Chapter 1

Introduction & Literature Survey

1.1 General Introduction

A sensor is a device that detects a change in the environment or a change on account of the interaction of the analyte and thereby converts it into an observable output signal. Generally, a sensor produces the output in the form of an electrical or optical signal. In our day-to-day life, we are surrounded by different types of sensors in several applications like television remotes, LDR sensors for the street lighting system, automatic door opening systems, and so on. These sensors help to lead our lives with easiness. They find a large number of significant applications in several fields such as home appliances, automobiles, weather monitoring, pollution monitoring, different alarms, robotics, medical diagnostics, pharmaceuticals, medicine, chemistry, synthesis, molecular engineering, materials engineering, biotechnology, etc. The sensors are fascinating to track down the various bio-components in the body through small-sized biological samples during medical analysis. They are employed to monitor the onsite pollution and guide us to achieve the environmental requirements. The probability of automation and construction of small sensors is highly beneficial to meet the scientific requirements [Simões and Xavier, 2017].

The sensors can be broadly classified into physical, chemical and biosensors. A physical sensor quantifies the physical quantity and no chemical reaction takes place in this case. Common examples include those based on the measurement of temperature, absorbance, pressure, conductivity, refractive index, or mass change. A chemical sensor identifies any chemical reaction with the involvement of the analyte yielding the analytical signal. A biosensor has biological receptor moieties participating in a biochemical process and acts as the source of the analytical response, for instance,

microbial immunosensors or potentiometric sensors. There are three components of a sensor – a receptor, a transducer and a signal processing unit [Chen et al., 2019]. The receptor is the active recognition part and it is the heart of a sensor that comes into physical contact with the analyte. Upon interaction with the analyte, it transfers the information to the transducers. There can be various types of probable binding or interaction between the analyte and the receptor depending upon the sensor such as chelating interaction via coordination bond, steric recognition (antigen-antibody interaction), enzyme-substrate binding, etc. The transducer intakes the information of the interaction between the receptor and analyte and convert it into a corresponding measurable form such as voltage, current, resistance, colour, etc. Finally, the signal processing unit helps to produce a readable output [Putzbach and Ronkainen, 2013].

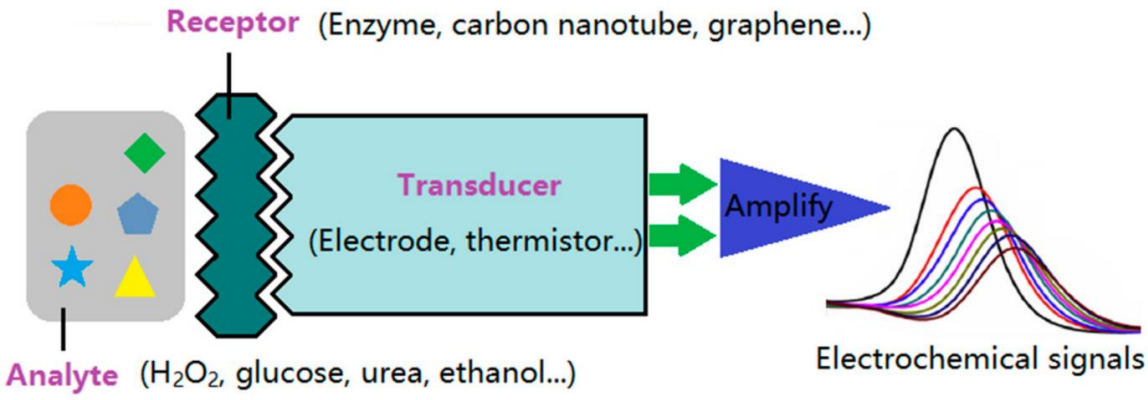

Figure 1.1 Schematic illustration of a sensor with its various components [Chen et al., 2019].

1.2 Classification based on Transducers

1.2.1 Optical sensors: These sensors pertain to the changes of optical phenomena arising out of an interaction between analyte and receptor. The optical properties that are commonly recorded through optical transducers include absorbance, luminescence,

reflectance, fluorescence, refractive index, scattering of light, optothermal effect, and surface plasmon resonance [Hulanicki et al., 2009].

1.2.2 Mass sensitive sensors: These sensors convert the change of mass observed at a specifically modified surface into the variation in certain measurable properties of the involved material. The variation in mass is mainly observed as a result of the accumulation of the analyte. For example, a piezoelectric device measures the variation in the frequency of a quartz oscillator plate which occurs due to the adsorption of the analyte at the oscillator.

1.2.3 Electrochemical sensors: Electrochemistry has delivered a fascinating and strong analytical tool for research in a wide variety of sectors like medicine, water, wastewater, environment, food, health, safety and quality of human life [Maduraiveeran et al., 2018]. Electrochemistry signifies the charge transfer between a solid/ liquid phase and an electrode. When there is no convection or there is an undisturbed environment, the transfer of charge may occur due to the existence of an electric field (referred to as migration current) or due to the concentration gradient of an electroactive species/analyte (referred to as diffusion current). Mass transport mostly occurs through the migration current in the bulk solution and mainly leads to electrical conductivity [Scozzari, 2008]. Electrochemical sensing technology is an essential part of modern analytical chemistry and has grabbed significant attention from researchers. Electrochemical sensors constitute a very large category of chemical sensors employing electrochemical methods which are among the oldest measurement techniques. In these sensors, the chemical informations such as concentration and properties of the analyte are obtained by a change in output signal in the form of current, voltage, resistance, etc.

Most of the electrochemical sensing applications employ a two-electrode or a three-electrode cell assembly.

In a two-electrode system (Figure 1.2), a Working Electrode (WE) is combined with a Reference Electrode (RE) which is non-polarizable and the electrical potential difference is measured between the WE and the constant potential of the RE. Two electrodes are separated by the electrolyte and connected to the electrochemical analyzer. A three-electrode assembly (Figure 1.2) comprises a WE, a RE and a large auxiliary or counter electrode (AE). The AE possesses a small charge-transfer resistance so that the ohmic potential drop (due to current flow) can be overcome. This setup functions well with solutions possessing poor electrical conductivity. The three electrodes are separated by a thin layer of electrolyte and connected to the electrochemical analyzer [Rathee et al., 2016]. The selection of the electrolyte is based on the nature of the analyte. The electrochemical sensors help to furnish a good selectivity and sensitivity, and a low limit of detection with portability, and low cost. That's why they are very much preferred over other types of sensing techniques.

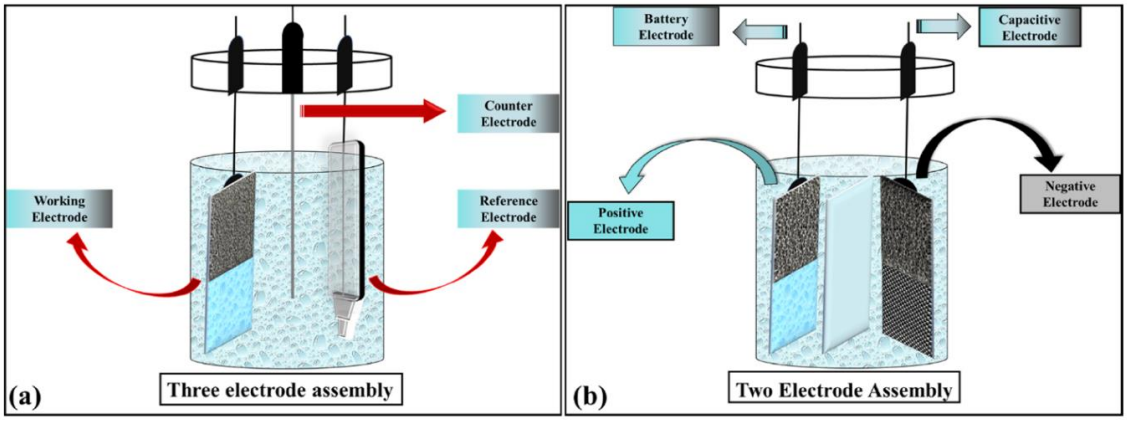

Figure 1.2 Pictorial representation of a) a three-electrode system and b) a two-electrode system [Iqbal and Aziz, 2022]

Based on the transducer, the electrochemical sensors can be further categorized as follows [Banica, 2012]:

1.2.3.1 Potentiometric sensors: They are also referred to as potentiometric ion sensors. Here, the ion under investigation is estimated on the basis of potentiometric transduction. A membrane is a primary sensing element that has ion-selective receptor sites or molecular receptors. This membrane is positioned in between the two solutions, one of them is the sample under investigation and the other is the analyte (ions) solution with known concentration. When ion exchange occurs across the membrane, a potential difference is created between these two sections. This potential difference may be easily determined through measurement and directly related to the concentration of analyte in the sample. These sensors are sometimes termed ion-selective electrodes. They are widely used in gas sensing applications for gases such as CO_2, HCN, NH_3 and HF. They are also applied as enzymatic sensors since many enzymatic reactions involve ions (e.g. H^+ or NH_4^+) or produce gases that can be detected such as CO_2 or NH_3.

1.2.3.2 Amperometric Sensors: These sensors rely on the measurement of electric current produced in the electrochemical cell when an appropriate fixed voltage is applied. If a reducible species (analyte) is present in the sample, the cell potential enhances and the resulting diffusion current varies directly with the analyte concentration [Worsfold et al., 2019]. This method helps to selectively distinguish among several electroactive species present in a test solution by judicious selection of the applied potential. In comparison to the potentiometric sensors, these sensors are rapid, sensitive, and precise, with a linear response but they suffer the limitation of interferences and poor selectivity [Alaejos and Montelongo, 2004]. Figure 1.3 displays the example of an amperometric setup for sensing dissolved chlorine.

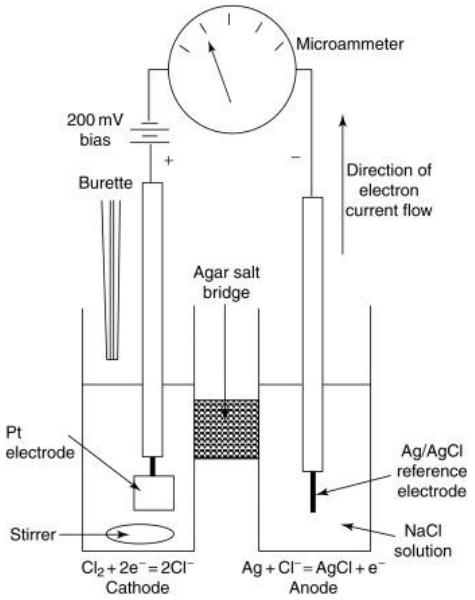

Figure 1.3 Amperometric titration apparatus for the determination of dissolved chlorine [Worsfold et al., 2019]

1.2.3.3 Conductometric sensors: Conductometric sensors involve the assessment of change in the electrical conductance of a solution due to the presence of an analyte since the electrical conductance is affected by the variation in analyte conductivity and electrochemical reactions. Sometimes the sensor directly measures the conductivity of the analyte. A sharp distinction between amperometric and conductometric sensors is unable to be defined many a time.

1.2.3.4 Impedimetric sensors: The measurement of electrochemical impedance is the basis of impedimetric sensors and it implies the extent of obstruction to the AC current flow through an electrochemical cell. These evaluations deliver a series of details of the physicochemical processes occurring inside the electrolytic environment under study like the migration of ions, charge distribution at the electrode / electrolyte interface, and kinetics of the electrochemical reaction(s). All these processes may be correlated to the characteristics of the sensing element combined with the electrochemical setup. Specifically, an AC voltage is applied to the system and the variation in electrochemical

impedance at the electrode / electrolyte interface is measured. For exploring the metabolic processes occurring in a biological system, both conductometric and impedimetric sensors are usually employed [Banica, 2012].

1.2.3.5 Voltammetric sensors

Voltammetry is a possible method for characterizing solutions through a non-conventional chemometric concept. It is an important electroanalytical tool employing the three-electrode system for determining the electrochemical behaviour of a system and extracting information about single or multiple analytes through current measurement as a function of applied potential. So, the potentials between the WE and RE are varied and the corresponding pattern of change in current is examined. Depending upon the decomposition potential, mass transfer limits and diffusion coefficient showed by different electroactive species present in the test solution, a complex signal is obtained which is called a Voltammogram. Different kinds of experiments may be executed to garner the details of the system and based on the waveform of the excitation input applied to the test solution, various kinds of voltammetry can be categorized. Some of the common techniques are cyclic voltammetry (CV), linear sweep voltammetry (LSV), stripping voltammetry, etc. Further, another voltammetric technique is prevalent in a series of potential rectangular steps having distinct amplitudes applied to obtain a detailed signature of the electrochemical system. Square wave voltammetry (SWV) and differential pulse voltammetry (DPV) belong to such pulsed techniques. So, there can be a broad range of feasible implementations of measurement routes of voltammetry according to the desired electrochemical experimentation [Kimmel et al., 2012; Scozzari, 2008]. Figure 1.4 depicts an electrochemical cell commonly employed for voltammetric experiments.

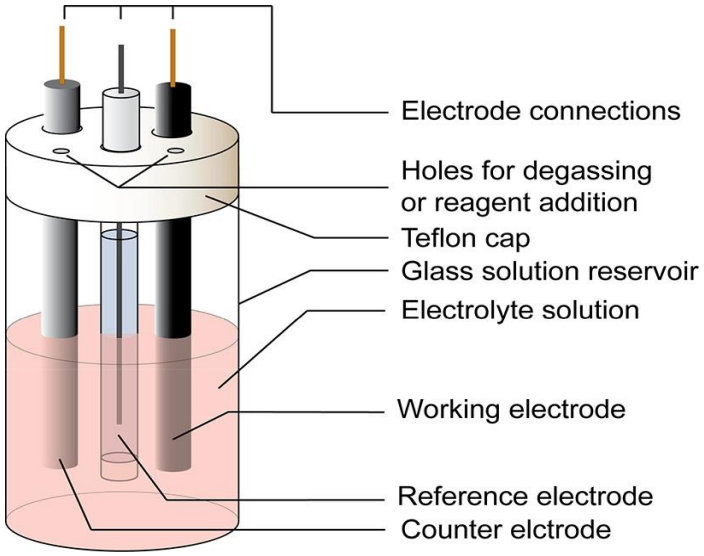

Figure: 1.4 Schematic representation of an electrochemical cell for voltammetric experiments [Elgrishi et al., 2018]

1.2.4 Electrical sensors: Here, the signal is observed due to the change of electrical properties which is caused as a result of the interaction between the receptor moiety and analyte. No electrochemical process is observed in this case.

1.2.5 Magnetic sensors: These sensors rely on an increase or decrease in the paramagnetic properties of the analyte under investigation.

1.2.6 Thermometric sensors: Thermometric sensors measure the heat changes associated with a particular chemical reaction or adsorption process involving the analyte. For example, a catalytic sensor exhibits the measurement of heat in an enzymatic reaction or a combustion reaction through a thermistor.

1.3 Classification based on receptors/recognition layer

Sensors can also be categorized into various classes depending on the type of receptors and the nature of the interaction involved. A series of recognition processes is observed which follows the reaction scheme:

$$\mathbf{A + R \rightleftharpoons P} \qquad \text{(Eq. 1.1)}$$

where A represents the analyte/sample, R refers to the receptor or recognition element and P represents the product of the interaction between the analyte and receptor.

This process of recognition is reversible in nature and the reversibility is indicative of noncovalent interactions in the product P, for instance, hydrogen bonds, electrostatic, and weak van der Waals forces.

The equilibrium constant is written as:

$$\mathbf{K_a = C_P / (C_A \times C_R)} \qquad \text{(Eq. 1.2)}$$

where C represents the concentration of various species depicted by the subscript. The equilibrium constant K_a signifies the chemical affinity of the sensing element to the analyte. So, the higher the value of K_a, the stronger the affinity and interaction between the two components. Such a recognition process is highly selective. In other words, it relies on the interaction of the recognition layer with the analyte only, not with any other interfering species [Banica, 2012]. There can be various types of recognition processes which are described below:

1.3.1 Ion Recognition: These are the first kind of chemical sensors that emerged extensively. The pH glass electrodes pioneered the development of ion sensors and were based upon the innovative efforts of Z. Klemensiewicz and F. Haber in 1908. Electric charge is the basic principle behind ion recognition in this case. Hence, such reagents and materials are generally used for ion recognition which possess the opposite electric charge than that of the analyte. Selectivity in case of ion recognition is achieved with the help of other properties of recognition material such as the dimension of the ion receptor, the partial covalent nature of the receptor-analyte bond, etc.

1.3.2 Recognition by Affinity Interactions: This technique makes use of the non-covalent interactions between the analyte and the receptor such as ion-ion interactions, hydrogen bonding, and weak van der Waals attraction forces. Such interactions result in the production of a molecular association complex in which the engaged chemical species must be complementary to each other in terms of their shape, size, and reactivity. The strength of this complex is designated by its stability constant value and such complexes can be very much stable. The affinity interaction can be observed most commonly in a biological system. For example, lectin proteins recognize carbohydrates by forming the association complex. Antibody–antigen interaction is another example of affinity interaction. Antibodies are the glycoproteins that the immune system of the organisms produces for identifying and neutralizing pathogenic microorganisms like viruses and bacteria. An antigen is a part of a pathogen which interacts with a specific antibody. This interaction between antibody and antigen is an immunochemical reaction. This reaction forms the basis of various clinical investigations and diagnoses. Specific antibodies are used as recognition receptors to identify pathogens.

1.3.3 Recognition through Enzymes: The proteinaceous compounds that serve as catalysts in the biological systems are termed enzymes. They are selective to a substrate (target compound) or a group of substrates. In contrast to other chemical sensors, the process of enzyme recognition involves three basic steps. The first step is the binding of a substrate with the active site present in the enzyme to yield an enzyme-substrate complex. Then, this complex is followed by a chemical transformation to yield an enzyme-product complex. Finally, the product is released followed by the replenishment of the enzyme's active site which becomes ready for the next sequence with other molecules. Many enzymes which are capable of retaining their catalytic activity after isolation are used as recognition agents in the chemical sensor. The

enzymatic sensor can be utilized for the qualitative as well as quantitative estimation of the substrate, detection of inhibitors, etc. It can also be employed as transduction labels in sensors centered on affinity recognition.

1.3.4 Recognition by Nucleic Acids: Nucleic acids (DNA and RNA) in living organisms are responsible for the storage as well as transmission of genetic information. They are composed of nucleobases grafted polymeric backbone. DNA composition is comprised of four nucleobases, namely adenine (A), guanine (G), cytosine (C), and thymine (T). RNA contains uracil (U) in place of thymine. Significantly, the hydrogen bonds are present in between two definite nucleobase pairs, i.e. A-T and G-C in DNA (A-U in RNA). As a result, two complementary chains of nucleic acids wound around each other to create a double-stranded association complex during hybridization. Nucleic acid hybridization is the basic principle behind nucleic acid sensors and serves as the recognition process. A short DNA/RNA strand plays the role of a receptor for recognizing a particular sequence of nucleobases within the nucleic acid under investigation (analyte) through hybridization. This technique is utilized in clinical diagnosis, for example, the identification of the pathogen, genetic abnormalities, etc. Moreover, this technique is also employed in forensic science.

1.3.5 Recognition by Cells and Tissues: Enzymes were isolated initially before being used in chemical sensing. But it was realized that enzymes present in cells and tissues can function better because of being in their natural environment. So, recognition through biological cells and tissues has become an important tool in chemical sensing. They may respond to any chemical stimuli by altering their metabolic pathway. Such alteration results in the utilization of oxygen or elimination of any other chemical entity which is further exploited for sensing.

1.3.6 Sorption of Vapour and Gas: Detection of vapours and gases is very much practically applicable in air quality monitoring, and emission management of hazardous gases/vapours in environmental and industrial investigations. Adsorption and absorption of gases and vapours in a solid material are utilized as basic principles for sensing. Keeping in mind the type of analyte species, different materials are utilized in sensing and recognition such as polymeric materials, inorganic materials, certain metals, etc.

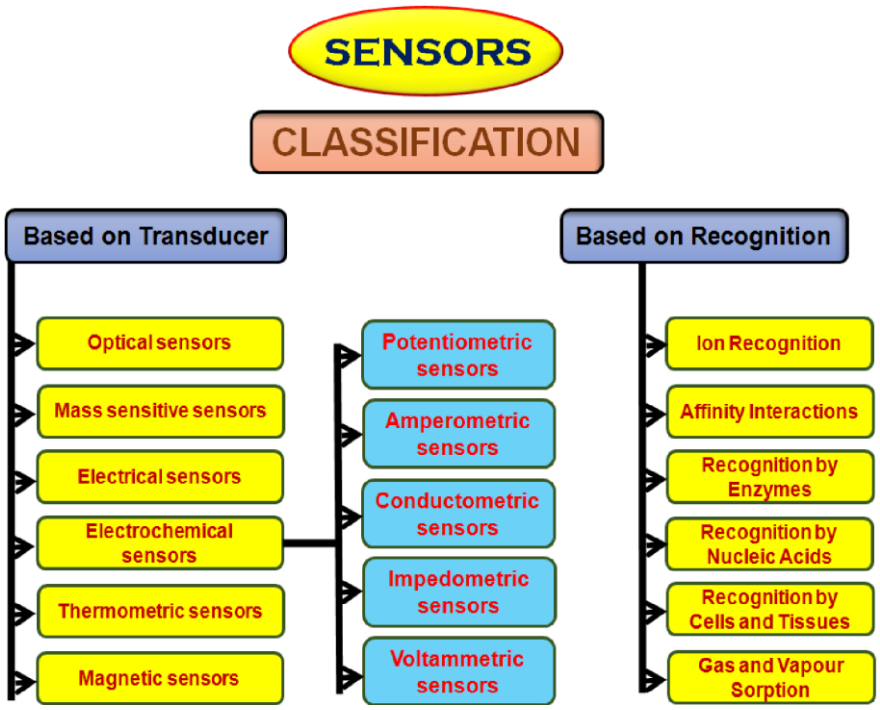

Figure 1.5 Classifications of Sensors

1.4 Parameters of a sensor

Various static and dynamic parameters are used for the characterization of a good sensor [Gründler, 2007]. These important parameters are described as follows:

1.4.1 Sensitivity: It can be defined as the extent of variation in the measurement/ output per unit change in the analyte concentration. It is calculated as the slope of the calibration curve.

1.4.2 Limit of Detection (LoD): It is the minimum concentration value of the analyte that can be determined under defined conditions. Generally, the LoD is determined when the fixed value signal-to-noise ratio is 3. Mathematically, it is equal to three times the standard deviation of a blank, in the absence of the analyte. The procedure for LoD evaluation depends on the type of sensor under consideration.

1.4.3 Accuracy and Precision: Accuracy is the extent of the proximity of a measured value to the actual value of a property. Precision shows how reproducible a particular measurement is. For a sensor to be accurate as well as precise, the measurement value must be around the average value and the different measurement values are very much close to each other.

1.4.4 Linearity and Linear Range: Linearity of a sensor is the relative deviation of a calibration curve (derived from an experiment) from perfectly straight line. Generally, the linearity values are stipulated for a defined concentration range of the analyte and, this range in which the linear response of the sensor is observed, is termed as Linear Range.

1.4.5 Dynamic Range: It is defined as the minimum to maximum measurable linear range of the output signal. Over this dynamic range, it can show the deviation from the sensing behaviour or in other words, it shows how the sensor response varies at various operating points. The dynamic range can also be defined as the concentration range from the limit of detection to the uppermost limiting concentration.

1.4.6 Selectivity: Selectivity refers to the indication of whether a sensor selectively responds to a specific analyte or a group of analytes present in the test solution. An ideal

sensor selectively shows interaction with only the analyte(s) under investigation without being affected by the effect of interfering species.

1.4.7 Resolution: Resolution of a sensor refers to the minimum concentration change that can be distinguished in terms of the output signal when the concentration is varied continuously.

1.4.8 Response time: It refers to the time consumed to produce the output signal when there is one step change in the concentration of the analyte. More specifically, it is the time consumed for the chemical interaction between the analyte and receptor, and the conversion of this interaction into the output signal by the transducer.

1.4.9 Stability: It refers to the ability of a sensor to keep its performance unchanged for a definite period of time. For measuring the stability, drift values are utilized such as variation in output signal for zero concentration.

1.4.10 Life cycle: Life cycle of a sensor is the time period over which the sensor actively operates or exhibits good sensing behaviour. The shelf life (maximum time of storage) of a sensor must be discriminated from the maximum operating life.

1.5 Advantages of electrochemical sensors

Electrochemical sensors offer various advantages over other conventional analytics that's why they are very much preferred in the present scenario. They have a fascinating technology because of the following merits they provide:

i. They are highly sensitive and selective towards the electroactive analytes, very specific to the analyte under investigation.

ii. They are very stable and provide reproducible results.

iii. They offer a very low detection limit for the analyte. These sensors can help to achieve the estimation of even the picomolar concentration of the analyte.

iv. They furnish very quick responses in comparison to other types of sensors. They are less time-consuming, flexible, and offer portability at low cost.

v. They offer a wide linear dynamic range in comparison to other techniques and help to obtain the qualitative and quantitative estimation of analyte in real samples also.

vi. These sensors are lightweight and transferrable tools, easy to operate, and compact.

Due to these reasons, electrochemical sensors are the first choice of researchers for the development of portable sensing devices [Simões and Xavier, 2017].

1.6 Convenient techniques employed for modification of electrode

The glassy carbon electrode (GCE) is a widely used working electrode in various electrochemical experiments since it is favourable in electrochemical applications and offers a large number of advantages [Abdel-Aziz et al., 2022]. GCE is generally exploited for electro-sensing applications because of its remarkable properties such as

- Provides a very homogeneous surface that can also be used repeatedly by polishing with alumina powder.
- Magnificent electrical conductivity
- Material in GCE is predominantly carbon
- An excellent chemical stability
- Reproducibility
- Absence of any redox peak within the selected potential windows in different experiments.
- Electrochemical inertness over a very broad potential window (about -0.1 to 0.1 V with respect to saturated calomel electrode)
- Low cost

- High hardness
- Impermeability

Prior to the electrochemical studies and applications, the electrode materials (or nanomaterials) with attractive properties are used to modify the electrode surface. Controlled or electrode modification in the desired manner can help to design electrodes with expected characteristics which can serve the purpose of numerous novel applications in electrochemistry [Adarakatti and Kempahanumakkagari, 2018]. There are various methods available for electrode modifications which are described below:

1.6.1 Dip Coating: In this technique, the bare electrode surface under investigation is dipped or immersed into the suspension of electroactive nanomaterial with required functionalities for an adequate period. As a result, a spontaneous film of the nanomaterial is adsorbed over the electrode surface. Then, the electrode surface is washed with an appropriate solution with the desired pH to remove the impurities adsorbed over the electrode.

1.6.2 Solvent Evaporation: It is also known as Drop Casting. The suspension of the electroactive nanomaterial in an appropriate solvent is drop cast over the surface of the electrode under consideration and kept undisturbed till the solvent is completely evaporated. The thickness of the film over the electrode can be tuned by controlling the concentration of the suspension. It is the most widely used technique of electrode modification.

1.6.3 Spin Coating: It is also known as Spin Casting. It permits to deposit a uniform thin film over the surface of the electrode. In this technique, a dilute suspension/solution of the requisite nanomaterial is introduced at the center of the electrode surface/substrate which is then rotated at a suitable speed so that the nanomaterials spread constantly and the excess solvent gets spinned off from

the edge of the electrode. Then the electrode was allowed to dry. This technique offers the advantage of uniformly depositing the various layers of the material up to the desired thickness.

After modification, the modified electrode can be undergone various characterizations, spectroscopic analysis, and electrochemical measurements to obtain a series of details such as the thickness of the deposited film, the porosity of the film, its morphology, its conductivity, charge transfer process through the film, etc. [Chaki et al., 2002; Raj and Behera, 2007].

1.7 Nanomaterials

Nanoscience is the chemistry sub-discipline pertaining to unique and exciting domains, to hunt for novel approaches and applications, for creatively exploring the small world [Bashir and Liu, 2015]. Nanomaterials can be described as natural or artificial materials exhibiting at least one external dimension in the range of 1-100 nm. They have chemical and physical properties different from their bulk counterparts and the surface properties are dominant. Nanomaterials include a large number of nanostructures such as nanoparticles, nanotubes, nanosheets, nanofibers, nanorods, nanowires, nano polymers, fullerenes, dendrimers, nanocomposite, etc. as shown in Figure 1.6 [Poh et al., 2018]. The nanomaterials have attracted interest for employment in sensing applications because of their distinct and significant characteristic properties which are mentioned as follows:

a. They offer a large specific surface area or surface-to-volume ratio which is extremely desirable for the analyte species to absorb over the surface or as a substrate for electocatalytic reactions to occur.
b. They facilitate fast electron transfer kinetics.

c. They facilitate the easy functionalization of the recognition layer.
d. They provide a possibility to tune their size and morphology to obtain the desired properties.
e. They exhibit a long shelf life along with long operational life.
f. They provide the benefit of easy processing since they mostly solubilize in organic solvents or they get dispersed easily so that can be efficiently applied on the electrode surface during modification of the electrode.
g. They are biocompatible which is essential for biomedical applications.

So, overall they furnish improved physical, chemical, and biological properties which are exploited for application in a wide variety of fields. Depending upon the dimension and quantum confinement of electrons, nanomaterials can be classified into the following categories:

1.7.1 Zero dimensional (0D) nanomaterials

These materials have grabbed extensive research interest in recent times with respect to sensing applications. This category includes materials such as graphene quantum dots (GQDs), carbon quantum dots (CQDs), inorganic quantum dots, fullerenes, noble metal nanoparticles, magnetic nanoparticles (MNPs), etc. Due to the beneficial features of ultra-small size, quantum confinement, rich exposed edges, large surface-to-volume ratio, commendable chemical, and physical properties, and excellent biocompatibility, they have presented a significant potential in biomolecular recognition, disease diagnosis, ion detection, and pathogen sensing [Wang et al., 2020].

1.7.2 One dimensional (1D) nanomaterials

These materials exhibit two dimensions in the nanoscale and the electrons in these materials are confined in these two dimensions, suggesting that the electrons cannot freely move. Examples include nanotubes, nanorods, nanowires, nanobelts, nanofibres, nanofilaments, etc. The 1D nanomaterials can be crystalline or amorphous, monocrystalline or polycrystalline, and metallic, ceramic, or polymeric [Bashir and Liu, 2015]. These materials possess a high surface-to-volume ratio which leads to noticeable changes in their electrical conductance upon surface modification, which are beneficial for sensing applications. The most exploited 1D material is the carbon nanotube (CNT).

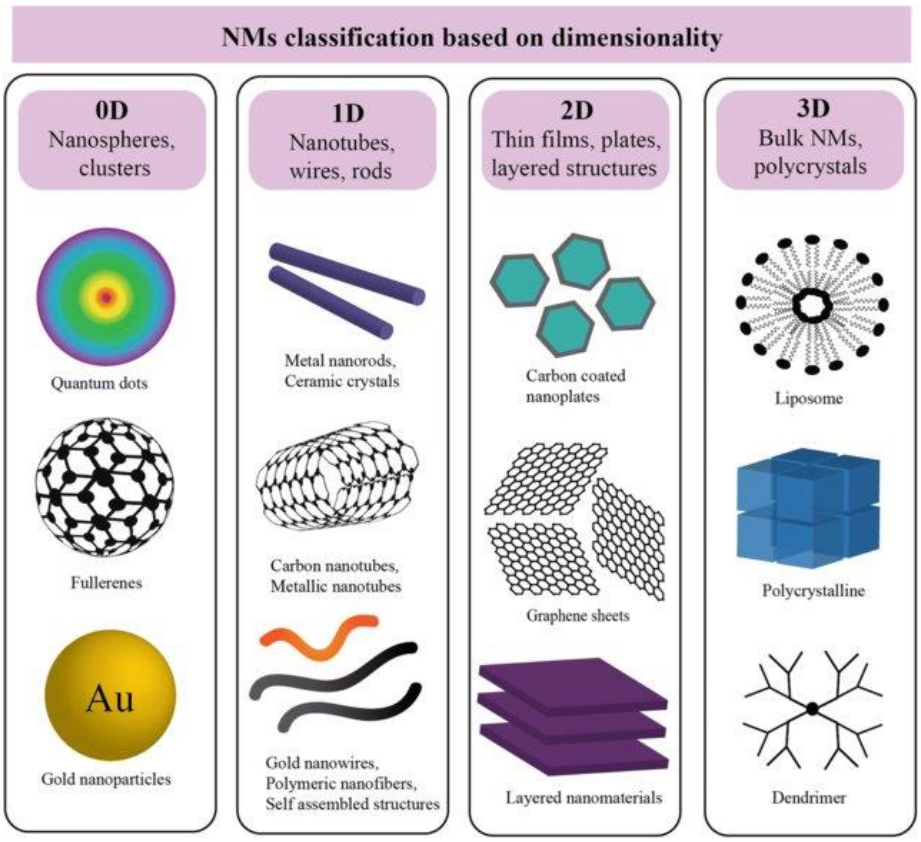

Figure 1.6 Schematic illustration of dimension-wise different categories of nanomaterials - zero (0D), one (1D), two (2D), and three dimensional (3D) with examples [Poh et al., 2018]

1.7.3 Two dimensional (2D) nanomaterials

2D nanomaterials are sheet-like structures with transverse dimensions >100 nm and width generally <5 nm. Due to their sheet-like morphology, they possess high surface area as well as anisotropic chemical and physical properties. These 2D layered materials have been a matter of extensive research in the recent decade that has been triggered and exemplified by the rapid growth of graphene materials [Hu et al., 2019; Pumera and Loo, 2014]. Figure 1.7 showcases a variety of functional 2D nanomaterials.

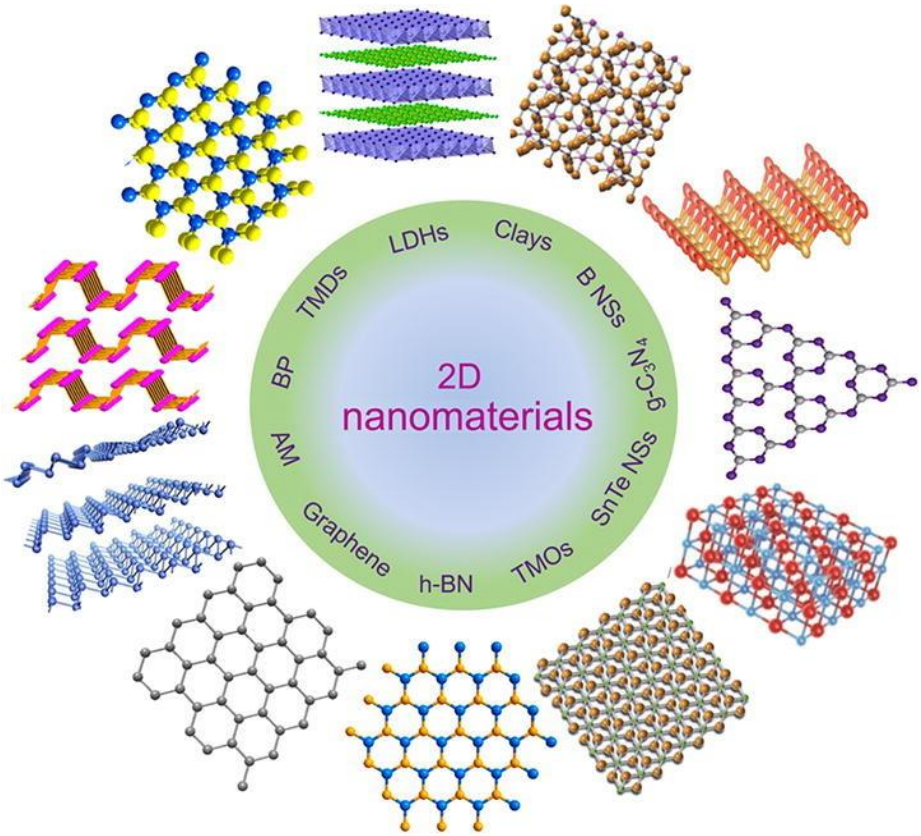

Figure 1.7 Schematic representations of 2D nanomaterials [Hu et al., 2019]

The first 2D nanomaterial was reported in 2004 by exfoliating graphene from graphite by Novoselov et al. [Novoselov et al., 2004]. Graphene is a one-atom-thick layered carbon crystalline film having sp^2 hybridized carbon atoms and it offers a large number of beneficial properties like large surface area, high electrical and thermal conductivity,

excessive mechanical strength, high stability, and rapid charge carrier mobility. There are majorly two derivatives of graphene namely graphene oxide (GO) and reduced graphene oxide (rGO). Regarding chemistry, GO and rGO carry enormous oxygen-containing functional groups such as carboxylic acid (COOH), epoxides (COC), and hydroxyls (OH) on their surface that create huge scope for further functionalization and modification of graphene and also allow them to get coupled to other chemical moieties [Aliyev et al., 2019].

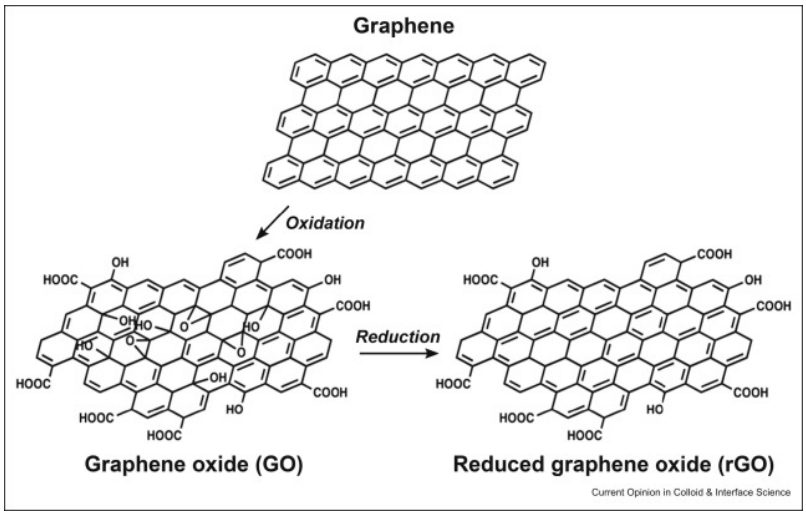

Figure 1.8 Structural representation of graphene, graphene oxide, and reduced graphene oxide [McCoy et al., 2019]

Due to the exceptional properties of graphene and its derivatives, they have been employed for application in the field of sensors, catalysis, electronics, optoelectronics, energy storage, etc. It is noteworthy that the graphene is just the tip of the iceberg in the class of 2D nanomaterials [Zhang et al., 2013]. The success with graphene triggered the interest in the exploration of other 2D nanomaterials and a large number of such ultrathin materials have been discovered, for instance, transition metal dichalcogenides (TMDs), transition metal oxides, black phosphorus, hexagonal boron nitride (h-BN), graphitic carbon nitride (g-C_3N_4), tin telluride nanosheets (SnTe NSs), etc. These 2D

nanostructures vary in their size, shape, thickness, composition, and crystal phases, which have been termed nanosheets, nanoflakes, nanoprisms, nanodisks, nanoribbons, nanoplates, nanobelts, nanorings, nanocones, nanowheels, and so on. These materials possess the highest specific surface area among other known materials, hence possess a large number of anchoring sites that help in loading the analyte or making composite with other nanomaterials. Therefore, these nanomaterials are employed in promising applications such as sensing, catalysis, bioimaging, solar cells, surface-enhanced Raman scattering (SERS), photothermal therapy, and so on [Chen et al., 2018]. TMDs possess interesting properties similar to that of graphene. TMDs are generally expressed as MX_2, where M designates transition metals like molybdenum (Mo), tungsten(W), titanium (Ti), zirconium (Zr), or hafnium (Hf), and X denotes chalcogen atoms like sulfur (S), selenium (Se) or tellurium (Te).

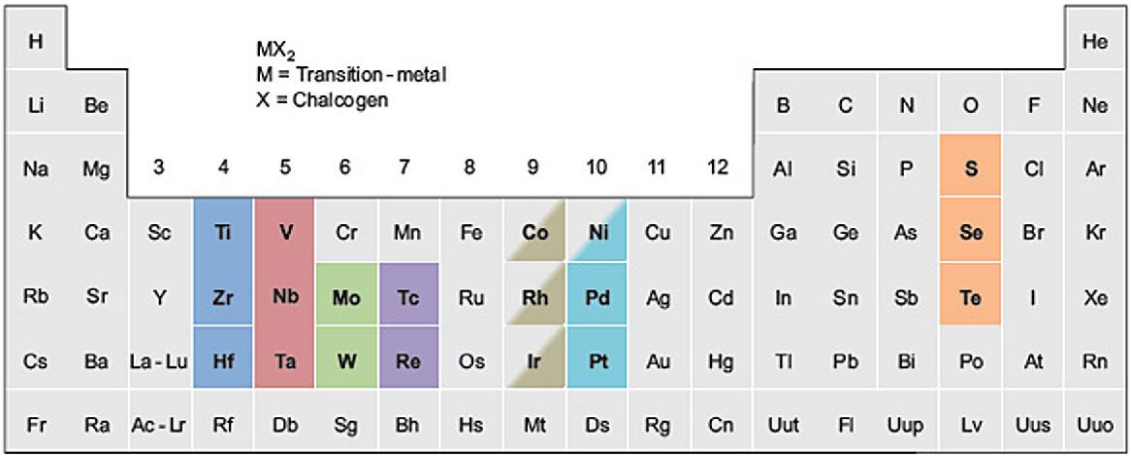

Figure 1.9 Representation of elements of the periodic table comprising TMDs [Zhao et al., 2020]

Around 40 various 2D TMD compounds exist. The transition metals along with the three chalcogens that primarily crystallize in 2D nanostructures are highlighted in Figure 1.9. Partial highlights of Ni, Co, Rh, and Ir specify that only a few of the dichalcogenide compounds attain a layered structure [Chhowalla et al., 2013]. The

structure of TMDs consists of building blocks of X-M-X layers coupled with each other with the help of weak van der Waals interactions (Figure 1.10). Each layer is built up of an intermediate plane of transition metal atoms sandwiched in between the two layers of chalcogen atoms with strong covalent bonds between M and X. The existence of weak van der Waals interaction between X-M-X layers makes it feasible to exfoliate the TMD crystal into individual layers that exhibit properties that are very much contrasting from the bulk material.

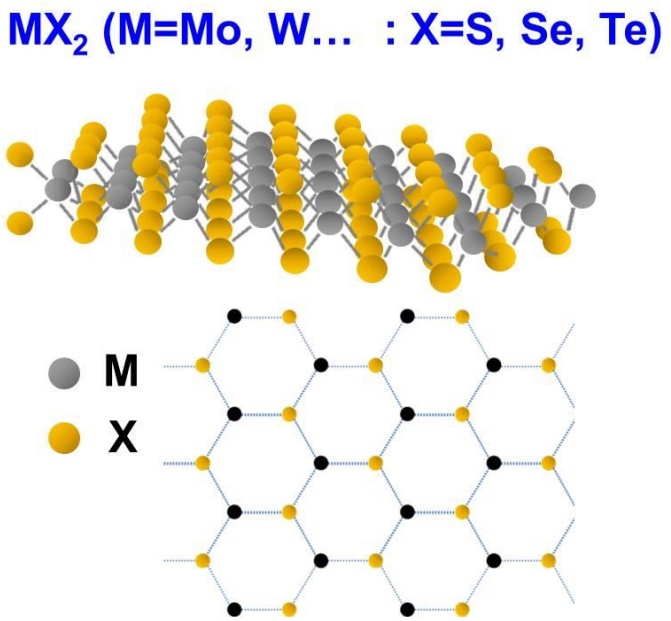

Figure 1.10 Schematic representation of sandwiched structure of 2D (TMDs) [Mouri et al., 2013]

2D TMDs offer a plethora of properties. Along with a large specific surface area, these layered materials also provide a tunable band-gap, that can be controlled by changing the orientations of M and X atoms or by varying the composition of the material, inside the TMD layer. These factors result in various possibilities including the possibility of variation in conductivity, thereby tuning electrochemical and fluorescence performances [Chhowalla et al., 2013]. Since these layered TMDs possess large specific surface area, rapid heterogeneous electron transfers, high electrical conductivity and fluorescence,

they have been employed for application in sensing, biosensing, energy production and storage, hydrogen evolution electrocatalysis, supercapacitors, and lithium-ion batteries.

1.7.4 Three dimensional (3D) nanomaterials

The 3D nanomaterials are comprised of interlinked network nanostructures, for example, graphene foam, carbon aerogel, CNT sponge, etc. They have grabbed significant interest due to their remarkable characteristics like large specific surface area, great electrical conductivity, highly porous structure, low apparent density, good stability, and environmental compatibility. With the help of their interconnected network structure and resulting physical properties, they find wide applications in the field of advanced sensors, energy storage, adsorption, catalysis, etc. In the case of other nanomaterials, the electrochemical performance is diminished because of the limited number of active sites and blocked ions, and mass transfer. In contrast, the 3D nanostructures have effectively solved these aforementioned shortcomings with the help of their large specific surface area as well as the short distance for ion and mass transfer. The research is continuously going on to develop high-quality 3D materials that have also been achieved on a large scale with the help of cost-effective and sustainable methods which are desired for practical applications [Wu et al., 2016; Yun et al., 2017].

1.8 Nanocomposites of 2D materials

Nanocomposites play a very pivotal and comprehensive role in fabricating sensing platforms. Nanocomposites are composite materials comprising two or more constituents having at least one of the dimensions of any of the constituents belonging to the nanosize scale (<100 nm). The individual components possess chemical and physical properties different from each other and they are combined to produce a new

material that possesses properties different and superior to the individual constituents. These materials are the combination of synergistic effects and unique properties of constituent nanostructure and exhibit their unique electrical, electronic, catalytic, and optical properties, hence they have been extensively exploited in electrochemical applications in the past decade [Hrapovic et al., 2004].

Table 1.1 Primary advantages and limitations of graphene and its derivatives [F. Catania et al., 2021]

	Advantages	**Disadvantages**
Graphene	❖ High thermal and electrical conductivities ❖ Great control over functionalization	❖ Hydrophobicity ❖ Expensive ❖ Difficult workability ❖ Small production
GO	❖ Water dispersibility ❖ Polar functionalization ❖ Low cost ❖ Easy workability	❖ Lower thermal and electrical conductivities ❖ Random functionalization on the surface ❖ Inferior control over post-synthesis functionalization

rGO	❖ High thermal and electrical conductivities ❖ Great control over functionalization ❖ Less expensive than neat graphene	❖ Hydrophobicity ❖ Difficult workability ❖ Properties related to the procedure followed for the synthesis

Graphene and its derivatives find various electrochemical applications as a result of their beneficial properties highlighted in Table 1.1. In contrast, there are various limitations also associated with these materials which restrict their applications up to a great extent in the electrochemical fields including sensors [Sajedi-Moghaddam et al., 2017]. Similarly, TMDs have extensively been employed in various electrochemical applications because of their superior electrochemical behaviour and large specific surface area. However, 2D TMDs suffer from the demerit of low conductivity which has imposed limitations on their application as electrode materials for electrochemical sensors. To conquer this limitation, such 2D carbonaceous and TMD-based materials are hybridized with other conducting materials, for instance, conductive polymers, conducting layered materials, noble metal nanoparticles, and such nanocomposites have been investigated and explored for trace-level detection of heavy metals, environmental pollutants, biological molecules, and therapeutic drugs.

1.8.1 Nanocomposites with Quantum Dots (QDs)

The layered TMDs possess a limited number of edge sites that behave as active sites during electrocatalytic applications due to the sheet structure, but the literature survey

suggests that the functionalization with the QDs has significantly introduced the basal active sites in the layers of TMDs, thereby remarkably enhancing the catalytic activity for electrochemical applications. Gopalakrishnan et al. designed a heterodimensional nanocomposite of molybdenum disulphide (MoS_2) QDs interspersed in few-layered MoS_2 nanosheets, through organic solvent-assisted liquid exfoliation for electrocatalytic applications. The synthesis methodology involves bath sonication accompanied by ultrasound probe sonication. The tailored heterodimensional nanostructured material exhibited highly concentrated active edges. As a result, the nanocomposite-based electrode when used in hydrogen evolution reaction (HER) delivered a remarkable electroactivity along with lower overpotential due to the synergistic effect of the two components [Gopalakrishnan et al., 2014].

Guo et al. reported the hydrothermal synthesis of MoS_2 nanosheets doped with GQDs and engineered the defects in the edge plane as well as the basal plane of nanosheets. The defect-rich nanostructure of GQDs-MoS_2 significantly enhanced both conductivity and intrinsic electrocatalytic activity of the material. The designed material with peculiar tailored nanostructure delivered a high-performance electroactivity in HER with low onset overpotential and good stability. The experimental results also expressed the possibility that the catalytic activity of the developed nanocomposite could be further enhanced by tailoring the composition, framework, configuration, and morphology [Guo et al., 2016].

Similar to TMDs, the nanocomposites of graphene and its analogs have been reported with improved electrochemical and functional properties. Hu et al. prepared a composite film of rGO and carbon dots (CDs) and exploited it for the electrochemical determination of dopamine (DA). The CDs possessed negatively charged carboxyl

groups which provided stability as well as facilitated the fruitful interaction with $–NH_2$ functional groups present in DA via electrostatic interaction to improve the specificity towards DA. Further, the interaction between rGO and DA was empowered through π-π interaction. The composite modified GCE (rGO-CDs/GCE) displayed a superior electrochemical response in comparison to bare GCE, GO/GCE, and CDs/GCE towards DA determination. The reported DA sensor was very sensitive, selective, and stable with a broad linear range of 0.01-450.0 μM and an exceptional LoD of 1.5 nM [Hu et al., 2014].

Dang et al. reported a material based on rGO anchored by CDs for supercapacitor application. The specific electrochemical capacitance of rGO was significantly enhanced by adding an optimum amount of CDs. The electrochemical results revealed that CD/rGO with a CD: rGO ratio of 5:1 exhibited rapid charge transfer kinetics, a good rate capability, excellent reversibility, and a superior specific capacitance that was 74.3% greater than that of rGO. So, the fabricated composite is an encouraging electroactive material with high-performance supercapacitor applications [Dang et al., 2016].

1.8.2 Nanocomposites with Conducting Polymers

Conducting polymers and their substituents have gained tremendous attention because of their exceptional electrical, electronic, optical, and optoelectronic characteristics, and they are a matter of great scientific and technological research. Conducting polymers containing Nitrogen as heteroatom have been a matter of extensive research and polyindole (PIn) is one of them and it has grabbed significance because of its non-toxicity and environmental stability. In addition, PIn is magnificent polymeric material since it combines the properties of polypyrrole (PPy) and polyphenylene. PIn and its

derivatives have been employed in a wide variety of applications such as sensing, electrocatalysis, electronics, and anticorrosion [Kumar and Prakash, 2014].

Conducting polymers such as polyaniline (PANI), PIn, etc. are widely employed to synthesize the nanocomposites with graphene with the aid of non-covalent interactions. Bai et al. non-covalently functionalized the graphene by sulfonated polyaniline (SPANI) to yield a nanocomposite with enhanced electroactivity as well as electrochemical stability along with excellent conductivity. The composite showed a significant potential for application in electrocatalysis [Bai et al., 2019].

Phasuksom et al. reported the preparation of graphene-based materials and PIn composites by in situ polymerization and exploited for the detection of methanol. The methanol response varied with the amount of oxygen present in the graphene-based substrate acting as active sites. All the prepared composites delivered a superior response for methanol determination with good sensitivity and reproducibility [Phasuksom et al., 2020].

Muduli et al. reported a nanopetal shaped composite of MoS_2 and (PPy) through the hydrothermal method and utilized as anode material coupled with a cathode PbO_2 for the application in ultracapacitors based on the lead-carbon hybrid. The ultracapacitive characteristics of MoS_2–PPy exhibited a great enhancement in power density and capacitance as a result of the synergistic combination of the redox property of MoS_2 and the good conducting behaviour of the conjugated polymer network. In addition, the efficient H^+ ion intercalation into the framework of the material by the transportation of electrons along with facile doping/de-doping of sulfate ions into the PPy network played a crucial role in highly effective capacitive performance [Muduli et al., 2021].

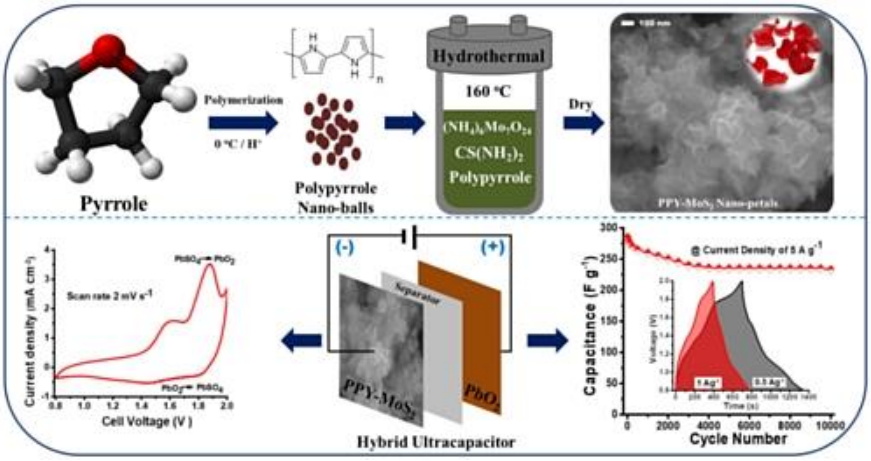

Figure 1.11 Schematic representation of the work of Muduli et al., 2021

1.8.3 Nanocomposites with Noble Metal Nanostructures

Noble metal nanomaterials form an important class of nanostructured materials and these materials hybridize the beneficial properties of noble metals with that of nanomaterials to yield enhanced performance of the materials which thereby increase the scope of nanomaterials in a wide variety of applications. The noble metal nanostructures possess a large number of advantageous features such as superior electrocatalytic activity, large specific surface area, excellent conductivity, rapid electron transfer kinetics, ability to tune the size and morphology, and biocompatibility [Pan et al., 2020]. To date, a huge number of noble metal nanostructures with various morphologies (balls, flowers, rods, cages, sheets, etc.) have been designed to fulfill the requisite demands in the research [Mitragotri et al., 2015; Chimene et al., 2015]. These nanostructures provide a broad scope of applications in the field of energy storage, information storage, new energy materials, functional catalysis, optics, photoelectronics, etc. because of their peculiar catalytic, electrical, and optical properties. Further, the flexibility of tuning the size, structure, and morphology make them an encouraging material for sensing application [Du et al., 2018; Aldewachi et al., 2018].

Zhou et al. reported a facile one-step synthesis of silver nanoparticles (Ag NPs) over the surface of GO and rGO without using any reducing agent or surfactant with an easy tuning of the size of Ag NPs. The designed material might find applications in catalysis, sensing, etc. [Zhou et al., 2009]. Xu and co-workers employed GO sheets as a substrate to develop Ag NPs film which was extremely flexible and capable of producing a stable aqueous suspension. The performance enhancement was tunable with the varying amounts of Ag NPs on the GO surface [Xu and Wang, 2009].

Dubey et al. modified the rGO sheets by PIn and incorporated the Ag NPs to yield Ag NPs/PIn-rGO nanocomposite and the performance was compared with Ag NPs/rGO and PIn/GO composites. The nanocomposite electrode material possessed superior processibility and electroactivity in comparison to Ag NPs/rGO and PIn/GO because of the synergistic effects of the individual constituents. The charge capacitive behaviour of the proposed material was examined and the results indicated its significant potential for applications in the field of charge storage devices, electrocatalysis, etc. [Dubey et al., 2015].

The functionalization of layered TMD surface with noble metal nanostructures have grabbed importance in recent literature since they have been developed as an effective engineering technique to improve the catalytic and electrosensing properties of the pristine 2D TMDs. The resulting nanocomposite displays more efficient electrochemical performance as compared to the individual components due to its nanostructural arrangement, morphology, and synergism.

Dolinska et al. reported a nanocomposite of gold nanoparticles (Au NPs)/MoS_2 nanopetals which was quite stable due to electrostatic interaction between the positively charged Au NPs and the negatively charged surface of MoS_2 nanopetals. The Au NPs

embedded nanosheets possessed a superior electrical conductivity and electrocatalytic activity towards glutathione, cysteine, and glucose due to the synergistic effect of the two constituents which was expressed by the shift in the oxidation potential along with larger current densities. The experimental results indicated that the developed material exhibited significant potential for application in sensing and energy conversion [Dolinska et al., 2015].

Sakhuja and co-workers functionalized the liquid-exfoliated WSe_2 nanosheets with Au NPs and platinum nanoparticles (Pt NPs) through a chemical synthesis route and exploited them for NO_2 detection at room temperature. The electrochemical results revealed that the sensing performance towards NO_2 was enhanced in manifolds in comparison to WSe_2 nanosheets at room temperature (RT) due to the decoration of nanoparticles over it. The composite formation victoriously tackled the limitation of recovery in the case of layered material-based NO_2 sensors. The functionalized NO_2 sensor was found to be extremely efficient, sensitive, selective, stable, reproducible, and very reliable to be exploited for real-time NO_2 determination [Sakhuja et al., 2022].

1.9 2D Nanomaterials and their nanocomposites in Drug sensing applications

The nanomaterials and their nanocomposites have a pivotal role in drug sensing applications. The introduction of nanotechnologies assisted in miniaturization, improving the efficiency and reliability of sensor devices. The nanocomposites of TMDs with noble metal nanostructures have garnered adequate attention in recent years since they have proved their potential to remarkably improve the conductivity and electrocatalytic properties of TMDs to be utilized for electrochemical sensing applications [Huang et al., 2014].

Chao et al. designed a nanocomposite of layered MoS_2 decorated with Pt NPs (PtNPs@MoS_2) via a microwave-assisted eco-friendly hydrothermal route which was further applied for the voltammetric sensing of uric acid (UA) and DA. As a result of the synergistic effect of Pt NPs and MoS_2 nanosheet, the nanocomposite-modified GCE expressed a superior electrocatalytic activity for oxidation of UA and DA, and also yielded two well-resolved anodic peaks (peak separation of 160 mV) of the analytes. Hence, the proposed sensor proved the capability of analyzing the two analytes individually as well as simultaneously. PtNPs@MoS_2/GCE was found to be very sensitive and selective towards the determination of UA and DA within a very broad concentration range of 0.5-150 µM and 5-1000 µM respectively. The developed sensor also showed excellent performance in real samples [Chao et al., 2016].

H. Sun and co-workers electrochemically deposited the Au NPs on the layered MoS_2 to synthesize the AuNPs@MoS_2 nanocomposite and this nanocomposite-modified GCE sensor was prepared for the electrochemical simultaneous detection of DA, ascorbic acid (AA) and UA. The synthesized material exhibited better electrocatalytic activity than MoS_2 nanosheets and Au NPs for the oxidation of DA, AA, and UA and yielded three appropriately resolved voltammetric peaks which allowed the sensor to simultaneously estimate the three analytes via the DPV technique. The developed sensor furnished a very wide linear concentration range of 0.05-30 µM, 0.05-100 mM, and 0.05-40 mM along with a good LoD towards DA, AA, and UA respectively. Moreover, the AuNPs@MoS_2/GCE displayed exceptional selectivity and sensitivity towards DA detection in human blood serum. The results suggested that the MoS_2-based nanocatalyst is a favourable candidate for developing selective and sensitive

biosensors and biofuel cells and it also possesses a great ability for the detection of chemicals and biomolecules [Sun et al., 2014].

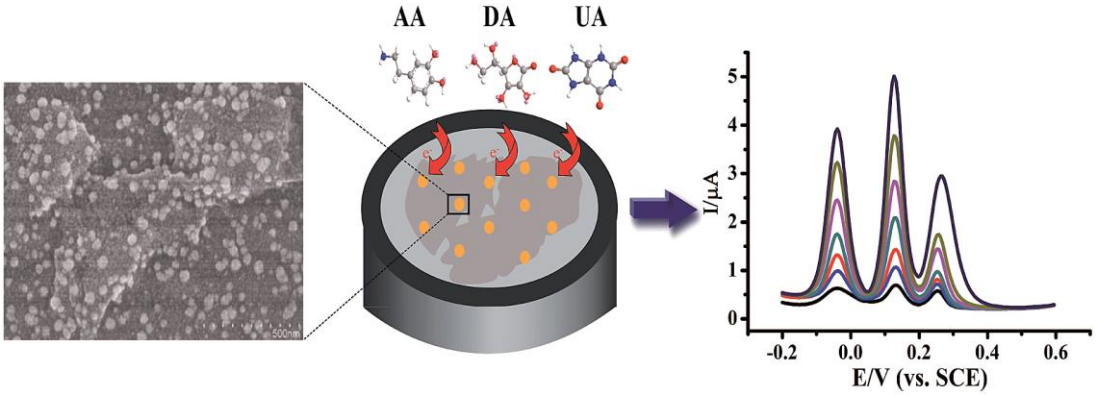

Figure 1.12 Schematic illustration of MoS_2-based simultaneous voltammetric detection of dopamine, ascorbic acid, and uric acid [Sun et al., 2014]

Yang et al. fabricated an electrochemical sensor for Clenbuterol (CLB) based on a 2D nanocomposite of MoS_2 nanosheet, Au NPs, and polyethylenimine (PEI) through the DPV technique. The designed material combined the beneficial properties of layered MoS_2, excellent conductivity of Au NPs, a large number of $–NH_2$ groups in PEI, and electrocatalytic behaviour of hemin. The nanocomposite-modified GCE showcased a remarkable DPV response towards CLB detection with a broad concentration range of 10-2000 ng/mL, a LoD of 1.92 ng/mL, good stability and reproducibility over a long period [Yang et al., 2017].

The hybridization of carbon-based materials such as graphene, CNTs, etc with TMDs has also been a matter of extensive research since these materials are capable enough to greatly enhance the conductivity of TMDs. Huang et al. reported the nanocomposite of layered MoS_2 and graphene through an L-cysteine-assisted solution-phase technique. The nanocomposite film was employed to modify the GCE for designing an electrochemical sensor for AC. The composite modified GCE showed a more

appreciative electron transfer kinetics and DPV response in comparison with MoS_2 or graphene modified GCE for the estimation of AC. The superior electrochemical response of the MoS_2–graphene nanocomposite has been designated to the robust nanostructure as well as the synergistic consequence between 2D MoS_2 nanosheet and the graphene. The nanocomposite can play an efficient role in fabricating electrochemical sensing and biosensing design. The reported results suggested that the sensing platform was highly sensitive, selective, and potent for the application of AC detection in real pharmaceutical samples [Huang et al., 2013].

Keerthana et al. reported the fabrication of an electrochemical sensor for a non-steroid anti-inflammatory drug Mesalazine (MZ) by developing a nanocomposite of WS_2 hierarchical flowers with rGO nanosheets through an eco-friendly hydrothermal method. WS_2 nanoflowers were found to be monodispersed uniformly over the rGO nanosheets which resulted in a substantial enhancement in the charge transfer kinetics through its large active surface area as well as the great conductivity of WS_2/rGO composite. The electrochemical studies illustrated that the WS_2/rGO modified GCE showcased the large cavities favouring the rapid electron transfer which further facilitated the remarkable enhancement in the activation of the WS_2/rGO electrocatalyst. As a result, the DPV response of WS_2/rGO modified GCE demonstrated excellent sensitivity and selectivity and a noteworthy reduced LoD of 3 nM toward MZ detection along with a wide linear range. In addition, the reported sensor exhibited significant reproducibility, rapid electrode kinetics, and long-term stability for quantitative estimation of MZ. Further, WS_2/rGO/GCE demonstrated the validity of MZ detection in various real samples, for instance, hemoglobin, water, human urine and bovine serum

albumin, that authenticated its extreme potential for real-time estimations [Keerthana et al., 2021].

Yang et al. reported the determination of CAP using a nanocomposite of MoS_2 and PANI modified carbon paste electrode through DPV. The nanocomposite was developed through the in situ polymerization of aniline over and in between the thin layers of MoS_2 nanosheets. The physisorption of aromatic aniline over the basal planes of MoS_2 nanosheets ameliorated the electrochemical behaviour of MoS_2/PANI nanocomposite. The developed material possessed a large specific surface area and remarkable conductivity. The benzene rings present in the nanocomposite facilitated the adsorption of conjugated CAP molecules. As a result, the voltammetric response of the nanocomposite for the CAP determination was significantly enhanced due to synergism. Hence, MoS_2/PANI/carbon paste electrode (CPE) showed a sensitive and selective determination of CAP with a low LoD and a wide linear range along with high stability and reproducibility [Yang et al., 2015].

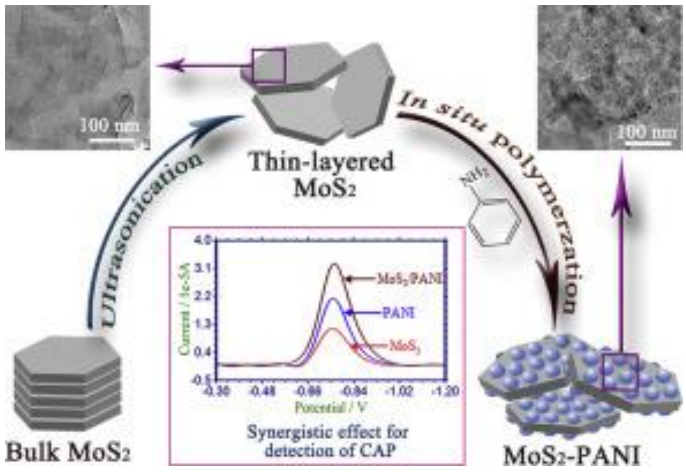

Figure 1.13 Schematic representation of the fabrication of MoS_2/PANI/CPE and DPV response towards CAP detection [Yang et al., 2015]

Huang et al. constructed a voltammetric sensor for trace-level detection of DA based on an integration of MoS_2–PANI and Au NPs. The AuNPs/MoS_2–PANI exhibited an

improved conductivity as well as specific surface area thereby enhancing the electrocatalytic activity of the material. The electrochemical results demonstrated that the composite-modified GCE was very sensitive toward DA detection with a very broad linear range from 1 to 500 µM and a fair LoD. The fabricated sensor also displayed a successful DA detection behaviour in real samples like a urine sample. [Huang et al., 2014]

Tiwari et al. proposed a voltammetric sensor for the trace level determination of Nevirapine (NVP), an anti-HIV drug with the help of a nanocomposite of Palladium (Pd) supported rGO with MoS_2 QDs (Pd@rGO/ MoS_2 QDs). It was proposed that the several Sulphur and Pd atoms in the composite imparted strong electrostatic anchorage for NVP. Further, a possibility was shown for the hydrogen bonding between electron-rich sites in NVP and electron-deficient sites in the designed material. Moreover, it was also proposed that there were probable hydrophobic interactions as well as π-π conjugation between aromatic rings of NVP and rings present in Pd@rGO. So, these synergistic interactions led to a high surface-to-volume ratio, electroactivity and hence, the Pd@rGO/ MoS_2 QDs modified GCE significantly lowered oxidation potential and provided an enhancement in DPV peak current for NVP due to rapid electron transfer kinetics. The electrochemical performance of GCE modified with the proposed material was found to be superior to Pd@rGO/GCE and MoS_2 QDs/GCE electrodes. The developed sensor was found to be very much sensitive, stable, and reproducible in the concentration range of 0.1-80 µM with an extremely low LoD of 50 nM and found to be suitable for NVP detection in human blood serum. The designed material also exhibited huge potential for constructing portable NVP sensing devices [Tiwari et al., 2018]

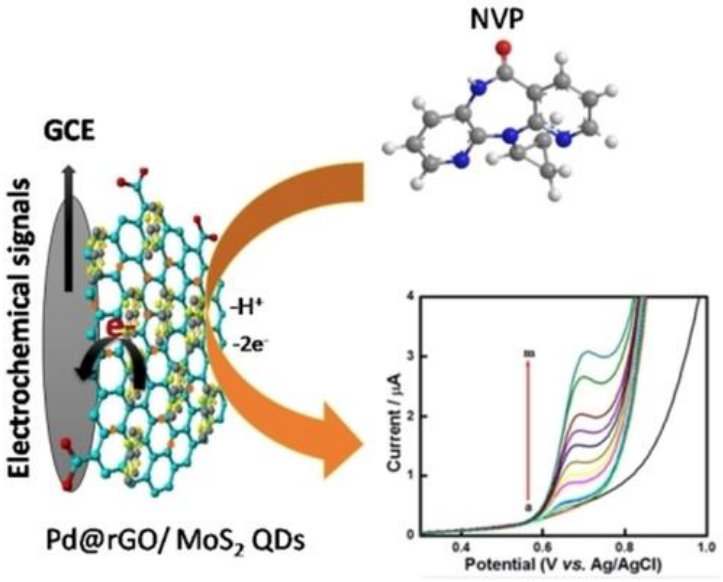

Figure 1.14 Schematic representation of the fabrication and sensing behaviour of Pd@rGO/MoS_2 QDs modified GCE towards Nevirapine detection [Tiwari et al., 2018]

Murugan and Dhamodharan developed a sensitive platform for the simultaneous detection of theophylline (TP), vanillin (VAN), and caffeine (CAF) based on MoS_2/PANI/f-MWCNTs nanocomposite utilizing DPV technique at GCE. The nanocomposite-modified GCE exhibits good electrochemical behaviour as a result of a large surface-to-volume ratio as well as rapid electron transfer kinetics which helped to achieve a good sensitivity, wide linear dynamic concentration window, remarkable selectivity, and repeatability with encouraging LoD values of 42 nM, 21 nM and 51 nM towards quantitative estimation of TP, VAN and CAF respectively. The DPV response clearly indicated three properly resolved peaks for the respective analytes. The sensing performance of the developed sensor was also validated for real-time use in drugs, food, and beverages with promising accuracy, sensitivity, and selectivity, and it was revealed that it possesses a great scope for the construction of commercial sensors [Murugan and Dhamodharan, 2022]

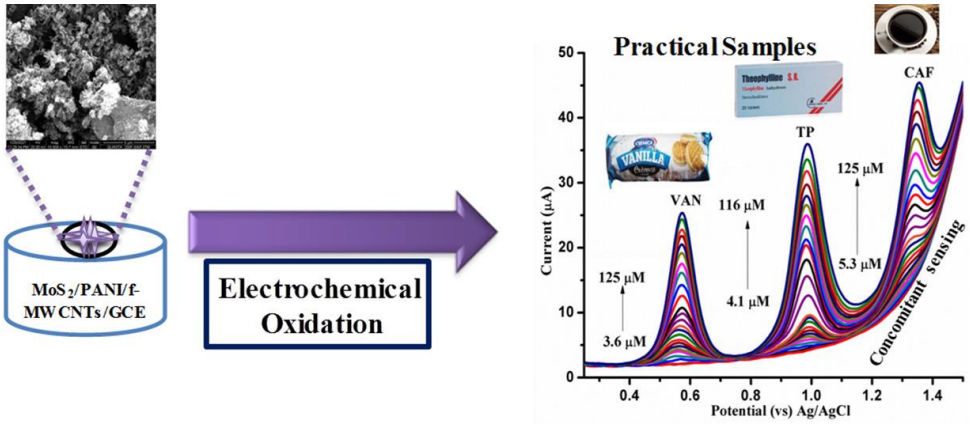

Figure 1.15 Schematic representation of the preparation and sensing behaviour of MoS_2/PANI/fMWCNTs nanocomposite modified GCE [Murugan and Dhamodharan, 2022]

Gao et al. reported the electrochemical detection of CAP using MoS_2 nanosheet supported by three carbonaceous materials i.e. MWCNTs, rGO, and carbon black (CB). The consequence of carbonaceous support was assessed and the results revealed that CAP sensing performance relied on the microstructures of the carbonaceous supports involved. rGO was proved as better material in terms of CAP detection performance since it exhibits larger electrochemically active surface area, superior conductivity, and lower interfacial resistance in comparison to CB and MWCNTs. DPV response MoS_2-rGO/GCE displayed a high sensitivity of 3.581 $\mu A \mu M^{-1} cm^{-2}$ towards CAP determination. The report also paved the way for the development of efficient electrochemical sensors and biosensors which rest on carbonaceous nanomaterials [Gao et al., 2021]. Some reports for the drug sensing have been listed in Table 1.2

Table 1.2 2D nanocomposites in drug sensing applications

S.N.	2D material	Filler	Analyte/Drug	Technique	Reference
1	MoS_2 nanosheet	PANI	CAP	DPV	Yang et al., 2015
2	MoS_2 nanosheet	PANI	CAP	DPV	Chen et al., 2016

3	MoS_2 nanosheet	PANI/f-MWCNTs	VAN, TP and CAF simultaneously	DPV	Murugan et al., 2022
4	MoS_2 nanosheet	PANI/GO	VAN, TP and CAF simultaneously	DPV	Murugan et al., 2021
5	MoS_2 nanosheet	PANI/Au NPs	DA	DPV	Huang et al., 2014
6	MoS_2 QDs	Pd@rGO	NVP	DPV	Tiwari et al., 2018
7	MoS_2 nanosheet	Pt NPs	DA and UA simultaneously	DPV	Chao et al., 2016
8	MoS_2 nanosheet	Au NPs	AA, DA and UA simultaneously	DPV	Sun et al., 2014
9	Graphene	PIn	DA	DPV	Kumar and Prakash, 2014
10	Graphene	Au NPs	Silodosin	DPSV	Er et al., 2015
11	rGO	Pd–Ag	AC	DPV	Reddy et al., 2018

1.10 Motivation and Objective of the thesis

Nanomaterials perform a very significant role in the development of advanced and efficient electrochemical sensors with the aid of their extensively large specific surface area, good electrocatalytic activity, and ease of functionalization furnishing a high sensitivity and selectivity. As per the literature survey and research findings, it has been observed that there is a necessity to develop sensitive, selective, fast, and cheap sensing tools for several therapeutic drugs administered to patients in due course of their treatment against various diseases such as malaria, typhoid, cancer or in case of various kinds of abnormalities in the body. When the concentration of these drugs is less than the optimum/desired level in the human body, the treatment of the disease becomes

ineffective. When the amount of such drugs is beyond the optimum/desired level in the body, they may create various kinds of adverse side effects. The normal metabolism of the body is harmed. This may seriously harm certain organ(s) of the body and this may also lead to death in severe cases. So, it becomes essential to keep the concentration of the therapeutic drugs in the human body within an optimum concentration window for efficient treatment of abnormalities and diseases. The maintenance of the desired amount of drug in the body further needs accurate and continuous monitoring. It motivated us to quantitatively determine the amount of therapeutic drugs in the body. In the current thesis, we have demonstrated the trace level sensors for antimalarial drugs Chloroquine (CQ) and Primaquine (PQ) as well as an immunosuppressive drug Azathioprine (Azp).

Recent research has shown that carbon and transition metal-based 2D nanomaterials such as GO, rGO, and MoS_2 nanosheet, and their composites have proved their potential for the development of high-performance electrochemical sensors because of their high surface areas, excellent conductivity, good electron transfer kinetics, etc.

Given these facts and the future perspective of nanotechnology's application in the field of sensing, the prime target of the thesis is:

- To design nanomaterial, their nanocomposites, and investigation for their electrochemical sensing applications with the help of various techniques.
- To explore physical, chemical, electrochemical and catalytic properties of designed nanomaterials and nanocomposites for fabrication of electrochemical sensors of antimalarial drugs (Chloroquine, Primaquine) and an immunosuppressive drug (Azathioprine).

Further, our thesis is aimed at the sub-objectives mentioned below:

- Synthesis of rGO and its nanocomposite with tungsten disulfide (WS_2) QDs, and its characterization. Further, fabrication of a voltammetric sensor for the antimalarial drug CQ based on the WS_2 QDs decorated rGO modified GCE.
- Synthesis of MoS_2 nanosheets and its nanocomposite with poly(5-carboxyindole) (CPIn), and its characterization. Further, fabrication of MoS_2-CPIn modified GCE for the voltammetric determination of an immunosuppressive drug Azp.
- Synthesis of MoS_2 nanosheet and its decoration with gold nanorods (GNR). Further, the characterization and utilization of the resulting nanocomposite (MoS_2-GNR) for the voltammetric detection of an antimalarial drug PQ utilizing the GCE.

1.11 Advantages of developed materials for sensing applications

Advanced 2D materials like rGO, MoS_2 nanosheet and their nanocomposites with QDs, conducting polymers, and metal nanostructures have been synthesized for improving their conductivity, stability, catalytic activity and electron-transfer properties like nanocomposite of rGO with WS_2 QDs, CPIn stabilized MoS_2 nanosheet and decoration of MoS_2 nanosheet with GNR. Further, these designed nanocomposites have been employed for the voltammetric sensing of therapeutic drugs CQ, Azp, and PQ.

rGO is a one-atom-thick layered crystalline carbon film offering a large active surface area, great electrical conductivity, high mechanical strength, and rapid electron transfer mobility. The resulting electrochemical, electronic, physiochemical, and optical properties make them a prominent candidate for different applications including sensing [Zhang et al., 2013]. The electrochemical properties of rGO are a little compromised due to the aggregation of the individual sheets which leads to reduced active surface area and a number of electrocatalytic active sites. This limitation can be overcome by the functionalization of rGO with WS_2 QDs in between and over the sheets resulting in

enhanced active surface area and a significantly larger number of electrocatalytic active sites. The electrochemical properties of the nanocomposite were also substantially improved due to the synergistic effect between rGO and WS_2 QDs. It motivated us to exploit the developed nanocomposite for the trace-level electrochemical determination of an anti-malarial drug CQ.

In the category of TMDs, MoS_2 has been explored to be analogous to graphenes and possesses a large specific surface area, excellent electrical conductivity, rapid heterogeneous electron transfer and fluorescence, rendering them to be used in sensing, biosensing, hydrogen evolution electrocatalysis, lithium-ion batteries, etc. [Pumera and Loo, 2014]. The conductivity and catalytic properties of layered MoS_2 are also compromised due to the stacking and aggregation of the individual sheets. Conducting polymers and their substituent possess various exceptional electrical, electronic, optical, and optoelectronic characteristics, and are employed in scientific and technological research [Kumar and Prakash, 2014].

We have exploited CPIn for preventing the restacking of the MoS_2 nanosheet and stabilize it. This nanocomposite formation has helped to greatly enhance the electrochemically active surface area of nanosheets and increase the number of active sites. Further, CPIn also aided to improve the conductivity and electron transfer kinetics of MoS_2 nanosheet. The synergistic effect of the two components has rendered to the development of a nanocomposite with excellent electrochemical properties to be exploited for sensing applications. We have employed the developed nanocomposite for fabricating the voltammetric sensor for trace-level detection of an immunosuppressive drug Azp.

The noble metal nanostructures are very well known for their variety of beneficial properties like as superior electrocatalytic activity, large specific surface area, excellent conductivity, and rapid electron transfer kinetics [Pan et al., 2020]. But, most of the time, they suffer a limitation of aggregation. GNR have been reported to improve the electrochemical properties of 2D carbonaceous nanomaterials by preventing their aggregation and incorporating synergism [Ojha et al., 2022]. We have decorated the MoS_2 nanosheet with GNR to prevent the restacking of the sheets as well as GNR, thereby excessively increasing the electrochemically active surface area. The synergism between MoS_2 nanosheet and GNR has helped to design a nanocomposite with a large specific surface area, great catalytic ability, good conductivity, and rapid electron kinetics and exhibiting all the desired properties for developing a high-performance electrochemical sensor. These properties motivated us for exploiting it for fabricating a voltammetric sensor for an antimalarial drug PQ.