface of the dots, one can use quantum dots as passive label probes or as active sensors in high-resolution cellular imaging. [37][38]

The dots' fluorescence can change as they react with the analyte. QDs cannot be employed in biological applications because they contain extremely poisonous heavy metal elements like cadmium. The use of nanomaterials in biological applications has raised concerns about toxicity and environmental pollution, thus it's critical to produce nontoxic and biocompatible nanomaterials. Due to their abundance of functional groups, QDs have proven to be straightforward to include into hybrid nanomaterials. Improved thermal and chemical stability, high quantum efficiency, extended excited state durations, and reduced toxicity can all be obtained by hybridizing QDs with other materials.[39][40]

- **NANOWIRES:**



One kind of nanowire sensor is a nanowire field-effect transistor (FET), which developed from ordinary planar FETs, which have a gate, source, drain, and body. The body's drain and source are made at the micro- or nanoscale using a metallic substance. The conductivity between the source and drain can be adjusted by creating electric potential fluctuations through the gate, a critically thin isolation layer that is constructed between them. Usually, the application of an external voltage causes these changes in electric potential. By binding the charged species to the gate, chemically or biologically charged species can also change the potential and hence the conductivity. Many years ago, a proposal was made for an electrical sensing mechanism that would use a build-up of charged species. Unfortunately, the low sensitivity of the planar gate FET sensor means that many applications cannot use it for detection without a large number of samples.

- **Nanorods:**

Nanorods are hollow tubes without an interior surface Thermally stable but less adaptable than nanotubes Made of metal, metal oxide, and carbon Uses: medication administration, bioimaging, photothermal therapy, nanocapacitors, etc. Nanorods are an intriguing component to study and perfect candidates for numerous applications because of their form anisotropy (physical characteristics). When compared to spherical particles, it was found that the nanorods' ability was improved. This is because the nanoparticles' higher surface plasmon excitation is caused by the increased aspect ratio of the particles. In particular, the increasing surface plasmons within a nanoparticle give rise to the strength of the dipole moment. Thus, in nanorods relative to spherical particles, an increase in surface plasmons results in an amplification of the electrical field. Partially aligned CdSe nanorods offered an efficient, guided channel for charge carriers to pass across the photovoltaic device and be collected, as established by Alivisatos and colleagues as one advantage of a rod-like form. In a similar vein, adding nanorods to P3HT film might boost the external quantum efficiency from 1 to 10 by a factor of 3.

As the aspect ratio of the nanoparticles rose, the electron accumulation improved. Additionally, one of the main factors in enhancing its qualities is the alignment of the nanorods. Anisotropic nanoparticle aspect ratio was found to be a factor in the electrical conductivity of polymer composites by the Winey group during their study of Ag nanorods for polystyrene composites. In particular, since rod-shaped particles have a lower percolation threshold than spherical ones. It has been discovered that percolation depends on the size and form of the nanoparticles. Greater length and diameter of rod-shaped particles are anticipated to confer numerous benefits on the oriental characteristics of nanorods. Last but not least, compared to isotropic (homogenous and uniform) particles, nanorods have greater advantages. In conclusion, it can be said that the aspect ratio, volume fraction, polydispersity, and orientation of nanorods have a significant impact on their efficiency.

- **Biosensors applications in medical field**

Modern medicine makes use of a wide range of biosensors. Tissues, microbes, organelles, cell receptors, enzymes, antibodies, and nuclear acids all employ these tools to find substances in delicate bio-elements. The creation of biosensors has been enormously important and has led to great advancements in the medical profession and the discovery of novel, powerful, and accurate analytical sensors.

A variety of processes, including the connection between anti-corps, catalytic enzymes, glucose thresholds, microbial diseases, tumor growth detection, pathogens, and toxins, are identified with the aid of the medical sector. The COVID-19 detection method now in use uses biosensors enabled by nanomaterials.

- **Significant applications of Biosensor in the medical field**[Table2]

Sr. No.	Applications	Description
1	Track biological abnormalities	Many medical problems are resolved with biosensors. It is capable of monitoring a patient's vital signs and detecting biological anomalies. Identification and monitoring of risk variables are essential to lowering healthcare costs because treatment costs are mostly determined by prevention and early intervention. The patient's treatment and care stakeholders guarantee that effective time management will help the patient achieve better results. A medical biosensor can swiftly identify the physiological modifications that can lead to proactive, early treatment. With current technology improvements, monitoring systems can be deployed for less money than hospital therapy.

Sr. No.	Applications	Description
2	Heart rate tracking	An athletic band or smartwatch that records heart rates continually and provides physiological data is an example of a biosensor. To gain a clinical understanding of the condition, sophisticated sensors can identify specific biomarkers. A bioreceptor detects the physiological state or activity of a biomarker and produces corresponding optical and electrochemical data. Biological data can be transmitted via a transducer, which transforms this unprocessed data into an electric signal. These technologies are being utilized in biomedical applications as an evolutionary algorithm to carry out a number of crucial tasks. This key piece of Industry 4.0 technology continues to advance and accomplish new milestones.
3	Track body chemistry	Diet Sensor allows users to check the molecules in food and track the amount of calories consumed. Those who suffer from severe allergies understand that excessive caution when it comes to food can lead to major problems, as individuals have little control over what they eat. To test an inpatient's breath for acetone molecules, healthcare uses a sophisticated nanosensor
4	Diet monitoring	Diet Sensor allows users to check the molecules in food and track the amount of calories consumed. Those who suffer from severe allergies understand that excessive caution when it comes to food can lead to major problems, as individuals have little control over what they eat. To test an inpatient's breath for acetone molecules, healthcare uses a sophisticated nanosensor.
5	Tracking Air quality	Modern sensor technologies make it simple to monitor air quality. This device notifies users and medical experts of disease diagnosis by tracking daily air quality and taking the body's core temperature. Accurately monitoring body temperature, sleep patterns, sports physiology, clinical testing, and hospital applications are all possible with its cable-free interface.

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