Thesis Abstract

Biosensors are crucial bioanalytical tools capable of detecting any analyte of interest within a sample solution. While the conventional diagnostic methods require certain demands such as trained personnel and advanced infrastructure, with the processes being time-consuming, they also have the biggest drawback of not being able to be accessed at remote locations. Electrochemical biosensors are emerging as newer alternatives to such conventional tools with the ability to function in remote settings, as point-of-care diagnostics as well. They are being continuously improved to detect clinical and environmental analytes with higher sensitivity and selectivity through incorporation of advanced materials and novel signal enhancement strategies. The surfaces of the sensors are functionalized with suitable biorecognition elements or the matrix components themselves are catalytic enough the detect the target analyte at suitable potentials. Functionalization with advanced nanomaterials often impart excellent catalytic properties to these sensing platforms along with increment in their surface area to many folds.

In this work, we have attempted to develop multiple sensing platforms with metal organic frameworks as essential matrix components, to detect a range of clinical and environmental analytes, both in ideal as well as real samples. They also offer potential for deployment for on-site detection of these analytes to ensure better health. In this thesis project, four different biosensors have been designed using metal organic frameworks and its composites to detect hydrogen peroxide, folic acid, nitrite, and uric acid. All materials and composites reported in the work has been thoroughly characterized through physical and electrochemical routes before their application in sensor development.

In the first work, creation of a nanohybrid platform has been attempted for rapid detection of hydrogen peroxide (H_2O_2), which has tremendous role in area of medical diagnostics. Conventionally, the peroxidase (POD) enzyme catalyses H_2O_2 however, it is prone to inherent chemical and thermal instabilities reducing the overall stability and shelf life of sensor probe. A possible solution for this problem has been attempted in this work where a non-enzymatic peroxidase mimic nanohybrid probe comprising of gold nanodendrites (AuND), nickel metal organic framework (Ni-MOF), and hydrazine has been synergistically deployed for rapid detection of H_2O_2. The developed sensor probe has been rigorously characterized through various physical as well as electrochemical characterization techniques. It demonstrated impressive analytical performance, with a linear dynamic range (LDR) between 1 x 10^{-8} M to 1 x 10^{-15} M, with the limit of detection

(LOD) being 0.34 (±0.05) x 10^{-15} M, making it suitable for trace analysis as well. The probe's average response time with changing H_2O_2 concentrations was 5.02 ± 0.42 seconds, making it an agile sensing platform for H_2O_2 detection. The nanohybrid probe displayed minimal response towards interferants such as superoxide radicals, ascorbic acid, cysteine, glucose, alanine, and citric acid, which usually co-exist in real sample matrix. In order to investigate the real-life applicability of the developed sensor probe, a real sample analysis involving synthetic serum was adopted which yielded a current recovery between 90.20 - 94.14%. The probe fabrication time and on-chip synthesis procedure are facile, making it a robust and efficient sensing platform for H_2O_2 free radical in clinical settings.

In the second work, an electrochemical sensor has been developed for folic acid (FA), an essential water-soluble vitamin and a precursor for enzymes which requires timely and precise monitoring in serum of individuals with varying clinical diagnosis. An attempt has been made in this direction through our work where, rapid detection of FA through its oxidation via. metal centres from hybrid nanomaterials, is deployed for signal generation. A non-enzymatic, non-immunometric approach involving a sandwich model comprising of NiMOF layered between gold nanoparticles (AuNPs) and gold nanodendrites (AuNDs) incorporated within a sensor matrix has been deployed for the purpose. The probe displayed great analytical performance with a LDR between 1 x 10^{-3} M to 1 x 10^{-11} M, with the LOD being 0.48 x 10^{-11} M. The probe's average response time with respect to changes in FA concentration was recorded as less than 2.1 seconds, making it a rapid sensing platform for FA detection. The real-life applicability of the developed sensor was tested in serum, followed by a breast cancer cellular microenvironment-based analysis which yielded a current recovery between 95.11-98.17%. The cancer cell FA uptake was also validated through a live cell imaging based on the standard method of fluorescence. The less fabrication time of the developed sensor when compared to existing ones makes it a facile and efficient sensing platform for FA in clinical settings. This current study is the first report on conjunction of 1D, 2D and 3D materials as sensing matrix for molecular detection application.

In the next chapter, we have attempted the stacking of two MOFs, a Ni-MOF, followed by Co-MOF, which was further functionalized with gold nanoparticles to detect nitrite ions (NO_2^-) in real/environmental water samples. Nitrite is a naturally occurring plant nutrient present in the soil and is also used as a preservative in industries however, can generate carcinogenic precursors at higher concentrations. The catalytic sensing probe

was developed to detect NO_2^- through its electrochemical oxidation to NO_3^- at a specific potential. The GCE/Ni-MOF/Co-MOF surface was deposited through a facile and faster approach of electrodeposition, with Co-MOF being developed through a novel electrodeposition route. The final sensing probe was thoroughly characterized by various physical and electrochemical techniques. It displayed worthy analytical performance in terms of its wide linear dynamic range between 1 x 10^{-3} M and 1 x 10^{-8} M and a limit of detection of 4.2 nM. It exhibited a rapid average response time of about <1.5 second, making it an ultrasensitive detection platform for NO_2^- in environmental water samples. A systematic integration with a smartphone application has also been proposed for on-site application of the sensor where a single-fed input value determines the real-time NO_2^- concentration in test water samples.

In the next and final work, novel sensing platform comprising of cobalt/molybdenum (Co/Mo) bimetallic MOF has been attempted for the sensitive detection of uric acid (UA) in clinical ranges. Conventionally, UA is detected through an enzyme called uricase which converts UA to allantoin. However, the enzyme-based diagnostic solutions are prone to chemical and thermal instabilities making the process cumbersome and tedious. To eliminate such challenges, the developed non-enzymatic detection system uses a highly catalytic bimetallic sensing module which electrochemically facilitates conversion of UA to allantoin, and yields electrochemical signal outcomes. The developed sensing probe was characterized through physical and electrochemical techniques. UA has been used as the sample target analyte to validate the efficacy of the bimetallic system using differential pulse voltammetry (DPV) and chronoamperometry (CA). The preliminary results hold immense promise for the developed system in application for sensing a wide range of analytes through electrochemical methods in clinical settings.

In the sixth and the final chapter/segment of the thesis, we have identified the possible challenges in development of such MOF-based sensing platforms to project better research opportunities for the upcoming researchers. The work is aimed towards the fabrication sensitive platforms exploring the potential of novel synthesis methods for MOF synthesis along with its deployment in the sensor matrix development. The work can be further extended to development of hand-held point-of care or miniaturized systems which can used for on-site diagnostics with little or no technical training requirements.