

# **Annexure**

## Annexure-I

### List of publications from thesis and associated works

1. **Divya**, I Nandi, N Mendki and **P. Chandra\***, “Software Integrated Personalized Biosensing Device for Serum Creatinine Detection based on Boron doped MXene Nanohybrid,” *ACS Biomaterials Science and Engineering*, 10, 6603-6614, 2024.
2. **Divya**, and **P. Chandra\***, “Bioengineered cellulosic paper micro-device for serum albumin detection in clinical range,” *International Journal of Biological Macromolecule*, 258, 128921, 2023.
3. **Divya**, and **P. Chandra\***, “ZIF-67- MWCNT Nanohybrid Based Electrochemical Immunosensing Device for Diagnosing Kidney Dysfunction,” *IEEE Sensors*, 1, 1-4, 2023.
4. **Divya**, S. Mahapatra, and **P. Chandra\***, “Design and Engineering of a Palm-Sized Optical Immunosensing Device for the Detection of a Kidney Dysfunction Biomarker,” *Biosensors*, 12 (12), 1118, 2023.
5. **Divya**, Darshna, A. Sammi, and **P. Chandra\***, “Design and Development of Opto-electrochemical biosensors for Clinical Biomarkers of Chronic Kidney Disease”, *Biotechnology and Bioengineering*, 120, 3116-3136, 2023.
6. **Divya**, M. G. Dastidar, S. Mahapatra, R. Kumari, D. S. Dkhar, S. Roy, and **P. Chandra\***, “Engineered nanomaterial-based implantable MicroNanoelectrode for in vivo Analysis: Technological advancement and commercial aspects,” *Microchemical Journal*, 187, 108431, 2023.
7. **Divya**, DS Dkhar, R Kumari, S Mahapatra, R Kumar, and **P. Chandra\***, “Ultrasensitive aptasensors for the detection of viruses based on opto-electrochemical readout systems”, *Biosensors*, 12(2), 2022.
8. **Divya**, A Sammi, S Mahapatra, R Kumar, **P. Chandra\***, “Nano-Bio-engineered Silk Matrix based Devices for Molecular Bioanalysis”, *Biotechnology and Bioengineering*, 119, 784-806, 2021.
9. **Divya**, S Mahapatra, VR Srivastava, and **P. Chandra\***, “Nanobioengineered sensing technologies based on cellulose matrices for detection of small molecules, macromolecules, and cells”, *Biosensors*, 11 (6), 168, 2021.
10. **Divya**, Shubhangi and **P. Chandra\***, “Bimetallic copper/Zinc Metal Organic framework-MoS<sub>2</sub> nanohybrid Based Electrochemical Sensor,” *IEEE BioSensors*, 2, 1-4, 2024.

11. **Divya**, Rohini Kumari, and **P. Chandra\***, “Co-MOF and c-MWCNT nanocomposite based impedimetric immunosensor for sensing of human serum albumin,” *Applied Organometallic Chemistry*, 2025.
12. **Divya**, Shubhangi, and **P. Chandra\***, “Electrochemical Approach for Synthesis of Bimetallic Iron-Nickel Metal Organic Framework for Caffeine Detection in Coffee and Green Tea Samples,” *Food Chemistry*, 2025.
13. **Divya**, Ankur Singh, and **P. Chandra\***, “Role of Surface Engineering in Advancement of Optoelectrochemical Sensing Platforms”, (revision submitted)
14. **Divya**, Shubhangi, Ratul Paul, Ankur Singh and **P. Chandra\***, “Electrochemically synthesized chromium metal organic framework nanocomposite with reduced graphene oxide based immunosensor for the detection of alkaline phosphatase,” 2024. (submitted)
15. D. S. Dkhar, R. Kumari, **Divya**, R. Kumar, T. Tripathi and **P. Chandra\***, “Antibody-receptor bioengineering and its implications in designing bioelectronic devices”, *International Journal of Biological Macromolecule*, 218, 225-242, 2022.
16. R Kumari, DS Dkhar, S Mahapatra, **Divya**, SP Singh, and **P. Chandra\***, “Nano-Engineered Surface Comprising Metallic Dendrites for Biomolecular Analysis in Clinical Perspective”, *Biosensors*, 12 (12), 1062, 2022.
17. R Kumar, DS Dkhar, R Kumari, **Divya**, S Mahapatra, A Srivastava, and **P. Chandra\***, “Ligand conjugated lipid-based nanocarriers for cancer theranostics”, *Biotechnology and Bioengineering*, 119, 3022-3043, 2022.
18. R Kumar, DS Dkhar, R Kumari, S Mahapatra, **Divya**, VK Dubey, and **P. Chandra\***, “Lipid-based nanocarriers: Production techniques, concepts, and commercialization aspect”, *Journal of Drug Delivery Science and Technology*, 74, 103526, 2022.
19. R Kumari, DS Dkhar, S Mahapatra, **Divya**, R Kumar, and **P. Chandra\***, “Nano-bioengineered Sensing Technologies for Real-time Monitoring of Reactive Oxygen Species in vitro and in vivo models”, *Microchemical Journal*, 180, 107615, 2022.
20. R Kumar, **Divya**, S Mahapatra, VK Dubey, **P. Chandra\***, “N-acetyl-d-glucosamine decorated nanolipid- based carriers as theranostics module for targeted anti-cancer drug delivery”, *Materials Chemistry and Physics*, 282, 125956, 2022.
21. Shubhangi, **Divya**, S. K. Rai, and **P. Chandra\***, “Shifting Paradigm in Electrochemical Biosensing Matrices Comprising Metal Organic Frameworks and their Composites in Disease Diagnosis”, *WIREs Nanomedicine & Nanobiotechnology*, 16, 4, 2024.

22. U. P. Azad, S. Mahapatra, **Divya**, A. Srivastava, N. P. Shetti, and **P. Chandra\***, “Electrochemical biosensors for monitoring of bioorganic and inorganic chemical pollutants in biological and environmental matrices,” *Microb. Biodegrad. Bioremediation, Elsevier*, ISBN: 978-0-323-85455-9, 2022.
23. B. Purohit, **Divya**, N. P. Shetti, and **P. Chandra\***, “Materials for wearable sensors,” *Wearable Phys. Chem. Biol. Sensors, Elsevier*, ISBN: 978-0-12-821661-3, 2022.

### **Patent**

**Title: “A METAL ORGANIC FRAMEWORK BASED SENSOR AND A METHOD OF FABRICATION THEREOF”**

**Authors: Pranjal Chandra, **Divya**, Shubhangi**


**Year: 2024**

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**Patent Application No.: 202511001234**

Article

# Design and Engineering of a Palm-Sized Optical Immunosensing Device for the Detection of a Kidney Dysfunction Biomarker

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**Abstract:** Creatinine is one of the most common and specific biomarkers for renal diseases, usually found in the serum and urine of humans. Its level is extremely important and critical to know, not only in the case of renal diseases, but also for various other pathological conditions. Hence, detecting creatinine in clinically relevant ranges in a simplistic and personalized manner is interesting and important. In this direction, an optical sensing device has been developed for the simple, point-of-care detection of creatinine. The developed biosensor was able to detect creatinine quantitatively based on optical signals measured through a change in color. The sensor has been integrated with a smartphone to develop a palm-sized device for creatinine analysis in personalized settings. The sensor has been developed following facile chemical modification steps to anchor the creatinine-selective antibody to generate a sensing probe. The fabricated sensor has been thoroughly characterized by FTIR, AFM, and controlled optical analyses. The quantitative analysis is mediated through the reaction between picric acid and creatinine which was detected by the antibody-functionalized sensor probe. The differences in color intensity and creatinine concentrations show an excellent dose-dependent correlation in two different dynamic ranges from 5 to 20  $\mu\text{M}$  and 35 to 400  $\mu\text{M}$ , with a detection limit of 15.37 ( $\pm 0.79$ ) nM. Several interfering molecules, such as albumin, glucose, ascorbic acid, citric acid, glycine, uric acid,  $\text{Na}^+$ ,  $\text{K}^+$ , and  $\text{Cl}^-$ , were tested using the biosensor, in which no cross-reactivity was observed. The utility of the developed system to quantify creatinine in spiked serum samples was validated and the obtained percentage recoveries were found within the range of 89.71–97.30%. The fabricated biosensor was found to be highly reproducible and stable, and it retains its original signal for up to 28 days.

**Keywords:** optical sensing device; paper sensor; personalized diagnosis; surface chemistry; kidney dysfunction



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## 1. Introduction

Chronic kidney disease has emerged as one of the most common conditions affecting more than 10% of the world's population, which equates to more than 800 million people. Over the last two decades, an exponential surge, i.e., a 42% increase in the number of deaths caused by chronic kidney disease was recorded worldwide [1]. According to the Global Burden of Disease Study, there has been a surge in mortalities due to chronic kidney disease and it has become one of the major diseases, leading to a global burden [2,3]. There are various risk factors associated with chronic kidney disease and co-morbid conditions which make the condition worse for patients. Chronic kidney disease was found to be more prevalent in cardiovascular patients [4]. In a recent study, it was shown that cases of chronic kidney disease have become common in children and thus the global burden has increased and is hampering children's quality of life. In most pediatric cases, it was observed that children require dialysis or kidney transplants which are not easily available in developing and under-developed countries [5,6]. In another study, it was established



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## Bioengineered cellulosic paper micro-device for serum albumin detection in clinical range

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## ARTICLE INFO

**Keywords:**  
Cellulose  
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Bioengineering

## ABSTRACT

Chronic Kidney Disease (CKD) is becoming one of the major causes of morbidity and mortalities in 21st century. We have developed a bioengineered cellulosic paper device for the quantification of albumin (ALB) in physiological samples. The paper surface was activated and antibodies specific to target biomarker was immobilized on engineered paper surface. Every step after modification was characterized by FTIR, XPS, SPM and optical analysis. Further, the device model was designed using CAD file, and a 3-D cascade device was fabricated with in-built constant light source to provide proper and controlled environment for in-situ image analysis. After adding the sample on the bioengineered paper, the antigen-antibody reaction takes place, after that addition of dye results in change of color from yellow to blueish-green within 40 s. An optical method was employed for the analysis of the images by recognizing the specific area and the color intensity. Additionally, the immunosensor specificity was evaluated on number of molecules that are usually found in the serum sample. The linear dynamic range of the developed immunosensor has been reported to be 1–60 mg/mL, covering the normal as well as clinical range of ALB in physiological samples with a detection limit of 0.049(±0.002) mg/mL. With good precision and recovery, the device was able to successfully determine the ALB concentrations in serum sample. The developed device has simple and user-friendly interface and it may also help diagnosing CKD in personalized settings.

## 1. Introduction

Paper-based optical sensors have been increasingly popular in recent years because of their advantages in terms of cost, speed, and portability for environmental, health diagnostics in areas with limited resources [1,2]. Due to their speed, portability, ease of use, low sample volume requirements, and ability to perform rapid analyses, paper-based sensors have gained interest as testing tools for the identification of analytes. A number of portable and user-friendly point-of-care diagnostic tools for colorimetric analysis have been recently reported using smartphone-based lab-on-a-chip devices [3]. The cost of diagnostic testing is significantly reduced when a lab-on-a-chip device is coupled with a smartphone for point-of-care testing [4]. As compare to the conventional optical assays, paper-based biosensing devices offers user-friendly analytical module and a personalized interface that don't require bulky instruments for signal generation and their analysis [5]. The lateral flow assay technique still has a number of drawbacks despite

being the most popular point-of-care platform, including a lack of quantitation capabilities and a lower level of sensitivity than the laboratory-based assays. The paper-based analytical instruments can be coupled with a variety of signal generation techniques viz. colorimetric and electrochemical, where the latter is the widely adopted transduction system due to numerous advantages [6–8]. In addition to these, surface plasmon phenomenon has also been widely used in sensing of numerous molecules that are coupled with various nanostructures [9]. In colorimetry, analysis is carried out by applying reagent(s) and the target analyte to the reaction zones within the paper device. A camera and scanner are used to measure or identify changes in the assay zone color on the paper device [10,11]. The optical parameters that are utilized for image analysis while using a smartphone camera are RGB (red, green, and blue) color intensities. Rapid optical detection of body fluid biomarkers and other samples can be achieved using a smartphone with an integrated a high-resolution camera [12]. A light source for imaging, such as a light-emitting diode, light diffuser, and optical chamber are

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# Software Integrated Personalized Biosensing Device for Serum Creatinine Detection Based on Boron doped MXene Nanohybrid

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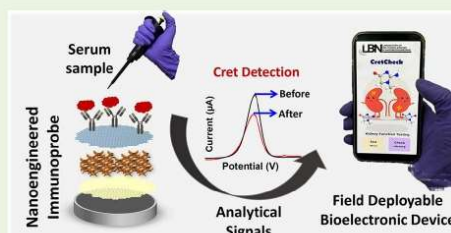
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**ABSTRACT:** In recent years, an increase in the number of chronic kidney disease (CKD) cases has led to a global health burden majorly affecting underdeveloped and developing nations. A key biomarker for assessing the kidneys' normal functioning is creatinine, which is filtered out from the blood by the kidney. Thus, timely and specific detection of creatinine becomes necessary for diagnosis and subsequent treatment of CKD. Hence, in this study, we have tried to develop a field-deployable, software-integrated immunosensor for the detection of creatinine in a serum sample. The immunosensor was developed by incorporating gold nanoparticles, boron doped MXene, polyaniline, and antireatinine antibody using an appropriate bioconjugation reaction. The developed sensor was able to detect creatinine in a linear dynamic range of 10 nM to 0.1 M with a limit of detection of 1.72 ( $\pm 0.07$ ) nM. The sensor was integrated with an indigenously developed software named "CretCheck" which simplifies the process of data analysis. The software integrated personalized biosensing device was used to find the creatinine concentrations directly from the obtained analytical signals. The developed immunosensor with the integrated software can also be implemented directly in primary health care facilities for creatinine detection in the future.

**KEYWORDS:** electrochemistry, human health, nanoengineering, personalized diagnosis, hand-held device, immunosensor



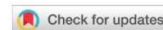
## 1. INTRODUCTION

Millions of people worldwide suffer from chronic kidney disease (CKD), which is a major global health burden and offers enormous challenges to healthcare systems.<sup>1</sup> The global burden of disease research 2017 estimated the contribution of 354 illnesses and injuries as well as 84 risk factors to morbidity and mortality between 1990 and 2017.<sup>2</sup> It was reported that there is a surge in morbidity and mortality at the national, regional, and worldwide levels due to CKD and reduced kidney function. To emphasize and garner attention on CKD, an initiative has been started that terms CKD as "Common, Harmful, and Treatable".<sup>3</sup> It affects more than 10% of the global population and it is reported that it will become the fifth major cause of mortalities by 2040.<sup>4,5</sup> Furthermore, it has become crucial to diagnose and treat CKD promptly in order to meet the 2030 UN Sustainable Development Goal of lowering the effect of communicable diseases to one-third. Therefore, to diagnose renal disease, developing methods for monitoring the levels of related biomarkers is required. Creatinine is a byproduct produced due to the breakdown of creatine, which is an essential component of muscles. Generally, creatinine is eliminated from the blood by the kidney and is considered as a key biomarker for diagnosing, tracking, and treatment of CKD.<sup>6,7</sup> Its accurate and timely identification is thus essential for prompt intervention and successful disease management.<sup>8,9</sup>

The conventional methods for the detection of creatinine are colorimetry, enzymatic assays, spectrophotometry, high pressure liquid chromatography, mass spectroscopy, capillary zone electrophoresis, flow injection analysis systems, and nuclear magnetic resonance.<sup>10–13</sup> These methods are frequently constrained by their intricate instrumentation, lengthy processing periods, and vulnerability to interference from other substances in biological samples. As a result, there has been a surge in interest for creating novel biosensing technologies that can get past these obstacles and transform the diagnosis industry.<sup>14,15</sup> The recent developments in the field of nanotechnology, material synthesis, and biorecognition components lead to novel sensing technologies with unmatched sensitivity, specificity, and speed of analysis.<sup>16</sup> These biosensors improve signal transduction and detection limits by taking advantage of the unique qualities of nanomaterials, such as high surface area-to-volume ratios, excellent conductivity, robustness, and biocompatibility.<sup>17,18</sup> Apart from their analytical capabilities, biosensors

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## RESEARCH ARTICLE

# Co-MOF and c-MWCNT Nanocomposite-Based Impedimetric Immunosensor for Sensing of Human Serum Albumin

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Cobalt metal–organic framework (Co-MOF), also called zeolite imidazole framework (ZIF-67), a subclass of MOF, is a burgeoning class of crystalline materials that features high porosity, large surface areas, remarkable stability, and flexibility. A coordination bond between an organic linker and a redox-active cobalt metal center forms ZIF-67 MOF, which has a unique architecture resembling zeolites. However, ZIF-67's limited conductivity impedes its application for electrochemical sensing. Considering this, we designed Co-MOF-carboxylated multiwalled carbon nanotubes (c-MWCNTs) nanohybrid, which was further functionalized with an anti-ALB antibody to enable the selective electrochemical evaluation of albumin (ALB), a clinically proven kidney biomarker. ALB, the most prevalent protein secreted by hepatocytic cells, performs a number of essential bodily functions; however, a deviation from a normal level is prognostic of kidney failure and other illnesses. Several physical and electrochemical methods were utilized to thoroughly characterize the developed immunosensing device. Following that, electrochemical impedance spectroscopy (EIS) was employed to evaluate its efficacy, and the linearity and detection limit were estimated as 0.1–60 mg/mL and 0.024 mg/mL, respectively. These remarkable outcomes are the result of c-MWCNT and Co-MOF synergistic effects, and they present a cutting-edge approach for point-of-care ALB detection using composite materials based on MOFs.

**1 | Introduction**

MOF is an emerging class of materials that is crystalline, porous, three-dimensional, and highly structured in nature [1]. Its constituents self-assemble into a range of 2D or 3D structures, comprising organic linker moieties like amines, carboxylates, or imidazolates and inorganic metal ions like cobalt, zinc, or copper [2, 3]. Thus, MOFs epitomize the elegance of chemical structures that unite organic molecules (linkers) and inorganic metal ions together in a single structure. These materials' large surface area, adjustable pore and channel size, and ease of functionalization have garnered a lot of interest

[4, 5]. They hold tremendous potential for applications in the healthcare, energy, and environmental sectors owing to their fine-tuning properties [6–8]. MOFs are categorized into a variety of subclasses, the ZIF subclass being one of them where imidazolyl ligands interact with transition metal ions to produce tetrahedral ZIFs [9, 10]. Among several ZIFs, ZIF-67 (Co-MOF) stands out as the most widely used material because of its facile synthesis procedure, enormous surface areas, enhanced adaptability, and exceptional mechanical, chemical, and thermal stability [4, 11]. The preparation of Co-MOF typically entails a self-assembly process involving the cobalt metal ion ( $\text{Co}^{2+}$ ) and the 2-methylimidazole linker, where the



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Food Chemistry

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## Caffeine detection in green tea and coffee samples using nanoelectronic device based on bimetallic FeNi-metal organic framework

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### ARTICLE INFO

**Keywords:**  
Beverages  
FeNi-MOF  
Caffeine consumption  
Electrochemical  
Bimetallic

### ABSTRACT

Caffeine, is a stimulant of the central nervous system, that is normally found in a range of foods, drinks and medications including tea, coffee, chocolate, energy drinks, and syrups. The levels of caffeine play an important role on the impact of its effect on human health. Hence, in this work, we have developed a nanoelectronic device employing the bimetallic metal-organic frameworks (MOFs) for the rapid detection of caffeine. The fabricated probe has been characterized through various physical characterization techniques, including SEM, EDX, FTIR, XPS, and electrochemical techniques. The developed chip was able to detect caffeine in a linear dynamic range of  $1 \times 10^{-5}$  to 50 mM with a detection limit of 1.26 ( $\pm 0.06$ ) nM. The developed probe was also tested against various interferants and its practical applicability was evaluated using green tea and coffee samples as real matrices. Further, 3D-printed cascade model was used for the device development and the developed chip shows its promising advantage in monitoring caffeine in diverse beverages.

### 1. Introduction

Caffeine, a naturally occurring alkaloid and an *N*-methyl derivative of xanthine, acts as a central nervous system (CNS) stimulant (Nehlig et al., 1992). It is commonly found in plants such as coffee, tea leaves, cocoa beans, yerba mate, and guarana berries, with its extracts primarily used as a flavoring agents in beverages (Reddy et al., 2024) (Burdan, 2015). Being a major component of coffee, tea, and other soft beverages, it offers various health benefits when consumed in moderation. Sensible intake of caffeine has shown to improve the performance of cardiac muscles, respiratory function, and CNS activity (Arauz et al., 2017) (Mari et al., 2024). It also finds its applications in the pharmaceutical field including use in pain relief preparations, flu remedies, and dietary aids. However, its excessive consumption (more than 200 mg per day) can lead to adverse effects, including overstimulation of the CNS, increased gastric acid secretion, diuresis, tremors, nervousness, nausea, seizures, and inhibition of DNA synthesis (Hughes, 2016) (Fiani et al., 2021) (Agrawal et al., 2013). Recently, its usage in a variety of beverages and medications is on the rise, which has increased interest in developing accurate and effective methods for its detection. Consequently, from a health perspective, the accurate determination of caffeine levels in food and beverages is crucial to prevent potential health risks. Because of this,

it is critical to keep an eye on the amount of caffeine in consumables to ensure consumer safety and regulatory compliance. The traditional methods for detecting caffeine like mass spectrometry (Torres Y Torres et al., 2015), UV-visible spectroscopy (Ahmad Bhawani et al., 2015), nuclear magnetic resonance (Okaru et al., 2020), and high-performance liquid chromatography (Lopez-Sanchez et al., 2018) are frequently used, but often suffer from few limitations. For instance, HPLC is a highly priced instrument which requires skilled personnel for its operation, making it unfeasible for general purposes. UV-vis spectroscopic method is cost-effective however may encounter spectral interferences, with poor sensitivity and a narrow dynamic range. Similarly, other methods such as nuclear magnetic resonance, mass spectrometry are costly, making them unsuitable alternatives for the purpose (Weldegebreel et al., 2017) (Saraban et al., 2024). This suggests a potential need for quick and affordable analytical methods to quantify caffeine in diverse matrices. Electrochemical sensors emerge as one of the plausible solutions which may provide faster, sensitive, reproducible, and affordable detection (Borse et al., 2022) (Azad et al., 2022) (Azad & Chandra, 2023). Due to their numerous advantages, we have tried to develop an electrochemical method for the analyte of interest. Sensor surface engineering using multi-dimensional materials has emerged as an important research prospect in the development of sensitive sensor development

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0308-8146/© 2025 Elsevier Ltd. All rights are reserved, including those for text and data mining, AI training, and similar technologies.

# ZIF-67-MWCNT Nanohybrid based electrochemical immunosensing device for diagnosing kidney dysfunction

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**Abstract**— Human serum albumin (HSA) is most abundant protein produced by liver hepatocytes. HSA (3.5–5 g/dL) accounts for half of the total protein in plasma in healthy individuals. HSA exhibits various functions such as antioxidant and immunomodulatory activities, and liver and kidney activity. Kidneys failure becoming one of the major problem of the 21<sup>st</sup> century which leads to global burden. In this study, we report electrochemical immunosensing device for the HSA detection using zeolite imidazole framework (ZIF-67) based nanohybrid including carboxylated MWCNT. The anti-HSA antibody were immobilized using ethyl(dimethylaminopropyl) carbodiimide - N-hydroxysuccinimide (EDC-NHS) conjugation reaction. The designed sensing surface has been characterized using different electrochemical techniques. Differential Pulse Voltammetry (DPV) was used for assessing the analytical performance of the sensor where dynamic range and detection limit were found to be 1–60 mg/mL and 4.65 µg/mL, respectively. This will help in determining the levels of HSA in kidney patients and provide a way towards timely treatment.

**Keywords**—zeolite imidazole framework; nanohybrid; electrochemical; sensing device; immunocomplexation

## I. INTRODUCTION

HSA is the most prevalent circulating protein in the bloodstream secreted by liver cells [1]. It prevents fluid from leaking out of bloodstream and circulates vitamins, enzymes, hormones and other substances throughout the body [2]. In chronic kidney disease, HSA may leak into the urine due to damage to the kidneys' filtering units called glomeruli. This condition is called albuminuria or proteinuria [3]. Eating adequate protein, preventing and treating infections, and maintaining good hygiene practices can also help improve HSA levels [4][5]. HSA's primary roles include transferring fatty acids, steroids, hormones, and certain medicines as well as preserving the plasma's osmotic pressure. Normal levels of HSA in healthy individuals' urine are 20 mg/L or less and 35–50 g/L in their serum [6][7]. Low levels of HSA can be a sign of chronic hepatitis, cirrhosis, and liver failure; conversely, large levels of HSA can be a sign of kidney failure [8][9]. Protein and hormone detection in

pathophysiological sample necessitates the creation of quick and trustworthy techniques for determining extremely low amounts of these analytes with high precision [10][11]. The immunocomplexation reaction possess high specificity and high sensitivity when integrated with electrochemical systems, thus immunosensors have drawn the most attention among these sensors [12]. The development of a stable combination by an antibody and an antigen is detected by immunosensors. This antigen-antibody reaction leads to change in electrochemical parameters such as potential, current, ion concentration, conductivity, or impedance [13][14]. Therefore, for the detection of HSA level in physiological samples we have designed electrochemical immunosensor because of the advantages they possess. For fabrication, Metal-organic frameworks (MOFs) are combination of both inorganic-organic crystalline materials have been explored [15][16]. MOF materials have recently explored because of their high specific surface area, configurable pore size, variety of central metals, organic ligands, and simple structure tunability [17][18]. Owing to their zeolite-like structure, ZIFs are one of these MOFs that have gained popularity and shows their potential use in various fields such as energy storage, adsorption, gas separation, catalysis, batteries, supercapacitors, and electrochemical sensors [19]. However, because most MOFs have weak electrical conductivity, there are fewer electron transfer channels, which also decreases the number of electron transfer paths on the electrode surface. To tackle the charge transport issue, it is crucial to incorporate materials with exceptional characteristics into MOFs [20]. Hence, for enhancing the signal we have incorporated multiwalled carbon nanotubes (MWCNTs) due to its outstanding qualities, including great chemical stability, a significant specific surface area, and good electrical conductivity [21][22]. Strong interfacial interactions between MOFs and MWCNTs can therefore foster reactant diffusion and charge migration, which increases the loaded components' electrochemical activity. Due to distinct characteristics of MOFs such as extremely high porosity, a large specific surface area, a customizable structure, and chemical and thermal durability can serve as immobilisation matrices. Hence, in this study we have used ZIF-67 for keeping the carboxylated MWCNTs intact on the electrode surface which further allows the immobilisation of anti-HSA antibody using carbodiimide bioconjugation. The fabricated sensor was able to

# Bimetallic Copper/Zinc Metal Organic Framework-MoS<sub>2</sub> Nanohybrid based Electrochemical Sensor

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**Abstract**— Acetaminophen is a globally used antipyretic analgesic drug to relieve pain. The excess usage of acetaminophen leads to various health implications including cardiovascular ailments, asthma, liver and kidney damage. Bimetallic MOFs are emerging materials in the field of electrochemical sensing domain utilizing the synergistic effect of both the metal ions present within. In this study, we report a sensing matrix comprising of an electrochemically fabricated novel bimetallic MOF (CoZn) conjugated with MoS<sub>2</sub> nanosheets to form an electroconductive nanocomposite. Layer-by-layer characterization of CoZn-MOF/MoS<sub>2</sub> modified electrode surface was done through different electrochemical analytical techniques like CV and EIS. The composite (GCE/CoZn-MOF/MoS<sub>2</sub>) can find its applications in sensing a plethora of analytes based on the catalytic potential of the metal nodes. In this work we have attempted the application of the developed nanocomposite probe in the electrochemical oxidation and thereby detection of acetaminophen. The developed nanocomposite was able to detect acetaminophen with enhancement in signal, proving the improved electroconductivity of the surface due to synergistic effect of CoZn-MOF and MoS<sub>2</sub>.

**Keywords**—metal organic framework; bimetallic; nanocomposite; electrochemical; sensing

## I. INTRODUCTION

Metal-organic frameworks (MOFs), often referred to 'porous coordinate polymers', are a class of recently developed porous materials that are multifunctional, crystalline compounds made up of clusters of metal ions coordinated to organic linkers to form one, two, or three-dimensional structures [1]. The high specific surface area, adjustable pore size, diversity in metal centres, organic ligands, and easy tunability in their morphology has contributed to their current significance in sensing applications [2][3]. The eminence of these structures have resulted to their potential applications in a number of industries, including batteries, supercapacitors, gas separation, adsorption, energy storage, and electrochemical sensors [4]. Contrary to this, a high electron transfer energy barrier of these materials when

synthesized through a variety of routes, including the most common solvothermal one makes their usage challenging in electrochemical biosensing [5]. A novel way to tackle this problem could be incorporation of a second metal ion in the MOF's lattice nodes or doping with a highly conductive metal within the MOF cavity or the sensor matrix. The first approach is a lesser transversed route that can be explored to achieve the synergistic effect of metal nodes in the developed bimetallic MOF. This could possibly be induced by lattice distortions, interfacial electronic coupling interactions, and increased porosity through combinational effects between distinct metal ions. Bimetallic MOFs are useful for catalyzing electron transfer-driven reactions because of their exposed active sites and great stability [6][7]. The common method of MOF synthesis can be replaced by electrodeposition-based methods which have been explored in recent times [8]. A range of bimetallic MOFs based on Ni/Cu catalytic bimetals [9], Cu/Co [10] for glucose, Fe/Ni for dopamine [11], Co/Ni for miRNA 126 [12], Cu/Ce for malathion [13], Mn/Fe for organophosphates [14], Ag/Zn for HCV-RNA [14] have been reported for a range of target analytes belonging to varied molecular strata. These research findings preach that bimetallic MOF are becoming one of the major areas which need to be explored more to utilize the potential lies in bimetallic MOFs for electrochemical sensing.

Acetaminophen is an antipyretic analgesic medication that is extensively used globally to relieve mild to moderate pain brought on by post-operative treatments, arthritis, headaches, and back pain [15][16]. Furthermore, it lowers fever in cases of viral and bacterial illnesses. An appropriate dosage of acetaminophen has no negative side effects; however, exceeding beyond this limit might result in a build-up of toxic acetaminophen metabolites, which can induce a variety of adverse effects, including skin rashes, pancreatic inflammation, hepatotoxicity, and nephrotoxicity. Specifically, the latter two effects may cause harm to the human body's kidneys and liver [17]. Numerous techniques, including titrimetry, UV-vis spectrophotometry, spectrofluorometry, and high-resolution liquid chromatography, have been used to measure acetaminophen in biological fluids, wastewater, and pharmaceutical formulations [18][19]. The evaluations become more challenging because of high expenses, prolonged processing time, and complex sample preparation requirements.



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## REVIEW

BIOTECHNOLOGY  
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# Design and development of opto-electrochemical biosensing devices for diagnosing chronic kidney disease

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**Abstract**

Chronic kidney disease (CKD) is emerging as one of the major causes of the increase in mortality rate and is expected to become 5th major cause by 2050. Many studies have shown that it is majorly related to various risk factors, and thus becoming one of the major health issues around the globe. Early detection of renal disease lowers the overall burden of disease by preventing individuals from developing kidney impairment. Therefore, diagnosis and prevention of CKD are becoming the major challenges, and in this situation, biosensors have emerged as one of the best possible solutions. Biosensors are becoming one of the preferred choices for various diseases diagnosis as they provide simpler, cost-effective and precise methods for onsite detection. In this review, we have tried to discuss the globally developed biosensors for the detection of CKD, focusing on their design, pattern, and applicability in real samples. Two major classifications of biosensors based on transduction systems, that is, optical and electrochemical, for kidney disease have been discussed in detail. Also, the major focus is given to clinical biomarkers such as albumin, creatinine, and others related to kidney dysfunction. Furthermore, the globally developed sensors for the detection of CKD are discussed in tabulated form comparing their analytical performance, response time, specificity as well as performance in biological fluids.

**KEYWORDS**

biosensing device, clinical biomarkers, electrochemical, Kidney dysfunction, nanobioengineering, optical

## 1 | INTRODUCTION

Chronic kidney disease (CKD) has emerged as one of the major health issues in which an individual's kidney is unable to perform its function (Anon, 2017). It has affected >10% of the human population which accounts for around 800 million people (Anon, 2009; Anon, 2019). In the last 20 years, an exponential increase in the number of deaths have been recorded worldwide. According to Kidney International reports, it will become the fifth major cause of death worldwide by the year 2050 (Kovesdy, 2022). One of the major concerns relating to CKD is that its cases are increasing in children which is becoming a

major public health issue. In one of the studies, it was found that there is a 30 times increase in mortality rate which severely affects "life quality" of children (Bates et al., 2014; Haffner, 2020). Most of the children depend on dialysis or a kidney transplant for their survival which is not simply accessible in developing and under-developed nations. Other major issues with CKD are the prevalence of other serious health conditions like cardiovascular diseases, depression, anxiety, and diabetes (Alshelleh et al., 2022; Jankowski et al., 2021). In a recent study, the risk associated with CKD and outcomes after coronary artery bypass surgery was established (Nowrouzi et al., 2022). These risk factors have increased social and

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Review

# Nanobioengineered Sensing Technologies Based on Cellulose Matrices for Detection of Small Molecules, Macromolecules, and Cells

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**Abstract:** Recent advancement has been accomplished in the field of biosensors through the modification of cellulose as a nano-engineered matrix material. To date, various techniques have been reported to develop cellulose-based matrices for fabricating different types of biosensors. Trends of involving cellulosic materials in paper-based multiplexing devices and microfluidic analytical technologies have increased because of their disposable, portable, biodegradable properties and cost-effectiveness. Cellulose also has potential in the development of cytosensors because of its various unique properties including biocompatibility. Such cellulose-based sensing devices are also being commercialized for various biomedical diagnostics in recent years and have also been considered as a method of choice in clinical laboratories and personalized diagnosis. In this paper, we have discussed the engineering aspects of cellulose-based sensors that have been reported where such matrices have been used to develop various analytical modules for the detection of small molecules, metal ions, macromolecules, and cells present in a diverse range of samples. Additionally, the developed cellulose-based biosensors and related analytical devices have been comprehensively described in tables with details of the sensing molecule, readout system, sensor configuration, response time, real sample, and their analytical performances.

**Keywords:** nanobioengineering; cellulose; matrix design; biosensors; cytosensing; human health

## 1. Introduction

Cellulose is a biopolymer of  $\beta$ -1,4 D-glucose units, a widely used biomaterial that exhibits unique properties and is used in various industries including textiles, electronics, biomedical, etc. [1]. Cellulose is the most commonly occurring biomaterial on earth [2], obtained mainly from different plant species [3] and some form of bacteria [4], i.e., *Acetobacter xylinum* [5]. Glucose molecules are bonded with van der Waal forces and hydrogen bonding to form a parallel stacking of cellulose microfibrils into crystalline cellulose [6]. Due to its structural form, cellulose exhibits unique properties such as high young's modulus, biocompatibility, biodegradability, high mechanical strength, transparency, and thermal stability, which allows high chemical modifications [7–9]. As well as appealing piezoelectricity, mechanical performance, dielectricity, and convertibility [10] have also been recorded. Cellulose has its application in a broad range of fields, such as in the pharmaceutical industry for coating of tablets, pellets, beads, granules [11], and in various other industries [12]. In addition to this, cellulose has also been widely used in the immobilization of different molecules, in wound healing, tissue engineering [13–15], and also has tremendous applications in flexible printed bioelectronics [16]. In recent times, further modification of cellulose with the nanostructures leads to its application as a matrix material for biosensor fabrication, which is generally called “nanocellulose”. Nanocellulose is a sustainable, renewable, and



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Review Article

## Engineered nanomaterial based implantable MicroNanoelectrode for *in vivo* Analysis: Technological advancement and commercial aspects

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## ARTICLE INFO

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## ABSTRACT

*In vivo* monitoring of essential biomolecules is crucial to address numerous critical diseases such as diabetes, cancer, and different neurological disorders that require continuous, rapid, and trace level recognition. In recent years, implantable biosensors conjugated with different kinds of nanomaterials are being used for *in vivo* detection as it supports minimal tissue invasion. Considering nanomaterials to design advanced *in vivo* biosensors has shown a substantial effect on imaging, diagnostics, and therapeutics. Nanomaterials i.e., nanoparticles, carbon fibers, dendrimers, quantum dots and nano-conjugates, have offered better biocompatibility, sensitivity, selectivity, and low detection limit to these *in vivo* opto-electrochemical biosensing platforms. In this article, the deployment of different kinds of nanomaterial for the fabrication of various *in vivo* sensors have been elaborated and discussed with various examples. Types of nanomaterial, analytes, mechanism, microelectrode dimensions, transduction system, testing model, and analytical details of such *in vivo* nano/micro sensors have been tabulated in detail. This article aims to provide a broader perspective regarding *in vivo* micronano sensors as in recent times, more interest has grown towards specified and real time detection in clinical settings. Various commercially available devices for *in vivo* monitoring have also been discussed. Major challenges during experimentation and their possible confronting strategies have also been depicted vividly.

## 1. Introduction

There is currently enormous and growing demand of *in vivo* micronano sensors towards the future generation of sensing mechanisms especially in the medical-healthcare domain. *In vivo* biosensors have great potential in disease diagnosis at an early stage in a continuous manner. Such biosensors detect the changes in concentration of a particular analyte which are not visible at tissue level initially but when the changes start occurring within the cells. Thus, continuous monitoring of an individual's health can broaden our understanding of even a small change from the normal condition [1]. *In vivo* biosensors are used for continuous real-time monitoring of target molecules in the animal/plant models. The traditional methods of diagnosing severe human health issues are typically time consuming and sometimes take up to several weeks for proper diagnosis, that would eventually affect the severity of the disease [2,3]. Moreover, traditional methods require well maintained, high-end labs, and are labor-intensive which strictly

implements the detailed established procedures [4,5]. For the first time in 1956, the idea of biosensor was proposed by Clark for developing a biosensor probe [6]. Biosensors are analytical devices which detects the changes in various forms of signals including electrical, thermal, optical and others [7,89]. It comprises of the following components: biorecognition element, transducer, amplifier, and detector [10–12]. It may also incorporate a biomimic as the recognition molecule which can be integrated with a transducing microsystem [13,14]. Biosensors can be categorized on the basis of type of biorecognition elements as bio-complexing, bio-catalytic, and on the type of receptor used such as DNAsensors, genosensor, immunosensors, aptasensors, enzymesensor, etc [15–19]. An appealing and one of the most crucial application of biosensors could be detecting the biomolecules and chemicals inside the organism. Such types of biosensors are majorly implantable in animal/plant body as a partially or fully introduced form in a way that cause minimum tissue invasion [20,21]. For developing implantable *in vivo* micronano biosensors, it is required to have specialized integrated

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# Nano-bio-engineered silk matrix based devices for molecular bioanalysis

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## Abstract

Silk is a fibrous protein, has been a part of human lives for centuries, and was used as suture and textile material. Silk is mainly produced by the members of certain arthropods such as spiders, butterflies, mites, and moths. However, recent technological advances have revolutionized silk as a biomaterial for various applications ranging from heat sensors to robust fibers. The biocompatibility, mechanical resilience, and biodegradability of the material make it a suitable candidate for biomaterials. Silk can also be easily converted into several morphological forms, including fibers, films, sponges, and hydrogels. Provided these abilities, silk have received excellent traction from scientists worldwide for various developments, one of them being its use as a bio-sensor. The diversity of silk materials offers various options, giving scientists the freedom to choose from and personalize them as per their needs. In this review, we foremost look upon the composition, production, properties, and various morphologies of silk. The numerous applications of silk and its derivatives for fabricating biosensors to detect small molecules, macromolecules, and cells have been explored comprehensively. Also, the data from various globally developed sensors using silk have been described into organized tables for each category of molecules, along with their important analytical details.

## KEYWORDS

biomaterial, biomolecular detection, biosensor, sericin, silk fibroin

## 1 | INTRODUCTION





Biomaterials (or bio-based materials), by definition, are materials that interact with the biological system as a part of fabricated systems to perform certain desired functions in a safe, reliable, and economical way (Park & Lakes, 2007; Srivastava et al., 2015). Since biomaterials interact directly with living tissues, it is crucial to understand their properties before any application. Based on properties such as biocompatibility, chemical stability, mechanical resilience, and biodegradability, biomaterials find various uses in several industries (Bandyopadhyay et al., 2019). The disposal of electronic devices has posed a massive risk to the environment because of the use of

nonbiodegradable materials; hence, biomaterials have easily entered the field of electronics and biosensors (Sun et al., 2018). They have been fabricated to be used for a wide array of applications which includes monitoring human and robot motion (He et al., 2017), solar cells (Li et al., 2020; Nie et al., 2014; Xiong et al., 2021), drug delivery (Ahsan et al., 2018; Anon, 2020; Zhang et al., 2012), and sensors (Bhatnagar et al., 2018; Chandra et al., 2011; Noh, Chandra, Ok Moon, et al., 2012; Zhu, Chandra, Song, et al., 2012). Having learned the advantages of biomaterials over the traditionally used non-biodegradable materials like synthetic polymers and plastics, the search for new, better, and greener biomaterials have been a hot topic among researchers. Herein, we will focus on one of the most

Aditi Sammi and Divya contributed equally to this study.

Review

# Ultrasensitive Aptasensors for the Detection of Viruses Based on Opto-Electrochemical Readout Systems

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**Abstract:** Viral infections are becoming the foremost driver of morbidity, mortality and economic loss all around the world. Treatment for diseases associated to some deadly viruses are challenging tasks, due to lack of infrastructure, finance and availability of rapid, accurate and easy-to-use detection methods or devices. The emergence of biosensors has proven to be a success in the field of diagnosis to overcome the challenges associated with traditional methods. Furthermore, the incorporation of aptamers as bio-recognition elements in the design of biosensors has paved a way towards rapid, cost-effective, and specific detection devices which are insensitive to changes in the environment. In the last decade, aptamers have emerged to be suitable and efficient biorecognition elements for the detection of different kinds of analytes, such as metal ions, small and macro molecules, and even cells. The signal generation in the detection process depends on different parameters; one such parameter is whether the labelled molecule is incorporated or not for monitoring the sensing process. Based on the labelling, biosensors are classified as label or label-free; both have their significant advantages and disadvantages. Here, we have primarily reviewed the advantages for using aptamers in the transduction system of sensing devices. Furthermore, the labelled and label-free opto-electrochemical aptasensors for the detection of various kinds of viruses have been discussed. Moreover, numerous globally developed aptasensors for the sensing of different types of viruses have been illustrated and explained in tabulated form.

**Keywords:** aptamers; viral infection; COVID-19; human health; digital health; biosensor



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## 1. Introduction

According to the World Health Organization, hundreds of millions of people have viral infections every year, with millions of death worldwide [1]. Figure 1A illustrates the the outbreak of few major viral infections that have created havoc in the human population over the past few centuries. The current situation of the COVID-19 pandemic has brought scientist's focus towards infectious diseases caused by viruses. The ongoing pandemic by novel SARS-CoV-2 has reported more than 284 million infections and claimed around 5.4 million deaths [2]. In addition to this, various other viruses, such as HIV, Dengue, Zika, Ebola, West Nile, etc., lead to a large number of human infections and deaths. Therefore, simple, fast, accurate, and specific diagnostic techniques are in great demand for the early diagnosis, prognosis and surveillance of diseases, by targeting particular biomarkers/target sites. There are some reliable techniques which exist for virus detection such as cell culture, hemagglutination inhibition test, immuno-complexation, etc [3,4]. Furthermore, with advancement in technology, a few other techniques, for instance, ELISA, RIA, serological and PCR methods, have also been employed for virus detection [5,6]. However, these methods are costly, time consuming, and require laboratory infrastructure and skilled personnel. In contrast to these methods, point-of-care (POC) diagnostic tools have attracted



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## N-acetyl-D-glucosamine decorated nano-lipid-based carriers as theranostics module for targeted anti-cancer drug delivery

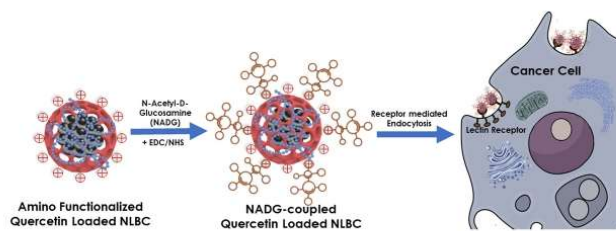
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### HIGHLIGHTS

- N-acetyl-D-glucosamine coupled quercetin-loaded nano lipid-based carrier (NADG-Q-NLBCs) has been constructed.
- The fabricated nanobioconjugate NADG-Q-NLBCs was characterized using several methods.
- The NADG-Q-NLBCs facilitate the controlled drug dissociation for long period in *in vitro* model.
- The developed nanocarrier enhanced the cellular uptake through receptor-mediated cell engulf.

### GRAPHICAL ABSTRACT



### ARTICLE INFO

**Keywords:**  
Material engineering  
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Cancer theranostics

### ABSTRACT

The present investigation was carried out to engineer N-acetyl-D-glucosamine (NADG) coupled quercetin-loaded (Q) nano-lipid-based carriers (NADG-Q-NLBCs) to target breast cancer. The constructed nano-bioconjugate was characterized by various techniques, and the *in vitro* drug release profiles were examined using zero and first-order kinetic models. The characterization data confirmed the morphology, size, charge distribution, crystallinity, and chemical interactions among the various moieties of the nano-bioconjugate. Further, the synthesized NADG-Q-NLBCs were applied to target the human breast cancer cells (MCF-7), which interestingly showed a more cytotoxic effect compared to the lone NLBCs and free Quercetin. The flow cytometry study confirmed NADG-Q-NLBCs induced apoptosis in MCF-7 cells in a targeted manner. The percentage of early apoptotic cells was found to be 25% in the case of NADG-Q-NLBCs, which is almost 2.5 times higher than the Q-NLBCs. However, the number of viable cells reached the maximum when treated with NLBCs. The present investigation suggests that the constructed nano-bioconjugate could be a capable carrier of drugs with sustained pharmacokinetics and improved physicochemical properties.

### 1. Introduction

Poor solubility, bioavailability, physiological, physicochemical, and pharmaceutical barriers are major problems allied with free drugs. Besides these limitations, multiple drug resistance is a major challenge

associated with them. All these limitations could be overcome through the novel material-based system comprising a ligand-based liposomal formulation of drugs, which has shown great promise in recent years [1]. Ligand-based drug delivery construct has the potential to accumulate more drugs inside the targeted cells through receptor-mediated

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# Shifting paradigm in electrochemical biosensing matrices comprising metal organic frameworks and their composites in disease diagnosis

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## Abstract

Metal Organic Frameworks (MOFs) are an evolving category of crystalline microporous materials that have grabbed the research interest for quite some time due to their admirable physio-chemical properties and easy fabrication methods. Their enormous surface area can be a working ground for innumerable molecular adhesions and site for potential sensor matrices. They have been explored in the last decade for incorporation in electrochemical sensor matrices as diagnostic solutions for a plethora of diseases. This review emphasizes on some of the recent advancements in the area of MOF-based electrochemical biosensors with focus on various important diseases and their significance in upgrading the sensor performance. It summarizes MOF-based biosensors for monitoring biomarkers relevant to diabetes, viral and bacterial sepsis infections, neurological disorders, cardiovascular diseases, and cancer in a wide range of real matrices. The discussion has been supplemented with extensive tables elaborating recent trends in the field of MOF-composite probe fabrication strategies with their respective sensing parameters. The article sums up the future scope of these materials in the field of biosensors and enlightens the reader with recent trends for future research scope.

This article is categorized under:

Diagnostic Tools > Biosensing

Diagnostic Tools > Diagnostic Nanodevices

## KEYWORDS

diagnosis, disease, electrochemical biosensors, metal organic frameworks, nanobioengineering

## 1 | INTRODUCTION

In recent times, the convergence of nanotechnology, materials science, and bioengineering has led to revolutionary progress in the advancement of biosensors, heralding a new age of accurate diagnosis and personalized healthcare (Borse et al., 2022; Chandra & Prakash, 2020; Huang, Zhu, & Kianfar, 2021). The increasing worldwide prevalence of infectious and fatal diseases, including those that can be transmitted and others that cannot, highlights the dire need for diagnostic methods that are simple, fast, accurate, and affordable (Mahato et al., 2016). Conventional



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Review

## Antibody-receptor bioengineering and its implications in designing bioelectronic devices

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Bioengineered antibody fragments  
Biosensors  
Bioreceptors  
Clinical diagnostics  
Nanobodies  
Healthcare  
Antibodies  
Antigen-antibody complex

### ABSTRACT

Antibodies play a crucial role in the defense mechanism countering pathogens or foreign antigens in eukaryotes. Its potential as an analytical and diagnostic tool has been exploited for over a century. It forms immunocomplexes with a specific antigen, which is the basis of immunoassays and aids in developing potent biosensors. Antibody-based sensors allow for the quick and accurate detection of various analytes. Though classical antibodies have prolonged been used as bioreceptors in biosensors fabrication due to their increased fragility, they have been engineered into more stable fragments with increased exposure of their antigen-binding sites in the recent era. In biosensing, the formats constructed by antibody engineering can enhance the signal since the resistance offered by a conventional antibody is much more than these fragments. Hence, signal amplification can be observed when antibody fragments are utilized as bioreceptors instead of full-length antibodies. We present the first systematic review on engineered antibodies as bioreceptors with the description of their engineering methods. The detection of various target analytes, including small molecules, macromolecules, and cells using antibody-based biosensors, has been discussed. A comparison of the classical polyclonal, monoclonal, and engineered antibodies as bioreceptors to construct highly accurate, sensitive, and specific sensors is also discussed.

### 1. Introduction

The 1980s was considered a decennium of 'enlightenment' in molecular immunology as antibodies were primitively foreseen as "magic bullets" by Paul Ehrlich in the late 19th century. His postulations described them as transporting cytotoxic agents to tumor cells [1]. Antibodies have been a dynamic tool for diagnosis, treatment, and research purposes. It is produced biologically as an element of the defense immune response when encountering a foreign substance or antigen. Owing to its dynamicity, it is considered the most frequently used diagnostic biorecognition element in biosensors [2]. Biosensors are robust and accurate analytical devices with a quick response, convenient for detecting and analyzing various biomarkers in eatables, medicinal, environmental, industrial, or pharmaceutical fields [3,4]. Until the late 1980s, antibody production was principally dependent on the immunization of experimental models such as rabbits, mice, and other

laboratory animals [5]. The immune response to an immunized antigen with multiple epitopes involves the activation of B-cells producing polyclonal antibodies. Polyclonal antibodies (pAbs) are the most basic antibodies produced with varying affinities. They can be generated in months at a low cost and require basic technical skills compared to monoclonal antibodies. On the other hand, monoclonal antibodies (mAbs) are homogeneous, monospecific, and generated by hybridoma technology [6]. However, pAbs are considered to have a superior specificity compared to mAbs because they are produced by a vast number of B-cell clones, each of which produces antibodies against a distinct epitope and also due to the presence of multiple binding sites [7].

Traditionally, the production of mAbs and pAbs is expensive, requires a range of techniques, and usually takes several months or even more. To encompass such issues, researchers have tailored antibody fragments through bioengineering to enhance their performance and

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## Review Article

Nano-bioengineered sensing technologies for real-time monitoring of reactive oxygen species in *in vitro* and *in vivo* models

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## ARTICLE INFO

## Keywords:

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Hydrogen peroxide

## ABSTRACT

Reactive oxygen species are produced as a by-product of the animal cellular metabolism and play an important function in cell signaling. Uncontrolled reactive oxygen species production is coupled with the evolution of acute diseases, namely, diabetes, cancer, tumors, cardiovascular and several neurodegenerative diseases, metabolic disorders, inflammation, and aging. Hydrogen peroxide, superoxide radicals, and hydroxyl radicals are the most frequently involved reactive oxygen species in various human diseases. Several traditional approaches such as fluorescence spectroscopy, electron spin resonance (ESR), high-performance liquid chromatography (HPLC), and mass spectrometry (MS) are available for detection of reactive oxygen species. However, these techniques have certain limitations, including a lack of miniaturization, onsite analysis, and time-consuming protocols. In the recent past, biosensing technology has emerged as the major approach for tracking the level of reactive oxygen species *in vitro* and *in vivo*. The goal of this review is to scrutinize recent biosensors for monitoring various

**Abbreviations:** ROS, Reactive oxygen species; •OH, hydroxyl; O<sub>2</sub><sup>-</sup>, superoxide; LOO<sup>•</sup>, alkoxy peroxy; ONOO<sup>-</sup>, peroxynitrite; H<sub>2</sub>O<sub>2</sub>, hydrogen peroxide; NOXs, nicotinamide adenine dinucleotide phosphate oxidases; COPD, chronic obstructive pulmonary diseases; ORR, oxygen reduction reaction; SOD, Superoxide dismutase; XOR, xanthine oxidoreductase; MAO, monoamine oxidase; NOX/DUOX, nicotinamide adenine dinucleotide phosphate oxidases/ dual oxidases; complex I, CoQ binding site; IF, FMN site; FMN site, complex II site IIF; IIIQo, complex III: site ubiquinone; ACON, aconitase; GPDH, α-glycerophosphate dehydrogenase; ETF dehydrogenase, ETF quinone oxidoreductase; ETF, Electron transfer flavoprotein; Q, oxidoreductase; PDH, pyruvate dehydrogenase; OGDH, 2-oxoglutarate dehydrogenase; UO, urate oxidase; EPHX2, epoxide hydrolase 2; CAT, catalase; Pxxs, peroxiredoxins; GST, glutathione s-transferases; ER, endoplasmic reticulum; Ero1p, Endoplasmic reticulum oxidoreductin 1p; PDI, protein disulfide isomerase; GSH, glutathione; NSCLC, non-small cell lung cancer; NF-κB, Nuclear factor-kappa light chain enhancer of activated B cells; IKK, I Kappa-κ kinase; MAPK, Mitogen-activated protein kinase; MKK3/6, mitogen-activated protein kinase kinase 3/6; MKK7, mitogen-activated protein kinase kinase 7; JNK, c-Jun N-terminal kinases; p38, p38 kinase; ARE, antioxidant response elements; Nrf2, nuclear factor erythroid 2-related factor 2; Keap1, Kelch-like ECH-associated protein 1; PI3K-Akt, phosphoinositide-3-kinase-protein kinase B; HCV, hepatitis C; NS 3, non-structural proteins 3; NSSA, non-structural proteins; α-KGDH, alpha-ketoglutarate dehydrogenase; ERK/MEK, extracellular signal-regulated kinase/mitogen-activated protein kinase kinase; COXs, cyclooxygenases; NOSs, nitric oxide synthases; CYP450, cytochrome P450; AngII, Angiotensin II; XO, xanthine oxidase; ICM, ischemic cardiomyopathy; DCM, dilated cardiomyopathy; PUFA, polyunsaturated fatty acids; ALS, Amyotrophic lateral sclerosis; IGF-1/AKT, Insulin-like growth factor (IGF)-1/protein kinase B pathways; AP-1, activator protein-1; TNF-α, tumor necrosis factor-alpha; (IL)-1b, interleukin; CFE/SWCNT/MB, carbon fiber microelectrode/single-walled carbon nanotube/methylene blue; DPV, Differential pulse voltammogram; SPECE, screen-printed carbon electrode; rGO@PDA, polydopamine encased graphene; CV, cyclic voltammetry; EIS, electrochemical impedance spectroscopy; SEED, substrate-enhanced electroless deposition; rGO, reduced graphene oxide; I-rGO, iodine nano spacer-impregnated reduced graphene oxide; Co<sub>3</sub>(PO<sub>4</sub>)<sub>2</sub>, cobalt phosphate; PEDOT, poly (3,4-ethylene dioxathiophene); SEM, scanning electron microscopy; AFM, atomic force microscopy; BSA, bovine serum albumin; TGA, thioglycolic acid; PbS QDs, PbS quantum dots; DMSA, dimercapto succinic acid; EDS, energy-dispersive X-ray spectroscopy; XPS, X-ray photoelectron spectroscopy; Co-CNT, cobalt/carbon nanotube hybrid nanocomplex; LPEG, Polyimide-laser-engraved porous graphene; GOD, glucose oxidases; FESEM, field-emission scanning electron microscopy; XRD, X-ray diffraction; TEM, transmission electron microscopy; ABTS, 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid); Mo<sub>2</sub>C@MoS<sub>2</sub>, MoS<sub>2</sub> nanosheets and Mo<sub>2</sub>C nanorods; FAGE, fluorescence assay by gas expansion; CIMS, chemical ionization mass spectrometry; ESR, spectroscopy; LIF, laser-induced fluorescence; 4-HBA, 4-hydroxybenzoic acid; MCH, 6-mercaptohexanol; HAT, 1-hexanethiol; APTMS, 3-aminopropyl trimethoxy silane; NPGL, nano porous gold layer; LDR, Linear dynamic range; LOD, limit of detection; GCE, Glassy carbon electrode; ATP, Adenosine triphosphate; LSV, Linear sweep voltammetry; AgNPs, Silver nanoparticles; NR, Not reported; MWCNTs, Multiwalled carbon nanotube; NGS, Nitrogen-doped graphene sheet; GO, Graphene oxide; ZIF-8, Zeolitic imidazolate framework-8; SDS, Sodium dodecyl sulfate; Ce-MOF, Cerium-metal organic framework; CVD, Chemical vapor deposition; pFeMOF/OMC, porphyrinic iron-based metal-organic framework/ordered mesoporous carbon; HRP, Horseradish peroxidase; GQDs, Graphene quantum dots; PET, photoinduced electron transfer; TMB, 3,3',5,5'-Tetramethylbenzidine; UCNPs, upconversion nanoparticles; mOG, modified azo dye; LRET, luminescence resonance energy transfer; GSSG, glutathione disulfide; NADP, nicotinamide adenine dinucleotide phosphate.

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E-mail address: [pranjal.bce@iitbhu.ac.in](mailto:pranjal.bce@iitbhu.ac.in) (P. Chandra).<https://doi.org/10.1016/j.microc.2022.107615>

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N-0001575513	Online Bank Transfer	0601250080229	27840.00	1475001020000001

## Annexure II

### Conferences/Symposium/Workshop attended

1. 7-day online workshop Karyashala on the "Advancements in in vitro Diagnostic methods in Healthcare" 19 – 25 July 2021 theme under [Accelerate Vigyan Scheme of DST-SERB](#).
2. 5-day Faculty Development Program, 'Smart and Functional Nanomaterials' 4 – 8th Aug 2021 at [National Institute of Technology Calicut](#).
3. **International Conference on Advanced Materials and Mechanical Characterization (ICAMM)**, 02 – 04 Dec, 2021 (virtual).
4. HEALTH 2021 Virtual Conference on "Cancer Biology: Advances and Challenges", held from 11 –13 Nov, 2021.
5. 7th **International Conference on Advanced Nanomaterials and Nanotechnology**, 14 –17 Dec, 2021.
6. **3rd Indian Materials Conclave (IndMac) and 32nd Annual General Meeting of MRSI**, 20 – 23 Dec, 2021.
7. Bionsangam 2022, **International Conference on 'Emerging Trends in Biotechnology'**, 10 – 12 March, 2022.
8. **International Conference on Electrochemistry for Industry, Health, and Environment**, EIHE–2023, 7 – 11 Feb, 2023, at [BARC, Mumbai](#).
9. 5-day workshop on "Computer Aided Drug Design and Structural Bioinformatics (CADD SB – 2023)", 13 – 17 March, 2023, at [IIT-BHU](#).
10. BioHeal-2023, **International Conference on Biomaterial and Health Care**, 13 – 16 April, 2023, at Rishikesh, organized by [IIT Roorkee](#).
11. **IEEE SENSORS 2023**, international conference held at [Vienna, Austria](#) from Oct 29 – Nov 01, 2023. (**Best young professional poster award**)

12. **Indo-Japan Symposium on Nanotheranostics** (InJaNa 2024), 23 – 25 Apr, 2024, at **IIT Roorkee. (Best oral presentation award)**
13. The **4<sup>th</sup> International Electronic Conference on Biosensors**, 20 – 22 May, 2024.
14. **IEEE BIOSENSORS 2024**, international conference held at Hinxton Hall, **Cambridge, UK** from 28 – 30 July, 2024.
15. **International Conference on Electrochemical Science and Technology (ICONEST) – 2024** at **CSIR-NPL, New Delhi** from 18 – 20 Sept, 2024.
16. **International Conference on Electrochemistry for Industry, Health and Environment, EIHE–2025** at **BARC, Mumbai** from 21– 25 Jan, 2025. (**Best poster presentation award**)
17. **35th Anniversary World Congress on Biosensors** from 19 – 22 May 2025 at **Lisbon, Portugal.**

## Annexure III

### Awards and Recognitions

#### PMRF ANNUAL REVIEW COMMENTS

**Name:** Divya  
**PMRF ID:** 1101114  
**Institute Name:** IIT BHU  
**Broad Area:** 10-Interdisciplinary areas in  
Science and Engineering including  
Indian Knowledge Systems



**May 2024 Review Comments:** 1. Recommended with commendation

**May 2024 Detailed Review Comments:** Ms. divya gave a presentation on chronic kidney disease and development of nanoengineered point of care device for its diagnostic. She talked about how paper can be used for such diagnostic application. She has published three papers in the last one year. She has also attended a few national and international conferences. Divya's basic concepts are clear. Overall, the committee was very happy with her progress for this year. Committee suggested that she can perhaps think about using mobile phones in replacing the device she is building. She should also think about increasing the shelf life for greater use in the field. She has also completed all her TA duties and uploaded the proof on the portal.

Completed my PMRF tenure with  
**Recommended with Commendation**  
(highest grade)



शिक्षा मंत्रालय  
MINISTRY OF  
EDUCATION

**P M R F**

Prime Minister's Research Fellows



**Gandhian Young Technological Innovation (GYTI) Award 2023** for “Paper-based point of care device for chronic kidney disease diagnosis” conferred by **Prof. Ajay Kumar Sood, Principal Scientific Advisor, Government of India** on 5<sup>th</sup> of November, 2024 at India International Centre, New Delhi.



**Best YP (Young Professional) Poster Award** at **IEEE SENSORS 2023** held at **Vienna, Austria** from October 29 to November 01, 2023.



**International Travel Award** by DST-SERB and CSIR to attend IEEE SENSORS 2023.



Science and Engineering Research Board (SERB)  
Department of Science and Technology (DST)  
Govt. of India



**Best Oral Presentation Award** at InJaNa held at IIT Roorkee from April 23-25, 2024.



**Best Presentation Award** at EIHE-2025 held at BARC, Mumbai from Jan 21-25, 2025.

**Annexure IV**

# Media Coverage

## IIT-BHU develops paper microchip for quick kidney disease detection

By **Sudhir Kumar** X, Varanasi

Nov 09, 2024 05:54 AM IST

Creatinine is measured via a smartphone-based imaging system, while albumin levels are assessed with an indigenously developed 3D-printed cascade, according to a press statement from IIT-BHU.



Left to Right: Prof Pranjal Chandra, Divya, PhD Scholar, and IIT-BHU Director Prof Amit Patra with the Gandhian Young Technological Innovation (GYTI) Award. (HT)

THE TIMES OF INDIA

## IIT (BHU) researcher wins GYTI Award

TNN | Nov 8, 2024, 09:51 PM IST

Varanasi: In a remarkable achievement, Divya, a PhD student under the mentorship of Prof Pranjal Chandra at the School of Biochemical Engineering, Indian Institute of Technology (IIT) BHU Varanasi, bagged the prestigious Gandhian Young Technological Innovation (GYTI) Award 2023 on Nov 5, at the India International Centre in New Delhi. She received this award for developing a groundbreaking paper-based micro device designed to diagnose kidney health.

Prof Ajay Kumar Sood, principal scientific advisor to the Govt of India, presided over the award ceremony. Distinguished attendees included R A Mashelkar, former director general of CSIR, Renu Swarup, former secretary of the department of Biotechnology (DBT), Govt of India, Prof T G Sitharam, chairman of the All India Council for Technical Education (AICTE), Prof P V M Rao, founder of the Honey Bee Network, and president of SRISTI Innovations.

## IIT-BHU develops CKD diagnostic tool

PHOTO: IIT BHU

Chronic kidney disease (CKD) has emerged as a global health crisis, affecting over 100 million people worldwide, or more than 10 per cent of the global population. The alarming rise in CKD-related mortality, recording a 42 per cent increase over the past two decades, has drawn attention to the urgent need for early diagnosis and treatment. CKD is now poised to become the fifth leading cause of death by 2040, as reported by the Global Burden of Disease Study. While factors such as cardiovascular conditions and pregnancy complications in women exacerbate kidney disease, developing nations are struggling with the financial burden of managing this growing epidemic. Despite no current cure for CKD, dialysis and kidney transplants remain the only viable options, both of which are difficult to access in many low-income countries. Researchers at the Indian Institute of Technology (IIT) BHU have developed a game-changing diagnostic tool aimed at addressing these challenges. Led by Divya, a PhD scholar, and Prof Pranjal Chandra from the School of Biochemical Engineering, the team has created a cost-effective paper



IIT-BHU scholar Divya with GYTI Award

microchip device designed for point-of-care testing of kidney health. The platform also underwent extensive validation using human serum matrices, and findings have been published in prestigious journals including ACS Biomaterials Science and Engineering by the American Chemical Society. Prof Chandra also explained that this is an integrated system and a platform technology that can be easily adopted for different markers for molecular detection in precision medicine. Divya wins award. Meanwhile, in a remarkable achievement, Divya was honoured with the prestigious Gandhian Young Technological Innovation (GYTI) Award 2023 at the India International Centre in New Delhi recently for developing the paper-based micro device designed to diagnose kidney health. Prof Chandra emphasised that this development aims to bridge the gap in healthcare access, particularly in primary healthcare centres, where resources are limited. Unlike conventional testing methods that require sophisticated instruments and long waiting times, this device delivers results in under 10 minutes, making it timely and efficient for early detection of

indicator of kidney function, is measured using a smartphone-based imaging system, while albumin levels are assessed using an indigenously developed 3D-printed cascade. The system incorporates a smartphone-based image processing software that automatically processes results, providing a clear 'green' or 'red' indication for healthy individuals and those with kidney disease. Dr Indrani Nandi, a DST National Postdoctoral Fellow under Prof Chandra's mentorship, and Nachiket Mendki, a BTech stu-

Thumbnail for IIT-BHU develops low-cost microchip for diagnosis of chronic kidney disease. Includes text: Varanasi: The research scholars at the Indian Institute of Technology (IIT) BHU, Varanasi, developed a game-changing diagnostic tool aimed at addressing the challenges of chronic kidney disease (CKD). Prof Pranjal Chandra from the School of Biochemical Engineering, who, along with a PhD student Divya, led the team. Chandra said that CKD emerged as a global health crisis, affecting over 100 million people worldwide, or more than 10% of the global population. The alarming rise in CKD-related mortality, recording a 42% increase over the past two decades, drew attention to the urgent need for early diagnosis and treatment. CKD is now poised to become the fifth leading cause of death by 2040, as reported by the Global Burden of Disease Study. While factors such as cardiovascular conditions and pregnancy complications in women exacerbate kidney disease, developing nations are struggling with the financial burden of managing this growing epidemic. Despite no current cure for CKD, dialysis and kidney transplants remain the only viable options to access in many low-income countries. He said that the team created a cost-effective paper microchip device designed for point-of-care testing of kidney disease. This novel solution could revolutionise kidney disease detection, offering a simpler, faster, and more affordable alternative to tra-

## IIT-BHU develops low-cost microchip for diagnosis of chronic kidney disease

TNN / Nov 8, 2024, 21:54 IST

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Varanasi: The research scholars at the Indian Institute of Technology (IIT) BHU, Varanasi, developed a game-changing diagnostic tool aimed at addressing the challenges of chronic kidney disease (CKD).

## IIT BHU Researchers Develop Low-Cost Diagnostic Tool for Early Detection of CKD

HEALTH TECH

Written by: Jayati Dubey November 11, 2024

## Varanasi News : किडनी के रोगों की जांच करेगी IIT BHU की पेपर माइक्रोचिप डिवाइस, जानें कैसे करेगा काम

अमर उजाला नेटवर्क, वाराणसी। Published by: अमन विश्वकर्मा Updated Fri, 08 Nov 2024 02:42 PM IST

## Biography



Divya is a Prime Minister Research Fellow at the School of Biochemical Engineering, Indian Institute of Technology (BHU) Varanasi. She has completed her M.Tech in Biotechnology from the Department of Biosciences and Bioengineering, Indian Institute of Technology Guwahati, where she worked on cellulose degradation using the novel isolation of fungi from Deepor Beel, a Ramsar site in Assam. She has also done her B.Tech in Biotechnology from the College of Biotechnology, Sardar Vallabhbhai Patel University of Agriculture and Technology, Meerut, where she worked on the detection of begomovirus associated with leaf curl disease.

She is working on the development of biosensing devices for affordable diagnosis, specially targeting the remote/primary healthcare centres. During her PhD tenure, her major focus is on the development of affordable diagnosis for kidney disease diagnosis. She has contributed to more than 20 peer-reviewed articles, 2 book chapters, and 1 patent during her PhD tenure. She has also received a few awards for her work on simple and affordable chronic kidney disease diagnosis devices, including the Gandhian Young Technological Innovation Award, which was awarded by the Principal Scientific Advisor, Government of India.