Chapter 1

Introduction & Literature Survey

1.1 General introduction

Mankind has been performing analysis since the beginning of time, using sensory nerve cells of nose to detect scent and enzymatic reactions in tongue to taste the food. However, toxic and poisonous materials could not be possible to detect from system therefore scientists have developed a new way of chemical testing that often has high selectivity of recognition systems e.g. receptors.

Sensing and catalysis have fascinated much attention in recent time due to their potential applications in devices, clinical diagnosis, environmental monitoring, pharmaceuticals and food processing industries etc. [Luo et al., 2006; Malhotra et al., 2006; Chun, 2009]. Earlier different conventional sensing methods have been used [Uludağ et al., 2010] for detection of different analytes. However, these methods are less sensitive, less specific and time consuming or complicated due to the need of expensive instrumentation and use of radioactive elements. Currently, optical, electrochemical, mass sensitive, etc. sensors are being used for detection of different molecules. However, these techniques suffer from the lack of stability, poor detection limit and requiring high amount of analytes [Scheller et al., 1991].

With advent of nanotechnology, catalysis and sensing is entering in a new era for the designing of advanced sensors, detecting low level concentration of analytes by using portable sensor device which was hardly possible earlier [Alivisatos, 2004]. Thus in the present chapter, we revisit the selected contributions in area of synthesis of metallic nanomaterials and coordination polymers and its applications in catalysis and sensing which is fascinating in both point of views, academic research as well as technological applications.

1.2 Brief history of sensors

A brief history of sensor explains wonderfully, how a simple and refined idea can generate an innovative infiltrate in the science and technology. The first generation sensor was proposed by Clark and Lyons in 1962. They used a combination of enzyme glucose oxidase incorporated into dialysis membrane and an electrochemical oxygen sensor (Clark oxygen electrode) to show the proficiency towards quantitative determination of glucose in aqueous medium [Clark et al., 1962]. A major problem with such sensor is their dependence on dissolved O_2 concentration in analytes. Cass et al. solved this problem in first generation sensor by using the mediators e.g. ferrocene etc. these molecules transfer electrons produced by biochemical redox reaction directly to electrode rather than reducing O_2 dissolved in analytes solution and are called the second generation sensor [Cass et al., 1984]. In 1970s, Yellow Springs Instruments company firstly promote an amperometric sensor which was a bench top glucose analyzer. At present most of the commercial bench top amperometric sensors depend on the reactions catalyzed by oxidase enzyme and successive detection of H_2O_2 at platinum electrodes. The high oxidizing potential (700 mV versus Ag/AgCl) is required for oxidation of H_2O_2 results in considerable interference from the oxidation of other compounds in complex matrices.

These early studies of sensors moved towards the integration of receptors i.e. recognition elements such as antibodies, enzymes, quantum dots, nanomaterials etc. onto physicochemical transducers leading to new Sensing/biosensing devices. This effort has striking the establishment of major research work towards environmental and biotechnological applications of sensors.

1.3 The sensor system

An analytical device which functions to analyze a sample to detect a specific compound is known as sensor. The receptors combine with various transduction methods have facilitated to create rapidly growing fields of analysis and related technologies are known as sensors and chips [Vo- Dinh et al., 2000]. In general there are three types of sensors: physical, chemical and biosensor. Physical sensor measures physical quantities like mass, pressure, distance, and temperature etc. Chemical sensors measures chemical substances by chemical responses. Biosensors measures chemical substances *via* biological sensing element.

A sensor typically consists of a transducer, receptors, and electronic system which include a signal amplifier, processor, and display (Figure 1.1).

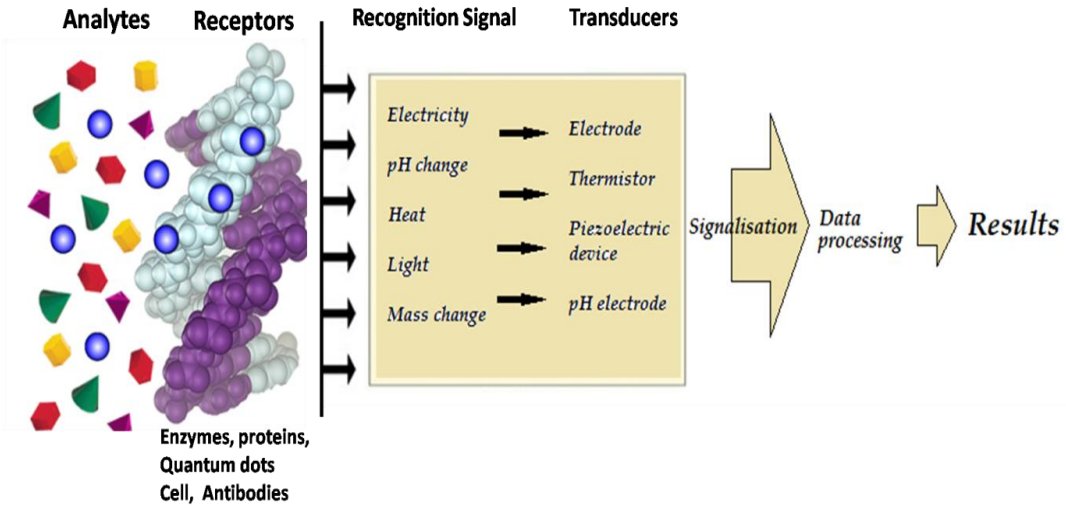

Figure 1.1 Schematic represents various component of a sensor involved in sensing.

1.3.1 Transducers

The interaction of analytes with receptors is proposed to create an effect measured by transducer, which converts the information into measurable signal. Based on the transducer, various methods have been viable towards sensor development technology; however most frequent methods are piezoelectric optical and electrochemical [Collings et al., 1997].

1.3.1.1 Types of Transducers

1.3.1.1.1 Electrochemical Transducers

Electrochemical transducers measure the electrochemical signal after the interaction of analytes with sensing surface of electrode [Collings et al., 1997]. The electrochemical technique is reliable, simple, reproducible, and highly sensitive/selective and can apply in the wide range of analyte concentration. The electrical changes could be potentiometric (a voltage change measured in between the reference electrodes and indicator), conductometric (change in the ability of the sensing material to transport the charge) and amperometric (a current change measured at applied voltage). Generally, amperometric electrochemical method is used in commercially existing sensors for clinical diagnosis.

1.3.1.1.2 Optical Transducers

The optical transducers are based on techniques such as surface plasmon resonance sensing and internal reflectance spectroscopy. Light entering to optical device is absorbed through planar waveguides or optical fibers toward a sensing surface. The reflected light intensity is measured by detector i.e. photodiode. Recorded optical signals commonly include fluorescence, absorbance, surface plasmon resonance and chemiluminescence. Most of the optical techniques of transduction need spectrophotometer for the detection of signal changes.

1.3.1.2 Types of sensors based on Transducers

1.3.1.2.1 Electrochemical sensor

Electrochemical sensor are typically based on the enzymatic catalytic reactions that consumes or produces electrons (redox enzymes e.g. glucose and cholesterol oxidase, etc). The electrochemical sensors usually made up of three electrodes system; a working electrode, a counter electrode and reference electrode. With involvement of target analytes, electron transfer reaction takes place across double layer on active electrode surface, and produces a current which are measured at a fixed potential. In electrochemical sensors signal transductions involves potential, impedance or current changes at electrode-electrolyte interface into electrical signal. Schematics of electrochemical sensors are shown in Figure 1.2 [Mandler et al., 2011].

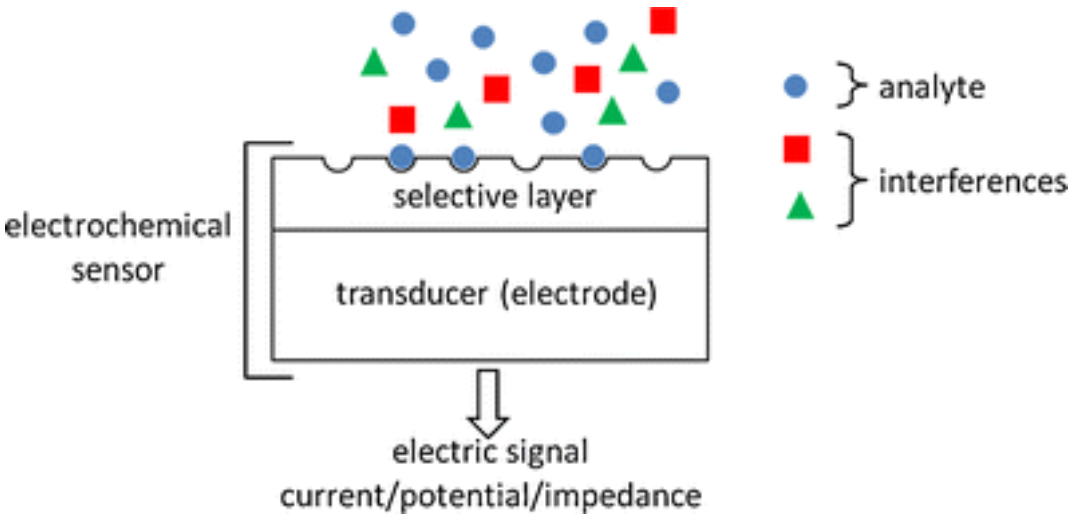

Figure 1.2 Schematics of electrochemical sensors [Mandler et al., 2011].

A number of electrochemical methods, like amperometric, photoelectrochemical, electrochemical luminescence and electrochemical impedance are widely used in detection of analytes but these methods suffer from poor sensitivity and stability. With significant achievement in nanoscience and nanotechnology, nanomaterials based electrochemical signal amplification has large potential for improving both stability and

sensitivity of electrochemical sensor [Zhu et al., 2015]. Recently, nanomaterials are the focus of scientists as advantageous tools for the development of electrochemical sensing platform with potential performance [Pandey et al., 2007; Willner et al., 2011]. Wang et al. investigated formation of poly (3-methylthiophene) based glassy carbon electrode, coated with Nafion– SWNTs used for sensing of dopamine [Wang et al., 2006]. Shan et al. illustrated graphene as a superior material to design a highly selective and sensitive glucose sensor by using glucose oxidase [Shan et al., 2013]. Kang and co-workers reported GOx/rGO/chitosan nanocomposite modified electrode for the study of glucose sensing by direct electrochemistry [Kang et al., 2009]. Hu et al. proposed a facile electrochemical sensing interface for the sensitive glucose detection based on Pt@BSA nanocomposites system along with covalent adsorption of Glucose oxidase [Hu et al., 2014]. The composition of graphene with the inorganic nanomaterials like metals and metal oxides, semiconductors, could open a new area for graphene based nanocomposites which improve the performance of electrochemical sensing platforms [Huang et al., 2012]. Mao et al. reported grapheme-gold nanoparticles hybrids as substrate for development of a highly selective and sensitive field effect transistor (FET) sensor [Mao et al., (2010]. Jiang et al. proposed Au@Pd-RGO nanocomposites as a promising candidate for highly selective and sensitive electrochemical detection of dopamine (DA), uric acid (UA), ascorbic acid (AA), with low limits of detection and wide concentration ranges (Figure 1.3) [Jiang et al., 2014].

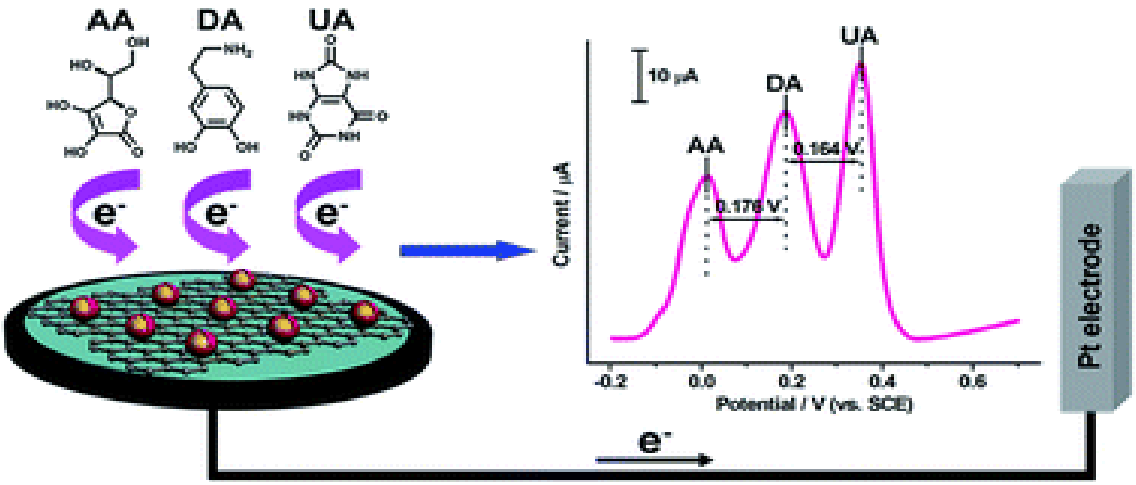

Figure 1.3 Au@Pd-RGO/GCE based sensors for the simultaneous determination of DA, AA and UA [Jiang et al., 2014].

The forensic detection of atropine was executed electrochemically by Ramdani et al. using economic screen printed and disposable graphite sensors in buffer solution of pH 10. The limit of detection for the developed sensor is 3.9 mM at S/N 3 in the concentration range of 5 mM–50 mM. The practical utility of the developed method is demonstrated through a systematic strategy of determination in coca-cola [Ramdani et al., 2013].

Several electrochemical sensors are designed for detection of various drugs. Titanium dioxide nanoparticles and amberlite XAD–2 modified carbon paste electrode (CPE) is developed for the estimation of trimipramine, imipramine and desipramine, using impedance spectroscopy, CV, DPV, and chronocoulometry [Sanghavi and Srivastava, 2013]. A silver nanoparticles and copper(II) complex modified CPE are employed for the assay of norepinephrine, dopamine, epinephrine and levodopa using chronocoulometry, impedance spectroscopy, stripping voltammetry and cyclic voltammetry (CV) [Sanghavi et al., 2013].

Electrochemical sensors have a range of advantages over various types of sensors i.e. high stability, low cost, high reproducibility and low limit of detection, fast response**,** high sensitivity and selectivity.

1.3.1.2.2 Optical sensors

The optical sensors measure optical signal of both catalytic and affinity reactions held at sensing surface in terms of change in fluorescence or in absorbance. The investigation and technological advancement of the optical sensors have practised an exponential progress during last era owing to large potential for real-time, label-free and direct detection of various biological and chemical substances [Soldatkin et al., 2003]. Optical sensors are good alternative of conventional analytical techniques, due to their sensitivity, small size, high cost, effectiveness, and specification, [Sant et al., 2003; Luo et al., 2004]. Optical sensors are used in pharmaceuticals, biomedical research, home land security, environmental monitoring, healthcare and the battlefield, etc. [Luo et al., 2004].

1.3.1.2.2.1 Colorimetric sensor

Currently, there is an increasing demand for development of low cost, simple, and effective sensors with an easy handling for detection of clinically significant molecules to assist in the diagnosis. Such sensing methods are tremendously important, mainly in the third world countries where advanced diagnostic technology is remote to bulk of population. Simple actions which could be accomplished at home without need of any sophisticated expensive instrumentations probably bring drastic changes in the rural health care management. Colorimetric sensing methods are rapid, suitable and simple for the onsite and real time detection of biomolecules along with naked eye detection without any expensive instrumentation.

Recently, gold nanoparticles used in development of colorimetric sensors have achieved considerable attention. These sensors are biocompatible and based on the color change due to interparticle plasmon coupling throughout aggregation (red-to- blue or purple) or re-dispersion (purple-to-red) of gold nanoparticles (GNPs) aggregate [Zhao et al.,2008]. The functionalized gold nanoparticles have been largely used for colorimetric assay of variety of analytes, including proteins [Ou et al., 2010], cells [Lu et al., 2010; Medley et al., 2008], DNA [Chandirasekar et al., 2011; Wang et al., 2012] and metal ions [Chai et al., 2010]. Jiang et al. demonstrated gold nanoparticles based colorimetric method for simple and effective glucose detection in rat brain by the reactions of GOx catalyzed oxidation of glucose, Fenton reaction of H_2O_2, and oxidative cleavage of ssDNA through OH radicals [Jiang et al., 2009; Radhakumary et al., 2011].

Yang et al. designed a colorimetric test strip for the sensing of mercury (II) based on nano-sized conjugated polymers **(**Figure 1.4). In the designed sensor, leucoemeraldine based PANI used as a probe, which specifically interact with Hg^{2+} and results in both "color-change" and "off–on" signals. The developed sensor shows a stunning naked eye colorimetric response distinctively towards Hg^{2+} ions (white–yellow/green–green–blue) over other interfering metal ions, with low limit of detection (5 nM) [Yang et al., 2014].

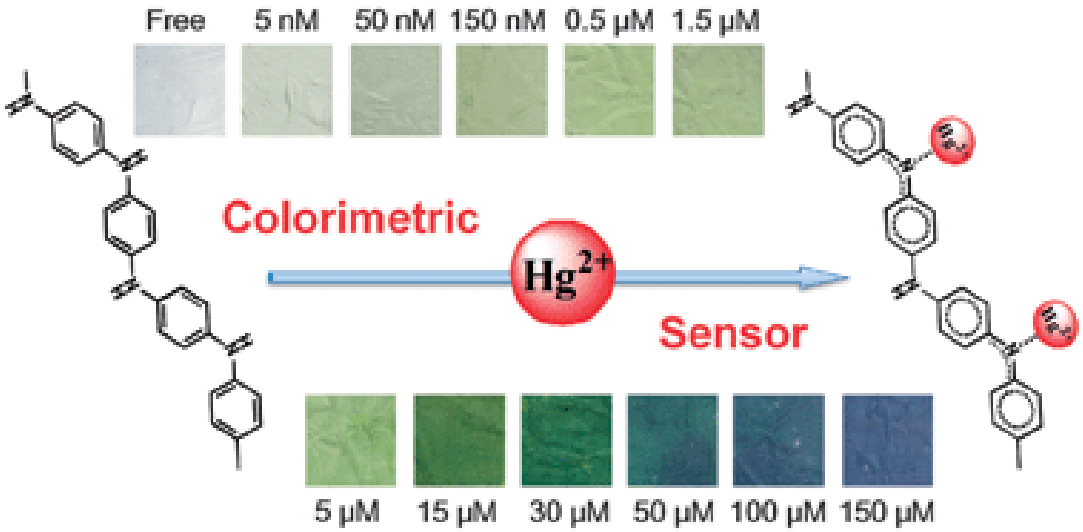

Figure 1.4 Optical colorimetric sensing of PANI-LBNF strips after 20 min incubation in aqueous solution of various concentrations of Hg^{2+} [Yang et al., 2014].

1.3.1.2.2.2 Fluorescence sensor

Fluorescence is the emission of light through a material that has absorbed light or other electromagnetic radiation. The good fluorescence is when the absorbed radiation is in the ultraviolet range of the spectrum, and therefore invisible to the human eye, although the emitted light is in the visible range, which gives the fluorescent that can be seen under UV light. Fluorescence has several applications such as biological detector, chemical sensor, fluorescent labelling and in the form of dyes etc.

1.3.2 Receptors or Recognition elements

In sensor, a receptor is intended to interact with particular analytes to produce measurable electrical signal by transducer. Superior selectivity for analytes in a mixture of other biological or chemical components is the main requirement of sensor. For example in glucose sensing, only glucose molecules are sensed from the mixture, because of the presence of a specific receptor i.e. GOx, H_2O_2 is generated as a result of biochemical redox reaction and breaks down, it generate two electrons which can be used for electrochemical sensing or is produces $OH^{\cdot}$ radicals and chromospheres as

results of catalytic reaction, which can be used in colorimetric biosensing of glucose *via* spectrometry.

1.3.2.1 Classification based on Receptors

Sensors can be classified on the basis of common type of receptors interactions involving: enzymes, nucleic acids, antibody, receptors, cells, quantum dots, nanomaterials and biomimetic materials (Vo-Dinh and Cullum, 2000).

1.3.2.1.1 Ion as receptor

These sensors are most primitive chemical sensors designed on huge amount. The first ion sensor, proposed by F. Haber and Z. Klemensiewicz was pH glass electrode based sensor. Electric charge is basis of the ion recognition. Opposite electric charge of materials to that of the analytes are appropriate for the ion recognition. Selectivity can be developed in the ion recognition by other factors i.e. size of the receptor and analyte-receptor bond.

1.3.2.1.2 Antibodies as receptor

Antibodies have very specific binding affinity toward specific compound or antigen for the development of immunosensors. Antibodies are generally immobilized on surface of the transducer *via* covalent attachment through the conjugation of carboxyl, amino, sulfydryl or aldehyde groups. The transducer surface must be earlier functionalized with hydroxyl, carboxyl, amino or other groups. The interaction between antibody and antigen is specific in nature which is based on lock and key fit model. The binding actions result in physicochemical change in signal into combination with a labelled, such as enzymes, fluorescent molecules, and radioisotopes. The use of antibodies in sensors is strongly dependent on antibody binding capacity, antibody-antigen interaction and assay conditions of temperature and pH [Leung et al., 2007].

1.3.2.1.3 Enzymes as receptor

Enzymes are made up of proteins with selectivity and high catalytic activity towards analytes [Guilbault, 1976]. Their commercial utility at high purity makes them remarkable for large fabrication of enzyme sensors. There are some limitations like ionic strength; chemical inhibitors, temperature, and pH affect their catalytic activity. Mostly enzymes lose their catalytic activity at temperatures above 60°C [Pohanka et al., 2013]. Most of the oxidase enzymes e.g. glucose oxidase and cholesterol oxidase, etc are used in fabrication of sensors which utilized dissolved oxygen and generate hydrogen peroxide. Enzymes are immobilized at the surface of transducers by various immobilization methods like adsorption, covalent attachment, and entrapment for the fabrication of biosensors [Bartlett et al., 1993; Cosnier, 1999]. Enzymes are usually attached to electrochemical and optical transducers.

1.3.2.1.4 Nucleic acid as receptor

Nucleic acids are used in development of genosensors which is based on the theory of complementary base pairing i.e. cytosine: guanine and adenine: thymine. If sequence of target nucleic acid is known then the complementary sequences is synthesized, labelled, and immobilized at sensor surface. The hybridization probes form pair with target sequences produce an optical signal. The ideal transduction theory works in optical detection of these sensors [Leung et al., 2007].

1.3.2.1.5 Cells as receptor

The cells are frequently used in sensor, sensitive to contiguous environment and can respond to every stimulating substance. The cells have a tendency to attach with surface and easily immobilized. They stay active for long time and their reproducibility makes them economical. They are frequently used for the detection of inclusive parameter like

toxicity, stress condition, organic derivatives and drug effect. The cells are also used for detection of herbicides which are main aquatic contaminant [Vedrine et al., 2003].

1.3.2.1.6 Polymeric, organic and inorganic materials as receptor

Amount of hazardous gases detection is incredibly significant for the controlling of air quality parameters. The recognition of vapours and gases is based on the sorption within the material or surface of electrodes. Organic-inorganic materials, Polymeric materials can be used as receptors for this purpose.

1.3.2.1.7 Nanomaterials as receptor

Nanomaterials also specifically recognise analytes and act as receptor in several processes. Analytes immobilized with nanomaterials through covalent interaction, adsorption, or entrapment method develop sensitive sensor. One common benefit of all the nanomaterials is high specific surface thus immobilizes an enhanced quantity of receptor units at reduced volume. Among such nanomaterials, quantum dots, carbon nanotubes, gold nanoparticles, polymer nanoparticles, graphene, and nanodiamonds are largely studied [Holzinger et al, 2014]. In some cases, enhanced sensitivity of the nano-enabled sensors is owing to fact that nanomaterials have comparable size as analytes of interest (e.g., pathogens, metal ions, antibodies, DNA, biomolecules) and are thus proficient to interrogating previously unreachable matrices. Additionally, incorporation of nanomaterials with natural receptors show highly selective and sensitive detection towards the target analytes, for example, nanobioelectronic tongues and noses for tastants, and odorants respectively and G-protein-coupled receptors for dopamine, hormones, geosmin, trimethylamine, cadaverine, etc. [Kwon et al, 2019].

1.4 Catalyst

Catalyst is a substance that increases rate of the reaction without being consumed. Current research work is more focused towards the nanostructured catalysts with

enhanced physiochemical properties. Natural enzymes such as horse radish peroxidase (HRP) and alkaline phosphatase are attractive catalyst mediating most of the biological reactions in the living organisms, and also accelerate the rate of reactions up to thousands times for particular substrates. Recently nanomaterials are emerged as catalytically active nanozymes which show a number of advantages over the natural enzymes, like controlled synthesis, low cost, tunability in catalytic process, and high stability against harsh conditions [Gao et al., 2007; Wei et al., 2008]. Recently, graphene and its derivatives, platinum and gold nanohybrids, quantum dots and their composite materials have been proved as fascinating materials with excellent peroxidase mimetic activities [Goa et al., 2015, Song et al., 2010]. The electrodes surfaces modified with nanomaterials are highly electro-catalytic which causes either reduction or oxidation of analytes at redox potential of mediator catalyst couple unless formation of the catalyst substrate adduct. A lot of work on the electro- and photoelectron-catalytic activity of MoS_2 proves it a capable candidate for the catalysis of hydrogen evolution reactions, [Jaramillo et al., 2007] and sensing [Wang et al., 2013]. Further nanocordination polymers are also emerged as potential catalyst due to the chemical tunability, porosity and high surface area [Jiang and Xu, 2011; Meilikhov et al., 2010]. Numerous innovative studies are reported for metal nanoparticles placed at coordination framework in catalysis [Lu et al., 2012; Kuo et al., 2012]. Qiu and co-workers developed porous and core shell nano-catalyst of Au/MIL-100 (Fe) and demonstrated its catalytic properties.

1.5. The role of nanomaterials for catalysis and sensing

For the development of nanotechnology, the role of nanomaterials is very important due to the fact that they exhibits remarkable properties such as high catalytic efficiency, high surface area, reaction activity, extraordinary electrical and thermal conductivities,

magnetic behaviour, good biocompatibility, ease of functionalization, high degree of selectivity and specificity and strong adsorption ability and are ideal for the development of highly efficient sensors [Fan et al., 2008; Huang et al., 2010]. Nanomaterials are defined as materials with at least one external dimension in the size ranges from approximately 1-100 nanometers [Buzea et al., 2007]. Variety of nanomaterials ranging from metallic nanoparticles (gold and silver nanoparticles), graphene and their derivatives, transition metal dichalcogenides, semiconductor nanoparticles (quantum dots) to polymeric, liposomal, dendrimers, and solid lipid nanoparticles have been explored broadly for sensing applications.

Developing a range of sensors has important impact on daily life. Fundamental issues towards the incorporation of sensing platform include the demand for low costs and have potential for real time measurement, mainly for point-of-care applications. With significant achievements in the nanoscience and nanotechnology, nanomaterials-based sensing signal amplifications have enormous potential for improving both selectivity and sensitivity of sensors. The growing demand for cost-effective, simple, rapid, and portable screen in methods for the qualitative and quantitative determination of analytes relevant to medical research, clinical diagnosis, environment and food safety monitoring, and biosecurity investigation has been accelerated the development of nanomaterials based sensors.

Further Composite nanomaterials (Figure 1.5) are the materials composed from two or more constituents with significant different chemical or physical properties. When combined together, produce a new material with different characteristics from the individual components. There are several reports available in literature to explore the usefulness of composite/ hybrid materials to tune the properties as well as to reduce the cost [Daniel et al., 1994; Nirala et al., 2015; Jones, 1998; Stankovich et al., 2006].

Currently, gold nanoparticles (AuNPs) decorated inorganic semiconductor composites have enhanced conductivity and catalytic activity for development of highly selective and sensitive sensors. In fact, these materials exhibit extensively better catalytic and electrochemical behaviours than nanomaterials alone, thus suggest the potential applications of nanocomposites in development of stable, low-cost and novel sensors. The inclusion of metal nanoparticles into transition metal dichalcogenides (TMDCs) e.g. Molybdenum disulphide (MoS_2), Tungsten disulfide (WS_2) resulted in the better catalytic activity, increased sensitivity and surface-enhanced Raman scattering (SERS), in sensing [Lin et al., 2014; Cao et al., 2017].

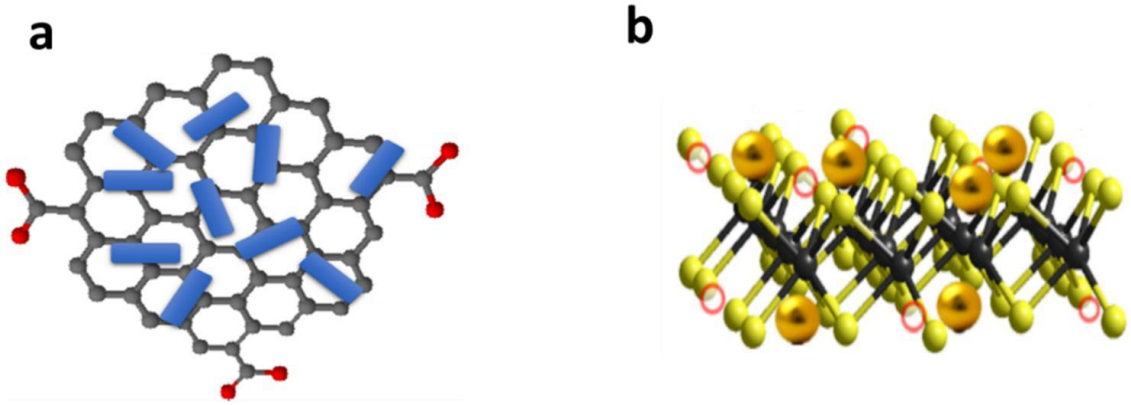

Figure 1.5 Schematic representation of the composite of (a) partially reduced graphene oxide- gold nanorods and (b) MoS_2-gold nanoparticles [Nirala et al., 2015].

1.5.1 Nanomaterials based sensors

The selectivity of a sensor mostly relies on the specificity of interaction between receptors and analytes. However, the sensitivity, stability, selectivity, response time and the detection limit of sensors strongly depends on the physicochemical properties of the transducer, which can be improved by the combination of nanomaterials as an interface between transducer and receptors. Metal nanostructures are ranging from noble to transition elements. Among metal nanostructures, noble metal nanostructures of well

tunable in their size and shape along with unique properties like extraordinarily catalytic activities and optical properties [Yan et al. 2010 ; Norouzi et al., 2011; Willner et al., 2011] have been extensively utilized in recent years, in various sensing applications. The uniqueness of optical, chemical and physical properties of the nanomaterials ascertain them very appropriate for developing new devices related to sensing. There are number of literature reported on nanomaterials based sensors.

Chen et al. developed electrochemical method for detection of hydrogen peroxide (H_2O_2) with palladium nanoparticles-graphene nanosheets (PdNPGNs) modified electrode. Ultrafine palladium nanoparticles were homogeneously modified on the graphene based glassy carbon electrode (GCE). The PdNPGNs-GCE voltammetry results, showed H_2O_2 reduction at low potential in linear response range (0.1 M to 1.0 mM) with 0.05 M detection limit (S/N = 3). The PdNPGNs-GCE system showed outstanding resistance toward poisoning from interfering species such as glucose, dopamine and ascorbic acid. Additionally, the electrochemical sensor existing excellent reproducibility and stability shows potential in practical analysis [Chen et al., 2013]. N. F. Atta et al. reported the electro-sensing of morphine based on gold nanoparticles modified graphite paste electrode (GPE) by DPV and CV techniques. Morphine is potent analgesic usually advised to patients suffering from pain. Electrochemical study of morphine showed an anodic peak response in buffer at pH 2 corresponding to oxidation of the tertiary amine into pseudo morphine as chief product. Electrodeposited gold nanoparticles modified electrode is used for study of oxidation behaviour of morphine. Due to the high electro catalytic effect and larger surface area of gold nanoparticles, the oxidation potential shifted towards the less positive potential region. Further the electrochemical sensing of morphine is performed at pH 7.4 by DPV in BR buffer and real sample (human urine and spiked) [Atta *el* al., 2011].

Li et al. developed sensitive and selective electrochemical sensor for glucose detection based on the anodized CuO nanowires (NW) with porous copper foam (CF). System showed excellent electro-catalytic activity and high sensitivity towards glucose detection due to high surface area of 3-dimensional porous copper foam. CuO-NWs/CF electrode shows good repeatability high selectivity, stability and reproducibility towards glucose detection. Proposed glucose sensor is also applied in human serum for practical applications and results obtained show good agreement with commercial available glucose sensor [Li *et al.* 2015].

Maleh et al. reported simultaneous electrochemical detection of three anti-cancerous drugs i.e. 6-thioguanine (6-TG) dasatinib (DA) and 6-mercaptopruine (6-MP) using modified electrode with Pt/MWCNTs and 1-butyl-3-methylimidazoleium hexafluorophosphate. Elevated concentration of these drugs in human blood serum causes many side effects. 6-TG and 6-MP are thiopurine anti-cancerous drugs advised for treatment of childhood acute lymphoblastic leukaemia [Kuśmierek *et al.* 2009]. DA is used for treatment of prostate cancer [Jesus *et al.* 2015]. Simultaneous detection of these drugs is important for the effective chemotherapy of cancer [Maleh *et al.* 2016].

Transition Metal Dichalcogenides (TMDCs) such as MoS_2, WS_2, $MoSe_2$, and WSe_2 show excellent catalytic, electronic, and optical behaviour. Lan et al. proposed a highly sensitive colorimetric sensor for assay of label-free DNA based on ultrathin transition-metal dichalcogenide nanosheet. Hybridization chain reaction is introduced for enhanced detection sensitivity. This label−free sensor exhibited excellent selectivity as well as low limit of detection [Lan et al, 2019].

Recently, ongoing works have been devoted for development of highly sensitive sensors for detection of hazardous molecules. In the view of human health and environmental protection, a lot of efforts have been proposed to rapid detection of pollutants using

nanomaterials. Several efforts have been performed to design the portable sensors for measuring pollutants like heavy metals in the environment. Inclusion of nanostructures and nanomaterials into the sensors leads to considerable enhancement in the performance of designed devices in the terms of selectivity, sensitivity, multiplexed detection capability and portability. Li et al., proposed nanostructure based sensors for the analysis of heavy metals and highlights strategies of the designed sensors and benefits of nanomaterials [Li et al.,2013]. Karimi et al. constructed simple, sensitive, selective, cost effective and rapid colorimetric sensor for the assay of Hg^{2+} ions based on Ag@AgCl nanomaterials. The limit of detection is 4.19 nM which is quite low, defined by Environmental Protection Agency of U.S. for the drinkable water. Additionally, selectivity test against various heavy metals at high concentration was demonstrated [Karimi et al, 2019].

1.5.2 Nanomaterials as Catalyst

Metal nanomaterials exhibit excellent catalytic properties and are different from their bulk counterparts since the catalytic property originates due to their quantum-size dimensions. Enzyme-mimetic nanomaterials are exposed as ultimate and significant tools for the detection of various analytes owing to their high stability, controllable structure, low cost, tunable catalytic activity and easy preparation, [Wei and Wang, 2008;]. First discovered nanomaterial, Fe_3O_4 magnetic nanoparticle (MNPs) exhibits surprising enzyme like catalytic activity [Gao et al., 2007]. Zero dimension nanomaterials such as AuNPs [Long et al., 2011], cerium oxide [Asati et al., 2009], $ZnFe_2O_4$ MNPs [Su et al., 2012], carbon nanodots [Shi et al., 2011], one dimension nanomaterials such as carbon nanotube [Song et al., 2010b],V_2O_5 nanowires [André et al., 2011], two dimensions (2D) nanomaterials such as graphene oxide [Song et al.,

2010a], have been explored as peroxidase mimics in catalyzing H_2O_2 -mediated color reaction and further used in the bioassays and medical diagnostic.

Ivanova et al developed Pt-decorated Boron Nitride Nanosheets as artificial nanozymes for the detection of dopamine. These Nanocomposites possess peroxidase like catalytic activity and accelerates oxidation of peroxidase substrate 3,3',5,5'-tetramethylbenzidine (TMB) in presence of hydrogen peroxide (H_2O_2). Oxidation of TMB gives an efficient platform for colorimetric detection of essential biomolecules i.e. dopamine. The increased amounts of the dopamine slowly inhibit catalytic activity of nanocomposites for the oxidation of TMB by H_2O_2. Present study contributes to knowledge of nanomaterials with excellent enzyme like catalytic activity for dopamine sensing [Ivanova et al, 2019].

Introduction of metal nanomaterials into the electrochemical sensors decreases over potential of different analytically important reactions. Nanomaterials can also alter the irreversibility of several chemical reactions which are irreversible at surface of unmodified electrode. Osaka and coworkers proposed a highly sensitive and selective electrochemical sensor used for selective detection of dopamine in presence of ascorbic acid based on catalytic activity of the gold nanoparticles falling over-potential of ascorbic acid [Raj *et al.,* 2003]. Nigra et al used calixarene capped gold nanoparticles for catalysis of the 4-nitrophenol reduction to 4-aminophenol (Figure 1.6) [Nigra. et al., 2013].

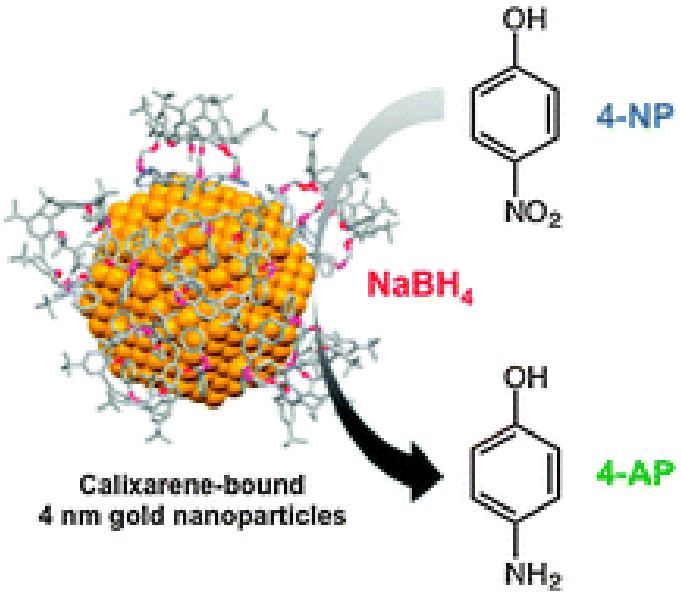

Figure 1.6 Calixarene capped gold nanoparticles act as catalyst for the 4-nitrophenol reduction to 4-aminophenol [Nigra. et al., 2013].

Kamali et al. reported excellent catalytic activity of low-temperature synthesized copper oxide nanosheets (CuO-NSs) for colorimetric sensing. CuO-NSs act as catalyst in degradation process of methylene blue dye in presence of sodium borohydride ($NaBH_4$). CuO-NSs were introduced to propose a cost-effective, highly selective, simple and fast optical sensor for the assay of Fe^{2+}/Fe^{3+} ions [Kamali et al., 2019].

1.6 The role of coordination polymers for catalysis and sensing

The area of coordination polymers has been emerging and extremely fashioned in scientific domain of material science. Coordination polymers (CPs) deals with the organic–inorganic hybrid materials, in which metal ions or clusters are linked by organic ligands *via* coordination bonds into indefinite crystal structures. The CPs shows an attractive polyfunctionality, stability, adjustability and often has tunable porous structures with very large specific surface area. Robson, Hoskins and co-workers sketched an assembly based approach to engineer the coordination polymers; they described crystal structures of coordination polymers in terms of networks and

employed it to develop new coordination polymers with fascinating topology and interesting properties that may be advantageous in several applications of catalysis and sensing [Wells, 1977, 1979, 1984].

Hybrid inorganic and organic materials; metal organic frameworks and coordination polymers have received much attention in the recent years. These metal organic frameworks deal with the repeating unit of the organic ligand attached to a metal in an infinite array and the functioning of these materials can be controlled with the choice of their individual components [Robin et al., 2004; Fromm et al., 2005]. Recently the metal–ligand coordination bond has found versatile applications in the molecular organization of various supra-molecular architectures, introducing the strength and specific directionality to the coordination bonds affiliated with metals. Metal complexes or ions and their bridging organic ligands assembled throughout the materials with various dimensionalities (1D–, 2D–, and 3D–) are referred as metal–organic frameworks (MOFs) or coordination polymers (CPs). Outline of the synthesis, applications and properties of MOFs is shown in Figure 1.7 [Muhammad Bilal et al., 2018].

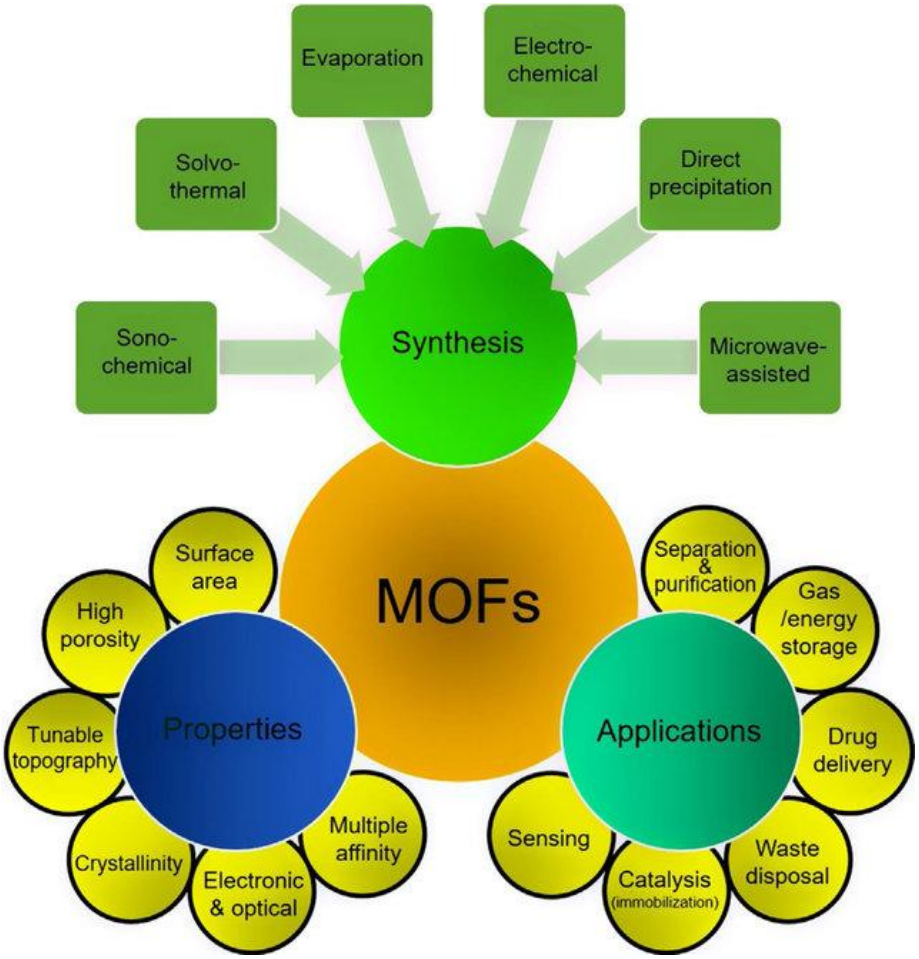

Figure 1.7 A schematic overview of MOFs synthesis, applications and properties [Muhammad Bilal et al, 2018].

1.6.1 Coordination polymer based sensors

Nano coordination polymers can be functionalized to bind selectively the specific moiety due to their larger surface area and porous structure, and thus can be used as effective sensors [Li et al., 2008; Hu et al., 2012; Yang et al., 2012; Zhang et al., 2011]. Qiu et al. have shown that $[Zn_3(BTC)_2 \cdot 12H_2O]$ nano–sized crystals exhibit high selectivity for ethylamine detection in acetonitrile solution, while $[Tb(BTC)(H_2O)_6]$ nanowires display strong luminescence emissions at 492 nm and 548 nm, and show high selectivity towards aromatic amines sensing, e.g. *p*–phenylenediamine and aniline [Qiu et al., 2008]. Zhang's group reported the luminescence property of nanostructured CPs $[Tb(BTC)(H_2O)_6]$, when dispersed in water and leading to a suspension that retain

its intrinsic stability in an aqueous medium for highly sensitive and selective sensing of metal ions in acetone and aqueous solution (Figure 1.8) [Yang et al., 2012].

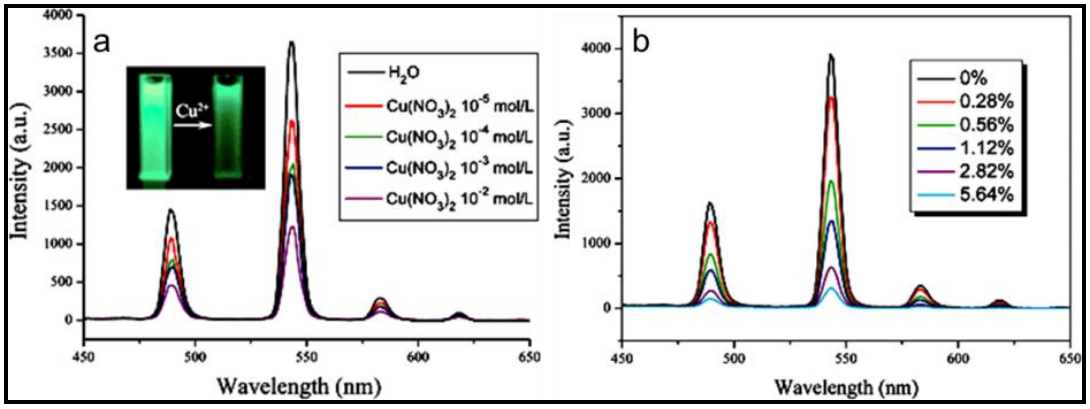

Figure 1.8 (a) Luminescence spectra of $Tb(BTC)(H_2O)_6$ in $Cu(NO_3)_2$ in aqueous solution at various concentrations (excition wavelength 300 nm). (b) Emission spectra of $Tb(BTC)(H_2O)_6$ in aqueous suspension in presence of different acetone contents (excitation wavelength 300 nm) [Yang et al., 2012].

Mursel Arici reported Zn(II) coordination polymer as a luminescent sensor for assay of 2,4-dinitrophenol (DNP), aluminium(III) and iron(III) ions. Designed luminescent coordination polymers based on tricarboxylic acid exhibit 2D layers and 3D supramolecular structures with H- bonding showing blue emission. Developed sensor is highly sensitive and selective towards detection of 2,4-dinitrophenol in the presence of other nitro compounds with low detection limit. Zn(II) coordination polymer was proficient to selectively detect Al^{3+} and Fe^{3+} ions over other interfering metal ions. [Mursel Arici, 2019]. Li at el. developed lanthanide coordination polymer-based sensor for the detection of Hg^{2+} ion by applying the inner filter effect. Designed coordination polymer contains europium ions as a metal center and isophthalic acid as bridging ligands that can sensitize the fluorescence of Eu^{3+} [Li at el., 2016]. Feng et al. outlines the recent progress and developments in the area of organometallic polymers based electrochemical chemosensors/biosensors. In these materials the metal centers provide function and allow materials to use in the electrochemical sensing based on different

transduction mechanisms. Due to intrinsic redox and affinity of metal, these types of polymers have been working in a range of electrochemical sensors by measuring the variation in current, resistance or redox potential of sensing system [Feng et al., 2015]

Tunsrichon et al. developed High-Performance Luminescent Sensor based on Zn(II) coordination polymer with 5-(3-pyridyl)-1,3,4-oxadiazole-2-thiol (Hpzt), used for the detection of 2,4,6-Trinitrophenol. It is highly selective and sensitive for sensing of 2,4,6-trinitrophenol through quenching process under UV light [Tunsrichon et al, 2019].

Fu et al. reported development of metalorganic coordination polymers (MOCPs) for efficient matrixes to immobilize enzymes for the amperometric sensing of phenols or glucose. Two metallic salts, Na_2PtCl_6 and $NaAuCl_4$, ligand, 2,5-dimercapto-1,3,4-thiadiazole (DMcT), and enzymes, tyrosinase and glucose oxidase (GOx) are used to display novel concept. After using MOCPs materials, mass-transfer efficiency and enzyme activity of sensor improved with high adsorption or encapsulation capability due to inimitable porous structure. The obtained limit of detection for catechol sensing is very low 0.2 nM (Figure 1.9) [Fu et al., 2011].

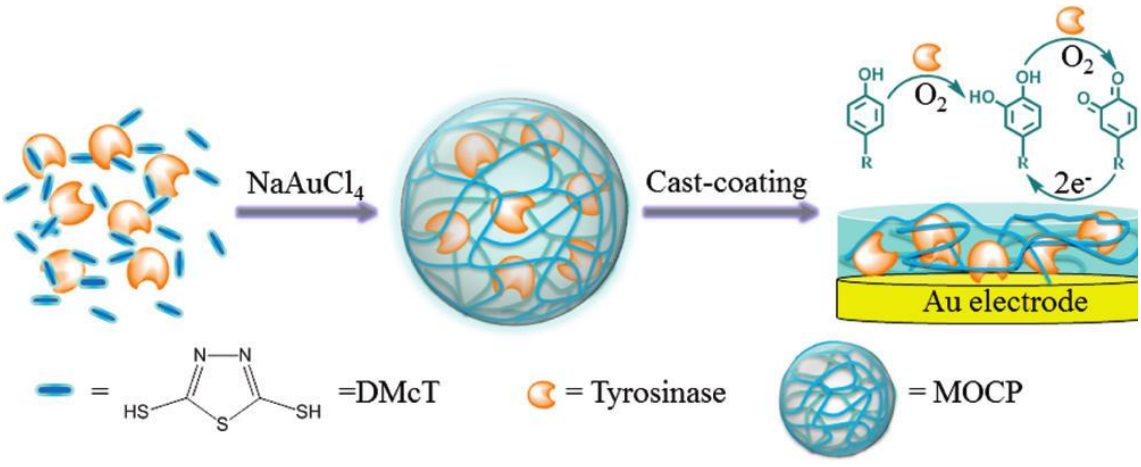

Figure 1.9 Biosensing mechanism and design of the MOCPs enzyme biocomposites (MEBCs)-based biosensor (e.g. MEBC) [Fu et al., 2011].

Song et al. reported synthesis of coordination polymer of chemical formula $[Cu_4Br(CN)(mtz)_2]_n$ (mtz = 5-methyl tetrazole). The fluorescence properties of this coordination polymer were executed in solid state and in different solvent emulsions. The results explain that the coordination polymer is very sensitive towards colorimetric sensor for NB and 2-NT (NB = nitrobenzene and 2-NT = 2-nitrotoluene) [Song et al., 2016]. Cheng et al reported, electrochemical and colorimetric sensors for thrombin assay, based on platinum nanoparticles (Pt NP) modified with metal-organic framework (MOF) (type Fe-MIL-88) and acts as a peroxidase mimic [Cheng et al, 2019].

1.6.2 Coordination polymer as Catalyst

Coordination polymers can act as efficient catalysts since they are porous in nature and have active metal centers; also they can be engineered to provide specific organic ligands and metal centers. Interestingly, several non–porous CPs also act as promising catalysts. NCPs are potential materials in heterogeneous catalysis mainly for "metal nanoparticles deposition into their pores" due to the chemical tunability, high surface area and porosity [Jiang and Xu, 2011; Meilikhov et al., 2010]. Several pioneering studies are reported for metal nano particles/bimetallic alloy nanoparticles placed at coordination framework in heterogeneous catalysis [Lu et al., 2012; Kuo et al., 2012]. Qiu and co-workers developed Au/MIL–100 (Fe) porous and core shell nano–catalyst through step wise method and demonstrated its catalytic properties. The improved catalytic activity of the nano–catalyst Au/MIL–100(Fe) rather than Au nanoparticles is due to the synergistic effect [Ke et al., 2013]. Additionally, coordination polymers are the potential candidate for heterogeneous catalysis in their solid form; since the major drawback in the liquid state heterogeneous catalysis is their short range stability. The catalytic cycle should progress without degradation or dissolution so that the ligand wouldn't react with the metal centers and vice–versa; that's why there are a few reports

in the literature for effective catalysis with these materials. Aoyama et al. have reported CPs formed by anthracenebisresorcinol (H_4L) and $Ti(O^iPr)_2Cl_2$, $Al(CH_3)_3$, $La(O^iPr)_3$ or $Zr(O^tBu)_4$, that exhibit effective catalysis [Dewa et al., 2001; Sawaki and Aoyama, 1999].

Now a days, a number of coordination polymers are developed that are suitable in asymmetric heterogeneous catalysis [Dai, 2004]. The specific purpose to choose these materials is to allow the pores with chiral environment to regulate the enantio–selectivity and the metal ions as a catalytic center. For instance, Sasai et al. have developed chiral motifs assembled through 1,1'-2,2'-binaphtol based chiral ligand (Figure 1.10) and Ti(II), Al(III) ions. They are extremely insoluble in commonly used organic solvents. The motif, $\{[Ti_2(\mu\text{–}O)_2(binol)]\}_n$ catalyses the asymmetric carbonyl–ene reaction (Figure 1.11) and the product of the reaction was related to the classical homogeneous catalysis.

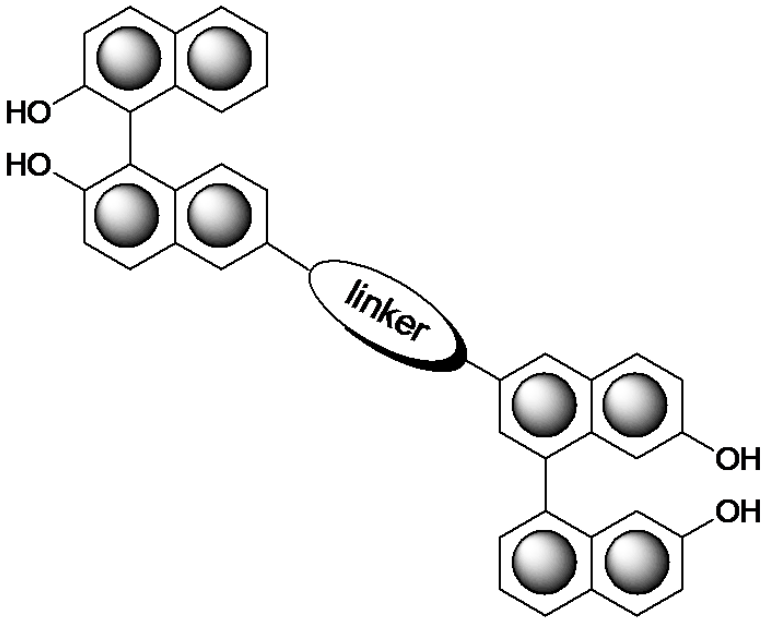

Figure 1.10 Structure of 1,1'-2,2'-binaphtol based ligand.

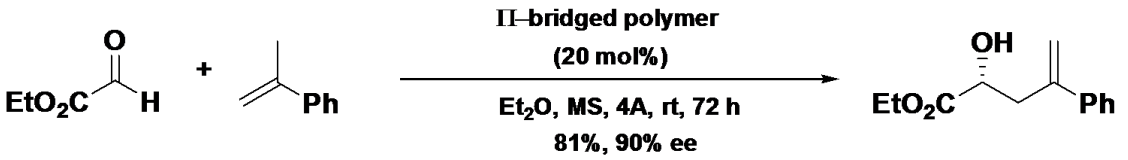

Figure 1.11 Catalytic activity of $\{[Ti_2(\mu\text{-}O)_2(binol)]\}_n$ in asymmetric carbonyl–ene reaction.

Inorganic–organic hybrid materials have been explored as a peroxidase mimics in catalyzing H_2O_2 -mediated color reaction and used in bioassays and medical diagnostic. Ai et al. explained the catalytic activity of MIL-53(Fe) complex in the presence of H_2O_2 color reaction and further utilized in bioassays [Ai et al., (2013)]. Luo et al. synthesized new metal−organic frameworks based solid catalysts, encapsulating with Hemin into MOF materials. These functionalized MOFs show an excellent catalytic activity and utilized as solid mimic peroxidases. Further the designed materials applied to develop sensors for the detection of H_2O_2 and glucose with low limits detection in broad response ranges [Luo et al.; 2015].

1.7 Nanomaterials and coordination polymers used as artificial enzyme: a substitute of natural enzymes

Enzyme mimetic possesses various advantages over the natural enzymes such as simple preparation, low cost, greater stability against denaturing and has been utilized in colorimetric assay and therapeutic diagnostics. Natural enzymes such as horse radish peroxidase (HRP) is an attractive biocatalyst mediating most of the biological activities in the living organisms, and is proficient to increase rate of the chemical reactions up to thousands times for definite substrates. There is large attention in using enzymes for applications in pharmaceutical processes, sensor, agrochemical production and food

industry [Wulff et al., 2002; Pang et al., 2009]. Though, the realistic applications of natural enzymes is often troubled by their intrinsic limitations, such as high costs, low operational stability, purification, sensitivity of the catalytic activity towards environmental conditions [Ellis et al., 2009].

Therefore, the development of artificial enzymes is highly needed [Wei et al., 2008]. Recently, emergence of nanotechnology with the biology has ignited broad research interests for developing functional nanomaterials and metal organic frameworks that expose exciting intrinsic catalytic properties to enzymes mimetic. The artificial enzymes or catalytically active nanomaterials show numerous advantages over the natural enzymes, like controlled synthesis, high stability against harsh conditions, tunability in catalytic activities, low cost etc [Gao et al., 2007; Wei et al., 2008]. These nanomaterial based artificial enzyme mimetic could catalyze the oxidation of a peroxidase substrate 3,3',5,5' tetramethylbenzidine (TMB), an important colorimetric agent in presence of H_2O_2 to the oxidized colored product (Figure 1.12). Recently, graphene and its derivatives have been proved as interesting materials with strong peroxidase mimetic activities [Song et al., 2010].

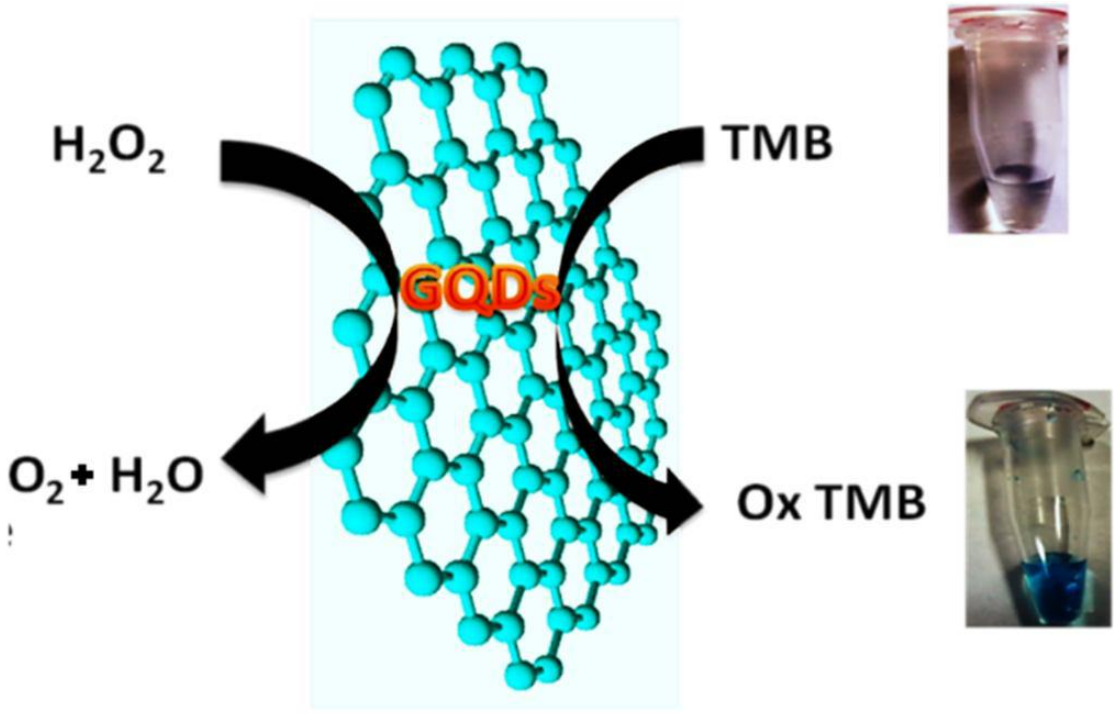

Figure 1.12 Schematic illustration of oxidation reaction of TMB in the presence of H_2O_2 catalyzed by GQDs.

Numerous investigations have proved the catalytic activity of metal nanomaterials as potential candidates for enzyme mimetic [He et al., 2011]. Among the metal nanoparticles, gold nanoparticles with either negative or positive surface charges remarkably show peroxidase mimetic activity. Wang and co-workers have explored the origin of peroxidase-like catalytic activity in gold nanoparticles [Wang et al., 2012]. Carbon nanomaterials, such as carbon nanotubes (CNTs), fullerene, graphene and their derivatives are performing great potential in different applications [Gao et al., 2014]. They have also gained significant attention as nanozymes owing to their capability to mimic activity of the natural enzymes [Liu et al., 2012 Song et al., 2010]. Scientists have proposed a colorimetric assay for the glucose detection by using GO–COOH exhibited peroxidase-like catalytic activity in presence of peroxidase substrate (TMB) and glucose oxidase.

Numerous work on electro- and photoelectro-catalytic activity proved that transition metal dichalcogenides could be a promising candidate in the catalysis of hydrogen evolution reactions, [Jaramillo et al., 2007] and biosensing [Wang et al., 2013]. Enzyme-mimetic inorganic nanomaterials such as MoS_2 and WS_2 have emerged as an ideal and significant tools for the colorimetric assay owing to their easy preparation, high stability, controllable composition and structure, as well as tunable catalytic activity [Sun et al., 2013].

Metal organic frameworks have explored (MOFs) excellent prospect in construction of novel nanozymes. Zhang et al reported method for cancer therapy and sensing based on the metal-organic frameworks based nanozymes. Further, 2D MOFs contain higher catalytic activities owing to their larger active sites and ultra large specific surface area for the substrates [Zhang, 2015; Wu, 2017].

1.8 Immobilization of biomolecules on nanomaterials

One of ceaseless challenges is immobilization scheme used to conjugate strongly the bio-specific units on such nanomaterials. Thus, the method applied to immobilize enzyme is key factor in designing a reliable sensor [Holzinger et al, 2014]. There are various methods *viz.* adsorption, entrapment and covalent used for immobilization of biomolecules described in Figure 1.13 and Table 1.1.

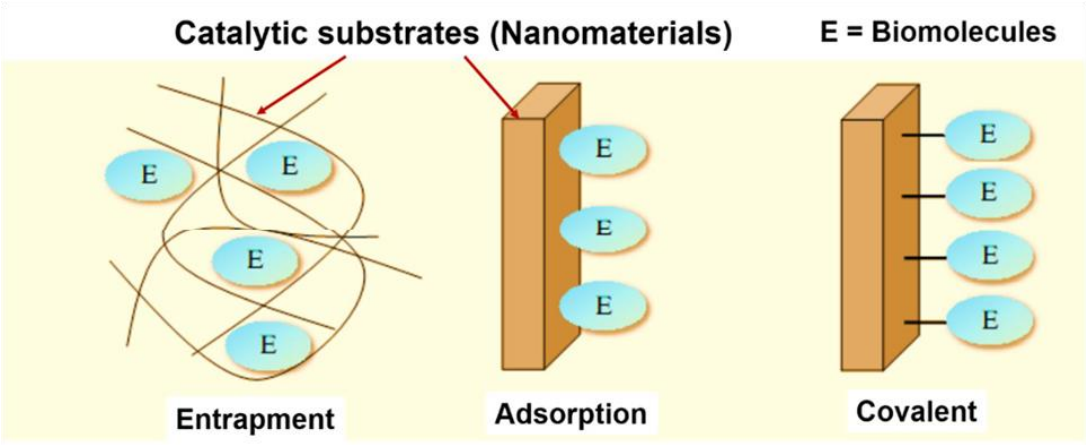

Figure 1.13 Schematic representations of immobilization methods.

Table 1.1 Various immobilization methods

	Type of Immobilization	Type of Interaction
1.	Adsorption	Electrostatic Hydrophobic interactions Vander Waals forces
2.	Entrapment	Entrapment
3.	Covalent	Covalent Coupling
4.	Affinity based	Affinity bonds between a functional group on a support and affinity tag on a protein sequence

In adsorption method, biomolecules (e.g. enzymes and antibodies) adsorbs onto solid surface represents easiest technique of physical immobilization [Choi, 2004]. The adsorption immobilization is based on weak interactions such as electrostatic, hydrophobic interactions or Van der Waal's forces. This method does not require any functionalization and is commonly non-destructive for the enzyme activity. The direct adsorption of proteins on polystyrene microtiter wells to use in enzyme linked immunosorbent assays (ELISA) has develop into a common immobilization method

owing to its low cost and simplicity. In entrapment method, generally a solution of polymeric materials is prepared containing biologic material that will be entrapped onto the working electrode. Covalent coupling of the enzymes with polymeric supports is common immobilization technique used for designing enzymatic sensors. In this process, catalysts are bound to the surface through their functional groups but they are not necessary for catalytic activity [Sassolas et al., 2012].

Table 1.2 Importance of immobilization methods

Immobilization methods	Advantages
Adsorption	▪ Simple and easy ▪ Limited loss of enzyme activity
Covalent Coupling	▪ No diffusion barrier ▪ Stable ▪ Short response time
Entrapment	▪ No chemical reaction between the monomer and enzyme that could affect activity ▪ Several types of enzymes can be immobilized within the same polymer
Affinity	▪ Controlled and oriented immobilization

Binding of the enzymes in to solid support is usually performed by initial activation of surface by multifunctional reagents (e.g. carbodiimide or glutaraldehyde), followed by the enzyme coupling to activated support, subsequently removal of unbound excess biomolecules [Choi, 2004; Fernandez et al., 2011]. Biomolecules can also be immobilized with nanomaterials by covalence, adsorption and entrapment to design a sensitive sensor. Nanomaterials have fascinating immobilization surfaces with large surface area [Luo et al., 2006]. Furthermore, direct adsorption of the enzymes on the bulk metal surfaces often results in the denaturation of proteins and loss of activity which can be improved if enzymes are primary adsorbed on metal nanomaterials prior to being electrodeposited on to the surface of electrode [Peng et al., 2005].

1.9 Motivation and Objective of the thesis

Recent investigations have indicated the future promises of Transition Metal Dichalcogenides (TMDCs) e.g. MoS_2-QDs, WS_2-QDs and their composites; nanoparticles and nano coordination polymers for the development of efficient sensors. However, bio-mimic catalysts and sensing using artificial enzymes are less explored and reported in the literature for development of stable and low cost sensors. Colorimetric detection based on nanomaterials is showing potential for screening large number of samples. Fast and low cost sensors for toxic chemicals and biologically important analytes are in great demand.

Considering these facts and futuristic applications of nanomaterials and coordination polymers in bio-mimic and sensors, the major objective of the thesis is:

- To synthesize metal nanomaterials, nanocomposites and nanocoordination polymers for simple and low cost biomimic catalysts and sensors and their characterization by using various techniques.
- To explore the outstanding physical, chemical and catalytic properties of nanomaterials and nano-coordination polymers for catalysis and sensing of biomolecules (glucose, choline), hazardous analytes (picric acid) and drug (6-mercaptopurine) and developing portable sensing kits for early and accurate detection of different analytes of interest.

Further, thesis is focused on following sub-objectives as given below:

- Facile synthesis of gold nanoparticles (AuNPs) decorated over MoS_2 quantum dots (AuNPs@MoS_2-QDs) composite as a robust peroxidase- mimetic detection of glucose in serum, saliva and tear and further development of portable kit.

- Facile synthesis of nanoporous palladium (II) bridged coordination polymer for peroxidase mimic for visual detection of glucose in tear and saliva and further development of portable kit.
- Facile and sensitive colorimetric assay of Choline based on gold nanoparticles (AuNPs) decorated over WS_2 quantum dots (AuNps@WS_2-QDs) composite as a peroxidase mimetic further development of portable kit.
- Simple and low cost colorimetric detection of picric acid using silver nanoparticles modified with 4-amino-3-hydrazino-5-mercapto-1,2,4-triazole.
- Simple and low cost sensors for effective and broad spectrum detection of 6-mercaptopurine in urine and blood serum based on nano network of coordination polymer AHMT-Ag.

1.10 Benefits of the proposed materials for catalysis and sensing applications

In this study, we made the surprising discovery of nanomaterials and coordination polymer that they possess intrinsic peroxidase-like activity. We have explored the typical properties of nanomaterials such as metal nanoparticles, transitions metal dichalcogenides, their composites and nanocordination polymers in present work for the development of sensor prototype (Table 1.3).

Table 1.3 Typical properties of nanomaterials and coordination polymers used in sensing and catalysis pathway.

	AuNPs@MoS_2-QDs	AuNPs@WS_2-QDs	Ag@AHMT NPs	AHMT-Pd NPCP	AHMT-Ag NCCP
High Surface Area	✓	✓	✓	✓	✓
Nano size	✓	✓	✓	✓	✓
Highly Catalytic	✓	✓	✓	✓	✓
Conducting	✓	✓	✓	✓	✓
Stability	✓	✓	✓	✓	✓
Biocompatible	✓	✓	✓	✓	✓
Sensitive	✓	✓	✓	✓	✓
Highly Functionalized	✓	✓	✓	✓	✓

Over the last decade, the incorporation of marvellous properties of nanomaterials has witnessed an enormous impact on sensing field. Nanomaterials and nanocoordination polymers have shown fabulous physicochemical properties such as biocompatibility, high surface area, outstanding electrochemical conductivity and catalytic activity etc. and these make them a suitable candidate for development of efficient sensor.

Synthesized materials (AuNPs@MoS_2-QDs, AuNPs@WS_2-QDs, AHMT-Pd nanoporous coordination polymer) show excellent catalytic activity and mimic the enzyme which is suitable for the detection of different biomolecules (glucose, choline) by colorimetric method. These nanomaterials are stable in harsh conditions such as high or low pH and temperature so we can design a portable test kit for detection of the level of particular biomolecules present in body fluids like blood serum, saliva and tear. Here,

the method was also used to detect glucose in non-invasive samples (tear, saliva). Nanomaterials (AHMT capped silver nanoparticles) are used for detection of hazardous molecules like picric acid by colorimetric method. Due to the high conductivity, AHMT-Ag coordination polymer is used for the detection of anticancer drug 6-mercaptopurine.