www.ThePharmaJournal.com

The Pharma Innovation

ISSN: 2277- 7695
TPI 2016; 5(6): 18-25
© 2016 TPI
www.thepharmajournal.com
Received: 04-04-2016
Accepted: 05-05-2016

Suravi Pandit
Girijananda Chowdhury Institute of Pharmaceutical Science (GIPS) Guwahati, Assam, India, Pin- 781017.

Debaprotim Dasgupta
Assistant Professor, Pharmaceutical Chemistry Girijananda Chowdhury Institute of Pharmaceutical Science (GIPS) Guwahati, Assam, India.

Nazneen Dewan
Girijananda Chowdhury Institute of Pharmaceutical Science (GIPS) Guwahati, Assam, India, Pin- 781017

Prince Ahmed
Girijananda Chowdhury Institute of Pharmaceutical Science (GIPS) Guwahati, Assam, India Pin- 781017.

Corresponding Author
Suravi Pandit
Girijananda Chowdhury Institute of Pharmaceutical Science (GIPS) Guwahati, Assam, India, Pin - 781017

Nanotechnology based biosensors and its application

Suravi Pandit, Debaprotim Dasgupta, Nazneen Dewan and Prince Ahmed

Abstract
Biosensor is an analytical device which is used to detect a biological product. In the development of biosensors, nanotechnology is playing an increasingly important role. The nanotechnology based biosensor or nanobiosensor technology is revolutionizing the health care industry such as the nanobiosensor technology is used in the measurement of metabolites, monitoring of diabetes etc., forensic medicine, homeland security. In food and drink industry these are used for remote sensing of water quality, determination of drug residue in food etc. For environment protection these are used in the detection of pesticides and river water contaminants like heavy metal ions, and genome analysis of organisms and communications.
The use of nanomaterials for the construction of biosensors has improved the sensitivity and performance of them, and has allowed the introduction of many new signal transduction technologies in biosensors. The development of tools and processes used to fabricate, measure and image nanoscale objects, has led to the development of sensors that interact with extremely small molecules that need to be analysed.
Several nanobiosensor architecture based mechanical devices, optical resonators, functionalised nanoparticles, nanowires, nanotubes and nanofibers have been in use. In particular, nanomaterials such as gold nanoparticles, carbon nanotubes, magnetic nanoparticles and quantum dots have being actively investigated for their application in biosensors, which have become a new interdisciplinary frontier between biological detection and material science.
With the advent of nanotechnology and its impact on developing ultrasensitive devices, it can be stated that it is probably one of the most promising way to solve some of the problems concerning the increasing need to develop highly sensitive, fast and economic method of analysis in medical diagnostics, food and drink industry, environment protection etc.

Keywords: Nanotechnology, Biosensors, Nanomaterials, Nanoparticles

1. Introduction
As per IUPAC, biosensor is defined as "A self-contained integrated device which is capable of providing specific quantitative or semi-quantitative analytical information using a biological recognition element which is in direct spatial contact with a transducer element." Biosensor is a device that combines a biological recognition element with a physical or chemical transducer detects a biological product. It is a probe that integrates a biological component with an electronic component to yield a measurable signal. These biosensors consists of three components –
(1) Bioreceptors that bind the specific form to the sample;
(2) An electrochemical interface where specific biological processes occurs giving rise to a signal;
(3) A transducer that converts the specific biochemical reaction in an electrical signal;
(4) A signal processor for converting the electronic signal into a meaningful physical parameter and finally
(5) A proper interface to display the results to the operator

1.1 Basic characters of a Biosensor
1) Linearity: - Maximum linear value of the sensor calibration curve. Linearity of the sensor must be high for the detection of high substrate concentration
2) Sensitivity: - The value of the electrode response per substrate concentration
3) Selectivity: - Interference of chemicals must be minimised for obtaining the correct result
4) Response time: - The necessary time for having 95% of the response

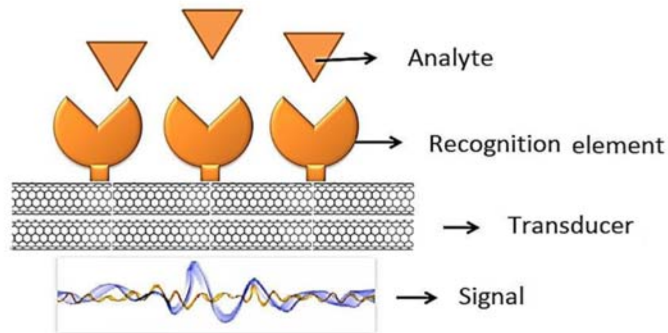

Fig (a): Schematic presentation of a biosensor

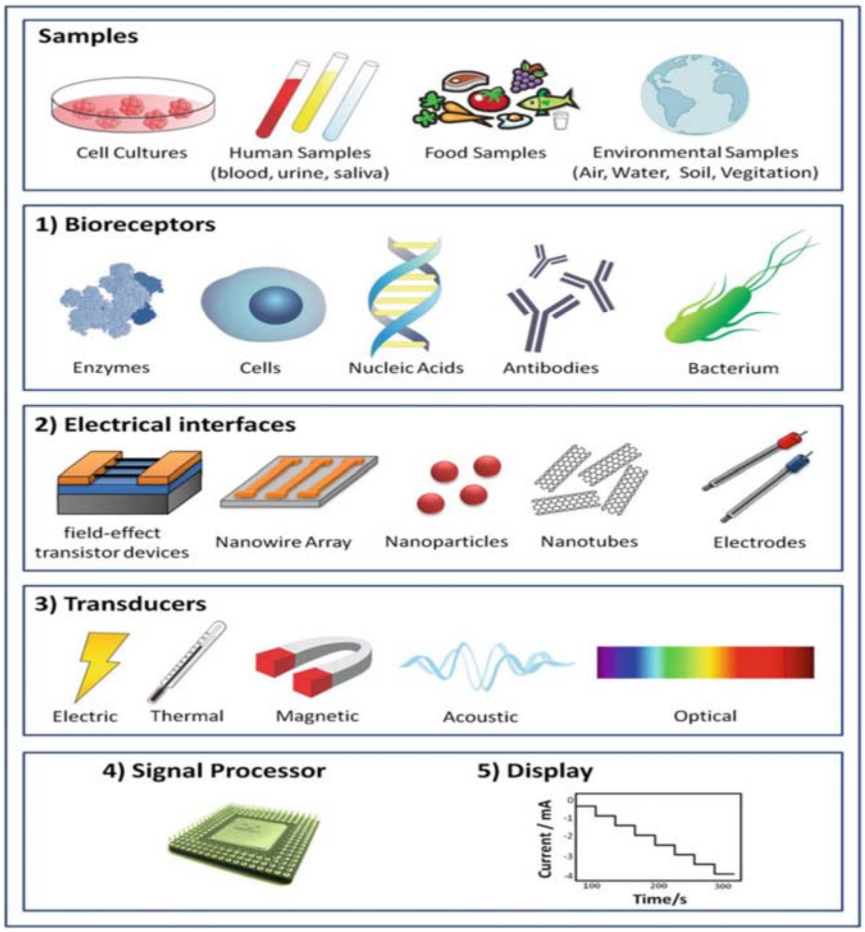

Fig (b): Components of a typical Biosensors

Nanotechnology is not a single technology or discipline but it encompasses various technologies that crosses sectors, such as nanomaterials, medicine, devices, fabrication, electronics, communication and energy. It is the ability to measure and to control matter at the nanometer scale. Nanotechnology deals with the generation and alteration of materials to nanosize (10^{-9} m). Nanomaterials based biosensors which represents the integration of material science, molecular engineering, chemistry and biotechnology can markedly improve the sensitivity and specificity of biomolecule detection, hold the capability of detecting or manipulating atoms and molecules, and have great potential in application such as biomolecular recognition, pathogen diagnosis and environment monitoring.

The nanotechnology products can be classified into three categories based on the number of dimensions "pushed" to the nanometer scale:

(1) thin films, such as coatings of implants for biocompatible purposes, anticoagulant coatings of stents, and coatings of pills and other therapeutic agents, have only one dimension pushed to the scale of few tens or hundreds of nanometres, while the other two dimensions can still extend up to millimetres;

(2) Nanomaterials (NMs), such as carbon nanotubes (CNTs), silicon nanowires, nanorods, and fibres, have two dimensions pushed to the nanometer scale; and

(3) Nanomaterials (NMs), such as quantum dots, gold, magnetic and polymeric nanoparticles, and liposomes, have all the three dimensions pushed to the nanometer scale.

2. Nanotechnology based biosensors

Nanobiosensors- the merging of Nanotechnology with Biosensors. Nanobiosensors are basically the sensors which are made up of nanomaterials and interestingly these are not the specialized sensors which can detect the nanoscale events and happenings. The question that sustains interest from the above description is that why nanomaterials are intended to be used in making biosensors or whether they are going to drive in any significant difference in the overall technology. Nanomaterials are a unique gift of nanotechnology to the mankind; these are the materials which have dimensions between 1-100 nanometres. The size constrains of these materials makes them very special as they have most of their constituent atoms located at or near their surface and have all vital physicochemical properties highly different from the same materials at the bulk scale. They can play very efficient roles in sensing mechanism of the biosensing technology. Integrated devices of the nanomaterials with electrical systems give rise to nanoelectromachenical system (NEMS) which are very active in their electrical transduction mechanisms. Several nanomaterials have been explored on the mechanism of their electronic and mechanical properties for their use in improved biological signalling and transduction mechanisms. Some of such materials that are widely employed include nanotubes, nanowires, nanorods, nanoparticles and thin films made up of crystalline matter. These can be as diverse as using amperometric devices for enzymatic detection of glucose to using quantum dots as fluorescence agents for the detection of binding and even using bioconjugated nanomaterials for specific biomolecular detection. These include colloidal nanoparticles which can be used to conjugate with antibodies for immunosensing and immunolabeling application. These materials can also be used to enhance the electron microscopic detections. Further, metal based nanoparticles are very excellent materials for electronic and optical applications that can be efficiently used for detection of nucleic acid sequences through the exploitation of their optoelectronic properties.

Various nanomaterials have been discussed to analyse their properties and recent applications in biosensors. The research in biosensor technology shows a constant increase in relation to the various nanomaterials with the interest to be implemented either into transducers or receptors operation parts, so as to enhance their multi detection capability and sensitivity. These nanomaterials are nanoparticles, nanotubes, quantum dots or other biological nanomaterials. These nanomaterials can contribute to either the bio-recognition element or the transducer or both. Nanosensors, nanoprobes and other nano systems have revolutionized in the fields of chemical and biological analysis, to enable the rapid analysis of multiple substances *in vivo*. In recent years, a wide variety of nanoparticles with different properties, such as small size, high speeds, smaller distances for electrons to travel, lower power, and lower voltages, Important advances in the field of nanotechnology have led to the utilization of nanomaterials such as metal nanoparticles, oxide nanoparticles, magnetic nanomaterials, carbon materials, Quantum Dots and metallophthalocyanines to improve the electrochemical signals of biocatalytic events that occur at the electrode/electrolyte interface. Functional nanoparticles that bound to biological molecules (e.g. peptides, proteins, nucleic acids) have been developed for use in biosensors to detect. The top-to-bottom approach involves micro-/nano-machining of macroscopic materials down to the desired nanometer scale using physical (anisotropic) or chemical (isotropic) processes. This process includes combination of techniques such as lithography, laser ablation, ion milling, and chemical etching. On the other hand, in the bottom-up approach, the material is "built" by the formation of an initial critical mass followed by the subsequent accumulation of material. Most commonly used techniques for bottom-up nanofabrication are molecular beam epitaxy, physical or chemical vapour deposition and evaporation, and the (bio) chemical processes for the production of (supra)molecular complexes, self-assembled monolayers, and protein–polymer nanocomposites. Several promising NMs, such as carbon nanotubes (CNTs), graphene, quantum dots (QDs), nanoparticles (NPs), and nanocomposites, have been used for diagnostics and biosensors in the last decade. The first major application has almost always been the glucose sensing mainly due to the multi-billion dollar glucose monitoring market. The field of nanotechnology has grown by leaps and bounds in the last two decades. However, the post-hype era of nanotechnology has posed serious challenges in the commercialization of nanotechnology-based products. The growing public concerns about the safety of NMs, the regulatory concerns in the absence of international guidelines for assessing the safety of NMs, and the industrial/healthcare (I/H) requirements are the most critical issues to be addressed before these products become commercially viable. This report provides the critical review of nanotechnology based biosensors by evaluating the technology push versus the I/H requirements.

2.1 Nanostructured Thin Films for Biosensing

Nanostructured thin films have opened the possibility to fabricate electrochemical sensors and biosensors with high power of detection due to intrinsic properties associated with their dimensions at nanoscale level. These interesting properties can be explained based on the organization level obtained when molecular arrangement is obtained at a solid conductor substrate. Also, the materials that can be used include a large range of organic and inorganic materials for films growth. Moreover, the possibility to improve the detection limit in biosensing devices can be also explained by using compatible materials such as natural polymers. The aim objective behind the utilization of these materials is to combine the high power of detection with preservation of the structural integrity of the biomolecules and, also, maintaining their biocatalytic activity.

2.2 Nanostructured Materials for Biosensing Devices

Nanostructured materials are well known as interesting tools with specific physical and chemical properties due to quantum-size effects and large surface area that provides unique and different properties compared to bulk materials. The exploration of these different characteristics provides the possibility to improve biosensors properties and increase the power of detection throughout size and morphology control. Interesting approaches has reported about the high increase in electronic properties when metallic nanostructures are used as components for electrodes modification. These includes the utilization of nanostructured materials with specific forms such 0D (quantum dots, nanoparticles), 1D (nanowires or carbon nanotubes) or 2D (metallic platelets or graphene sheets) orientation that reflects in their final properties. The next topic will be emphasize in biosensors fabrication using metallic nanoparticles (MNPs) as transducing elements on modified electrodes and some interesting electrochemical approaches used to improve biosensing performance.

2.2. A) Carbon Nanotubes (CNTs)

During the past decade, CNTs have been one of the most extensively used NMs in biosensors, diagnostics, tissue engineering, cell tracking and labelling, and delivery of drugs and biomolecules. They are hollow cylindrical tubes composed of one, two, or several concentric graphite layers capped by fullerenic hemispheres, which are referred to as single-, double-, and multi-walled CNTs, respectively. They have unique structures, excellent electrical and mechanical properties, high thermal conductivity, high chemical stability, remarkable electrocatalytic activity, minimal surface fouling, low overvoltage, and high aspect ratio (surface to volume). CNTs-based biosensors and diagnostics have been employed for the highly sensitive detection of analytes in healthcare, industries, environmental monitoring, and food quality analysis. They have been predominantly used in electrochemical sensing, mainly for glucose monitoring but also for the detection of fructose, galactose, neurotransmitters, neurochemicals, amino acids, immunoglobulin, albumin, streptavidin, insulin, human chorionic gonadotropin, C-reactive protein, cancer biomarkers, cells, microorganisms, DNA, and other biomolecules.

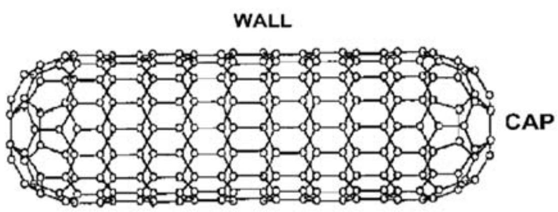

Fig (c): Structure of a single walled Carbon Nanotube

2.2. B) Graphene
Graphene, an atomically thin layer of sp2-hybridized carbon, is another most extensively used NM for diagnostics and biosensors in the last few years due to its interesting and exciting properties, such as high mechanical strength, high thermal conductivity, high elasticity, tunable optical properties, tunable band gap, very high room temperature electron mobility, and demonstration of the room temperature quantum Hall effect. It is a transparent material with a very low production cost and low environmental impact. It has been extensively employed in electrochemical, impedance, fluorescence, and electrochemiluminescence biosensors for the detection of a wide range of analytes such as glucose, cytochrome c, NADH, haemoglobin, cholesterol, ascorbic acid, dopamine, uric acid, hydrogen peroxide, horseradish peroxidase, catechol, DNA, heavy metal ions, and gases.

2.2. C) Quantum Dots (QDs)
QDs are inorganic nanocrystals, approximately 1–10 nm in size, with unique optical properties of broad excitation, narrow size-tunable emission spectra, high photochemical stability, and negligible photobleaching. They have been widely used, mainly as alternatives to fluorophores, for the development of optical biosensors to detect ions, organic compounds, pharmaceutical analytes, and biomolecules such as nucleic acids, proteins, amino acids, enzymes, carbohydrates, and neurotransmitters. They have also been employed for the in vivo detection of target sites in cancer. In fact, they are the ideal candidates for multiplexed optical bioanalysis due to their ultra-high sensitivity, high specificity, cost effectiveness, miniaturized size, size-dependent emission wavelength, and rapid analyte detection.

2.2. D) Nanoparticles (NPs)
NPs have also been extensively used in various bioanalytical applications, especially for the development of biosensors, diagnostics, imaging, drug delivery, and therapy, due to their unique optical and other properties. They change colour in response to the binding of molecules to their surface. The change in the properties of nanoparticles by varying their size or shape has been exploited for various bioanalytical applications. The most widely used NPs are GNPs, which have a nontoxic, biocompatible, and inert core. The prominent plasmon absorption and scattering properties of GNPs are highly useful for the early stage detection and photothermal therapy of cancer and other diseases. They have been used for the development of immunoassays, diagnostics, and biosensors for various analytes. Based on their preferential accumulation at the tumor sites, they have been used for the therapy of cancer and other diseases by acting as nanocarriers for the delivery of drugs, DNA, and genes. The multivalent GNPs facilitate efficient drug delivery to the target sites by shielding the unstable drugs, while their strongly enhanced surface plasmon resonance absorption enables the photothermal therapy of cancer. They have been extensively used in imaging due to their enhancement of the Raman and Rayleigh signals that provide greater chemical information. Therefore, it will be highly useful to combine all the benefits of GNPs, such as diagnostic, specific targeting, and therapeutic, into a single multifunctional GNPs based platform, which can be chemically tailored for a particular disease. Magnetic NPs are the second most widely used NPs, which have been extensively employed in biosensors and diagnostics for the detection of proteins, enzymes, DNA, mRNA, drugs, metabolites, pathogens, and tumor cells. Various types of magnetic sensors based on different signal transduction mechanisms, such as magnetic relaxation switch assay sensors, magnetic particle relaxation sensors, and magneto resistive sensors, have been developed. The diagnostic magnetic resonance (DMR) technology has also been employed extensively for magnetic biosensing. The development of miniaturized chip-based nuclear magnetic resonance detector (μNMR) has further enhanced the capabilities of DMR for the highly sensitive analyte detection in microliter sample volumes, multiplex analysis, and development of cost-effective, portable, and high through put platforms for point-of-care diagnostics. The magnetic NPs are being extensively used by industries such as Phillips Research, Eindhoven, Netherlands for the development of immunoassays and rapid integrated biosensor for multiplexed immunoassays.

2.2. E) Chitosan
Chitosan is one of the most promising NMs for the integration of biological components in medical device due to its excellent biocompatibility, complete biodegradability, and non-toxic nature. The degradation products of chitosan are harmless natural metabolites. It is obtained by the deacetylation of chitin, the second most abundant natural polymer after cellulose, which is found in the shells of crustaceans (crabs and shrimp), the cuticles of insects, and the cell walls of fungi. It is suitable for optical sensors due to its transparent nature. It is also appropriate for electrochemical sensors as the chitosan films are porous and highly permeable to ions. The pH-dependent solubility of chitosan enables the formation of stable films under neutral and basic pH conditions, whereas its amine groups aid in the covalent binding of biomolecules and the formation of nanocomposites with polymers or NPs. But it requires chemical modification such as carboxymethylation to increase its solubility in water and other common solvents. It has been extensively used in biosensors, diagnostics, lab-on-a-chip devices, and other biomedical or bioanalytical applications

2.2. F) Dendrimers

Dendrimers are hyperbranched, monodispersed, star-shaped, and nanometer-scale three dimensional macromolecules with a very high density of surface functional groups. They are composed of three distinct components, i.e., the core, the interior dendron, and the exterior surface with terminal functional groups. They have been used extensively in various biosensors and diagnostics, such as those based on electrochemistry, fluorescence, surface enhanced Raman scattering, impedimetry, and surface plasmon resonance, mainly as they increase the analytical sensitivity, stability, and reproducibility but reduce the no specific interactions. They have also been used for other bioanalytical applications such as drug delivery, gene transfection, and catalysis.

2.2. G) Biological and Other NMs

Lipid vesicles, thin lipid films, and liposomes are biological NMs formed via the bottom-up nanotechnology approach. They have very similar composition to the cell membrane, being composed of phospholipids or other amphiphiles. The bilayer lipid membrane structure provides a biomimetic environment for embedding the biocomponents, such as receptors and proteins, under non-denaturing conditions. Due to their inherent biocompatibility, effective encapsulation of hydrophilic or hydrophobic drugs, and sensitivity to pH and temperature, they have been used as drug-delivery carriers for controlled drug release and for the development of biosensors and diagnostics. The amphiphilic nature allows them to spontaneously form organized structures. They have been used for the amplification of optical, electrochemical, and acoustic signals. Hybrid nanoparticles composed of lipids and polydiacetylene (PDA) have been employed for the development of smart colorimetric biosensors, where the externally induced conformation change of PDA due to specific biomolecular interactions results in remarkable blue-to-red chromatic transition. This approach has been employed for the rapid diagnosis of diseases, study of peptide–membrane interactions, and the colorimetric screening of enzyme catalysts, antibacterial peptides, and physiological ions. Besides these, other NMs (such as cellulose nanocrystals, biomolecules [, and a wide range of nanocomposites with unique properties have also been used. The nanoscale features of the bioanalytical platforms have also been modified for signal enhancement and better assay sensitivity. Moreover, the tools and instruments being employed for nanoscale probing and manipulation have also evolved. The Scanning Probe Microscope that was previously used only for the topographical mapping/imaging of surfaces can now be employed to probe nanometer localized electrical, optical, and nanomechanical properties, and to monitor interactions in real time. It has evolved from a tool to a nanotechnology instrument for bottom-up nanofabrication and for imaging biomolecule assemblies, surfaces, and cells, both in ambient and liquid environment, with special modifications for the sensitive biological surfaces. Therefore, the last decade has seen significant developments in nanotechnology and the continuously increased use of NMs in diagnostics and biosensors.

2.3 Miniaturized Devices and Implantable Biosensors

Besides the modification of electrodes surface by nanomaterials, in recent years, some studies have been done in trying to build biosensors and bioelectronics devices with nanometric geometry, where the individual 1D structures are applied as working electrodes for current measurements low, typically on the order of femtoamperes (f) and picoamperes (pA). Several types of electrodes such as single-walled carbon nanotubes (SWNTs), boron-doped silicon nanowires (SiNWs) and Sn doped In2O3 nanowires (ITO-NWs) have been shown to be interesting for building nanodevices. For example, in a pioneer work, Lemay and co-workers performed electrochemical measurements, on reduced scale of redox enzymes to study a small amount of molecules. This approach was based 2 Nanomaterials for Biosensors and Implantable Biodevices 41 on lithographically fabricated gold (Au) nanoelectrodes with dimensions down to 70 9 70 nm, where was demonstrated successfully for the first time a distinct catalytic response from less than 50 enzymes ([NiFe]-hydrogenase) molecules. These results were obtained using cyclic voltammetry in which were observed a turnover current of 22 fA (femtoampere). However, because of high surface-to-volume ratio and tunable electron transport properties related to the quantum confinement effect present in these nanodevices, their electrical properties are strongly influenced by minor perturbations. This way, when an electrode with nanometer dimensions is used, various types of noises can affect the measurements and compromise the interpretation of the results. Recently, the noise and distortions are the main factors limiting the accuracy of measurements in devices at low current conditions (sub-pico-Ampere). In experiments using electrodes macro-scale (centimetres, micrometres) problems related noises can be easily overcome by the use of programs for signal smoothing. However, for nanoelectrodes, the use of conventional methods of smoothing of signals can lead to loss of useful information. Thus, many research efforts have been observed in the development of methodologies capable of minimizing the effects of external disturbances in the low currents measurements in nanoelectrodes. Like most of the noise frequency affecting the measurements are known (thermal, flicker, burst and shot noise) smoothing filters were used to promote a better visualization of the useful signal. Numerical methods have proven useful for the treatment of the signal due to its simplicity and speed of processing, allowing the identification of unwanted signals, changes in control parameters related to the final quality of the processed signal and quick view of the desired signal. The miniaturization of electrochemical platforms is an important feature in the development of the new generation of implantable clinical devices for monitoring metabolites at living organisms. The implantable biosensors are presented as ideally devices desirable for the diagnosis and management of metabolic diseases such as, diabetes, which currently is based on data obtained from test strips using drops of blood. Although widely used, this procedure is unable to reflect the general situation of the patient and point out trends and patterns associated with their daily habits. Thus, many studies focused on the development of implantable biosensors for continuous monitoring of several biologically important metabolites have been reported in bio electrochemical area with the purpose to improve human quality of life and too in recent trends, the capability to generate energy from biomass fuels. For example, shows a catheter microchip that consists of flexible carbon fibre electrodes modified with neutral red redox mediator (FTCF-NR) being implanted in jugular vein of rat. This system can be used both to monitor glucose levels and for power generation in biofuel cells utilizing enzymes and microorganisms. Despite promising, the reliability of implantable systems is often undermined by factors like bio fouling and foreign body response in addition to sensor drifts and lack of temporal resolution. The prospects of implantable devices and in particular the metabolic monitoring can only be achieved if they can be readily implanted and explanted without the need for complicated surgery. This sense, for facilitated the implantation, the implantable device should be extremely small, which calls for miniaturization of various functional components, such as electrodes, power sources, signal processing units and sensory elements. This way, miniaturized biosensors can cause less tissue damage and therefore less inflammation and foreign body response.

3. Application of Nanotechnology Based Biosensor Technology

The definition and description of the concept of operation of nanobiosensors do not leave any room for their application as they are highly versatile and multifunctional. From the estimation and diagnosis in the health related in vivo aspects, biosensors can also be used for environment monitoring of pollutants, toxicants and physical aspects like humidity, heavy metal toxicity, and even presence of their carcinogens

A) **Biomedical and Diagnostic Application:** Biosensors have been used for biological detection of serum antigen and carcinogens, and causative organism of so many metabolic disorders since a long time. The routine application in diagnosis is best described by the use of biosensors in the detection of disorders like diabetes, cancer, allergic responses, and so many other disorders on the basis of serum analysis. To talk about most of the studied and effectual applications of nanobiosensors from clinical point of view, there are numerous clinical applications that are principally being enabled by using biosensors in routine. The applications include the detection of glucose in diabetic patients, detection of urinary tract bacterial infections, detection of HIV-AIDS and diagnosis of cancer. The advent of biosensors has really improved the diagnosis of all these diseases and related malfunctions. With the addition of nanoscale interventions, this diagnosis has further been benefited and made more precise. The incorporation of nanomaterials has enabled the detecting enzyme system to be immobilized, and this has allowed the recycling and reuse of costly enzymes. Besides they have improved sensitivity and accuracies that make them good candidate. The implementation of nanoscale innovations like NEMS and MEMS has enabled several advantages to the overall testing procedure. Biochips and microarray based technique has enabled the testing of many disease in no time. With controlled synthesis, even magnetic nanoparticles have been synthesised and used for isolation and heavy metal resembling in properties with iron from the blood serum of living organisms.

B) **Environmental Applications:** This is a relatively broader area of application. This is so as environment undergoes so many rapid scale changes almost every second. The determination of pollutants, toxic intermediate, heavy metals from waste streams, and the monitoring of the weather conditions like the estimation of humidity and many other vital features are really highly detailed and comprehensive task. The sensors based on nanomaterials can be very versatile in many terms of their detection and monitoring. The use of devices such as cantilever based electronic probes and the provisions which require very little amount of analyte are very good invaders of the technology. The nanomaterials based sensing tools can be used to find the particular kind of damaging extent of a material present or prevailing in the environment. Carcinogen and harmful intermediates leading to the disruption of proper hormonal systems in the living beings have been isolated through the use of highly sophisticated and specific compounds, particularly named as endocrine-disrupting compound. Using substrate specific detection mechanism, biosensors have been developed for detection of nitrates, inorganic phosphates and biological oxygen demand like parameters have been proved to be environmentally restoring in their working mechanisms. These application can be integrated an a single sensor can be developed by the use of nanomaterials which can sense the different contaminants equally well in a single operation. These applications are highly energy saving, economical and time saving in nature.

C) **Miscellaneous Applications:** Nanobiosensors can also be employed to optimize several other detection. In the industrial operations, feeding of nutrient media and substrate mixtures into the bioreactors for diverse applications can be regulated using these sensors. On an industrial scale many commercial preparation and separation can be enhanced with these sensors. For instance, in the metallurgical operation requiring separation of impurities existing in a complexed form combined in the form of ores, nanobiosensors can be used to separate the impurities selectively by trying out different configurations of the sensing enzymes. Developing microbiological and biochemical assays coupled with bioengineering based innovations are really very handy applications of these sensing materials.

3.2 Advantages of Nanotechnology Based Biosensors

The numerous advances in nanotechnology based biosensor technology have generated tremendous technology push, as evident from the exponentially increased number of publications, patent applications, projects, and focused nanotechnology initiatives/themes. Some of which are discussed: -

- ❖ It is a detection of target molecules, a key factor in early detection of diseases such as breast cancer an AIDs
- ❖ Rapid and high throughput detection
- ❖ Detection processes are simple, user friendly, fast and cost effective
- ❖ Reduced material requirement to fabricate and easier recycling
- ❖ Novel properties and new capabilities
- ❖ Repetitive, portable and stability
- ❖ With the advent of nanotechnology and its impact on developing ultrasensitive devices, mycotoxins analysis has also been benefiting from the advances taking place in applying nanomaterial in sensors development
- ❖ Nanotechnology are also been used in the detection of pathogen in environment.
- ❖ It is been used in toxicity analysis

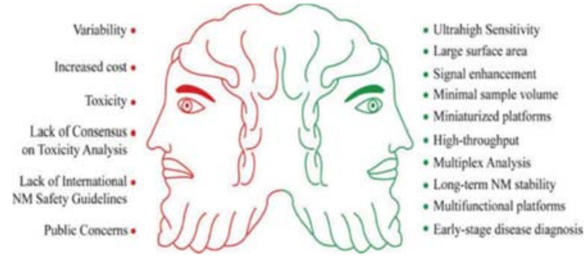

Fig (d): Nanotechnology based Biosensors – the two sides of Janus

4. Current trends in Nanobiosensors

There is a big demand for fast, reliable and low-cost systems for the detection, monitoring and diagnosis of biological molecules and diseases in medicine. This demand exists in the areas of environmental pollutant monitoring, detection of foodborne pathogens, and the potential danger of bioterrorism. The development of ultra-sensitive biological and chemical sensors is one of the grand scientific, engineering, and educational challenges of the 21st century. The next generation biosensor platforms require significant improvements in sensitivity and specificity, in order to meet the needs in a variety of fields including in vitro medical diagnostics, pharmaceutical discovery and pathogen detection. Advances in diagnostic technology have been essential to the progress of medicine. The ability to identify diseases and pathogens by detecting associated proteins, nucleic acid sequences, organelles, cell receptors, enzymes, and other markers, can provide biomedical researchers and healthcare professionals with a detailed knowledge of disease pathways and patients conditions. However, many of the conventional tests currently available are slow, and require large amounts of sample materials, and may lead to false positive or negative results. Thus, there is a need for rapid, trustworthy, low-cost, multiplexed screening to detect a wide range of biomaterials. The current state-of-the art diagnostic biosensors are based on several technologies, often including either the enzyme-linked immunosorbent assay (ELISA), or amplification of a sample by polymerase chain reaction (PCR), using appropriate primers and detection methods. The research on nanobioelectronics & biosensors aims at the integration of nanoelectronics, tools and materials into low cost, user friendly and efficient sensors and biosensors, with interest in several fields such as diagnostics, food analysis, environment monitoring and other industries.

5. Future trends

Nanotechnology has really proved to be a very significant blessing in the development of biosensors. It has been revolutionized the case of biological detection. The overall mechanism have become quicker, smarter, less costly and user friendly. The transduction mechanisms have been significantly improved with the use nanomaterials and nanostructures like those of quantum dots, nanoparticles for enzyme immobilization, and hybrid nanostructure with multiple functionalities. Future argues very well for this dynamic, versatile and quick recognition system considering their multidimensional potential. These materials are right now being increasingly considered for the merging of chemical and biological sensors to make the overall processes fast, easy to execute, and better in terms of performance. The increasing advancement of miniaturization and nanomaterials research has stimulated the application of these materials for sensing several key pathways and regulatory events. With the current progress and exhaustive research pace of nanomaterial exploration, the sensing technology has become more and more versatile, robust and dynamic.

The tremendous advancement in the sensor technologies are due to the great technological demand for rapid, sensitive, and cost-effective biosensor systems in vital areas of human activity such as health care, genome analysis, food and drink, the process industries, environmental monitoring, defence, and security. At present, the nanotechnology-based biosensors are at the early stage of development. The vast applications of nanotechnology in such diverse fields such as semiconductors, biological and medical devices, polymer composites, optical devices, dispersions, and coatings are amazing.

6. Conclusion

Nanobiosensor research focuses on developing innovative technologies that have the ability to make significant contributions in the areas of human and animal disease marker detection, promising therapeutic compound identification and analysis, nano-and biomaterials characterization, and biocatalyst development. These technologies take the form of nanometrically engineered, biologically active surfaces, or liquid-solid interfaces, and the tools necessary to characterize them. The emergence of nanotechnology has opened up new horizons for the development of nanosensors and nanoprobes with submicron-sized dimensions, which are suitable for intra cellular measurements. The attention is being focussed on the study of various nanoeffects, such as the quantum size effect, mini size effect, surface effect, and the macro-quantum tunnel effect, that is unique to nanomaterials, and is actually their most attractive aspect. New nanomaterials and nanostructures need to be explored for use in biosensors. Preferably, nanotechnology-based biosensors should be integrated within tiny biochips with on-board electronics, sample handling and analysis. This will greatly enhance their functionality, by providing devices that are small, portable, easy to use, low cost, disposable, and highly versatile diagnostic instruments. Laser nanosensors can be used for the *in vivo* analysis of proteins and biomarkers in individual living cells. Even though a wide range of nanobiosensors have been developed in the past two decades, the futuristic goal of low-cost, high throughput, multiplexed clinical diagnostic lab-on-a-chip devices is yet to be truly realized. It is still unclear which nanobiosensor architectures are best matched to which diagnostic tasks. Moreover, nanobiosensors that are functional in the lab may not be of use in the field or clinic for several reasons. Well-structured interdisciplinary research programs that involve, life science researchers, engineers and physicians have to be conducted, to reveal more refined and affordable biosensors.

7. Acknowledgement

The authors sincerely thank Girijananda Chowdhury Institute of Pharmaceutical Science, Guwahati, Assam, India for providing all information to carry out this study.

8. Reference

1. Sangadevan S, Periasamy M. Recent trends in Biosensors and their Application. Revised Advance Material Science, 2014, 62-69.
2. Vashist SK, Venkatesh AG *et al.* Nanotechnology-Based Biosensor and Diagnostics: Technology Push versus Industrial/Healthcare Requirements. BioNano Science, 2012, 115-126.
3. Otles S, Yalcin B. Review on the application of nanobiosensors in food analysis. ACTA Scientiarum Polonorum, Technol. Aliment 2012; 1(11):7-18.
4. Reddy MNK, Ratna NP. Nanobiosensors. Advance in Electronic and Electric Engineering 2013; 3(3):321-326.
5. Tothill IE. Biosensors and Nanomaterials and their Application for Mycotoxin Determination. World Mycotoxin Journal. 2011; 4(4):361-374.
6. Janfaza S, Razavi H. Medical Nanobiosensors: A Tutorial Review. Nanomedicine Journal. 2015; 2(2):74-87.
7. Cui D, Guo Q, Zhang X. Recent Advances in Nanotechnology Applied to Biosensors. www.mdpi.com/journal/sensors. 2009; 9:1033-1053.
8. Luz RAS, Lost RM, Crespilho FN. Nanobio electrochemistry. Springer-Verlag Berlin Heidelberg, 2013.
9. Weiss PS. Nanoscience and nanotechnology: present and future. ACS Nano 2010; 4:1771-1772.
10. Jiarong C, Yuqing M, Nongyue H, Xiaohua W, Sijiao L.

Nanotechnology and biosensors. Biotechnology Advances 2004; 22:505-518.
11. Vaddiraju S, Tomazos I, Burgess DJ, Jain FC, Papadimitrakopoulos F. Emerging synergy between nanotechnology and implantable biosensors: a review. Biosensors and Bioelectronics 2010; 25:1553-1565.
12. Stylios GK, Giannoudis PV, Wan T. Applications of nanotechnologies in medical diagnostics. Injury, International Journal of the Care of the Injured. 2005; 36S:S6-S13.
13. Fournier-Wirth C, Coste J. Nanotechnologies for pathogendetection: future alternatives? Biologicals 2010; 38:9-13.
14. Vashist SK, Zheng D, Pastorin G, Al-Rubeaan K, Luong JHT, Sheu FS. Delivery of drugs and biomoleculesusing carbon nanotubes. Carbon 2011; 49:4077-4097.
15. Kim KY. Nanotechnology platforms and physiological challenges for cancer therapeutics. Nanomedicine: Nanotechnology, Biology, and Medicine 2007; 3:103-110.
16. Kawasaki ES, Player A. Nanotechnology, nanomedicine, and the development of new, effective therapies for cancer. Nanomedicine: Nanotechnology, Biology, and Medicine 2005; 1:101-109.
17. Fortina P, Kricka LJ, Bonnell D, Kulkarni A, Wang J, Miyahara Y *et al.* Nanotechnology: improving clinical testing? Clinical Chemistry 2010; 56:1384-1389.
18. Zarbin MA, Montemagno C, Leary JF, Ritch R. Nanotechnology in ophthalmology. Canadian Journal of Ophthalmology. 2010; 45:457-476.
19. Sahoo SK, Parveen S, Panda JJ. The present and future of nanotechnology in human health care. Nanomedicine: Nanotechnology, Biology, and Medicine 2007; 3:20-31.
20. Brambilla D, Droumaguet BL, Nicolas J *et al.* Nanotechnologies for Alzheimer's disease: diagnosis, therapy, and safety issues, Nanomedicine: Nanotechnology, Biology, and Medicine 2011; 7:521-540.
21. Sawhney APS, Condon B, Singh KV, Pang SS, Li G, Hui D. Modern applications of nanotechnology in textiles. Textile Research Journal. 2008; 78:731-739.
22. Bonnell D. The next decade of nanoscience and nanotechnology ACS Nano 2010; 4:6293-6294.
23. Gabellieri C. Nanomedicine in the European Commission policy for nanotechnology. Nanomedicine: Nanotechnology, Biology, and Medicine 2011; 7:519-520.
24. Horton MA, Khan A. Medical nanotechnology in the UK: a perspective from the London Centre for Nanotechnology. Nanomedicine: Nanotechnology, Biology, and Medicine 2006; 2:42-48.
25. Cash KJ, Clark HA. Nanosensors and nanomaterials for monitoring glucose in diabetes, Trends in Molecular Medicine 2010; 16:584-593.
26. Hutchison JE. Greener nanoscience: a proactive approach to advancing applications and reducing implications of nanotechnology ACS Nano 2008; 2:395-402.
27. Parveen S, Misra R, Sahoo SK. Nanoparticles: a boon to drug delivery, therapeutics, diagnostics and imaging. Nanomedicine: Nanotechnology, Biology, and Medicine 2012; 8:147-166.
28. Malik P, Katyal V, Malik V, Asatkar A, Inwati G, Mukherjee TK. Nanobiosensors: Concepts and Variations. ISRN Nanomaterials, 2013, 9.