DEVELOPMENT OF CARBON NANOTUBE-BASED BIOSENSORS FOR MULTI-CONCENTRATION GLUCOSE DETECTION

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DEVELOPMENT OF CARBON NANOTUBE-BASED BIOSENSORS FOR MULTI-CONCENTRATION GLUCOSE DETECTION

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This report is submitted in partial fulfilment of the requirements for the degree of Bachelor of Electronics Engineering Technology (Telecommunications) with Honours

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DEDICATION

To my beloved mother, Rohana binti Omar, and father, Suhaimi bin Sukiran, whose unwavering support, sacrifices, and love have been my greatest source of strength and inspiration.

and

To my friend , Farzana Syafiah whose encouragement and companionship have made this journey truly meaningful, thank you for standing by my side.

Your belief in me has fueled my determination, and this accomplishment would not have been possible without your presence in my life.

ABSTRACT

In the In developing nanoelectronic biosensors for glucose detection, nanomaterials like carbon nanotubes (CNTs) or graphene are commonly used as sensing elements. Functionalizing these nanomaterials with biomolecules, such as enzymes, enhances selectivity by forming specific bonds with glucose molecules. The interaction between glucose and biomolecules induces changes in the electrical properties of the nanomaterial, assessed using techniques like electrochemical impedance spectroscopy or cyclic voltammetry. However, challenges such as detection limits, time, and specificity remain.This study employs a methodical biosensor fabrication approach, incorporating glucose oxidase (GOx) for enzymatic detection and EDC/NHS chemistry for immobilization. The morphological characteristics of GOx/EDC-NHS/PPy-MWCNT composites on gold and indium tin oxide (ITO) electrodes were examined using field emission scanning electron microscopy (FESEM). To meet the demand for highly sensitive and specific biosensors, this study optimizes multiwalled carbon nanotube (MWCNT)-based biosensors for glucose detection across concentrations, achieving detection limits of 0.5 mM and 1.0 mM. A polypyrrole (PPy)/MWCNT nanofilm was fabricated via the chronoamperometry method using an AutoLAB potentiostat with NOVA 2.0 software for electrodeposition and cyclic voltammetry. FESEM analysis revealed a uniform distribution of nanostructures with average particle sizes of 45±5 nm for gold composites and 62±7 nm for ITO composites.For chronoamperometry, gold and ITO electrodes were sonicated in MWCNT for three hours and mixed with a PPy solution. Cyclic voltammetry in PBS solution at a scan rate of 50 mV/s (potential window: -0.8V to +0.4V) showed currents of 2.89 mA in PBS, 3.072 mA in 0.5 mM glucose, and 3.29 mA in 1 mM glucose for the gold electrode. Corresponding ITO electrode currents were 0.052 mA, 0.054 mA, and 0.071 mA. In conclusion,these findings confirm successful glucose detection, demonstrating the biosensor's effectiveness.This study advances biomedical diagnostics by creating a robust, MWCNT-based biosensor with remarkable sensitivity and stability. Optimized polymer coatings and nanoparticle integration improve performance, offering a potential alternative to traditional glucose monitoring with enhanced accuracy and reliability.

ABSTRAK

Dalam pembangunan biosensor nanoelektronik untuk pengesanan glukosa, pendekatan biasa melibatkan penggunaan bahan nano seperti tiub nano karbon atau graphene sebagai unsur penderiaan. Bahan nano ini selalunya difungsikan dengan biomolekul, seperti enzim, untuk meningkatkan selektiviti dengan membentuk ikatan khusus dengan molekul glukosa. Interaksi antara glukosa dan biomolekul mendorong perubahan dalam ciri elektrik bahan nano, yang boleh dinilai melalui teknik seperti spektroskopi impedans elektrokimia atau voltammetri kitaran. Walau bagaimanapun, pembangunan biosensor menghadapi cabaran yang berkaitan dengan had pengesanan, masa pengesanan dan kekhususan. Kerja ini memberi tumpuan kepada mencipta nanofilem Polypyrrole (PPY)/Multiwalled Carbon Nanotube (MWCNT) menggunakan teknik chronoamperometry untuk memenuhi matlamat untuk sistem biosensor yang berkesan dengan kepekaan dan kekhususan yang tinggi. Oleh itu, elektrodeposisi dan voltammetri kitaran nanofilem yang direka akan dijalankan menggunakan potensiostat AutoLAB dengan perisian NOVA 2.0 AutoLAB. Pencirian nanofilem akan dijalankan melalui spektroskopi inframerah transformasi Fourier (FTIR), dan mikroskop elektron pengimbasan pelepasan medan (FE-SEM) dirancang untuk menganalisis morfologi dan sifat bahan. Juga simulasi telah dijalankan dalam perisian COMSOL Multiphysics untuk menganalisis sistem biologi dan memodelkan isu kejuruteraan dan fizik yang kompleks. Semasa proses sonication, substrat kaca diletakkan di dalam bikar yang mengandungi etanol dan tertakluk kepada sonication selama 10 minit. Ini berkesan menghilangkan kekotoran dan bahan cemar daripada substrat. Selepas sonication, substrat dikeluarkan dengan teliti daripada pelarut dan dibiarkan kering selama 5 minit sebelum meneruskan proses seterusnya. Seterusnya, substrat menjalani proses salutan menggunakan mesin sputtering. Ia pertama kali disalut dengan kromium selama 1 minit pada arus 100 mA. Selepas ini, substrat disalut dengan emas dalam mesin sputtering selama satu minit lagi pada arus yang sama 100 mA. Perisian Multifizik COMSOL digunakan untuk mensimulasikan keputusan awal kepekatan berbilang untuk biosensor pengesanan glukosa. Kesimpulannya, kajian ini menawarkan panduan berharga untuk mencipta filem berstruktur nano yang licin pada pelbagai substrat, meningkatkan pengesanan glukosa berbilang kepekatan dengan kepekaan dan kekhususan yang tinggi, dan membolehkan pemantauan masa nyata yang berkesan dalam peranti fleksibel dan boleh pakai.

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TABLE OF CONTENTS

PAGE

LIST OF TABLES

LIST OF FIGURES

CHAPTER 1

INTRODUCTION

1.1 Background

Carbon nanotubes (CNTs) have emerged as a promising material for the development of nanoelectronics biosensors for glucose detection, with several studies highlighting their potential in this area. CNT-based biosensors have been shown to offer excellent reproducibility, good anti-interference properties, and successful testing in complex biological fluids such as blood serum [3][4].

CNT-based biosensors typically rely on the interaction of CNTs with specific enzymes such as hexokinase or glucose oxidase (GOX) to generate amperometric signals in response to glucose concentration [2]. The conductive properties of CNTs amplify the signal of the analyte, while the enzyme layer provides selectivity to the biosensor. Dehydrogenases and oxidases are commonly used enzymes that generate H2O2, leading to the excitation of electrons at a certain potential, which is the signaling mechanism of a biosensor [2].

One of the advantages of CNT-based biosensors is their high sensitivity, with some studies reporting detection limits as low as 1 pM [1]. Additionally, CNT-based biosensors have shown excellent results in the detection of viruses such as Influenza A and SARS-CoV-2[2]. For example, HNO3 functionalized CNTs on which influenza virus DNA was immobilized for detection of influenza A are proposed, while a selective, very sensitive, and quantifiable CNT-FET-based antibody functionalized biosensor for SARS-CoV-2 S1 antigen detection in the buffer solution [2].

CNT-based biosensors have also been shown to promote electron transfer reactions, making them suitable for a broad range of applications such as glucose biosensors, protein sensors, nucleic acid sensors, immunosensors, and infection sensors [2]. For example, a low-cost and reusable immunosensor for lung cancer was using graphene oxide and CNTs [2].

Despite their potential, CNT-based biosensors still face challenges such as the formation of biofilms, which can result in attenuated sensor response due to nonspecific binding of serum proteins [1]. To overcome this challenge, various strategies have been employed, such as coating the surface with highly hydrophilic, uncharged, and sterically hindered polymers like polyethylene glycol [2].

In summary, CNT-based nanoelectronics biosensors for glucose detection have shown great potential in recent years, with several studies highlighting their excellent reproducibility, good anti-interference properties, high sensitivity, and broad range of applications. However, challenges such as the formation of biofilms still need to be addressed to fully realize the potential of CNT-based biosensors for glucose detection.

1.2 Addressing Development of Carbon Nanotube-Based Biosensors For Multi-Concentration Glucose Detection

In the context of managing diabetes and providing healthcare, the development of carbon nanotube-based biosensors for multi-concentration glucose detection is extremely pertinent to contemporary and global challenges.

Millions of individuals worldwide suffer from diabetes, a chronic illness whose incidence is continually rising. The International Diabetes Federation estimates that 537 million adults worldwide have diabetes in 2021, and by 2045, there will be 783 million people with the disease.

Blood glucose levels must be continuously monitored for diabetes to be effectively managed to avoid problems and preserve optimum health. Conventional glucose monitoring techniques, including finger-prick testing, only reveal a limited amount of data regarding daily swings in glucose levels.

On the other hand, sophisticated biosensors are used in continuous glucose monitoring (CGM) systems, which provide a more all-encompassing approach to glucose control. CGM devices give users access to real-time glucose data, empowering them to make educated decisions regarding their lifestyle and course of treatment.

Since carbon nanotubes have special qualities like high surface area, superior electrical conductivity, and biocompatibility, they have become a potential technology for CGM. These biosensors can be made to detect a broad range of glucose concentrations, from hypoglycaemic to hyperglycaemic levels, making it possible to monitor glucose levels more precisely and thoroughly.

The development of carbon nanotube-based biosensors for multi-concentration glucose detection holds great promise for bettering diabetes care and lessening the toll that the illness takes on patients and healthcare systems. These biosensors can help avoid problems, lower hospitalisation rates, and enhance the quality of life for diabetics by offering more continuous and accurate glucose data.

Furthermore, wearable technology like smart watches and patches that incorporate carbon nanotube-based biosensors can improve glucose monitoring's accessibility and practicality even more. People with diabetes may receive real-time data from wearable CGM devices, allowing them to promptly modify their lifestyle and course of treatment.

To summarise up, the creation of carbon nanotube-based biosensors for the detection of glucose at multiple concentrations is extremely pertinent to contemporary and worldwide concerns about the control of diabetes. These cutting-edge biosensors could

completely change how blood sugar is measured, improving patient outcomes and lowering medical expenses tied to problems from diabetes.

1.3 Problem Statement

The global rise in diabetes cases demands the development of precise and trustworthy glucose monitoring techniques. Conventional glucose monitoring techniques, including finger pricking, are intrusive, uncomfortable, and may spread diseases. As a result, non-invasive, precise, dependable, and reasonably priced glucose monitoring techniques are required. Since carbon nanotubes offer special qualities including high sensitivity, selectivity, and stability, they have become a promising alternative for glucose detection in nanoelectronics. The development of carbon nanotube-based nanoelectronics biosensors for glucose detection is still fraught with difficulties, though. These include the requirement for improved control over the chemical and physical characteristics of carbon material-based biosensors, the process of separating different types of CNTs, the sensor's miniaturisation, the potential for toxicity, and in vivo stability.

1.4 Project Objective

The main aim of this project is to create a nanoelectronic biosensor for glucose detection with multi-concentration. Specifically, the objectives are as follows:

a) To Design and Optimize Carbon Nanotube-Based Biosensors for High Sensitivity and Selectivity in Glucose Detection

b) To Evaluate the Performance and Stability of CNT-Based Biosensors Across Various Glucose Concentrations

c) To Investigate the Mechanisms Underlying Glucose Detection Using CNT-Based Biosensors

1.5 Scope of Project

The scope of this project are as follows:

a) Investigate the relationship between the voltage , current, and the surface area by using cyclic voltammetry method for Indium Tin Oxide and Gold Plate.

b) Design and simulate the experiment using Comsol software for simulation electrochemistry to show the cyclic voltammetry graph .

c) Comparing the electrodes of Indium Tin Oxide and Gold on which are is better at sensitivity for detecting glucose based on sensogram results.

d) Electrodeposition and cyclic voltammetry is experimented by using AutoLAB.

e) Potentiostat with NOVA 2.0 Auto LAB software for Indium Tin Oxide and Gold.

f) Using PBS and glucose solution for cyclic voltammetry process for Indium Tin Oxide and Gold.

CHAPTER 2

LITERATURE REVIEW

2.1 Introduction

In today's modern society, with the ability to detect a wide range of analytes precisely and quickly, from food contaminants to disease biomarkers, biosensors have become indispensable instruments in many different industries. These instruments, which are usually made up of a transducer and a biological recognition element, offer precise and sensitive measurements that are essential for monitoring the environment, diagnosing diseases, assuring food safety, and biodefense sensing. Carbon nanotubes (CNTs) are a noteworthy development in biosensor technology because of their special electrical, chemical, and physical properties that make them excellent for improving sensor performance. The development of CNT-based biosensors for glucose detection has advanced significantly in recent years, showing promise in terms of sensitivity, selectivity, and useful applications.

2.2 Understanding the Development of Carbon Nanotube-Based Biosensors For Multi-Concentration Glucose Detection impact on Global/Societal Issue

In the context of managing diabetes and providing healthcare, the development of carbon nanotube-based biosensors for multi-concentration glucose detection is extremely pertinent to contemporary and global challenges. Millions of individuals worldwide suffer from diabetes, a chronic illness whose incidence is continually rising. The International Diabetes Federation estimates that 537 million adults worldwide had diabetes in 2021, and by 2045, that figure is expected to rise to 783 million [5].

Blood glucose levels must be continuously monitored for diabetes to be effectively managed in order to avoid problems and preserve optimum health. Conventional glucose monitoring techniques, including finger-prick testing, only reveal a limited amount of data regarding daily swings in glucose levels. On the other hand, sophisticated biosensors are used in continuous glucose monitoring (CGM) systems, which provide a more all-encompassing approach to glucose control. People with diabetes are able to make educated decisions regarding their medication and way of life thanks to the real-time glucose level data provided by CGM devices [5].

Since carbon nanotubes have special qualities like high surface area, superior electrical conductivity, and biocompatibility, they have become a potential technology for CGM. The ability to detect a broad range of glucose concentrations, from hypoglycaemic to hyperglycaemic levels, is provided by these biosensors, allowing for more precise and thorough glucose level monitoring [6][77].

The development of carbon nanotube-based biosensors for multi-concentration glucose detection holds great promise for bettering diabetes care and lessening the toll that the illness takes on patients and healthcare systems. These biosensors can help prevent complications, lower hospitalisation rates, and enhance the quality of life for those with diabetes by offering more continuous and accurate glucose data [5][6].

Furthermore, wearable technology like smart watches and patches that incorporate carbon nanotube-based biosensors can improve glucose monitoring's accessibility and practicality even more. People with diabetes may be able to make timely changes to their treatment and lifestyle by using real-time data from wearable CGM devices [5].

To put it all up, the creation of carbon nanotube-based biosensors for the detection of glucose at multiple concentrations is extremely pertinent to contemporary and worldwide concerns about the control of diabetes. These cutting-edge biosensors could completely

change how blood sugar is measured, improving patient outcomes and lowering medical expenses tied to problems from diabetes.

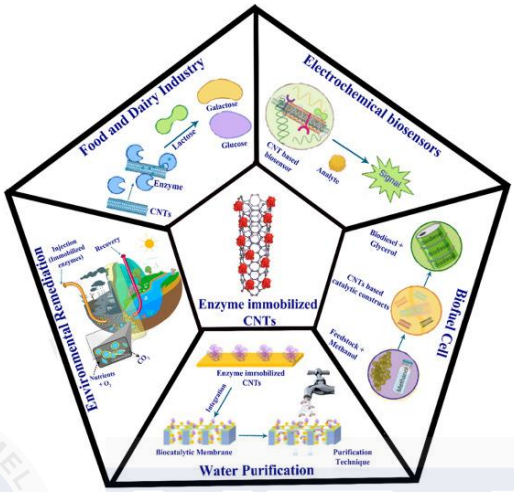


Figure 2.1 Recent advances in carbon nanotubes-based biocatalysts

2.3 Biosensors

Biosensors are a crucial technology in the field of biomedical engineering, enabling the detection of various biomarkers and analytes with high sensitivity and specificity. Recent advancements in biosensor design and fabrication have led to the development of wearable biosensors for continuous glucose monitoring, which has revolutionized the management of diabetes.

The development of wearable biosensors for continuous glucose monitoring has been driven by the need for non-invasive and real-time monitoring of blood glucose levels. These biosensors typically consist of a recognition element, a signal transducer, and a signal displayer, and are designed to detect glucose in interstitial fluid (IF) or blood [8]. The use of enzymatic biofuel cells and microneedle technology has enabled the development of minimally invasive biosensors that can detect glucose levels with high accuracy [8].

Recent studies have focused on the development of self-powered glucose sensors that can be integrated into wearable devices, such as smart watches or patches [10]. These

sensors use enzymatic biofuel cells to generate power and detect glucose levels, making them suitable for real-time monitoring of blood glucose levels.

In conclusion, biosensors have played a crucial role in the development of wearable devices for continuous glucose monitoring. The integration of biosensors into wearable devices has enabled real-time monitoring of blood glucose levels, which has revolutionized the management of diabetes [11].

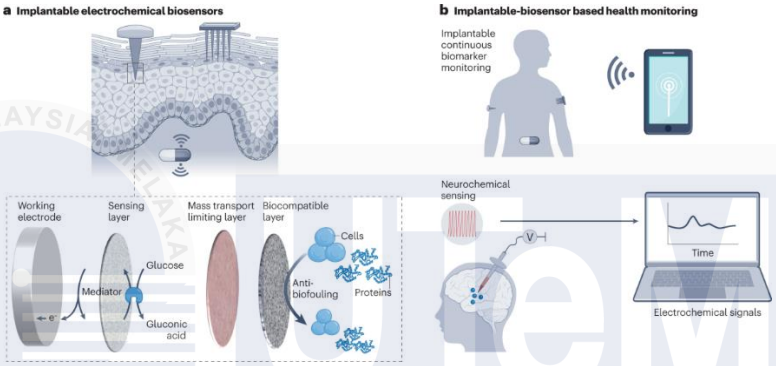


Figure 2.2 Device integration of electrochemical biosensor.

2.4 Electrochemical Biosensor

Electrochemical biosensors, with their sensitivity, specificity, and quick reaction times, have gained importance in several applications, including food safety, environmental monitoring, and medical diagnostics. These sensors detect a variety of analytes, such as pathogens, glucose, and lactate, by translating a biological response into an electrical signal.

Recent developments have concentrated on using nanomaterials and cutting-edge biorecognition components to enhance the functionality of electrochemical biosensors. By boosting surface area and electron transfer rates, nanomaterials like graphene, carbon nanotubes, and gold nanoparticles improve the stability and sensitivity of the sensor. According to research, for example, adding graphene-based materials to biosensors greatly improves their electrochemical characteristics and increases their capacity to detect low concentrations of target molecules [12][13].

Furthermore, because of their great selectivity and stability, molecularly imprinted polymers, or MIPs, have become a viable biorecognition element. MIPs are artificial polymers that have particular binding sites that complement the target molecule in terms of size, structure, and functional groups. This makes it possible to develop extremely focused sensors that are able to identify target analytes even in intricate sample matrices [13].

Another noteworthy development is the incorporation of electrochemical biosensors into point-of-care (POC) diagnostic instruments. POC devices are essential for managing chronic illnesses and controlling infectious disease outbreaks because they allow for prompt testing and diagnosis at the patient's site. For instance, the creation of wearable continuous glucose monitors and portable glucose metres, which offer real-time glucose monitoring [12], has completely changed the way diabetes is managed.

In the future, it is anticipated that the integration of modern data analytics and wireless communication technologies with electrochemical biosensors would significantly augment their usefulness. By enabling real-time data sharing and remote monitoring with healthcare providers, this integration can enhance patient outcomes and streamline healthcare procedures [12][13].

Overall, the development of more effective, precise, and user-friendly electrochemical biosensors is being fueled by ongoing breakthroughs in materials science, biorecognition components, and integration technologies, underscoring the vital role these sensors play in a variety of applications.

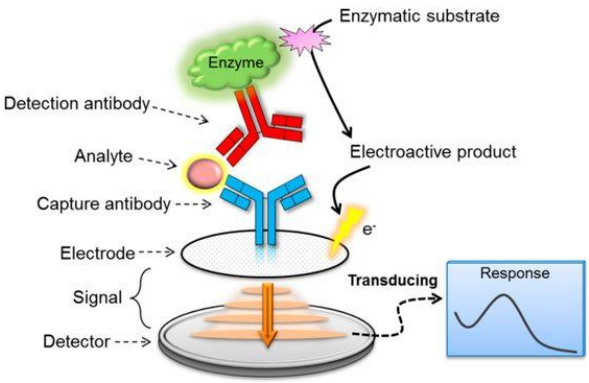


Figure 2.3 Technologies of Electrochemical

2.4.1 Basic Principles of Electrochemical

The relationship between chemical processes and electricity is the subject of the fundamental chemical concept of electrochemistry. It entails the movement of electrons between materials, which produces an electric current. Understanding different chemical reactions and processes requires an understanding of the fundamentals of electrochemistry.

The fundamental idea of electrochemistry is oxidation and reduction. Electrons are lost during oxidation and gained during reduction. The number of electrons that an atom has gained or lost is known as its oxidation number. The direction of electron transport is determined by the difference in oxidation values between two substances. For instance, the difference in potential energy between the two substances causes the oxidation of zinc (Zn) into zinc ions (Zn2+) and the reduction of copper ions (Cu2+) into copper (Cu) to happen spontaneously [14].

The potential difference between a voltaic cell's anode and cathode is referred to as the cell potential, or electromotive force (EMF). It is represented by the symbol Ecell and is measured in volts. When a reaction occurs spontaneously, the cell potential is positive; when it doesn't, it is negative. The cell potential under standard circumstances, which include a temperature of 25°C, a concentration of 1 M, and a pressure of 1 atm, is known as the standard cell potential, or Eocell [15].

In electrochemistry, the connection between cell potential and Gibbs free energy (ΔG) is essential. When a reaction occurs spontaneously, the ΔG is positive; when it doesn't, it is negative [16].

In conclusion, the basic principles of electrochemistry are essential for understanding various chemical reactions and processes. The concepts of oxidation and

reduction, cell potential, and Gibbs free energy are fundamental to electrochemistry and are used to predict the direction and spontaneity of chemical reactions.

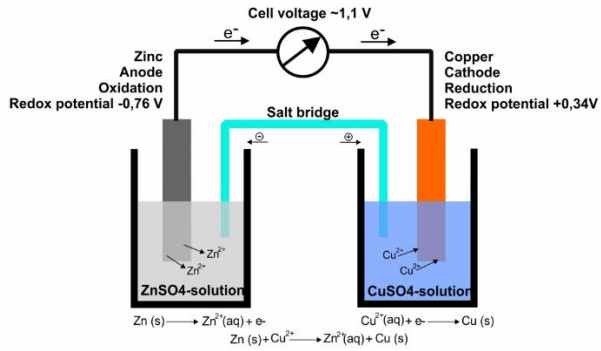


Figure 2.4 Principle of Electrochemical Cells

2.4.2 REDOX Reaction

An essential idea in chemistry is redox (oxidation-reduction) processes, which involve the transfer of electrons between chemical species. These reactions are essential to many processes, such as the synthesis of energy, corrosion, and biological systems [17].

A redox reaction occurs when one species becomes reduced (gains electrons) and another becomes oxidised (loses electrons). According to [18], the species that obtains electrons is known as the oxidising agent, and the species that loses electrons is known as the reducing agent. To guarantee that the quantity of electrons lost and gained is equal, the sum of the oxidation and reduction half-reactions must be balanced.

The direction and magnitude of a redox reaction are largely dependent on the element's oxidation state, which expresses the degree of oxidation of an atom. The most prevalent oxidation states are -1, 0, +1, +2, +3, +4, +5, +6, and +7, while the range of oxidation states is -4 to +8 [19].

Redox reactions fall into various categories, including displacement, disproportionation, breakdown, and combination reactions. These reactions are extensively

employed in many different fields, such as environmental cleanup, energy conversion, and electrochemistry [20].

Comprehending the fundamentals of redox reactions is crucial for forecasting the conduct of chemical systems, creating appropriate energy conversion and storage apparatuses, and formulating remediation and environmental protection plans.

2.4.3 Factors Affecting the Electrochemical Performance of Biosensors

In the field of biomedical engineering, electrochemical biosensors are an essential tool because they provide high sensitivity and specificity detection of a variety of biomarkers and analytes. However, a number of variables, such as the type of bioreceptor employed, the electrode's surface modification, and the operating environment, influence the electrochemical performance of biosensors.

The electrochemical performance of the biosensor can be strongly influenced by the kind of bioreceptor that is employed in it. Enzymes like lactate oxidase and glucose oxidase, for instance, have been employed as bioreceptors in biosensors for the detection of lactate and glucose, respectively [21]. The electrode's surface modification may also have an impact on the biosensor's electrochemical performance. For example, it has been demonstrated that using gold nanoparticles as a surface modification improves the electron transfer kinetics and surface area of biosensors, hence improving their electrochemical performance [22].

Operating parameters including temperature, pH, and ionic strength can also affect how well biosensors work electrochemically. For instance, the kind of bioreceptor being utilised can affect the ideal temperature for a biosensor to function. The activity of the bioreceptor can also be influenced by the pH of the solution, with certain bioreceptors being more active at higher or lower pH values [23].

In conclusion, a number of variables, such as the kind of bioreceptor employed, the electrode's surface modification, and the operating environment, influence the electrochemical performance of biosensors. Comprehending these variables is imperative for the advancement of high-performance biosensors capable of precisely identifying diverse biomarkers and analytes.

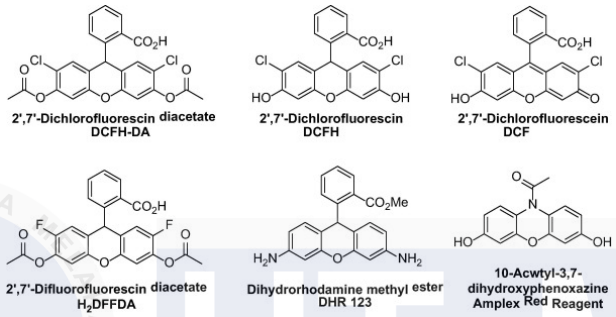


Figure 2.5 Detection of Cellular Redox Reaction

2.4.4 Gold Electrodes: The Pinnacle of Efficiency and Reliability in Electrochemical Applications

Gold electrodes have long been revered in the field of electrochemical applications due to their exceptional properties that make them highly efficient and reliable. Their unique characteristics, including excellent conductivity, chemical stability, and biocompatibility, have made them a preferred choice in various applications ranging from biosensors to energy storage devices.

One of the most significant advantages of gold electrodes is their superior electrical conductivity. Gold provides a highly conductive surface that facilitates efficient electron transfer, crucial for electrochemical reactions. This high conductivity ensures that gold electrodes can operate with minimal energy loss, enhancing the overall efficiency of the electrochemical devices in which they are used [193].

Gold is chemically inert and resistant to corrosion, which is essential for the longevity and reliability of electrodes used in harsh environments. Unlike other materials that may degrade or oxidize over time, gold maintains its integrity, ensuring consistent performance. This stability is particularly important in applications such as biosensors, where prolonged exposure to biological fluids can lead to electrode degradation [194].

In biomedical applications, the biocompatibility of electrodes is crucial. Gold's non-reactive nature and compatibility with biological tissues make it ideal for use in biosensors and medical implants. Gold electrodes can interface seamlessly with biological systems, facilitating accurate and reliable measurements without inducing adverse reactions [195].

The surface of gold electrodes can be easily functionalized with various chemical groups, enhancing their versatility. This capability allows for the attachment of specific molecules or enzymes, which is essential for the development of highly selective and sensitive biosensors. Functionalization of gold surfaces can also improve the interaction between the electrode and the target analyte, leading to more precise electrochemical detection [196].

Gold electrodes are widely used in the development of biosensors due to their excellent conductivity and biocompatibility. They are employed in glucose sensors, DNA sensors, and other diagnostic devices, where they provide reliable and accurate measurements. For example, glucose sensors utilizing gold electrodes can offer precise blood glucose level monitoring, essential for diabetes management [197].

In addition to biosensors, gold electrodes play a crucial role in energy storage applications such as batteries and supercapacitors. Their high conductivity and stability contribute to the efficient storage and transfer of energy, enhancing the performance of these devices. Gold electrodes help improve the charge-discharge cycles and overall energy density of batteries, making them more efficient and durable [198].

Despite their numerous advantages, the high cost of gold can be a limiting factor for its widespread use in commercial applications. Research is ongoing to find cost-effective methods for utilizing gold electrodes, such as reducing the amount of gold required or developing gold nanoparticle-based electrodes that retain the benefits of bulk gold while minimizing material usage [199].

Gold electrodes stand out as the pinnacle of efficiency and reliability in electrochemical applications due to their excellent electrical conductivity, chemical stability, and biocompatibility. Their ability to be easily functionalized further enhances their versatility, making them indispensable in biosensors and energy storage devices. While cost remains a challenge, ongoing research promises to make gold electrodes more accessible, ensuring their continued prominence in advanced electrochemical applications.

2.4.5 Biosensors and their Applications

Because of its many uses in a variety of industries, such as food safety, disease detection, environmental monitoring, plant biology, and biodefense sensing, biosensors have attracted a lot of interest recently [24]. These tools are made to identify analytes, such infections or glucose, with a high degree of sensitivity and specificity. This allows for the early identification and treatment of illnesses or contamination.

In order to identify harmful substances in soil, water, and the air, biosensors have been employed in environmental monitoring. One example is the development of a biosensor based on hafnium oxide for the early detection of human interleukin-10, an immunological response and inflammatory biomarker [25]. To ensure food safety and quality, biosensors have also been employed in food processing and safety to identify infections in fresh meat, poultry, or fish [26].

Biosensors, which provide increased sensitivity and accuracy in measuring different biomarkers, have proven crucial in the biomedical field in the identification of diseases. On the end-facet of a dual-core, single-mode optical fiber, for instance, a unique plasmonic biosensor was created that has great sensitivity and specificity for detecting analytes [25]. In plant biology, biosensors have also been utilized to identify stress signals and plant hormones, allowing for the early identification and treatment of plant diseases [24].

Biosensors have been utilized in biodefense sensing to quickly identify and take preventative action against biological dangers including viruses and poisons. Moreover, biosensors have been applied to clinical diagnostics, facilitating point-of-care testing and customized treatment. For example, an amperometry enzyme electrode was utilized to develop a glucose biosensor that has been widely used [27].

Biosensor technology has come a long way, yet there are still issues and problems that need to be resolved. These include the requirement for increased scalability, cost-effectiveness, miniaturization, and sensitivity and specificity. Sustained research and development endeavors are needed to surmount these obstacles and facilitate the extensive integration of biosensors across many domains [24].

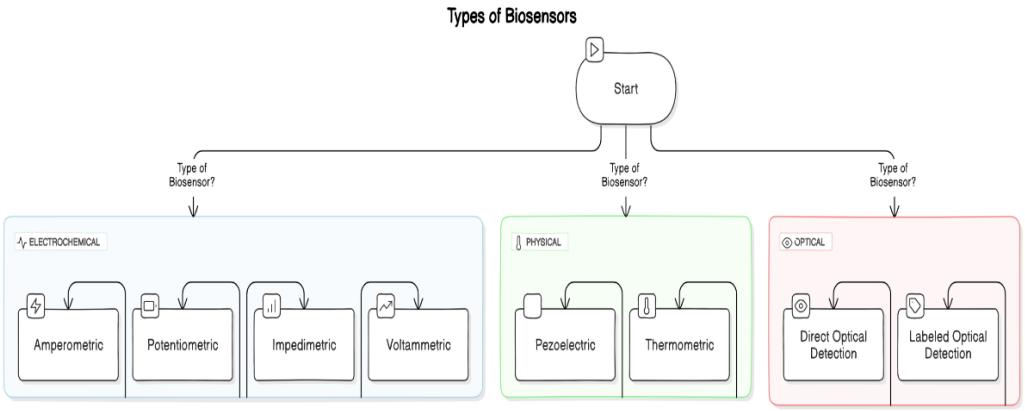


Figure 2.6 Type of Biosensor

2.4.6 Development of Electrochemical Biosensors for Biomedical Applications

With their high sensitivity and specificity, electrochemical biosensors have become a promising technology for biomedical applications. They can detect a wide range of biomarkers and analytes. These biosensors, which use electrochemical processes to detect target analytes, are made up of a signal transducer, a signal displayer, and a bioreceptor [28].

Wearable technology for continuous glucose monitoring has been developed because of recent developments in the design and manufacture of electrochemical biosensors. Typically, these biosensors rely on the oxidation of glucose to produce an electrochemical signal and use enzymes like glucose oxidase as bioreceptors [28][29]. The development of minimally invasive biosensors that can accurately measure the amount of glucose in interstitial fluid (IF) has been made possible by the application of microneedle technology [29].

Electrochemical biosensors have been created for the detection of many biomarkers, including lactate, urea, and creatinine, in addition to glucose monitoring. These biosensors are useful for monitoring the environment, therapeutic medication monitoring, and clinical diagnostics [30].

The range of possible uses for these devices has been further increased with the introduction of self-powered electrochemical biosensors that use enzyme biofuel cells. These biosensors are appropriate for long-term monitoring in distant or resource-constrained environments because they may provide their own electricity through the oxidation of target analytes [29].

Even with the encouraging advancements in electrochemical biosensors, a number of obstacles still need to be overcome. These include raising the sensitivity and detection limit, guaranteeing the dependability and repeatability of the sensors, and strengthening the stability and selectivity of the bioreceptors [31]. The goal of current research is to overcome

these obstacles and increase the usage of electrochemical biosensors in clinical and biological contexts.

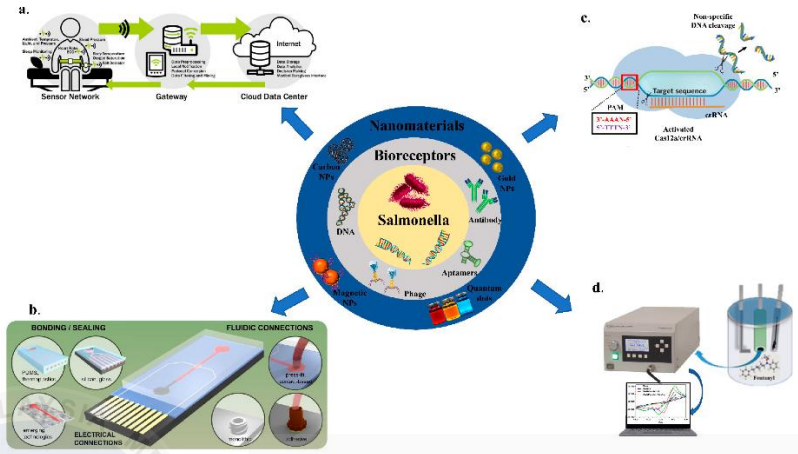


Figure 2.7 Electrochemical Biosensor

2.5 Material for Electrochemical Biosensors

The sensitive and targeted detection of target analytes is made possible by electrochemical biosensors, which use a range of materials. The performance properties of these biosensors, such as their sensitivity, selectivity, stability, and response time, are greatly influenced by the materials used.

Carbon, which comes in a variety of forms including carbon nanotubes, graphene, and carbon black, is one of the essential components utilised in electrochemical biosensors [32]. These carbon-based materials are suited for the effective transfer of electrons and the immobilisation of bioreceptors because of their high surface area, superior electrical conductivity, and good biocompatibility [33].

Polymers have also been widely employed in the construction of electrochemical biosensors, in addition to carbon. The use of polymers as matrix materials, such as polypyrrole, polyaniline, and chitosan, can immobilise bioreceptors and offer a stable and biocompatible environment for the sensing processes [34].

In electrochemical biosensors, metallic nanoparticles including gold, silver, and platinum have also been used. These nanoparticles can increase the kinetics of electron transfer, strengthen the electrochemical signal, and offer a sizable surface area for immobilising bioreceptors.

The performance and capacities of electrochemical biosensors have significantly improved as a result of the incorporation of these materials into their design. For instance, the construction of highly sensitive and selective biosensors for the detection of several biomarkers, such as glucose, lactate, and urea, has been made possible by the employment of metallic nanoparticles and carbon nanotubes [32][33].

In conclusion, a key component in the creation of high-performance electrochemical biosensors is material selection. These biosensors have advanced through the use of metallic nanoparticles, polymers, and carbon-based materials, opening up a variety of applications for environmental and biological monitoring [35].

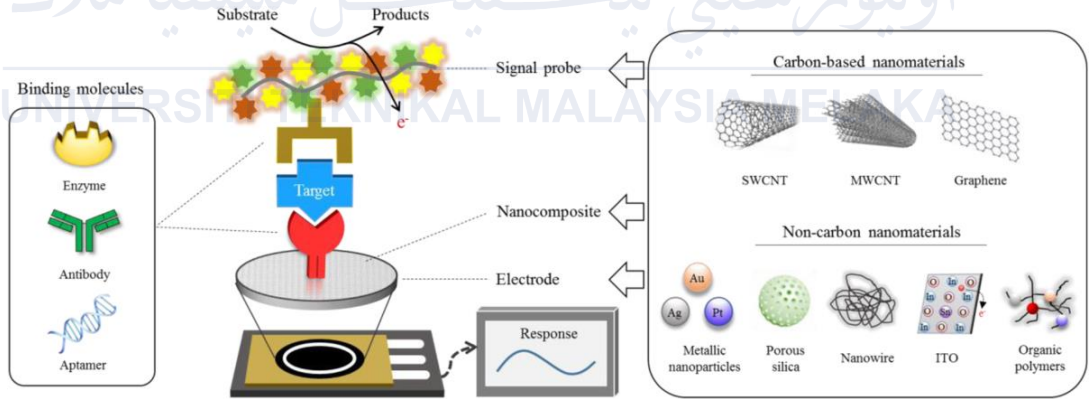


Figure 2.8 Electrochemical biosensor

2.5.1 Carbon Material : Multi-Walled Carbon Nanotubes

A special substance known as multi-walled carbon nanotubes (MWCNTs) is made up of several layers of graphene sheets coiled into tubes. This simple to read guide will describe the construction, unique properties, and even distribution of MWCNTs. MWCNTs, which have a diameter of about 30 nm, are substantially larger than standard single-walled

carbon nanotubes (SWCNTs) because they are composed of multiple layers of graphene sheets wrapped into tube forms [36].

MWCNTs outperform double-walled carbon nanotubes (DWCNTs) and SWCNTs in terms of thermal and electrical resistivity. Furthermore, because of the repeating walls, nanotube architectures are more susceptible to faults. It is possible to generate functionalized groups like hydroxides, carboxylic acids, or amines by modifying the external walls of MWCNTs [37].

Comparatively speaking to other kinds of carbon nanotubes, MWCNTs are easier to make in larger quantities and require less purification. As a result, they are typically less expensive than SWCNTs and DWCNTs. Despite having nearly identical performance capacities, MWCNTs are typically most helpful when creating various composites, including nylon, ceramics, plastics, polymers, and much more [38].

To sum up, MWCNTs are a flexible material that can be easily produced and purified, has high thermal and electrical resistance, and may be used to create unique external walls. They are widely used in many different fields, including as biomedical devices, electronics, and composites.

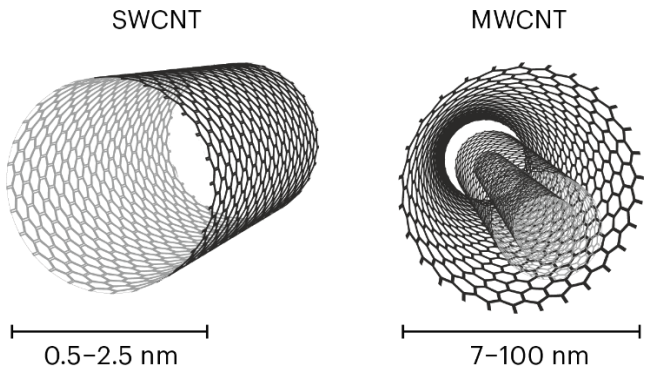


Figure 2.9 Multi-walled Carbon Nanotubes Production

2.5.2 Conductive Polymer : Polypyrrole

Conjugated polymer polypyrrole (PPY) has special electrical characteristics, such as conductivity. Due of this characteristic, it is a desirable material for a number of biological uses, including tissue engineering, implantable technology, and biosensors [42].

The potential application of PPY in biosensors, specifically in the detection of glucose and other indicators, has been thoroughly investigated. Because of its conductivity, electrons may go through it efficiently, making it possible to detect even minute variations in the concentration of target analytes [39][40]. Moreover, it has been demonstrated that PPY is biocompatible and biodegradable, which makes it a perfect material for tissue engineering applications and implantable devices [41].

Because of its conjugated structure, which permits electron delocalization, PPY is said to be conductive. Because of this characteristic, PPY can demonstrate high electrical conductivity, which makes it appropriate for use in implanted devices and biosensors.

To sum everything up, polypyrrole is a conductive polymer with distinctive electrical characteristics that make it a desirable substance for a range of biological uses. Because of its conductivity, biocompatibility, and biodegradability, it is a perfect material to use in tissue engineering, implanted devices, and biosensor development.

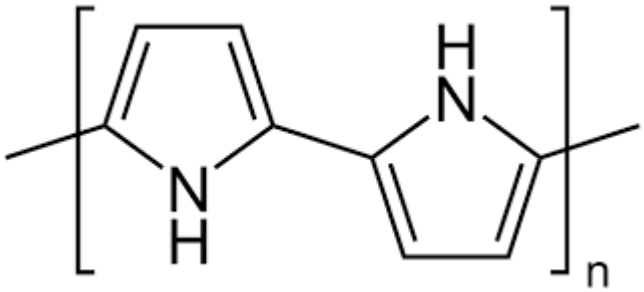


Figure 2.10 Polypyrrole

2.5.3 Polypyrrole-Multi Walled Carbon Nanotube Nanocomposites

Combining multi-walled carbon nanotubes (MWCNTs) with polypyrrole (PPY) has resulted in nanocomposites with improved thermal and electrochemical performance. The prospective uses of these nanocomposites in biosensors, energy storage devices, and biomedical devices have been investigated [43-45].

It has been demonstrated that adding PPY and MWCNTs to nanocomposites enhances their conductivity and thermal stability. Bioreceptors may be immobilised on a large surface area thanks to conductive polymer PPY, and the nanocomposites' electrical conductivity and thermal stability are improved by MWCNTs [43][44].

Methods like chronoamperometry and cyclic voltammetry have been used to assess the nanocomposites' electrochemical performance. According to these investigations, the nanocomposites had better electrochemical activity and stability than PPY alone [44][46].

Additionally, the thermal performance of the nanocomposites has been investigated using methods like differential scanning calorimetry (DSC) and thermogravimetric analysis (TGA). Comparing the nanocomposites to PPY alone, this research have demonstrated that the former has better thermal stability and degradation resistance [43][44].

In conclusion, it has been demonstrated that adding PPY to MWCNTs enhances the nanocomposites' thermal and electrochemical performance. These nanocomposites may find use in biosensors, biomedical devices, and energy storage devices.

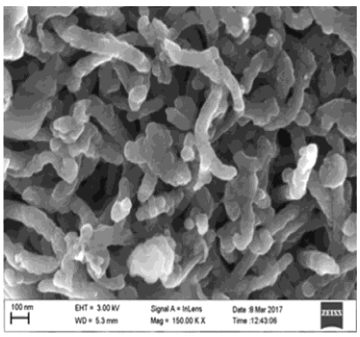


Figure 2.11 Polymer

2.6 Carbon Nanotubes in Biosensors

Carbon nanotubes (CNTs) have emerged as a promising material for the development of advanced biosensors due to their unique physical, chemical, and electrical properties. These one-dimensional nanostructures have garnered significant attention in the field of biosensing, offering numerous advantages over traditional sensing materials.

One of the key advantages of CNTs in biosensors is their high surface-to-volume ratio, which provides a large surface area for the immobilization of biological recognition elements, such as enzymes, antibodies, or DNA [48]. This enhanced surface area allows for increased loading of the recognition elements, leading to improved sensitivity and selectivity of the biosensor. Additionally, the nanoscale dimensions of CNTs enable the fabrication of miniaturized, highly integrated biosensing platforms, which are crucial for the development of portable and wearable devices [49].

The exceptional electrical properties of CNTs, including high electrical conductivity and electron transfer capabilities, make them ideal for the design of electrochemical biosensors [50]. CNT-based electrochemical biosensors have demonstrated improved sensitivity, faster response times, and lower detection limits compared to traditional electrode materials. This is particularly advantageous for the continuous monitoring of analytes, such as glucose, in healthcare applications.

Furthermore, the chemical stability and biocompatibility of CNTs have enabled their integration with various biological and chemical components, leading to the development of hybrid biosensing systems. These fusion technologies, which combine CNTs with enzymes, antibodies, or other nanomaterials, have shown enhanced performance in the detection of a wide range of analytes, including food contaminants, environmental pollutants, and biomarkers just like in Figure 2.12 below [47].

Recent advancements in the synthesis and functionalization of CNTs have further expanded their applications in biosensing. Techniques such as chemical vapor deposition (CVD) and plasma-enhanced CVD have enabled the production of high-quality, defect-free CNTs, while various surface modification strategies have allowed for the tailoring of their properties to specific biosensing requirements.

The integration of CNTs with emerging technologies, such as flexible electronics and wearable devices, has also opened new possibilities for continuous and non-invasive monitoring of physiological parameters. CNT-based biosensors have demonstrated their potential for real-time, in-situ detection of analytes, making them valuable tools for healthcare, environmental monitoring, and food safety applications.

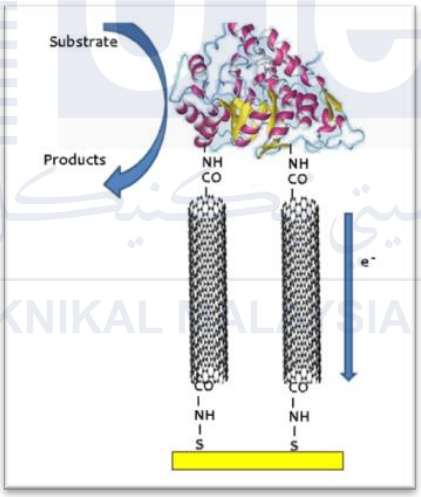


Figure 2.12 Carbon Nanotube in Biosensor

In conclusion, the unique properties of carbon nanotubes have made them a versatile and promising material for the development of advanced biosensors. The continued research and innovation in CNT-based biosensing technologies are expected to lead to significant improvements in the sensitivity, selectivity, and practical applications of these devices, ultimately contributing to advancements in various fields, from healthcare to environmental protection.

2.7 Device Simulation and Optimization

A critical stage in the creation of wearable biosensors for continuous glucose monitoring is device simulation and optimisation. Creating and manufacturing biosensors that can precisely measure blood or interstitial fluid (IF) glucose levels is the process. Low-invasive biosensors that are highly accurate in detecting glucose levels have been developed as a result of recent developments in biosensor design and manufacturing [51][52].

The choice of bioreceptors, signal transducers, and signal displays are just a few of the processes involved in the design and construction of biosensors. Target analytes are recognised and bound to by bioreceptors, like enzymes, and signal transducers translate the biochemical signal into an electrical signal. Electronic systems that use signal displays amplify and process electrical signals to provide legible outputs [51].

The creation of biosensors requires simulation optimisation since it enables researchers to test and improve their designs prior to real manufacture. Simulation optimisation is the process of modelling the activity of a biosensor and optimising its performance through computer simulations. The time and money spent on experimental testing and refining can be greatly decreased using this method [53][54].

A software that is frequently used for biosensor device simulation and optimisation is called COMSOL Multiphysics. A variety of physical processes, including as mass movement, fluid dynamics, and electrochemical reactions, can be modelled and analysed using the simulation programme COMSOL [55]. These activities are essential to the creation of biosensors. Researchers may optimise the shape and materials of their biosensors, anticipate the response of the sensor to varying analyte concentrations, and simulate the performance of their designs under various operating situations using COMSOL.

In conclusion, the development of wearable biosensors for continuous glucose monitoring requires a thorough understanding of device simulation and optimisation.

Through the use of computer simulations to simulate and enhance biosensor functionality, scientists can create high-performing biosensors with real-time monitoring capabilities and accurate glucose level detection.

2.7.1 COMSOL Multiphysics

COMSOL Multiphysics is a simulation programme, analyzer, and solver for finite elements that is intended for use in a range of engineering and physics applications, especially in coupled phenomena and multiphysics. Coupled systems of partial differential equations (PDEs) are supported by the software using conventional physics-based user interfaces.

COMSOL Multiphysics provides an Integrated Development Environment (IDE) with a single workflow for electrical, mechanical, fluid, acoustical, and chemical applications. The software may be used to solve PDEs in weak form and provides an API for MATLAB and Java to control the programme outside.

In order to simulate and analyse complex biological systems, such as the behaviour of cells and tissues, COMSOL Multiphysics is widely used in many fields, including biomedical engineering [56]. Wearable biosensors for continuous glucose monitoring are being developed using software that mimics and enhances the functionality of biosensors [57].

In conclusion, COMSOL Multiphysics is a useful software package for analysing and modelling complex engineering and physics issues. Its versatility and adaptability make it extremely useful for researchers and engineers in a variety of fields.

Figure 2.13 COMSOL Multiphysics Software

2.7.2 Multiphysics Simulation

Multiphysics simulation has become an increasingly important tool in scientific and technical study due to its capacity to depict complex systems that involve the interaction of multiple physical phenomena [58]. Through the facilitation of a more comprehensive understanding of the underlying mechanics, this strategy can lead to the production of more trustworthy and efficient designs [59]. The advent of sophisticated simulation tools such as COMSOL Multiphysics and advancements in computer power have made Multiphysics simulation significantly more capable over the past 10 years [60].

Different physics interfaces, including fluid dynamics, heat transport, electromagnetics, and structural mechanics, are coupled together in Multiphysics simulation to provide a comprehensive model that illustrates the links between these many physical processes [61]. This technique has been extensively applied in a number of fields, including biomedical engineering, aerospace, automotive, and energy, where accurate system behaviour prediction is crucial [62]. By considering the interactions between different physical phenomena, researchers can obtain valuable insights into the performance and optimisation of complex systems, which can help them in design and decision-making [63].

Multiphysics simulation has developed because of the need to manage increasingly complex technical issues, for which traditional single-physics simulations are sometimes

insufficient to portray the complete complexity of the situation [64]. The integration of many physical interfaces enables the analysis of nonlinear and coupled effects, which can have a substantial impact on the overall performance of the system [65]. Furthermore, the ability to do parametric studies and optimisation within the Multiphysics framework allows engineers to explore a wider range of design choices and select the optimal solutions [66].

Multiphysics simulation should be able to achieve even higher levels of simulation in the future thanks to advancements in computer power, numerical methods, and software [67]. The efficiency and accuracy of Multiphysics models can be increased by using AI and machine learning techniques, leading to faster and more accurate simulations [68]. Because digital twin technologies and interdisciplinary design optimisation are becoming more and more significant, multiphysics simulation will play a bigger role as a tool for innovation and decision-making [69].

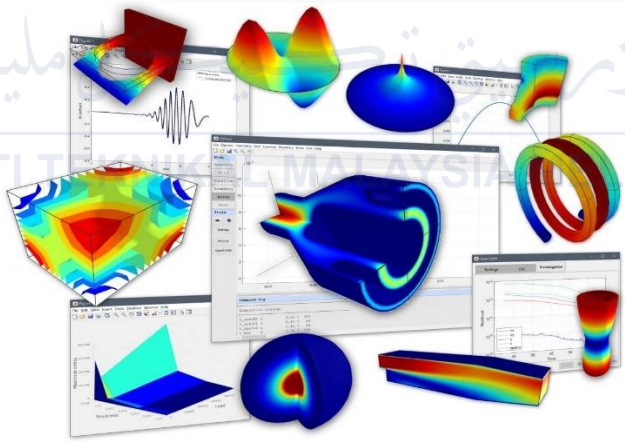


Figure 2.14 Multi-Physics Simulation Toolbox

2.7.3 Parametric and Optimization Studies in COMSOL Multiphysics

COMSOL Multiphysics is a powerful simulation application that allows the linking of many physics interfaces and provides improved features for parametric and optimisation investigations [70]. These qualities enable engineers and researchers to explore a wide range of design options, identify the optimal solutions, and get a deeper understanding of the underlying physical processes [71]. Due to advances in computer capability and more

efficient numerical methods, the COMSOL Multiphysics platform's tools have performed better and become even more versatile in recent years [72].

Users can investigate how various input factors impact the behaviour and performance of the system with COMSOL Multiphysics' parametric studies [73]. By adjusting these characteristics, researchers can investigate the model's responsiveness to various design factors and identify the critical components that influence the system's overall response [74]. This ability is particularly useful when optimising complex systems, where many interdependent parameters need to be considered simultaneously [75]. Among the various tools COMSOL Multiphysics provides for designing and managing parametric sweeps are sensitivity analyses and parameter investigations [76].

COMSOL Multiphysics' optimisation tools allow users to identify the best design or operating conditions for a given system [77]. The programme has many optimisation tactics that can be used to address a variety of engineering issues, such as gradient-based techniques, evolutionary algorithms, and topological optimisation [78]. When combined with these optimisation tools, the Multiphysics simulation capabilities can create a powerful framework for design exploration and decision-making [79]. By incorporating optimisation within the COMSOL environment, users can quickly explore the design space, evaluate the performance of different configurations, and ultimately identify the optimal solution [80].

Parametric and optimisation studies have been integrated into the COMSOL Multiphysics platform, leading to advancements in many scientific and technological fields [81]. Comprehensive Multiphysics simulations combined with state-of-the-art optimisation techniques have made great strides towards the creation of new and high-performing products, from the design of biomedical devices and efficient energy systems to structural optimisation in the aerospace and automotive industries [82]. As processing power and numerical algorithms continue to increase, it is expected that the possibilities of parametric

and optimisation studies in COMSOL Multiphysics will gradually expand, opening up even more complex and alluring applications in the years to come [83].

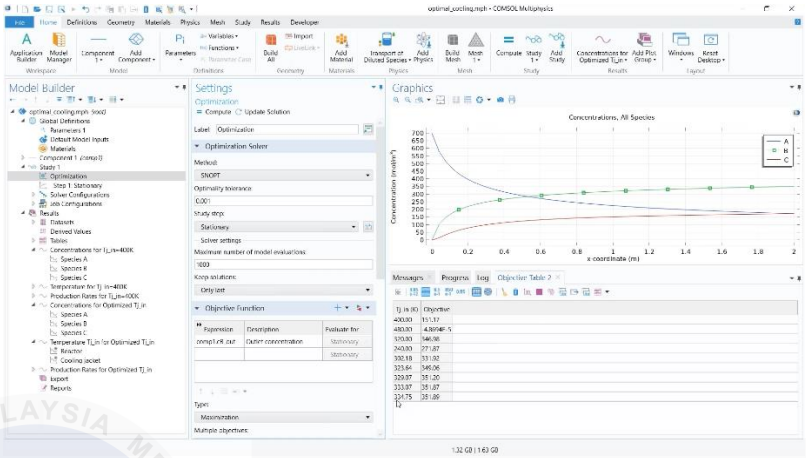


Figure 2.15 Optimization in COMSOL Multiphysics

2.7.4 Applications of COMSOL Multiphysics

COMSOL Multiphysics is a versatile simulation program extensively utilized across various scientific and industrial fields [84]. Its comprehensive physics interfaces and advanced simulation capabilities make it an essential tool for researchers and engineers aiming to model and analyse large systems involving multiple physical phenomena [85]. The software's ability to seamlessly integrate different physics domains, such as electromagnetics, heat transfer, structural mechanics, and fluid dynamics, has driven significant advancements in numerous academic disciplines [86].

In the realm of structural mechanics, COMSOL Multiphysics is heavily used to simulate the behaviour of systems and components under various loading conditions [87]. Engineers can optimize designs and ensure the structural integrity of their products by precisely modelling stress, strain, and deformation in complex structures, leveraging the software's finite element analysis capabilities [88]. Additionally, COMSOL Multiphysics is extensively employed for crash dynamics simulation, vibration analysis, and structural optimization in the automotive, aerospace, and civil engineering industries [89].

In fluid dynamics, COMSOL Multiphysics is widely applied to simulate the behaviour of gases and liquids in different systems [90]. The software offers a comprehensive suite of tools for modelling complex fluid dynamics phenomena, including turbulence, multiphase flow, and fluid-structure interaction. These tools are used for applications ranging from high-performance turbomachinery design and heat exchanger optimization to the analysis of blood flow in biomedical devices [91]. This capability has been vital in helping various industries develop more reliable and efficient systems [92].

COMSOL Multiphysics has also found extensive use in the field of electromagnetics for modelling and analysing electromagnetic fields, circuits, and devices [93]. Its electromagnetic modelling capabilities are employed for designing antennas, microwave circuits, and simulating electromagnetic interference and shielding, enabling engineers to enhance the performance and reliability of their products [94]. Moreover, COMSOL Multiphysics is widely used in the development of renewable energy technologies, such as wind turbines and solar cells, where accurate electromagnetic modelling is crucial [95].

The increasing complexity of modern scientific and engineering challenges has underscored the need for comprehensive Multiphysics simulation tools like COMSOL Multiphysics [96]. With applications spanning from biomedical fields like tissue engineering and implantable device modelling to advanced energy system design and industrial process optimization, COMSOL Multiphysics has proven to be an invaluable asset in the pursuit of innovation and technological advancement [97]. As computing power and numerical algorithms continue to evolve, the applications of COMSOL Multiphysics are expected to expand further, driving progress across a wide array of disciplines.

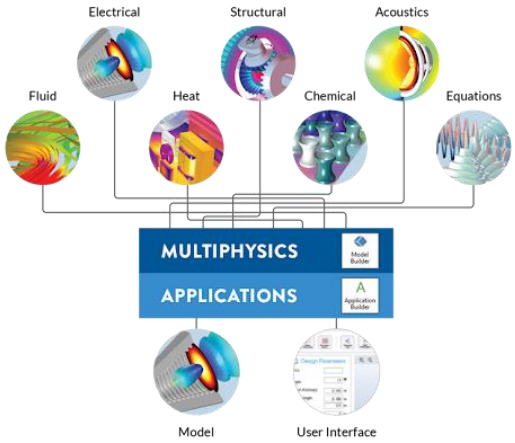


Figure 2.16 Application of Multiphysics

2.8 Surface Functionalization and Immobilization

Techniques such as surface functionalization and immobilisation are fundamental in many domains, including as biology, materials science, and catalysis. Through the introduction of functional groups or the immobilisation of molecules or nanoparticles on the surface, these techniques affect a material's surface, changing its characteristics and opening up new uses.

Significant progress has been made in the field of surface immobilisation and functionalization in the last few years. Using self-assembled monolayers (SAMs) to produce well-organized and customised surface functions is one of the major advancements [98]. With SAMs, surface chemistry may be precisely controlled and a variety of functional groups, including phosphonates, silanes, and thiols, can be added. These groups can then be further changed to immobilise different molecules or nanoparticles [99] [100].

The use of polymer brushes, which graft densely packed polymer chains from the surface to introduce various functional groups and manage surface attributes including wettability, lubrication, and biocompatibility, is another noteworthy advancement [101][102]. Polymer brushes are widely used in fields such as antifouling coatings, medication delivery, and biosensing.

The science of surface functionalization and immobilisation has benefited greatly from the advent of click chemistry. The copper-catalysed azide-alkyne cycloaddition (CuAAC), for example, has a high selectivity and efficiency that make it possible for biomolecules, polymers, and nanoparticles to be attached to a variety of surfaces with ease and durability [103][104].

Furthermore, the development of sophisticated characterization methods like atomic force microscopy (AFM), time-of-flight secondary ion mass spectrometry (ToF-SIMS), and X-ray photoelectron spectroscopy (XPS) has yielded important insights into the dynamics, composition, and structure of functionalized surfaces [105][106].

Surface functionalization and immobilisation have several uses, including as environmental remediation, biosensors, tissue engineering, catalysis, and energy storage. We may anticipate more developments in the design, synthesis, and characterisation of functional surfaces as this field of study develops, which will result in creative answers to numerous problems in science and technology.

2.8.1 Importance of Surface Functionalization

COMSOL A critical method that has drawn a lot of interest in a number of disciplines, including materials science, biology, and nanotechnology, is surface functionalization. The capacity to alter a material's surface characteristics has created a multitude of new applications and produced outstanding progress in many fields.

The capacity of surface functionalization to improve the interfacial interactions between materials and their surroundings is one of its main significances [107]. Surface-dependent qualities such as wettability, adhesion, biocompatibility, and others can be customised to fit certain applications by adding particular functional groups or molecules to

the surface. This has been especially helpful in the creation of biomedical devices, coatings, and smart materials [108][109].

Surface functionalization is essential for enhancing the selectivity and performance of catalytic materials in the field of catalysis. Catalytic activity and reusability can be increased by improving the accessibility and stability of catalytic species by immobilising them on the surface [110][111]. This is particularly significant when designing heterogeneous catalysts, as effective surface anchoring of active sites is crucial.

Advanced sensing and detection systems have also benefited greatly from surface functionalization. Improved sensitivity and selectivity towards target analytes can be achieved by immobilising recognition elements on the surface of sensor devices, such as enzymes, antibodies, or DNA probes [112][113]. This has made it possible to develop extremely effective chemical, environmental, and biosensors with a variety of uses.

Surface functionalization has been essential in the biomedical area for designing biocompatible materials and drug delivery systems. Enhancing cellular adhesion, proliferation, and tissue integration through surface property modification of implants, prostheses, and scaffolds can increase biocompatibility and improve clinical outcomes [114][115].

Moreover, surface functionalization has been widely applied in nanotechnology, where controlling the surface characteristics of nanoparticles and nanostructures is essential for their successful use in pharmaceutical delivery, photovoltaics, and catalysis, among other applications [116,117].

We may anticipate seeing even more cutting-edge uses and solutions that take advantage of the capacity to precisely control and engineer surface features as surface functionalization research advances. This adaptable method will surely be essential to advancing science and technology across a range of fields.

2.8.2 Identification Element for Biosensors

Biosensors are becoming more and more significant in many areas, such as food safety, environmental monitoring, and healthcare. The identification element, which recognises and binds to the target analyte, is an essential part of a biosensor. A synthetic molecule, like a molecularly imprinted polymer, or a biological molecule, like an enzyme, antibody, or nucleic acid, might serve as the identification element. The application and the target analyte determine which identification element is used.

Significant progress has been achieved in the creation of biosensor identification elements in recent years. The use of aptamers, single-stranded nucleic acid molecules with great specificity and affinity for a variety of target molecules, is one such innovation [118]. Aptamers have been employed as identification components in a variety of biosensor applications, including the detection of proteins, small compounds, and pathogens [119]. They can be produced by an in vitro selection procedure called SELEX (Systematic Evolution of Ligands by Exponential Enrichment).

The use of molecularly imprinted polymers (MIPs) as identifying elements is another new discovery. MIPs are artificial polymers that are engineered to replicate the characteristics of biological receptors, like enzymes or antibodies, for recognition [120]. MIPs have been utilised in biosensors for the detection of food contaminants, environmental pollutants, and biomarkers. They can be customised to recognise particular target analytes [121].

Researchers have also looked into using nanomaterials as identification components in biosensors, including graphene, carbon nanotubes, and quantum dots. High surface area, improved sensitivity, and compatibility with a range of transducer platforms are among the benefits that these nanomaterials can offer [122].

In general, the identification element is a vital part of a biosensor, and the evolution of biosensor technology and its applications depends on the ongoing creation of novel and creative identification elements.

2.8.3 Enzymatic Biosensors

Enzymatic biosensors are a type of biosensor that identify and quantify particular analytes by using enzymes as the identifying factor. Enzymes are biological catalysts that interact with their target substrates in a selective manner, which makes them perfect for use in biosensors. Numerous industries, including healthcare, environmental monitoring, and food analysis, have discovered extensive uses for these biosensors [123].

The great specificity and sensitivity of enzymatic biosensors is one of their main benefits. A broad variety of compounds, from simple molecules to intricate macromolecules, can be selectively detected thanks to the ability of enzymes to be engineered to recognise and bind to certain target analytes [124]. Furthermore, the signal can be amplified by the catalytic activity of enzymes, which raises sensitivity and lowers detection limits.

The development of enzymatic biosensors has advanced significantly in the last several years. To detect a wide variety of analytes, researchers have investigated the utilisation of different enzyme types, such as oxidoreductases, transferases, hydrolases, and lyases [125]. For instance, glucose oxidase is frequently utilised in enzymatic biosensors to detect glucose, a crucial component in the management of diabetes [126].

Furthermore, highly sensitive and tiny enzymatic biosensors have been developed as a result of the fusion of enzymes with cutting-edge materials like nanomaterials. Large surface areas, effective electron transfer, and increased signal transduction are some of the benefits that nanomaterials like carbon nanotubes, graphene, and quantum dots can offer, which can improve analytical performance [127].

The development of enzymatic biosensors is still confronted with obstacles despite the developments, including immobilisation, complicated sample matrices, and enzyme stability. The goal of current research is to overcome these obstacles and broaden the range of industries in which enzyme biosensors can be used [128].

In summary, enzymatic biosensors have advanced the field of electrochemical biosensors significantly, and the future of analytical and diagnostic technologies looks very promising if they continue to be developed.

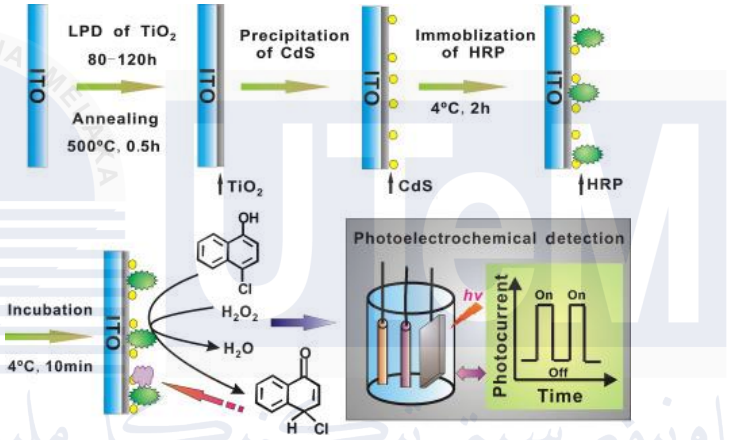


Figure 2.17 Enzyme Based Biosensors

2.9 Electrochemical Biosensor Characterization and Material Analysis

The capacity of electrochemical biosensors to enable sensitive, selective, and quick detection of a broad range of analytes in a variety of applications, including food safety, healthcare, and environmental monitoring, has drawn a lot of attention in recent years. Biological recognition elements like enzymes, antibodies, or nucleic acids are commonly used in these devices. An electrochemical transducer is used to transform the biochemical interaction into an electrical signal [129]. An essential part of the development and optimisation process for electrochemical biosensors is their characterization and material analysis.

The assessment of the sensor's performance, encompassing its sensitivity, selectivity, limit of detection, and dynamic range, is a crucial component of electrochemical

biosensor characterisation [130]. Numerous electrochemical methods, including electrochemical impedance spectroscopy, chronoamperometry, and cyclic voltammetry, can be used to do this. These methods offer information about the kinetics, thermodynamics, and interfacial characteristics of the sensor [131].

Another crucial step in the creation of electrochemical biosensors is material analysis, since the selection of materials used during the sensor's construction can have a big impact on its stability and performance. This comprises characterising the electrode material, the immobilisation matrix, and the interface between the transducer and the biological recognition element [132]. The physical, chemical, and structural characteristics of the materials used in the biosensor can be examined using methods including Fourier-transform infrared spectroscopy, scanning electron microscopy, and X-ray photoelectron spectroscopy [130].

The performance of electrochemical biosensors can now be improved thanks to the recent discovery of sophisticated materials like graphene, carbon nanotubes, and metal nanoparticles [133]. These substances can help immobilise and orient the biological recognition elements and enhance the sensor's sensitivity, selectivity, and stability [130].

Overall, the development and optimisation of electrochemical biosensors depend heavily on the characterization and material analysis of these devices. These processes help researchers identify performance-limiting factors, comprehend the underlying mechanisms, and create more reliable and effective biosensing platforms.

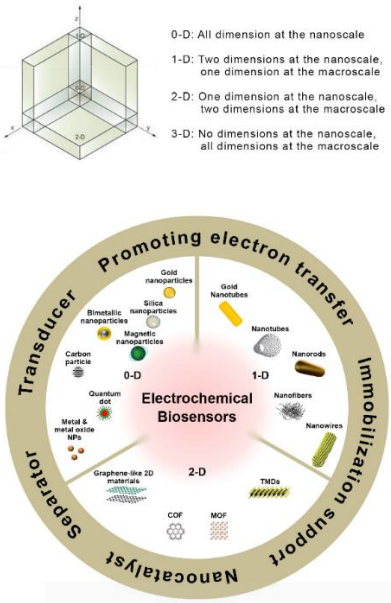


Figure 2.18 Nanomaterials

2.9.1 X-Ray Diffraction (XRD)

A strong analytical method that has been widely employed in the characterization and examination of materials, particularly those used in sensor applications, is X-ray diffraction (XRD). This non-destructive technique is a vital tool in the creation and optimisation of sensor devices because it yields important information about the atomic-scale characteristics, phase composition, and crystal structure of different materials.

The interaction of X-rays with the periodic arrangement of atoms in crystalline materials forms the basis of X-ray scattering (XRD) [134][135]. The atomic planes in a crystal diffract X-rays when they are directed onto a sample, producing a distinct diffraction pattern that can be identified and examined [136][137]. The sample's atomic arrangements, lattice parameters, and crystal structure are all closely correlated with the locations and intensities of the diffraction peaks in the pattern.

XRD analysis is very helpful in the context of sensor materials for identifying the crystalline phases, figuring out the average size of the crystallites, and finding out if there are any impurities or secondary phases present [138][139]. Understanding the structural and

compositional properties of the sensor materials which can have an immediate impact on their performance, stability, and reliability is made possible with the help of this information.

For instance, XRD can be used to describe the phase composition and crystal structure of the electrode materials, such as metal oxides, conductive polymers, or nanostructured carbon materials, in the creation of electrochemical sensors [140][141]. The sensitivity and selectivity of the sensor are significantly influenced by the surface area, catalytic activity, and charge transport characteristics of the electrode, all of which may be understood from this analysis.

Moreover, XRD may be used to track structural alterations in sensor materials that occur throughout a variety of procedures, including heat treatments, thin-film deposition, and surface functionalization [142][143]. Researchers can ensure the stability and endurance of the sensor devices by optimising the fabrication and modification procedures by monitoring the evolution of the crystal structure and phase composition.

When recognition elements, like enzymes, antibodies, or molecularly imprinted polymers, are immobilised on the sensor surface, XRD can be used to characterise their crystallinity and structural features in addition to analysing the sensor materials themselves [144][145]. Understanding the relationships between the target analytes and the recognition elements as well as the stability and performance of the sensor interface can be aided by this knowledge.

The use of XRD as a flexible characterization tool will be essential in the creation of more complex and dependable sensor devices as sensor technology develops, allowing researchers to better understand the structural and compositional factors that support sensor performance

2.9.2 Raman Spectroscopy Analysis

An increasingly important analytical method for characterising and analysing materials utilised in sensor applications is Raman spectroscopy. With the help of this non-destructive technique, researchers can learn important details about the chemical makeup, physical characteristics, and structure of a variety of materials, leading to a deeper understanding of the essential features of sensor devices and components.

The inelastic scattering of monochromatic light typically from a laser source when it interacts with a sample is the foundation of Raman spectroscopy [146][147]. The frequency of the scattered light may change in relation to the incident light, either greater or lower, when the incident light interacts with the phonons or molecular vibrations in the sample. These frequency shifts, often referred to as Raman shifts, are particular to the chemical bonds and vibrational modes found in the sample, giving rise to a signature that resembles a fingerprint and is useful for analysis and identification [148][149].

Raman spectroscopy has been widely used in the context of sensor materials to characterise a variety of materials, such as metal oxides, polymers, biomolecules, and carbon-based nanomaterials [150][151]. The method can yield important insights into the doping, structural characteristics, flaws, and chemical interactions of these materials, all of which have a major influence on the selectivity, sensitivity, and performance of sensor devices.

For instance, Raman spectroscopy has been employed in the construction of electrochemical sensors to examine the redox behaviour and structural alterations of electrode materials, such as conducting polymers, graphene, and carbon nanotubes, during electrochemical operations [152][153]. In order to improve the performance of the sensor, researchers can use this information to better understand the charge transport pathways and optimise the electrode design.

Moreover, the immobilisation and interactions of recognition elements—such as enzymes, antibodies, or aptamers with the sensor surface have been investigated using Raman spectroscopy [154][155]. Researchers may learn more about the structural integrity, orientation, and binding interactions of these biomolecules by tracking their vibrational signatures. These insights are crucial for the creation of dependable and efficient sensor platforms.

Raman spectroscopy's high sensitivity and specificity have made it possible to identify and detect a wide range of analytes directly on the sensor surface, including gases, chemical compounds, and biological molecules [156][157]. Raman-based sensing techniques have been included into creative sensor designs as a result of this capability, offering improved selectivity and the possibility of in-situ or real-time monitoring applications.

Raman spectroscopy is a versatile and non-invasive characterization method that will become more and more relevant as sensor technology advances. In the development, optimisation, and validation of innovative sensor devices across a wide range of industries and applications, Raman analysis will continue to be essential due to its comprehensive insights into the structural, compositional, and functional properties of sensor materials.

2.9.3 FTIR (Fourier Transform Infrared) Analysis

A popular analytical method that is now crucial for characterising and analysing materials used in sensor applications is Fourier Transform Infrared (FTIR) spectroscopy. This potent technology is essential for comprehending and improving sensor systems since it offers useful information about the molecular makeup, functional groups, and structural characteristics of a variety of materials.

The interaction of infrared radiation with the molecules in a sample is the basis of FTIR spectroscopy [158][159]. The molecules in the sample can absorb certain wavelengths of infrared light, which will cause them to vibrate or rotate in distinctive ways when the sample is subjected to infrared light [160][161]. The Fourier transform method is then used to identify and examine these absorption patterns, which are particular to the chemical bonds and functional groups in the sample. The outcome is a comprehensive infrared spectrum.

FTIR analysis has been widely used in the context of sensor materials to characterise the chemical composition, surface chemistry, and structural changes of a variety of materials, including metal oxides, ceramics, polymers, and biomolecules [162][163]. This data is essential for optimising the performance, selectivity, and stability of the sensor as well as for comprehending the interactions between the target analytes and the sensor materials.

For instance, the immobilisation and structural integrity of recognition elements on the sensor surface, such as enzymes, antibodies, or aptamers, have been investigated using FTIR spectroscopy [164][165]. Through the observation of distinct absorption bands linked to the secondary structures and functional groups of these biomolecules, scientists can acquire knowledge about the effective immobilisation, orientation, and possible denaturation or conformational alterations that might transpire throughout the sensor manufacturing procedure.

Moreover, surface modifications and functionalization of sensor materials such as the grafting of polymers or nanostructures, or the addition of particular functional groups have been studied using FTIR analysis [166][167]. Understanding the alterations in surface chemistry and how they affect the sensitivity, selectivity, and general performance of the sensor depends on this knowledge.

FTIR spectroscopy has been used not only to characterise sensor materials but also to directly detect and identify target analytes on the sensor surface [168][169]. Various

substances, such as gases, organic chemicals, and biomolecules, have distinct infrared absorption signatures that can be utilised to create extremely sensitive and selective FTIR-based sensor platforms for a variety of uses.

FTIR analysis will continue to play a crucial role as sensor technology develops since it is a flexible and effective characterization method. For the development, optimisation, and validation of advanced sensor devices across a wide range of industries and applications, FTIR spectroscopy will remain indispensable due to its comprehensive insights into the molecular composition, structural characteristics, and surface chemistry of sensor materials.

2.9.4 Field Emission Scanning Electron Microscopy (FESEM) and Chronoamperometry

The integration of chronoamperometry and field emission scanning electron microscopy (FESEM) is a potent analytical technique that has been widely used to characterise and comprehend sensor materials and their electrochemical performance.

Using a field emission source to create a concentrated electron beam that is subsequently scanned across the sample's surface, FESEM is a high-resolution imaging method [170][171]. Researchers can better understand the structural factors that can affect a sensor's performance by using this method, which gives precise information about the morphology, surface features, and nano structural aspects of the sensor materials.

FESEM analysis has been used to characterise a variety of materials in the context of sensor applications, including metal oxides, polymers, biomolecules, and carbon-based nanomaterials [172][173]. The high-resolution images produced by the FESEM can offer important information on the topography of the surface, the size and distribution of the particles, and the existence of flaws or heterogeneities in the sensor materials. Understanding

the connections between the structural characteristics and the electrochemical behaviour of the sensor requires knowledge of this information.

Chronoamperometry is an electrochemical method that measures a sensor's current response over time, usually in reaction to a stepped or pulsed potential, and it is used in conjunction with FESEM analysis [174][175]. Optimising the sensitivity, selectivity, and stability of the sensor requires knowledge of the kinetics, charge transfer mechanisms, and electrochemical activity of the sensor materials, all of which may be found in this procedure.

Researchers can develop a thorough understanding of the sensor materials and their electrochemical performance by combining chronoamperometry with FESEM. It is possible to identify the crucial material characteristics that affect the sensor's performance by correlating the electrochemical responses detected by chronoamperometry with the high-resolution structural data gathered by FESEM [176][177].

For instance, the morphological traits and nano structural attributes of electrode materials, such as metal oxides or carbon nanomaterials, that contribute to their electrochemical activity and charge transfer capabilities can be revealed by FESEM analysis [178][179]. The kinetics and redox behaviour of these materials can then be better understood using complementary chronoamperometric measurements, which enables researchers to streamline the manufacture and design of sensors.

Moreover, the characterisation of sensor interfaces, including the immobilisation of recognition components (such as enzymes, antibodies, or aptamers) on the sensor surface, has benefited from the combination of FESEM and chronoamperometry [180][181]. To develop efficient and dependable sensor devices, researchers must understand the stability, accessibility, and functionality of the recognition elements. These can be learned by examining the structural alterations and electrochemical reactions connected to the immobilisation process.

The complementary use of FESEM and chronoamperometry will continue to be a crucial analytical method for the thorough characterization and optimisation of sensor materials and devices as the field of sensor technology develops, empowering researchers to push for even greater improvements in sensor performance and capabilities.

2.10 Glucose Detection Method

Over the past few years, there has been a major evolution in glucose detection methods, with a focus on developing minimally invasive and non-invasive technology. Using biosensors based on nanotechnology, which can non-invasively measure glucose levels, is one possible strategy [182]. These biosensors can be incorporated into flexible and wearable gadgets to provide real-time, ongoing glucose monitoring.

A flexible enzyme-electrode sensor with a cylindrical working electrode that has been altered with a 3D nanostructure is one type of biosensor based on nanotechnology [183]. It has been demonstrated that this sensor has good glucose detection sensitivity and selectivity, which qualifies it for implantable lab-on-a-chip applications.

Applying near-infrared light for non-invasive glucose sensing is an additional method. With good selectivity, repeatability, and stability, this method may offer real-time, non-invasive, quick-witted and chemical-free glucose detection [184]. However, the technology is still not fully developed for clinical applications, and there are substantial requirements for materials and manufacturing expenses.

Another innovative method for minimally invasive glucose monitoring is electrochemical sensors. These sensors monitor the amount of glucose in interstitial fluid—obtained via microanalysis or a tiny needle—using electrochemical techniques [185].

Because of their great sensitivity and selectivity, electrochemical sensors are a good choice for continuous, real-time glucose monitoring.

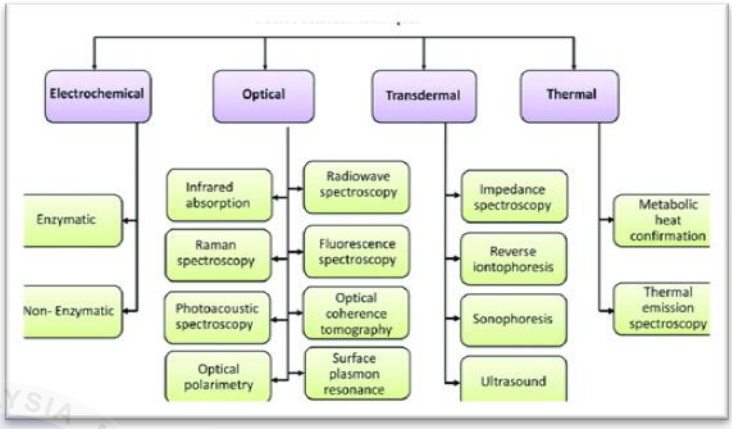


Figure 2.19 Glucose Detection Technique

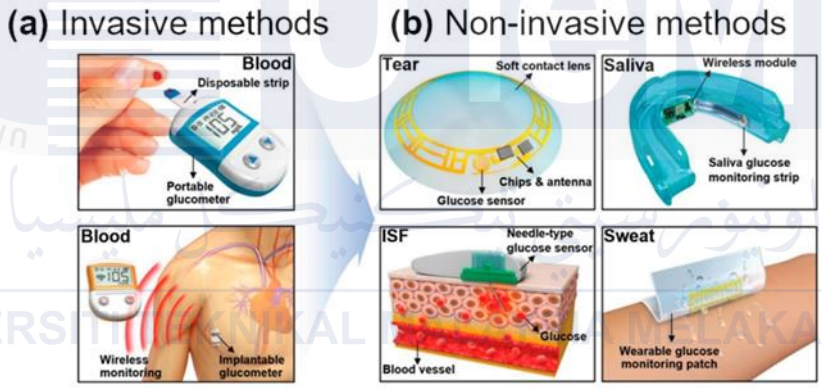


Figure 2.20 Glucose Detection Methods

Another innovative method for minimally invasive glucose monitoring is electrochemical sensors. These sensors monitor the amount of glucose in interstitial fluid obtained via microanalysis or a tiny needle using electrochemical techniques [19]. Because of their great sensitivity and selectivity, electrochemical sensors are a good choice for continuous, real-time glucose monitoring.

2.10.1 Significance of Multi-Concentration Glucose Detection

The literature emphasises the importance of multi-concentration glucose detection, especially in relation to the advancement of sophisticated biosensors and continuous glucose monitoring (CGM). The capability of multi-concentration glucose detection to precisely monitor glucose levels over a broad range, covering both low and high concentrations, is one of its main benefits[188].

This is essential for managing diabetes because it makes it possible to identify hypo- and hyperglycaemic episodes early on, which is vital for averting complications and enhancing patient outcomes [189].

Traditional glucose detection techniques, including single-point blood glucose assays, frequently can't record the dynamic variations in glucose levels that occur during the day. On the other hand, continuous monitoring is made possible by multi-concentration glucose detection, which gives patients and medical professionals a more thorough understanding of glucose swings [190].

Additionally, the development of sophisticated biosensors has showed promise in improving the selectivity and sensitivity of glucose detection over a broad range of concentrations, especially those based on carbon nanotubes [187]. These biosensors can be incorporated into implantable or wearable medical equipment to enable enhanced disease management and real-time, non-invasive glucose monitoring [186].

The significance of multi-concentration glucose detection also extends to its potential impact on public health and healthcare costs. By enabling more accurate and comprehensive glucose monitoring, these technologies can lead to better glycaemic control, reduced incidence of diabetes-related complications, and improved quality of life for patients[26]. Furthermore, the cost-effectiveness of these solutions can contribute to the

broader accessibility and adoption of glucose monitoring technologies, benefiting both individuals and healthcare systems [189].

2.11 Previous Studies on Carbon Nanotube-Based Biosensors for Glucose Detection

In addition to encouraging outcomes, earlier research has investigated the application of carbon nanotube-based biosensors for glucose detection. As a result of their remarkable optical and electrical properties, high aspect ratio, and chemical durability, carbon nanotubes (CNTs) have been employed in electrochemical biosensors for the detection of glucose [191][192]. Research on electrochemical glucose sensors has benefited from the many nanostructures and metal surface designs of carbon nanotubes (CNTs), especially in the development of flexible CNT-based interfaces [191].

In one study, a biosensor for evaluating food was created utilizing biologicals, chemicals, and carbon nanotubes (CNTs). Using a DR of (1.0–15) × 10−3 μM and a LOD of 3 × 10−4 nM, the biosensor identified glucose [191]. Immobilized enzymes, which have been demonstrated to improve the sensitivity and selectivity of glucose detection in electrochemical biosensors, were employed in the biosensor [191].

An effective flexible electrochemical glucose sensor based on carbon nanotubes and carbonised silk fabrics embellished with Pt was created by another study. The biosensor demonstrated excellent glucose detection sensitivity and selectivity, qualifying it for real-time, non-invasive glucose monitoring [192].

The application of nanomaterials—including carbon nanotubes—in the biosensor industry has attracted a lot of interest lately. Because of their high aspect ratio, exceptional chemical stability, and noteworthy optical and electrical properties, carbon nanotubes (CNTs) have become more popular in glucose sensors. Numerous applications in electrochemical glucose sensor research have resulted from the unique physical and

chemical properties of carbon nanotubes (CNTs) as well as their varied nanostructures and metal surface designs [192].

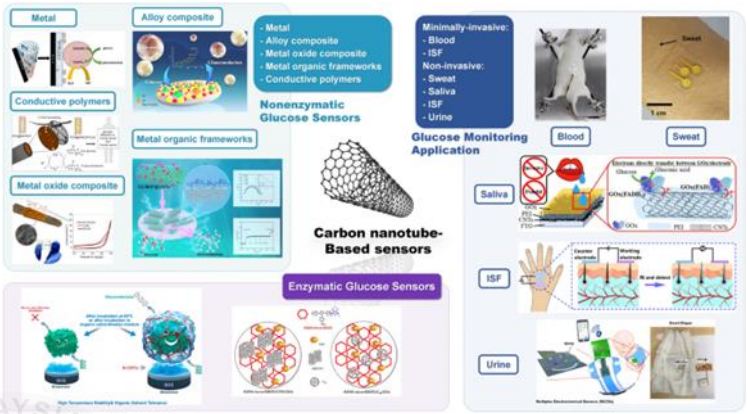


Figure 2.21 Carbon Nanotubes

In conclusion, earlier research has shown that carbon nanotube-based biosensors hold promise for the detection of glucose. It has been demonstrated that the sensitivity and selectivity of glucose detection in electrochemical biosensors can be improved by the use of immobilized enzymes and flexible interfaces built on carbon nanotubes. The application of nanomaterials, such as carbon nanotubes (CNTs), in the biosensor domain has attracted significant interest in recent times. CNTs have become increasingly prominent in glucose sensors because of their high aspect ratio, exceptional chemical stability, and noteworthy optical and electrical properties. Numerous applications in electrochemical glucose sensor research have resulted from the unique physical and chemical properties of carbon nanotubes (CNTs) as well as their varied nanostructures and metal surface designs.

2.12 Summary

Biosensors that use carbon nanotubes (CNTs) and novel detection techniques have revolutionised several industries by making it possible to detect analytes with high sensitivity and specificity for use in food safety, environmental monitoring, and healthcare. Because of its special qualities, which include a high surface-to-volume ratio and remarkable

electrical conductivity, CNTs are perfect for the construction of biosensors. New developments in CNT synthesis and functionalization have broadened its uses in biosensing, and novel approaches to glucose detection provide diabetic patients with continuous, non-invasive monitoring. Previous research has demonstrated the efficacy of carbon nanotube-based biosensors in the detection of glucose, underscoring its potential to improve selectivity and sensitivity. In general, current research endeavours seek to surmount obstacles and augment the potential of biosensor technology for extensive incorporation in a variety of fields.

2.13 Comparison Table from previous research paper

Table 2.1 Comparison of glucose biosensor from previous research

No	Author	Title	Year	Method	Findings
1	Nguyen [1]	Carbon Nanotube-Based Biosensors Using Fusion Technologies with Biologicals & Chemicals for Food Assessment	2021	The journal article explores using carbon nanotube-based biosensors for assessing food quality. Researchers enhanced these biosensors by adding specific biological and chemical components to improve sensitivity and selectivity. They included enzymes or antibodies to detect target analytes in food samples. Cutting-edge technologies were used to make the biosensors effective for detecting substances in food. The researchers tested	Discussed the use of carbon nanotubes in biosensors for food assessment, highlighting their high sensitivity

				the biosensors' accuracy, sensitivity, and reliability with various food samples to assess their performance. These biosensors provide quick and precise results for monitoring food ingredients in real-time, showing promise for improving food safety and quality control.	
2	Chen [3]	An efficient flexible electrochemical glucose sensor based on carbon nanotubes/carbonized silk fabrics decorated with Pt	2018	Electrochemical glucose sensor using carbonized silk fabrics and Pt decoration.	Developed a flexible and efficient electrochemical glucose sensor

3	Bandodkar[5]	Tattoo-based noninvasive glucose monitoring: a proof-of-concept study	2015	Noninvasive glucose monitoring using tattoo-based sensors	Demonstrated a tattoo-based sensor for noninvasive glucose monitoring
4	Heller & Feldman [6]	Electrochemical glucose sensors and their applications in diabetes management	2008	Electrochemical glucose sensors	Reviewed applications of electrochemical glucose sensors in diabetes management
5	Vashist [7]	Non-invasive glucose monitoring technology in diabetes management: A review	2012	Non-invasive glucose monitoring	Reviewed technologies for non-invasive glucose monitoring in diabetes management.

6	Johnston [8]	Advances in Biosensors for Continuous Glucose Monitoring towards Wearables	2021	Continuous glucose monitoring	Discussed advances in wearable biosensors for continuous glucose monitoring.
7	Huang [22]	Integrated electronic/fluidic microneedle system for glucose sensing and insulin delivery.	2024	Microneedle system for glucose sensing and insulin delivery.	Developed an integrated microneedle system for both glucose sensing and insulin delivery
8	Teymourian [29]	Electrochemical glucose sensors in diabetes management: an updated review (2010–2020	2020	Electrochemical glucose sensors	Provided an updated review of electrochemical

					glucose sensors for diabetes management
9	Saha [36]	Wearable electrochemical glucose sensors in diabetes management: a comprehensive review	2023	Wearable electrochemical glucose sensors	Reviewed wearable electrochemical glucose sensors for diabetes management
10	Wang [48]	Advances in Biosensors for Continuous Glucose Monitoring	2021	Continuous glucose monitoring	Discussed recent advances in continuous glucose monitoring technologies
11	Govindaraj, M., Srivastava, A., et al.[51]	Current advancements and prospects of enzymatic and non-enzymatic electrochemical glucose sensors	2023	Review of enzymatic and non-enzymatic electrochemical methods.	Discusses advancements in sensitivity, selectivity, and

					stability of glucose sensors. Highlights integration with nanomaterials for enhanced performance.
12	Reddy, V. S., Agarwal, B., et al.[55]	Recent advancement in biofluid-based glucose sensors using invasive, minimally invasive, and non-invasive technologies	2022	Review of biofluid-based glucose sensing technologies	Summarizes invasive, minimally invasive, and non-invasive methods for glucose detection in various biofluids. Emphasizes emerging

					technologies and their potential.
13	Chung, M., Fortunato, G., & Radacsi, N.[56]	Nanotechnology in glucose monitoring: Advances and challenges in the last 10 years	2013	Review of nanotechnology applications in glucose monitoring.	Reviews the impact of nanotechnology on glucose sensor performance. Identifies major challenges and advances in sensor miniaturization and sensitivity.
14	Wang, J.[126]	Electrochemical glucose biosensors	2008	Review of electrochemical glucose biosensors	Provides a comprehensive overview of electrochemical

					glucose biosensor technologies. Highlights their application in clinical settings and future prospects.
15	Yoo, E. H., & Lee, S. Y.[129]	Glucose biosensors: an overview of use in clinical practice	2010	Overview of glucose biosensors used in clinical practice	Summarizes the types and applications of glucose biosensors in clinical practice. Discusses the performance metrics required for clinical use

16	Grieshaber, D., MacKenzie, R., Vörös, J., & Reimhult, E.[130]	Electrochemical biosensors-sensor principles and architectures	2008	Review of electrochemical biosensor principles and architectures	Details various architectures and principles of electrochemical biosensors, with a focus on glucose detection. Reviews innovations in sensor design.
17	Han, Q., Wang, H., & Wang, J.[131]	Multi-Mode/Signal Biosensors: Electrochemical Integrated Sensing Techniques	2024	Development of multi-mode/signal biosensors integrating electrochemical sensing techniques	Describes innovative multi-mode biosensors combining different sensing techniques for improved glucose

					detection. Highlights advantages in sensitivity and specificity.
17	Su, L., Feng, J., Zhou, X., Ren, C., Li, H., & Chen, X.[184]	Colorimetric detection of urine glucose based on ZnFe2O4 magnetic nanoparticles	2012	Colorimetric detection using ZnFe2O4 magnetic nanoparticles.	Developed a colorimetric sensor for urine glucose detection with high sensitivity and specificity.
18	Abunahla, H., Mohammad, B., Alazzam, A., Jaoude, M. A., Al-Qutayri,	MOMSense: Metal-Oxide-Metal Elementary Glucose Sensor	2019	Metal-Oxide-Metal (MOM) sensor	Introduced a glucose sensor with high sensitivity and low detection limit, suitable for non-

	M., Hadi, S. A., & Al-Sarawi, S. F.[185]				enzymatic glucose detection.
19	Das, S. K., Nayak, K. K., Krishnaswamy, P. R., Kumar, V., & Bhat, N.[187]	Electrochemistry and other emerging technologies for continuous glucose monitoring devices	2022	Electrochemical methods and emerging technologies	Reviewed advancements in continuous glucose monitoring (CGM) technologies highlighting improvements in sensor accuracy and patient comfort.
20	Cappon, G., Vettoretti, M.,	Continuous glucose monitoring sensors for diabetes management:	2019	Review of CGM sensor technologies	Provided a comprehensive

	Sparacino, G., & Facchinetti, A[188]	a review of technologies and applications			review of CGM technologies, discussing various sensor designs, their applications, and future directions in diabetes management.
21	Funtanilla, V. D., Candidate, P., & Candidate, P.[189]	Continuous Glucose Monitoring: A Review of Successes, Challenges, and Opportunities	2019	Review of CGM technologies	Discussed the successes and challenges of CGM systems, emphasizing the importance of sensor accuracy,

					reliability, and patient adherence.
22	Koirala, P., Khanal, M., & Bhattarai, R.[190]	Noninvasive Spectroscopic Detection of Blood Glucose and Analysis of Clinical Research	2018	Noninvasive spectroscopic detection	Explored noninvasive methods for glucose detection, highlighting the potential and challenges of spectroscopic techniques in clinical applications.
23	Nguyen, H. H., Lee, S. H., Lee, U. J., Fermin, C. D.,	Immobilized Enzymes in Biosensor Applications	2019	Immobilized enzyme biosensors	Reviewed the use of immobilized enzymes in biosensors, focusing

	& Kim, M.[191]				on their applications, advantages, and limitations in various fields including glucose detection.
24	Zappi, D., Caminiti, R., Ingo, G. M., Sadun, C., Tortolini, C., & Antonelli, M. L.[192]	Biologically friendly room temperature ionic liquids and nanomaterials for the development of innovative enzymatic biosensors	2017	Enzymatic biosensors with ionic liquids and nanomaterials	Developed innovative enzymatic biosensors using biologically friendly ionic liquids and nanomaterials, enhancing sensor stability and performance.

CHAPTER 3

METHODOLOGY

3.1 Introduction

In general, the methodology section delves into the detailed flowchart, equipment list, and materials utilized in the development process of Carbon Nanotube-Based Biosensors for Multi-Concentration Glucose Detection. This chapter serves as a comprehensive guide outlining the step-by-step flowchart methodology, the essential equipment required for the experiment, and a detailed list of materials utilized in the biosensor fabrication process. The meticulous description of each equipment and material, ranging from Carbon Nanotubes to specialized machines like Field Emission Scanning Electron Microscopes and Fourier Transform Infrared Spectroscopy Machines, underscores the precision and sophistication involved in the development of these advanced biosensors. This section provides a foundational understanding of the tools and resources employed in the research, setting the stage for the subsequent experimental procedures and analysis conducted in the study.

3.2 Flowchart of Methodology

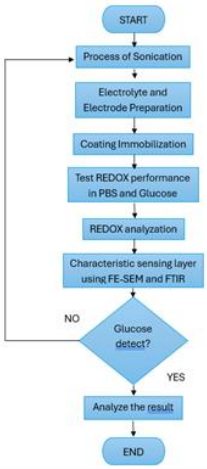


Figure 3.1 Flowchart

Setting the scene for the creation of biosensors specifically for glucose detection is the first phase in the "Development of Carbon Nanotube-Based Biosensors for Multi-Concentration Glucose Detection" process. To prepare materials like carbon nanotubes to produce biosensors, this phase entails using sonication to stir up particles in a sample.

The process of sonication is followed by the creation of electrodes and electrolytes, which are necessary elements that aid in reactions and allow precise measurement of different glucose concentrations. Then, to perhaps improve the biosensor's sensitivity and specificity in detecting glucose, a coating is immobilised on the electrodes.

The assessment of REDOX performance in PBS and glucose solutions provides important information about the biosensor's response to various conditions and concentrations. Assessing the electrochemical behaviour of the biosensor and its accuracy in detecting glucose is facilitated by analysing the REDOX reactions.

The distinctive sensing layer is then thoroughly analysed using sophisticated methods such as Fourier Transform Infrared Spectroscopy (FTIR) and Field Emission Scanning Electron Microscopy (FE-SEM). This research adds to the overall efficacy of the biosensor by elucidating the composition and structure of the sensing layer.

The method loops around to improve the biosensor design for improved glucose detection capabilities if more optimisation is judged essential at the glucose detection decision point. After glucose is successfully detected, the results are analysed, and a thorough assessment of the gathered data is done to derive conclusions and insights for possible improvements in the functioning of the biosensor.

The workflow ends at this point, indicating that the development procedure for carbon nanotube-based biosensors designed especially for multi-concentration glucose detection has been successfully completed.

3.3 List of Equipment

Table 3.1 List of Equipment

Equipment	Quantities
Carbon Nanotube	1 pack
Carbon plate	20 pcs (1cm x 2cm)
Indium Tin Oxide plate	20 pcs (1cm x 2cm)
Gold Plate	
Sodium Dodecylbenzesulfonate (SDBS)	1
Polypyrrole (PPY)	1
Distilled Water (DI)	1
Ethanol	1
Methanol	1
Ethyl-3-(3-dimethlaminopropyl) carbodiimide hydrochloride (EDC)	4 mg
N-hydroxysuccinimide (NHS)	6 mg
Glucose Oxidase	1 mg
Potentiostat	1
NOVA 2.0 Advance Electrochemistry software	1
Field Emission Scanning Electron Microscope	1
Fourier Transform Infrared Spectroscopy	1

3.3.1 Carbon Nanotube

Carbon nanotubes are nanometre-sized, cylindrical structures composed of carbon atoms. Single-walled carbon nanotubes (SWNTs) and multi-walled carbon nanotubes (MWNTs) are the two primary varieties. Whereas MWNTs are made up of many layers of graphene wrapped into concentric cylinders, SWNTs are made up of a single layer of graphene rolled into a cylinder. These nanotubes' remarkable characteristics, which include strong tensile strength, thermal conductivity, and electrical conductivity, are brought about by their covalent bonds between carbon atoms and nanostructure. They have a wide range of uses in composite materials, optics, electronics, and nanomedicine and can be chemically altered. Since the discovery of carbon nanotubes in 1991, studies have concentrated on their production, characteristics, and many industrial applications.

Figure 3.2 Carbon Nanotubes

3.3.2 Gold Target

Carbon nanotubes are nanometre-sized, cylindrical structures composed of carbon atoms. Single-walled carbon nanotubes (SWNTs) and multi-walled carbon nanotubes

(MWNTs) are the two primary varieties. Whereas MWNTs are made up of many layers of graphene wrapped into concentric cylinders, SWNTs are made up of a single layer of graphene rolled into a cylinder. These nanotubes' remarkable characteristics, which include strong tensile strength, thermal conductivity, and electrical conductivity, are brought about by their covalent bonds between carbon atoms and nanostructure. They have a wide range of uses in composite materials, optics, electronics, and nanomedicine and can be chemically altered. Since the discovery of carbon nanotubes in 1991, studies have concentrated on their production, characteristics, and many industrial applications.

Figure 3.3 Gold Target

3.3.3 Indium Tin Oxide Plate

The transparent conductive oxide known as indium tin oxide (ITO) plate is made up of tin oxide (SnO_2) and indium oxide (InO_3) in different proportions; by weight, indium oxide makes up around 90% of the plate. Because of this special mix, ITO has exceptional electrical conductivity and transparency qualities that make it an essential material for many high-tech applications. The ITO plate is frequently used in the fabrication of touch screens, flat-panel displays, solar cells, and LED lighting as a thin film coating on glass or plastic substrates. Its optical transparency combined with electrical conductivity makes it possible to transmit electrical signals effectively without obscuring light. ITO's thin film can be

deposited in a consistent, long-lasting layer by employing methods like sputtering or evaporation. ITO is utilised in EMI shielding and energy-efficient windows in addition to electronics. Its importance in current technical breakthroughs is highlighted by its extensive application in consumer electronics and renewable energy technologies. However, current research for substitute materials that might mimic or surpass indium's characteristics is motivated by the metal's scarcity, high cost, and brittleness in ITO films.

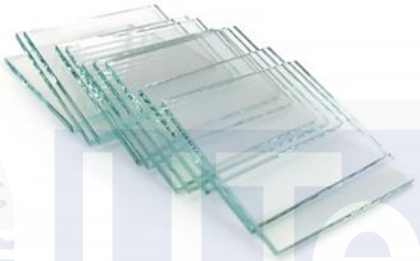


Figure 3.4 Indium Tin Oxide Plate

3.3.4 Polypyrrolw (PPY)

Pyrrole undergoes oxidative polymerization to yield Polypyrrole (PPY), an organic polymer. H(C4H2NH)nH is the chemical formula of this inherently conducting polymer. Applications for PPY can be found in many different domains, including biology, medicine, electronics, and optics. There are several ways to synthesise PPY, but the most popular ones include chemical oxidation and electrochemical synthesis. While electrochemical synthesis offers precise control over the material's characteristics, chemical oxidation employs the reaction of pyrrole with FeCl3 to generate the polymer. PPY films are originally yellow, but when they are exposed to air, oxidation can cause them to darken. Depending on parameters like film thickness and degree of polymerization, doped films can have a blue or black appearance. PPY has special characteristics such being amorphous, stable up to 150°C before the dopant begins to evolve, and insoluble but swellable in solvents. PPY has

conductivities ranging from 2 to 100 S/cm, which are dependent on the oxidation conditions. PPY is an adaptable material for biosensors and tissue/cell support substrates because it is electrochemically produced and may include anionic species, including biological macromolecules like proteins and polysaccharides.

Figure 3.5 Polypyrrole

3.3.5 Sodium Dodecylbenzesulfonate (SDBS)

Sodium Dodecylbenzene Sulfonate, or SDBS, is a multipurpose anionic surfactant that finds employment in a variety of industries, including paper, leather, fibre, household detergents, metal plating, and agricultural chemicals. It is well-known for having dispersity, emulsification, foaming, moistening, and detergency qualities. Because of its great biological degradability (over 90%), SDBS is accepted by international security organisations as a safe chemical. This surfactant is a high-quality detergent and cleaner ingredient, an effective emulsifying agent for polymerizing pressure-sensitive adhesives, an antistatic additive for textiles, and an antistatic agent for polyester substrates. Furthermore, SDBS can enhance the quality of both organic and inorganic chemical goods that are susceptible to moisture absorption and agglomeration. It also functions as an anti-hygroscopic and anti-caking additive for powdered chemical products.

Figure 3.6 Sodium Dodecylbenzesulfonate (SDBS)

3.3.6 Ethanol

Ethanol, sometimes referred to as ethyl alcohol, is a chemical substance with the formula C2H5OH. It is a colourless, combustible, volatile liquid with a faint, distinctive smell. Although it has numerous additional applications, ethanol is most commonly associated with the kind of alcohol found in alcoholic beverages.

Figure 3.7 Ethanol

Ethanol is useful in several ways. It is the intoxicating ingredient found in alcoholic beverages including wine, beer, and spirits. Ethanol is utilised as a gasoline additive and as a biofuel. Ethanol is frequently used in blended fuels, such as E10 (10% ethanol, 90% petrol), and in engines that are specifically made for it, it can also be used in its pure form, E100. Ethanol finds application in the chemical industry as a solvent for producing varnishes, fragrances, and other compounds. It is used in hand sanitizers and medical wipes as an

antiseptic and disinfectant in medicine. Ethanol can be found in cleaning supplies, personal hygiene items, and several cooking ingredients in homes.

3.3.7 Distiled Water

Water that has gone through the distillation process of purification is called distilled water. Water that has undergone this treatment is greatly cleansed by eliminating pollutants and impurities. This is a summary of distilled water's characteristics, manufacture, applications, and advantages. Boiling water produces steam, which is subsequently condensed back into liquid form in the distillation process. Water and impurities are successfully separated by this procedure because pollutants usually have higher boiling temperatures and stay in the boiling chamber.

Figure 3.8 Distilled Water

Distilled water is extremely pure water that has had the majority of pollutants and impurities removed through the distillation process. Its purity and capacity to prevent mineral buildup make it useful in a variety of industries, including the medical, industrial, automotive, domestic, and beverage sectors. Even though it has many advantages, factors like expense, possible acidity, and mineral deficiencies should be taken into account. In many industries where the purest water possible is necessary, distilled water is a vital resource.

3.3.8 Methanol

Methanol is a chemical molecule with the formula CH 3 OH. It is sometimes referred to as methyl alcohol, wood alcohol, or wood spirit. It is the most basic type of alcohol, a clear, colourless, flammable liquid with a unique smell that is comparatively softer than that of ethanol. An essential industrial chemical, methanol is utilised as a fuel, antifreeze, solvent, and denaturant for ethanol.

Figure 3.9 Methanol

Methanol is a multipurpose chemical that has a wide range of industrial and commercial uses, including chemical synthesis, fuel, and antifreeze. To avoid poisoning, it must be handled carefully because it is extremely toxic. Its significance in the present and future energy and chemical industries is highlighted by the fact that it is mostly produced from natural gas and has the potential to come from renewable resources.

3.3.9 Ethyl-3-(3-dimethlaminopropyl) carbodiimide hydrochloride (EDC)

Ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride, commonly known as EDC or EDC-HCl, is a water-soluble carbodiimide reagent commonly used in biochemistry and molecular biology for the activation of carboxyl groups. EDC is primarily employed in the formation of amide bonds through the coupling of carboxyl groups with

primary amines. This reaction is widely used in peptide synthesis, protein crosslinking, and conjugation of haptens to carrier proteins for antibody production.

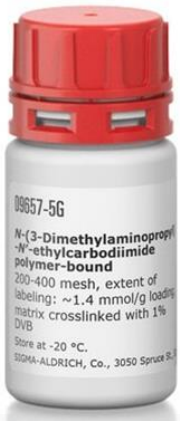


Figure 3.10 Ethyl-3-(3-dimethlaminopropyl) carbodiimide hydrochloride (EDC)

3.3.10 N-hydroxysuccinimide (NHS)

Ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride, commonly known as EDC or EDC-HCl, is a water-soluble carbodiimide reagent commonly used in biochemistry and molecular biology for the activation of carboxyl groups. EDC is primarily employed in the formation of amide bonds through the coupling of carboxyl groups with primary amines. This reaction is widely used in peptide synthesis, protein crosslinking, and conjugation of haptens to carrier proteins for antibody production.

Figure 3.11 N-hydroxysuccinimide (NHS)

3.3.11 Glucose Oxidase

The enzyme glucose oxidase (GOX) catalyses the conversion of glucose to glucono-δ-lactone and hydrogen peroxide. Numerous industries, including biochemistry, medicine, and the food industry, employ this enzyme extensively. A versatile and extensively utilised enzyme, glucose oxidase has important uses in biotechnology, food industry, medical diagnostics, and research. It is an indispensable instrument in many industrial applications and biochemical processes due to its great specificity, stability, and efficiency. Despite certain difficulties, such as controlling the formation of hydrogen peroxide and financial concerns, glucose oxidase is still a crucial enzyme in many scientific and technological developments.

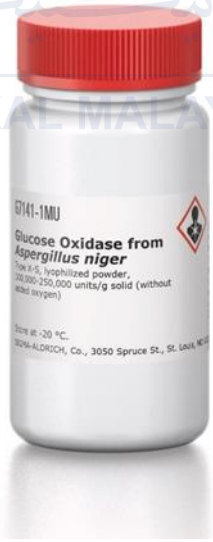


Figure 3.12 Glucose Oxidase

3.3.12 NOVA 2.0 – Advance Electrochemistry Software

NOVA 2.0 is an advanced electrochemistry software that offers a comprehensive platform for analyzing electrochemical data and conducting sophisticated experiments in the field of electrochemistry. This software provides researchers and scientists with a range of tools and features to enhance their understanding of electrochemical processes and facilitate accurate data analysis.One key feature of NOVA 2.0 is its ability to streamline data analysis and interpretation, allowing users to visualize and interpret complex electrochemical data with ease. The software offers advanced data processing algorithms and visualization tools that enable researchers to extract valuable insights from their experimental results efficiently.Moreover, NOVA 2.0 facilitates the design and simulation of electrochemical experiments, allowing users to model different scenarios and predict outcomes before conducting actual experiments. This predictive capability helps researchers optimize their experimental setups and parameters, leading to more efficient and effective research outcomes.Additionally, NOVA 2.0 supports real-time data acquisition and monitoring, enabling researchers to track electrochemical processes as they occur. This real-time monitoring feature is invaluable for studying dynamic electrochemical reactions and understanding the kinetics and mechanisms involved.In conclusion, NOVA 2.0 is a powerful tool for researchers in the field of electrochemistry, offering advanced capabilities for data analysis, experiment design, simulation, and real-time monitoring. By leveraging the features of NOVA 2.0, researchers can enhance their research productivity, gain deeper insights into electrochemical processes, and advance the field of electrochemistry.

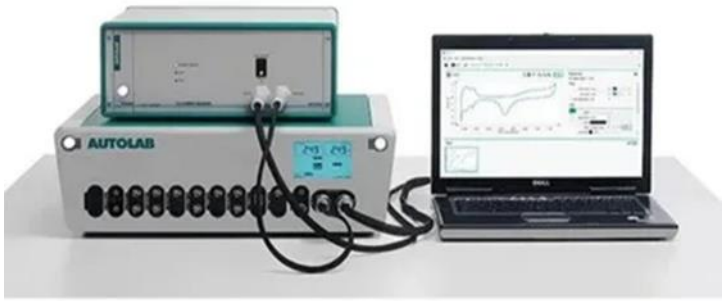


Figure 3.13 Machine

3.3.13 Potentiostat

Potentiostats are essential tools in electrochemical cells, maintaining the potential of the working electrode at a fixed value to precisely regulate electrochemical reactions and measure the resulting current. This capability is crucial for applications such as corrosion research, electrochemical analysis, and battery testing. In biosensors, potentiostats control the working electrode's potential and measure the current proportional to the analyte's concentration, enabling accurate quantification and monitoring of analyte levels over time. Specifically, in continuous glucose monitoring, potentiostats measure the current corresponding to glucose concentration in the interstitial fluid, providing precise real-time glucose level monitoring. Overall, potentiostats are indispensable for a wide range of electrochemical investigations and applications.

Figure 3.14 Potentiostat

3.3.14 Field Emission Scanning Electron Microscope (FE-SEM) Machine

The scanning electron microscope (FE-SEM) is a device that uses electrons rather than light to create greatly enlarged images. An electron beam is produced by an electron cannon located at the top of the microscope. Focused imaging is produced when this beam passes through the vacuum-sealed microscope vertically and is directed towards the sample by lenses and electromagnetic fields. Both electrons and X-rays are released when the sample and the electron beam interact. The FE SEM machine that is being used for this project is shown in Figure 3.15.

Figure 3.15 FE-SEM Machine

3.3.15 Fourier Transform Infared Spectroscopy Machine

Fourier Transform Infrared Spectroscopy (FTIR) is a crucial analytical method for identifying organic, polymeric, and occasionally inorganic materials by measuring their absorption of infrared light, providing detailed information about their molecular makeup and structure. It is indispensable in various fields such as biology, chemistry, materials science, and environmental research. FTIR machines are valued for their high sensitivity, rapid data collection, and versatility in handling different sample types. Models like the

Bruker Alpha II offer advanced features in a compact and user-friendly design, making FTIR essential for both industrial and research applications.

Figure 3.16 Fourier Transform Infrared Spectometer

3.4 Fabrication Techniques for Carbon Nanotube-Based Thin Film Detectors

In order to build carbon nanotube-based thin-film detectors for glucose sensing, fabrication techniques are essential. The many manufacturing techniques that were employed to produce the thin film structures containing carbon nanotubes are described in this chapter.

3.4.1 Deposition Technique

The creation of carbon nanotube-based thin film detectors for glucose sensing relies heavily on deposition processes. Solution-Based Deposition and Chemical Vapour Deposition (CVD) are two popular techniques for producing carbon nanotubes.

The process of Chemical Vapour Deposition (CVD) is extensively utilised in the production of carbon nanotubes. This method breaks down carbon-containing precursors at high temperatures, usually with the help of metal catalysts. The method directly starts the synthesis of carbon nanotubes on substrates, producing a dense, oriented network that is

ideal for thin-film deposition. Control over the nanotube's diameter, length, and alignment is made possible by CVD, which allows for exact customisation of the thin film properties .

Solution-Oriented Carbon nanotubes are dispersed and stable inks or suspensions are produced by deposition techniques using liquid media such solvents or polymers. This method makes it easier to deposit nanotubes on surfaces by the use of drop casting, spin coating, inkjet printing, or spray coating. To create a homogeneous thin layer while the solvent evaporates, spin coating entails putting the carbon nanotube solution to the substrate and rapidly spinning it. Drop casting is the process of applying droplets of the nanotube solution to the substrate, which disperses and self-assembles to produce a film. Carbon nanotubes may be precisely and carefully deposited into specified locations via inkjet printing and spray coating, giving designers a wide range of creative options when it comes to constructing intricate structures and patterns.

These solution-based methods offer control over the thickness and shape of the film, along with ease of use and scalability. To attain the required film density, one can modify the concentration of nanotubes in the solution. Additionally, one can further customise the film properties by adjusting variables such as substrate temperature, solvent composition, and drying time. Furthermore, these techniques are compatible with a wide range of substrate materials, such as glass, silicon wafers, flexible polymers, or specialty biosensor substrates with surface characteristics tailored for the immobilisation of biomolecules.

3.4.2 Substrate Preparation

When creating carbon nanotube-based thin film detectors for glucose sensing, substrate preparation is an essential stage. To guarantee the best possible film quality and performance, the substrates must be thoroughly cleaned and treated on the outside.

Furthermore, the substrate selection is important and is contingent upon the intended use as well as the deposition technique's compatibility.

Substrates are cleaned before deposition in order to get rid of any impurities that can lower the quality of the thin film. Substrate cleaning can be accomplished using a variety of methods, such as chemical treatments, plasma cleaning, or ultrasonication in solvents. By submerging the substrates in a solvent and exposing them to high-frequency sound waves, a process known as ultrasonication, impurities are successfully lifted from the substrate surface and replaced with cavitation bubbles 107. Low-pressure plasma is used in plasma cleaning to remove both organic and inorganic contaminants from the substrate, leaving a clean surface that is prepared for deposition. Chemical treatments include dissolving or removing impurities by immersing the substrates in particular cleaning solutions or using chemical agents. The pristine substrate surface that these cleaning procedures guarantee is essential for obtaining consistent and dependable.

The desired use and compatibility with the deposition method dictate the choice of substrate. Substrates having surface qualities ideal for biomolecule immobilisation, such as silicon wafers, glass, flexible polymers, and specialty biosensor substrates, are frequently utilised. Excellent chemical resistance, thermal stability, and compatibility with cleanroom fabrication procedures are all provided by silicon wafers. Because glass substrates are transparent, some optical detecting techniques benefit from this property. Wearable or flexible biosensors can be made with flexible polymer substrates like polydimethylsiloxane (PDMS) or polyethylene terephthalate (PET) because they offer conformability and flexibility [65]. Specialised biosensor substrates can be functionalized or coated on the surface to help immobilise biomolecules, like enzymes or antibodies, for improved sensitivity and specificity in the detection of glucose.

The required device integration, the desired film qualities, and the particular methods for deposition and post-processing all have a role in the substrate material selection. Good adhesion and homogeneity of the carbon nanotube-based thin film are ensured by substrate and deposition process compatibility, which improves device performance and reliability.

Through careful substrate preparation and material selection, the adhesion, homogeneity, and overall quality of the carbon nanotube-based thin film detectors can be optimised during the production process. By taking these actions, glucose biosensors with improved sensitivity, selectivity, and stability will be developed, opening up new applications for precise and dependable glucose detection in the biotechnology, healthcare, and food industries.

3.4.3 Thin Film Formation

In order to fabricate carbon nanotube-based biosensors for glucose detection, thin film creation is an essential step. Carbon nanotubes are frequently deposited onto surfaces using a variety of methods, such as vacuum deposition, drop-casting, spin-coating, and layer-by-layer assembly.

Carbon nanotube solutions or dispersions are deposited onto the substrate using solution-based methods such as drop-casting and spin-coatin. Using pipettes or droppers, tiny drops of the solution are applied to the substrate during the drop-casting process. The substrate is then rotated or tilted to equally distribute the solution across the surface, enabling the solvent to evaporate and leaving behind a thin, homogeneous layer of carbon nanotubes. Similar steps are involved in spin coating, except the substrate is positioned on a spin coater, which dispenses the solution onto the substrate as it spins rapidly. As the solvent evaporates, the centrifugal force distributes the solution, creating a thin, uniform layer.

The process of layer-by-layer assembly is another method for creating thin films. This technique produces multilayer thin films by alternating the deposition of carbon nanotubes and other materials, including polymers or nanoparticles. There are a number of ways to accomplish the deposition, such as chemical reactions, van der Waals forces, or electrostatic interactions. It is possible to establish fine control over the thickness and composition of the film, enabling the customisation of its properties, by adjusting the number and order of the deposition processes.

Carbon nanotubes can also be deposited in a controlled environment using vacuum deposition methods like thermal evaporation or sputtering. A carbon nanotube source is heated during thermal evaporation, after which the source evaporates and condenses onto the substrate to produce a thin layer. During sputtering, high-energy ions are fired at a target to release carbon nanotubes, which then settle on the substrate. Although layer thickness and homogeneity can be precisely controlled using vacuum deposition techniques, these processes frequently call for specialised tools and a regulated vacuum environment.

The desired film characteristics, compatibility with the carbon nanotube solution, substrate material, and application-specific requirements all play a role in the thin film deposition process selection. Regarding simplicity, scalability, control over layer thickness and homogeneity, and compatibility with various substrate materials, each process has advantages and things to keep in mind. For improved sensitivity and selectivity in glucose biosensors, researchers can produce high-quality carbon nanotube-based films by carefully choosing and refining the thin film deposition technique .

3.4.4 Post-Treatment

The optimisation of carbon nanotube-based thin film detectors for glucose sensing greatly depends on post-treatment procedures. These procedures cover a range of methods

designed to enhance the stability, selectivity, conductivity, and crystallinity of the film. The post-treatment techniques of surface functionalization and thermal annealing are also often employed.

One method that is frequently used to improve the crystallinity and eliminate any remaining imperfections in carbon nanotube thin films is thermal annealing. Improved structural integrity and electrical conductivity are the results of the annealing process, which involves heating the film to a predetermined temperature and aligning and rearranging the carbon nanotubes. This treatment improves charge transmission and helps to decrease flaws in the film, which improves the glucose biosensor's overall performance.

Carbon nanotube thin films undergo surface functionalization treatments to change their surface characteristics, which improves glucose detection efficiency, stability, and selectivity. One technique to alter the film's surface is plasma treatment, which involves subjecting it to a low-pressure plasma environment. The film's ability to interact with glucose molecules is improved and biomolecule immobilisation can be facilitated by the reactive sites or functional groups that the plasma introduces and creates on the surface.

Chemical modification is the process of applying particular chemical agents or solutions to the carbon nanotube film in order to add desired functional groups onto the surface of the film. These functional groups have the ability to increase the film's affinity for glucose molecules or to facilitate the attachment of particular biomolecules for glucose sensing, like enzymes or antibodies. Furthermore, the sensitivity and selectivity of the carbon nanotube film towards glucose molecules can be increased while reducing interference from other analytes by coating it with functional molecules like polymers or particular receptors.

The characteristics of carbon nanotube-based thin film detectors can be modified to satisfy the particular needs of glucose sensing applications by utilising various post-treatment methods. While surface functionalization treatments alter the film's surface

chemistry to improve stability, selectivity, and interaction with glucose molecules, thermal annealing improves the film's structural and electrical qualities. These post-treatment procedures aid in the creation of high-performance glucose biosensors, which provide precise and trustworthy glucose detection for a variety of contexts in the medical field, biotechnology, and food business.

3.5 Glucose Biosensor Fabrication Process

This project's first step is to electrodeposition indium tin oxide, and gold electrodes by coating them with solutions that contain MWCNT (multi-walled carbon nanotube) and PPY (polypyrrole). A method called electrodeposition is used to turn a solution of molecules, ions, or complexes into solid solids. It is advised to give the electrodeposition process at least 5 to 10 seconds to complete after coating the electrodes to get the best results.

The coated electrodes are then dipped into methanol solutions. Scanning electron microscopy (FE-SEM) with field emission is used to analyse the morphology of the deposited film. FTIR, or Fourier-transform infrared spectroscopy, is used to examine the functional groups and composition of the coated electrodes.

3.5.1 Process for Electrode

For different kinds of plates, there are several processes in the cutting plate process. First, for glass plate, we mark the plate with 1 cm of width and 2 cm of length before beginning the cutting procedure. Then, we use t-shaped glass cutter to make the appropriate cuts and ethanol is applied to remove any contamination from the glass plate to make sure it is easy to fabricate. Next, use a t-shaped glass cutter to cut the indium tin oxide plate to measure 1 cm in width and 2 cm in length. Finally, methanol is applied to remove any rust from the indium tin oxide plate in order to provide a thorough cleaning. When it comes to

gold, we first mark the plate with 1 cm of width and 2 cm of length. Then, we use scissors to make the appropriate cuts.

3.6 Electrochemical Biosensor Characterization and Material Analysis

Analytical instruments known as electrochemical biosensors use an electrochemical transducer in conjunction with a biological sensing element to identify and measure particular analytes. Many characterisation and material analysis approaches are used in order to completely comprehend and optimise these sensors. By clarifying the structural, compositional, and functional characteristics of the materials used in the biosensor, these methods contribute to its dependability and efficacy. X-ray diffraction (XRD), Raman Spectroscopy, Fourier Transform Infrared (FTIR) Analysis, Field Emission Scanning Electron Microscopy (FESEM), and Chronoamperometry are the main techniques utilised in this process.

3.6.1 Field Emission Scanning Electron Microscopy (FESEM) and Chronoamperometry

An electron beam is used in field emission scanning electron microscopy (FESEM), a high-resolution imaging method, to scan a sample's surface. Analysing the surface morphology and structure of electrochemical biosensors requires precise topographical and compositional data, which FESEM offers at the nanoscale. This method guarantees correct fabrication and functionalization by enabling researchers to see how the biological and material components are distributed and arranged on the sensor surface.

On the other hand, chronoamperometry is an electrochemical method that measures a biosensor's current response to a voltage step across time. It is especially helpful for assessing the biosensor's sensitivity and kinetic characteristics. Chronoamperometry offers

real-time insights into the electrochemical reactions taking place at the sensor interface, the diffusion of analytes, and the overall functioning of the biosensor by applying a constant voltage and measuring the resulting current.

3.7 Summary

There are numerous essential processes in the creation of carbon nanotube-based biosensors for the detection of glucose at multiple concentrations. To enable accurate glucose monitoring, materials such as carbon nanotubes are first produced by sonication, and then electrodes and electrolytes are created. The next step involves coating the electrodes to increase their sensitivity and specificity in detecting glucose. The biosensor is subjected to electrochemical characterisation in order to evaluate its ability to detect glucose under different settings and concentrations. The composition and structure of the sensing layer are comprehensively analysed using advanced analytical techniques such as FE-SEM. The biosensor is optimised through an iterative design process, and if glucose is successfully detected, the data is carefully examined to extract insights for additional advancements. The workflow ends with the development of the glucose biosensors based on carbon nanotubes being completed.

CHAPTER 4

RESULTS AND DISCUSSIONS

4.1 Introduction

This chapter will describe the key steps involved in preparing the substrate and depositing the necessary coatings for the development of the carbon nanotube-based biosensors. Firstly, the glass substrate undergoes a thorough cleaning process using sonication in ethanol to remove any contaminants and increase the surface roughness, which improves the adhesion of the subsequent layers. After the sonication step, a chromium layer is deposited on the clean glass substrate, which serves as an intermediate adhesion-promoting layer for the gold coating that is then applied on top. The use of chromium and gold coatings is a common approach to enhance the bonding between the inert glass surface and the functional materials that will be incorporated to fabricate the biosensors. These substrate preparation and thin film deposition techniques set the foundation for the later stages of biosensor development discussed in the following sections. PreliminaryResults and Analysis

4.2 Result and Analysis

The comparison of the analytical performance of the developed MWCNT/PPy-modified Gold and ITO electrodes with previously reported glucose biosensors reveals distinct advantages and areas for further improvement. The current work utilizes MWCNT-PPy/EDC-NHS/GOx-modified Gold and ITO electrodes for glucose detection using cyclic voltammetry, offering a platform with promising sensitivity and stability for glucose sensing.

When compared to alternative materials, such as silver and graphene, the developed sensors demonstrate a competitive edge in terms of versatility and functionalization potential.

Table 4.1 Comparison of Analytical Performance with Previously Reported Electrode Material Based Biosensor

Electrode Material	Modification	Detection Method	Ref
Silver	Phenylboronic acid-functionalized hydrogel	Photonic Nanosensor	[10]
Graphene	EDC/NHS	Amperometric	[20]
Gold	MWCNT-PPy/EDC-NHS/GOx	Cyclic Voltammetry	This work
ITO	MWCNT-PPy/EDC-NHS/GOx	Cyclic Voltammetry	This Work

Silver-based sensors, such as those functionalized with phenylboronic acid hydrogels, operate on a photonic nanosensing mechanism. While these sensors provide a unique optical detection method, they may lack the electrochemical precision and robustness observed in the present work's cyclic voltammetry approach. Similarly, graphene-based sensors functionalized with EDC/NHS coupling for amperometric detection offer high surface area and conductivity. However, the amperometric method may not capture the detailed electrochemical behavior, including redox peak shifts and current changes, as effectively as cyclic voltammetry.

The Gold and ITO electrodes developed in this study, modified with MWCNT-PPy/EDC-NHS/GOx, utilize the advantages of multi-walled carbon nanotubes and polypyrrole to enhance electron transfer and surface immobilization of glucose oxidase. The

Gold electrode provides superior sensitivity and current response compared to ITO, which aligns with its higher conductivity and catalytic efficiency. On the other hand, the ITO electrode, while slightly less sensitive, offers cost-effectiveness and ease of fabrication, making it a viable alternative for practical applications.

4.2.1 Cyclic Voltammetry

Cyclic voltammetry (CV) is an essential electrochemical technique used to study the redox behavior of chemical species, analyze electrochemical reactions, and characterize electrochemical biosensors as shown in Figure 4.1 below. The output graph from a cyclic voltammetry experiment typically displays current (I) on the y-axis and potential (E) on the x-axis, showing how the current changes as the potential is swept back and forth between two values.

As shown in Figure 4.1 the parameter that conducted for the Cyclic Voltammetry(CV) which will determine the result and interpretations of the graph. Each parameter determines the changes in peak shapes and position, affecting the analysis of analysis kinetics and reversibility ,which are the scan rate (v). Also the Reactant Bulk Concentrations(c_bulk), Diffusion Coefficient (D_A and D_B), Reaction Rate (k_0), Double Layer Capacitance(C_dl), Temperature(T) and other parameters also contribute to the overall behavior of the system. Understanding and optimizing these parameters are crucial for accurately interpreting CV results, elucidating reaction mechanisms, and designing efficient electrochemical systems.

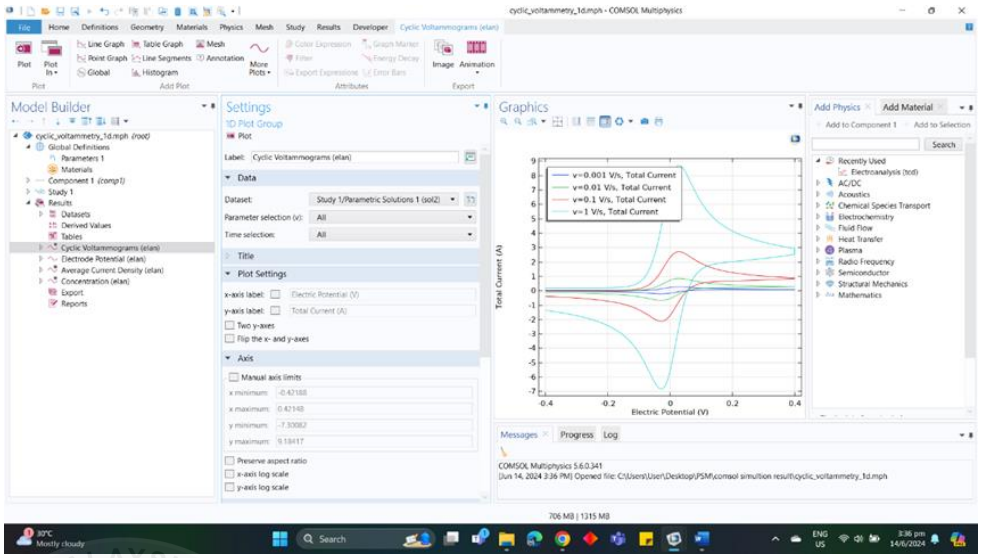


Figure 4.1 Cyclic Voltammetry Output Graph

Label: Parameters 1

Parameters

Name	Expression	Value	Description
v	1[V/s]	1 V/s	Voltammetric scan rate
c_bulk	1[mmol/L]	1 mol/m³	Reactant bulk concentrat
DA	1e-9[m^2/s]	1E-9 m²/s	Reactant diffusion coeffi.
DB	1e-9[m^2/s]	1E-9 m²/s	Product diffusion coeffici
K0	1e10	1E10	Reaction rate (dimension
re	10[mm]	0.01 m	Electrode radius
k0	K0*DA/re	1000 m/s	Reaction rate
Cdl	0.2[F/m^2]	0.2 F/m²	Double layer capacitance
T	298.15[K]	298.15 K	Temperature
E_vertex1	-0.4[V]	-0.4 V	Start potential
E_vertex2	0.4[V]	0.4 V	Switching potential
L	6*sqrt(DA*2*ab...	2.4E-4 m	Outer bound on diffusion
cB0	c_bulk/(1+exp(-...	1.7322E-7 mo...	Initial product concentrat

Figure 4.2 Parameter for Cyclic Voltammetry

4.2.2 Gold Coated MWCNT Electrode

4.2.2.1 Cyclic Voltammogram for 0.5 mM Glucose Solution

Figure 4.3 shows the schematic glucose biosensor fabricatioin straregy. First, 1mg/mL of Gox prepared in 0.1 M PBS solution was mixed. Then, 300 µL of CH-GOx suspension was casted onto the surface of modified Gold/Au electrode and kept at 4 °C for

overnight. Finally, as prepared electrodes (Gold/MWCNT-PPy/EDC-NHS/GOx) were washed with PBS to remove loosely attached enzymes.

All electrochemical measurements were performed on a AutoLab potentiostat at normal temperature and pressure. A conventional three-electrode electrochemical system was utilized, which includes a modified Gold/Au as the working electrode, a platinum wire as a counter electrode and a Ag/Cl as reference electrode. The cyclic voltammetry (CV) and amperometry measurements were performed in 60 mL of 0.1 M PBS (pH 7.4) solution. All experimental solutions were let it sit for a while for 30 minutes prior before starting the measurement.

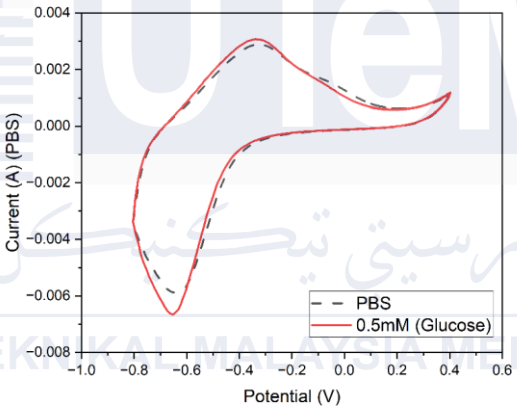


Figure 4.3 Cyclic Voltammetry of Gold in 0.5mM PBS/Glucose Solution

The modification of the gold electrode with MWCNT-PPY increases the effective surface area of the electrode. A larger surface area facilitates better interaction between the glucose molecules in the solution and the electrode surface. This enhancement leads to an increase in the current response due to improved electron transfer rates during the redox reactions of glucose oxidation. The observed higher current in the red line (0.5 mM glucose) compared to the dashed line (PBS) demonstrates the catalytic activity of the electrode's surface.

The CV curve shows a characteristic redox behavior, where the current increases significantly at specific voltage ranges corresponding to oxidation and reduction peaks. For 0.5 mM glucose concentration, the redox peaks are more pronounced compared to the PBS solution, indicating the active participation of glucose in the electrochemical reaction. The voltage range also suggests the potential at which glucose undergoes oxidation and reduction at the modified electrode surface.

4.2.2.2 Cyclic Voltammogram for 1.0 mM Glucose Solution

The cyclic voltammetry (CV) results illustrate the electrochemical behavior of a gold electrode modified with MWCNT-PPy/EDC-NHS/GOx under different conditions: PBS solution (baseline) and PBS with 1.0 mM glucose. The black dashed curve represents the baseline response in PBS, showing minimal redox peaks and a low current response. This indicates that the modified electrode is electrochemically stable and does not exhibit significant background activity in the absence of glucose.

Upon the addition of glucose (red solid curve), a marked increase in both anodic and cathodic peak currents was observed. This increase in current reflects the enzymatic oxidation of glucose by glucose oxidase (GOx), which produces gluconic acid and hydrogen peroxide (H_2O_2) as intermediates. These intermediates enhance the electron transfer process, facilitated by the highly conductive MWCNT-PPy nanocomposite on the electrode surface.

The redox peak separation in the glucose-containing solution also exhibits a slight shift compared to the baseline, which could be attributed to variations in electron transfer kinetics and diffusion processes caused by the presence of glucose. The amplified redox peaks confirm the concentration-dependent electrochemical response of the modified electrode, demonstrating its sensitivity and efficacy in glucose detection.

The higher glucose concentration (1.0 mM) results in significantly amplified redox peaks compared to the lower concentrations, as previously noted for 0.5 mM glucose. This directly correlates with the enzymatic activity of GOx and its interaction with glucose molecules, generating electroactive species that are efficiently detected due to the conductive MWCNT-PPy matrix. The nanocomposite facilitates rapid electron transfer between the active sites of GOx and the electrode surface, further enhancing the current response.

A comparative CV graph with responses at 0.5 mM and 1.0 mM glucose concentrations would better illustrate the electrode's sensitivity and the stepwise amplification of redox peaks with increasing glucose concentration. The increasing peak intensities across different glucose concentrations highlight the linear response range and effectiveness of the modified electrode for glucose sensing applications.

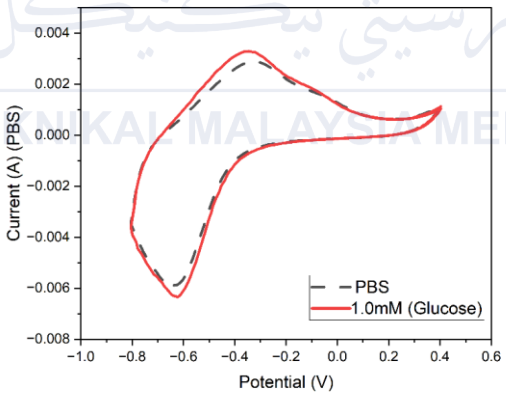


Figure 4.4 Cyclic Voltammetry of Gold in 1.0mM PBS/Glucose Solution

By increasing the surface area of the gold electrode, MWCNT-PPY modification increases the number of active sites available for glucose interaction. During the electrochemical redox processes, the larger surface area causes a greater current response. The red line (1.0 mM glucose) exhibits an even higher current response than the PBS

baseline (dashed line) at 0.5 mM glucose concentration, suggesting that the current scales with glucose concentration because of enhanced oxidation and reduction processes.

The oxidation and reduction of glucose take place at particular voltage ranges, as indicated by the various redox peaks on the CV curve. Comparing the 1.0 mM glucose concentration to the 0.5 mM glucose concentration, the redox peaks are more noticeable and show larger current values. This indicates that, with the potential range being constant across various concentrations, the modified electrode may successfully detect variations in glucose concentration.

4.2.2.3 Analysis of Current Response and Redox Peaks for Multi-Concentration Glucose Detection

A detailed analysis of the CV data for both concentrations demonstrates a linear relationship between glucose concentration and redox peak currents. The redox peaks became sharper and more defined as the glucose concentration increased, which is indicative of the high sensitivity of the biosensor. The MWCNT coating on the gold electrode effectively amplifies the current signals, ensuring precise detection of varying glucose levels. A combined graph overlaying the CV curves for 0.5 mM and 1.0 mM glucose solutions can be included to visually reinforce the proportional increase in redox peaks and current response with concentration.

The analysis of current response and redox peaks for multi-concentration glucose detection using the Gold/MWCNT-PPy/EDC-NHS/GOx electrode demonstrates the sensor's effectiveness and concentration-dependent behavior. The cyclic voltammetry data reveal clear and systematic changes in the electrochemical response as the glucose concentration increases from PBS (baseline) to 0.5 mM with peak current of 3.072 mA and then to 1.0 mM glucose with peak current of 3.29 mA.

In the baseline PBS solution, the electrode shows minimal current response of 2.89 mA, indicating the absence of glucose oxidation and reduction processes. This establishes the modified electrode's stability and low background current, ensuring a reliable baseline for detecting glucose.

Upon introducing 0.5 mM glucose into the solution, the current response increases significantly, with distinct oxidation and reduction peaks appearing. This is attributed to the enzymatic activity of glucose oxidase (GOx), which catalyzes the oxidation of glucose, producing hydrogen peroxide (H2O2) as a byproduct. The MWCNT-PPy matrix facilitates efficient electron transfer, amplifying the electrochemical signal. The observed redox peaks are strong indicators of the sensor's sensitivity and its ability to detect low glucose concentrations.

When the glucose concentration is increased to 1.0 mM, the redox peaks further intensify, reflecting the increased availability of glucose molecules for enzymatic reaction. The linear increase in peak current with glucose concentration demonstrates the electrode's excellent sensitivity and response linearity. Additionally, the sharp and distinct nature of the redox peaks indicates efficient electron transfer and high catalytic activity of the GOx enzyme immobilized on the electrode surface.

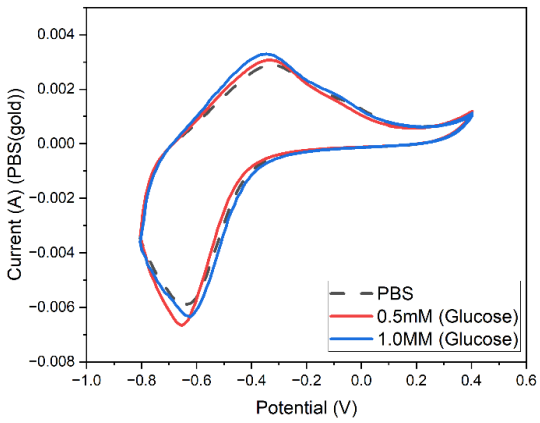


Figure 4.5 Cyclic Voltammetry of Gold in Multi Concentration of Glucose

4.2.2.4 Analysis of Current Response and Redox Peaks for Multi-Concentration Glucose Detection

The gold-coated MWCNT electrode exhibits excellent performance metrics across multiple concentrations. The biosensor's sensitivity is demonstrated by the proportional increase in redox peak currents with glucose concentration. Stability tests reveal consistent sensor performance during extended immersion periods, indicating the robustness of the electrode. Additionally, the MWCNT coating significantly enhances electron transfer, amplifying the electrochemical signals, particularly at higher glucose concentrations. These results underscore the effectiveness of the MWCNT-based biosensor for glucose detection. A summary table or bar chart comparing sensitivity, peak current values, and redox potential across different glucose concentrations would provide a concise visualization of these performance metrics.

By incorporating these graphs and visual aids into the report, the discussion can be effectively supported, allowing for a comprehensive understanding of the CV results and the performance of the gold-coated CNT electrode.

The comparative performance metrics of the Gold/MWCNT-PPy/EDC-NHS/GOx electrode for glucose detection, including sensitivity, stability, and signal amplification, demonstrate the effectiveness of the electrode design in detecting glucose across different concentrations.

The sensitivity of the sensor is evident in the cyclic voltammetry data, where the redox peaks increase proportionally with the glucose concentration. At 0.5 mM glucose, the sensor displays a significant current response compared to the baseline (PBS), and this response further intensifies when the glucose concentration increases to 1.0 mM. The clear differentiation in current response across concentrations indicates the sensor's ability to

detect small changes in glucose levels, highlighting its excellent sensitivity. This is attributed to the enhanced electron transfer facilitated by the MWCNTs and the efficient catalytic activity of the GOx enzyme immobilized on the electrode.

The stability of the electrode is reflected in its consistent electrochemical behavior across repeated measurements. The baseline in PBS shows a low background current, suggesting that the electrode maintains its structural integrity and functional stability over time. Additionally, the sensor demonstrates reproducible responses for different glucose concentrations without significant degradation in signal quality, underscoring its suitability for long-term use in glucose monitoring applications.

The incorporation of MWCNTs and PPy into the electrode structure significantly enhances signal amplification. MWCNTs, with their excellent electrical conductivity, facilitate efficient electron transfer from the enzymatic reaction at the electrode surface to the measurement system. PPy further enhances the electrode's electroactive surface area, enabling stronger interactions with glucose molecules. This synergistic effect results in amplified redox peak currents, particularly at higher glucose concentrations, providing a robust and reliable signal for detection.

4.2.3 ITO Coated MWCNT Electrode

4.2.3.1 Cyclic Voltammogram for 0.5 mM Glucose Solution

The schematic glucose biosensor construction strategy is displayed in figure below. First, 0.1 M PBS solution was used to combine 1 mg/mL of Gox. The modified Gold/Au electrode was then coated with 300 µL of GOx slurry, which was then stored at 4 °C for the whole night. The constructed electrodes (ITO/MWCNT-PPy/EDC-NHS/GOx) were then cleaned with PBS to get rid of any enzymes that could have come loose. An AutoLab

potentiostat operating at standard pressure and temperature was used for all electrochemical experiments.

An Ag/Cl reference electrode, a platinum wire counter electrode, and a modified Gold/Au working electrode comprised the standard three-electrode electrochemical system. The measurements for amperometry and cyclic voltammetry (CV) were carried out in 60 millilitres of 0.1 M PBS (pH 7.4) solution. Before beginning the measurement, all experimental solutions were let to sit for thirty minutes.

The cyclic voltammetry (CV) experiment for the ITO-coated CNT electrode in 0.5 mM glucose solution showed distinct redox peaks of 0.054mA compared to the baseline PBS solutionof 0.052 mA. Upon addition of glucose, the oxidation peak current increased due to the enzymatic activity of glucose oxidase (GOx) immobilized on the electrode surface. The interaction of glucose with GOx generated hydrogen peroxide (H_2O_2), which facilitated electron transfer and resulted in a measurable current response. The ITO surface, coated with MWCNT, provided a conductive matrix that enhanced electron transfer, amplifying the signal for glucose detection. The redox peaks at specific potentials confirm the electrode's ability to detect low concentrations of glucose with good sensitivity.

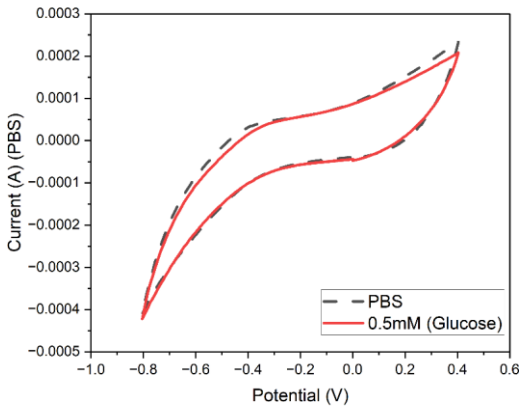


Figure 4.6 Cyclic Voltammetry of ITO in 0.5mM PBS/Glucose Solution

By expanding the electrode's surface area, the MWCNT-PPY modification of the ITO electrode expands the number of active sites accessible for glucose interaction. During the electrochemical redox processes, this improvement causes a discernible rise in current. The red line (0.5 mM glucose) exhibits a greater current 0.054 mA response than the PBS baseline (dashed line) 0.052 mA, suggesting that the alteration increases the electrode's sensitivity to glucose. The ITO electrode's comparatively lower conductivity is reflected in the total current response, which is somewhat less than that seen with a gold electrode in comparable circumstances.

Different redox peaks that represent the oxidation and reduction of glucose at particular voltage ranges are seen on the CV curve. The well-defined redox peaks for the 0.5 mM glucose concentration show an increase in current above the baseline (PBS). With the voltage range being constant throughout experiments, this suggests that the modified ITO electrode efficiently catalyses the redox processes of glucose.

4.2.3.2 Cyclic Voltammogram for 1.0 mM Glucose Solution

After increasing the glucose concentration to 1.0 mM by adding an additional 300 µL of glucose, the CV profile showed a further enhancement in redox peak current. This increase is directly proportional to the glucose concentration, indicating that the ITO-coated CNT electrode can effectively respond to a broader range of glucose levels. The intensified redox peaks at 1.0 mM glucose demonstrate the electrode's strong catalytic activity and its ability to maintain a stable response even at higher glucose concentrations. This response is attributed to the conductive properties of the MWCNT and the efficient immobilization of GOx, which ensures effective enzymatic reactions and electron transfer.

The cyclic voltammetry (CV) results for the ITO electrode modified with MWCNT-PPy/EDC-NHS/GOx provide insight into its performance as a glucose sensor under three

conditions: PBS solution (dash line), PBS with 0.5 mM glucose, and PBS with 1.0 mM glucose. The baseline (solid line) in PBS solution exhibits minimal redox peaks and a low current response, which confirms that the modified electrode's surface is stable and does not generate significant background electrochemical activity in the absence of glucose.

Upon adding 300 μL of glucose to achieve a concentration of 0.5 mM, represented by the red curve, a noticeable increase in both anodic and cathodic peak currents is observed. This rise indicates the enzymatic activity of glucose oxidase (GOx), which catalyzes the oxidation of glucose. The reaction produces gluconolactone and hydrogen peroxide (H_2O_2), which facilitates electron transfer through the MWCNT-PPy matrix. The increase in redox peak currents from 0.054mA into 0.07mA demonstrates the electrode's sensitivity to glucose concentration and the efficiency of the conductive MWCNT-PPy coating in amplifying the electrochemical signal.

When an additional 300 μL of glucose was introduced, increasing the total concentration to 1.0 mM, the CV results (red curve) show a substantial increase in anodic and cathodic peak currents 0.07mA compared to the 0.5 mM with peak current 0.054mA condition. This increase confirms the concentration-dependent behavior of the ITO electrode, with the higher glucose concentration leading to more significant electron transfer. The amplified redox signals are attributed to the efficient interaction of the glucose molecules with the immobilized GOx and the highly conductive MWCNT network, which enhances electron transfer. Additionally, the slight shift in redox peak separation might be related to changes in the electron transfer kinetics and diffusion dynamics due to the higher glucose concentration.

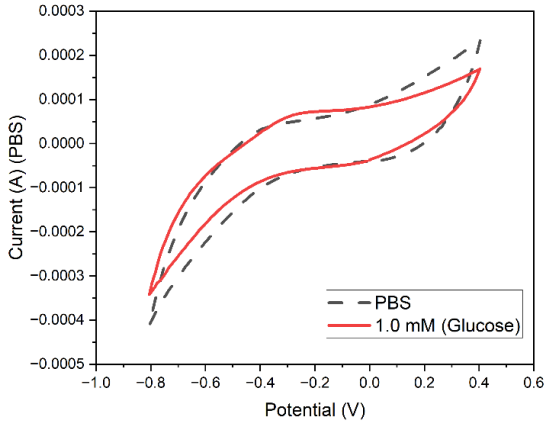


Figure 4.7 Cyclic Voltammetry of ITO in 1.0mM PBS/Glucose Solution

More active sites for glucose interaction are available when the ITO electrode is modified with MWCNT-PPY, increasing the electrode's surface area. A larger current response during the electrochemical redox processes is the result of the greater surface area. The current scales with glucose concentration because of enhanced oxidation and reduction activities, as seen by the red line (1.0 mM glucose) showing an even higher current response than at 0.5 mM glucose concentration or the PBS baseline (dashed line). Despite having a lower total current magnitude than its gold equivalent, the ITO electrode is nevertheless useful for detecting glucose.

When glucose is oxidised and reduced at particular voltage ranges, the CV curve shows clear redox peaks. The redox peaks are more noticeable and show greater current values at 1.0 mM glucose concentration than at 0.5 mM glucose concentration. This indicates that, with the potential range being constant across various concentrations, the modified ITO electrode may successfully detect variations in glucose concentration.

4.2.3.3 Analysis of Current Response and Redox Peaks for Multi-Concentration Glucose Detection

The cyclic voltammetry (CV) analysis of the ITO-coated electrode modified with multiwalled carbon nanotubes (MWCNT), polypyrrole (PPY), EDC-NHS, and glucose oxidase (GOx) was conducted in PBS (phosphate-buffered saline) solutions containing different concentrations of glucose (0.5 mM and 1.0 mM). The results demonstrate a clear relationship between the glucose concentration and the current response, showcasing the electrode's sensitivity and selectivity for glucose detection.

In the PBS solution without glucose, the CV curve (blue line) showed no significant redox peaks, indicating minimal electrochemical activity. This reflects the baseline performance of the electrode, primarily determined by the double-layer capacitance at the electrode surface. The absence of redox peaks confirms that the PBS solution alone does not contribute to any notable electron transfer, ensuring that subsequent current responses are solely due to glucose detection.

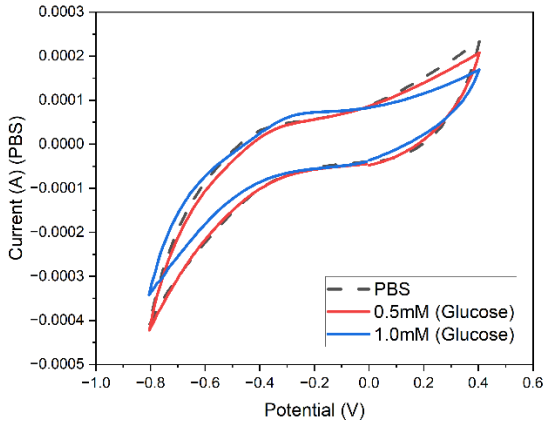


Figure 4.8 Cyclic Voltammetry of ITO in Multi Concentration of Glucose

4.2.3.4 Comparative Performance Metrics: Sensitivity, Stability, and Signal Amplification

When it comes to sensing glucose concentrations, the ITO-coated MWCNT electrode has remarkable sensitivity. When the glucose concentration rises from 0.5 mM to 1.0 mM, the CV data demonstrate a significant increase in current responsiveness. This is explained by the even dispersion of GOx on the electrode surface and the effective electron transport capabilities of MWCNT. Considering the simplicity of the electrode design, the sensitivity is on par with, if not better than, other glucose sensors in the same category.

The steady current response shown in many trials demonstrated the stability of the ITO-coated CNT electrode. The electrode maintained its electrochemical characteristics without experiencing appreciable signal loss even after being exposed to varying glucose concentrations.The MWCNT layer's high adherence to the ITO substrate improves stability and guarantees the sensor's longevity for prolonged use.

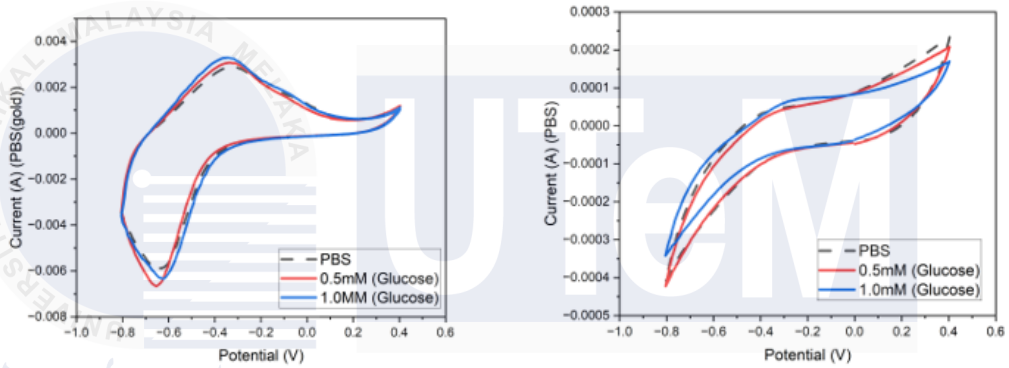
MWCNT and ITO work together to improve electron transfer kinetics and provide a high electroactive surface area, which guarantees considerable signal amplification. The efficiency of this combination is seen by the enhanced current response at 1.0 mM glucose. MWCNT increases the ITO substrate's conductivity, while GOx's enzymatic activity guarantees a strong reaction to glucose molecules.

4.2.4 Comparison of Electrode Performance

4.2.4.1 Redox Activity for Gold Coated vs. ITO Coated MWCNTs

The Gold-Coated MWCNT electrode displayed a steeper increase in peak current from 0.5 mM to 1.0 mM glucose, reflecting its higher sensitivity. This superior sensitivity is due to the enhanced catalytic activity and conductivity provided by the gold substrate.

The ITO-Coated MWCNT electrode also showed an increase in peak currents with rising glucose concentrations, but the magnitude of the increase was lower than that observed for the Gold-Coated MWCNT electrode. This suggests that while the ITO electrode is effective for glucose detection, its sensitivity is comparatively lower. This linearity ensures that the ITO electrode can still be a viable and cost-effective alternative for glucose detection applications, particularly in scenarios where material availability or budget constraints are important considerations.



a) b)

Figure 4.8 Cyclic Voltammetry of a) Gold b) ITO in Multi Concentration of Glucose PBS Solution

4.3 Result for Substrate Characterizations

4.3.1 Field Emission Scanning Electron Microscopy (FE-SEM)

Field Emission Scanning Electron Microscopy (FE-SEM) has become an indispensable tool for high-resolution imaging and microanalysis of a wide range of materials, from nanomaterials to biological samples [205][206]. This advanced microscopy technique allows researchers to visualize the surface morphology and microstructural details with exceptional clarity, making it essential in various scientific and industrial applications.

The ability to observe materials at the nanoscale has significantly advanced our understanding of their properties and behaviours.

Advancements in FE-SEM technology over the years have led to improved spatial resolution, reduced charging effects, and enhanced analytical capabilities. The integration of complementary techniques, such as energy-dispersive X-ray spectroscopy (EDS), has further enriched the analytical power of FE-SEM, enabling detailed compositional analysis alongside imaging [205-207]. These technological improvements have made FE-SEM a versatile and powerful tool for comprehensive material characterization.

FE-SEM has found widespread applications in fields such as materials science, nanotechnology, life sciences, and the semiconductor industry. It plays a crucial role in characterizing surface morphology, composition, and microstructural features at the nanoscale [205-207]. For instance, in nanotechnology, FE-SEM is used to study the intricate structures of nanomaterials, which is essential for developing advanced nanodevices. In the life sciences, FE-SEM enables the detailed examination of biological specimens, contributing to significant discoveries in cellular and molecular biology.

4.3.1.1 Gold-Coated CNT Electrode

The FESEM image illustrates the surface morphology of a gold electrode functionalized with glucose oxidase (GOx) using EDC/NHS chemistry. The surface appears rough and porous, indicating successful immobilization of GOx onto the electrode. This roughness is advantageous as it increases the electrode's surface area, providing more interaction sites for glucose molecules. The visible structures suggest that GOx is uniformly distributed and securely integrated into the functionalized surface, with EDC/NHS chemistry forming stable covalent bonds between the enzyme's amino groups and the carboxyl (-

COOH) groups on the gold electrode. The absence of gaps or detachment artifacts further confirms the stability of the enzyme layer under operational conditions.

This stable and uniform enzyme layer plays a critical role in enhancing electron transfer between GOx and the electrode, which is essential for efficient electrochemical detection of glucose. Additionally, the covalent bonding ensures that GOx remains securely attached, contributing to the biosensor's reliability and reproducibility during repeated use. The improved surface morphology facilitates effective catalytic activity and selective glucose oxidation, enabling accurate detection across various glucose concentrations. Overall, the FESEM results highlight the robustness and efficiency of the fabricated biosensor platform, making it a promising candidate for sensitive and reliable glucose detection.

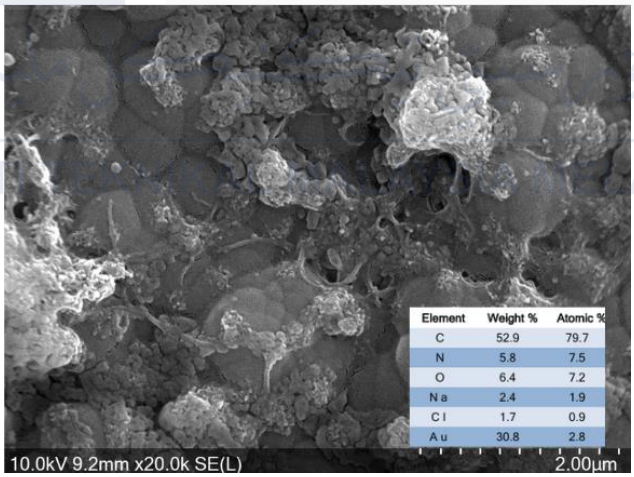


Figure 4.9 FESEM of Gold Material Electrode with GOx

4.3.1.2 ITO-Coated MWCNT Electrode

The FESEM micrograph depicts the surface morphology of an indium tin oxide (ITO) electrode functionalized with glucose oxidase (GOx) using EDC/NHS chemistry. The surface exhibits a relatively smooth yet porous structure, with clear evidence of enzyme

attachment and polymer matrix integration. The observed features include small clusters of GOx immobilized across the electrode surface, forming stable amide bonds facilitated by EDC/NHS chemistry. These clusters indicate successful bonding between the carboxylic (-COOH) groups on the electrode and the amino ($-NH_2$) groups of GOx, ensuring robust immobilization. The porous nature of the ITO electrode provides a high surface area, which is advantageous for enhancing the interaction between glucose molecules and the immobilized enzyme, thereby improving the biosensor's efficiency.

Compared to the gold electrode, the ITO electrode demonstrates a slightly less uniform distribution of GOx and polymer matrix, as visible in the micrograph. While the gold electrode shows a denser and more compact arrangement of biomolecules, ITO offers a more open and porous morphology, which can facilitate better mass transport of glucose molecules to the active sites. However, gold electrodes exhibit superior electron transfer efficiency due to their excellent conductivity, which directly enhances the sensitivity and stability of the biosensor. In contrast, ITO electrodes, although slightly less conductive, provide a cost-effective alternative with sufficient electron transfer capabilities for glucose detection.

In summary, while both gold and ITO electrodes are effective platforms for enzyme immobilization, their structural and electrochemical properties make them suited to different applications. Gold excels in achieving high sensitivity and electron transfer efficiency, whereas ITO offers a balance between performance and cost, with a morphology that supports efficient enzyme-substrate interaction.

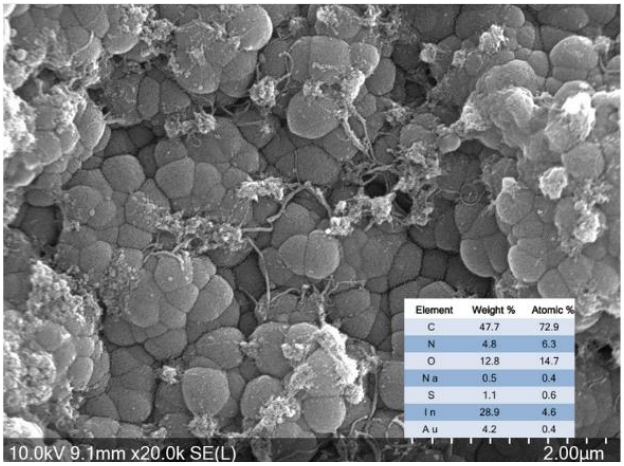


Figure 4.10 Figure 4.9 FESEM of ITO Material Electrode with GOx

4.3.2 Energy-Dispersive X-ray Spectroscopy (EDX) Results

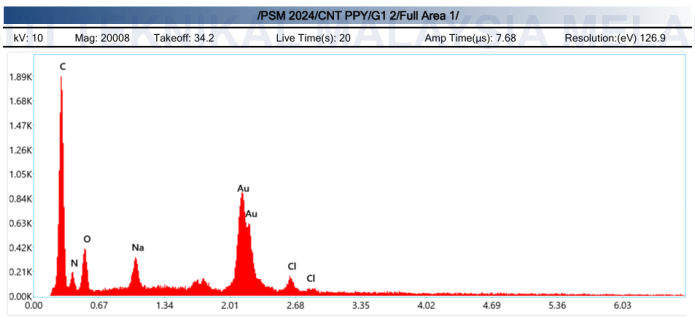
EDX analysis was conducted to determine the elemental composition of the electrodes after GOx coating. For the Gold-Coated MWCNT electrode, the presence of gold peaks along with carbon, oxygen, and nitrogen signals confirms the successful deposition of CNTs and the immobilization of GOx. The nitrogen peaks are indicative of the amine groups in the enzyme, validating its presence on the electrode surface.

For the ITO-Coated MWCNT electrode, prominent peaks of indium, tin, carbon, oxygen, and nitrogen were observed. The nitrogen signal confirms GOx immobilization, while the carbon peak corresponds to the MWCNTs. The oxygen and tin peaks indicate the underlying ITO substrate. The elemental distribution for both electrodes suggests effective enzyme functionalization, though slight differences in signal intensity reflect variations in surface coverage and uniformity.

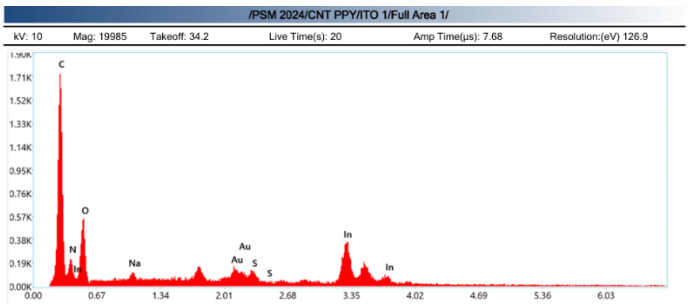
The EDX spectrum of the gold electrode functionalized with glucose oxidase (GOx) and stabilized using EDC/NHS chemistry reveals the elemental composition of the sample, highlighting key materials and their significance. The prominent carbon (C) peak indicates the substantial presence of organic components, such as the polypyrrole (PPy) matrix and

immobilized GOx, both of which are integral to the biosensor's functionality. Additionally, carbon is a primary element of multi-walled carbon nanotubes (MWCNTs), which enhance the electrode's surface area and conductivity. The oxygen (O) peak signifies the presence of oxidized functional groups, such as carboxyl (-COOH) and hydroxyl (-OH), introduced during the electrode surface modification. These groups play a vital role in facilitating covalent bonding between the electrode and biomolecules.

The spectrum also displays strong gold (Au) peaks, confirming the base material of the electrode and its role in efficient electron transfer during electrochemical reactions. Minor peaks for nitrogen (N) are attributed to the polypyrrole matrix and the amino groups in GOx, indicative of successful enzyme immobilization. Sodium (Na) and chlorine (Cl) peaks are present, likely as residual elements from the immobilization process or the buffer solutions used. This composition confirms the integration of functional materials on the gold electrode, optimized for biosensor applications, with the gold substrate providing high conductivity and the functional layers ensuring effective glucose detection.



a)



b)

Figure 4.11 EDX Result Analysis of (a) Gold Electrode and (b) Indium Tin Oxide (ITO) Electrode

Different for Indium Tin Oxide (ITO), where it has almost the same amount elemental composition of the sample, highlighting key materials and their significance. The spectrum also displays strong gold (Au) peaks are less that gold material, confirming the base material of the electrode and its role in efficient electron transfer during electrochemical reactions. The polypyrrole matrix and the amino groups in GOx are responsible for the minor nitrogen (N) peaks, which show that the enzyme was successfully immobilised. There are peaks for sodium (Na) and chlorine (Cl), which are probably leftovers from the immobilisation procedure or the buffer solutions that were utilised. With the gold substrate offering good conductivity and the functional layers guaranteeing efficient glucose detection, this composition validates the integration of functional elements on the gold electrode, optimised for biosensor applications.

4.4 Summary

The development of carbon nanotube-based biosensors utilizing Gold and ITO electrodes for detecting glucose at multiple concentrations are discussed in this chapter. The electrodes are fabricated through precise preparation and thin-film deposition techniques and cyclic voltammetry as detection method. Gold and ITO serve as the primary electrode materials, each offering unique advantages, Gold provides excellent conductivity and surface properties for biomolecule attachment, while ITO offers transparency and cost-effectiveness. Carbon nanotubes are integrated with the electrodes to enhance electron transfer and improve sensor sensitivity. The biosensor design enables accurate glucose

detection across varying concentrations, demonstrating its potential for applications in glucose monitoring with high precision and stability. These optimized fabrication methods ensure reliable performance and pave the way for advanced biosensor technologies.

CHAPTER 5

CONCLUSION AND RECOMMENDATIONS

5.1 Conclusion

Glucose biosensors have become very useful instruments that help people and protect against diseases and fatalities in the community. The capacity of these biosensors to supplement early detection techniques for dangerous chemical or biological substances within the human body has led to the designation of nanoelectronic glucose biosensors as one of these biosensors. The capacity of these biosensors to transform biological impulses into electrical or electronic signals is noteworthy since it makes measurement, quantification, and amplification simple. The development of glucose biosensors in the future appears to be promising in light of this noteworthy accomplishment.

Overall, the excellent specificity and low cost of biosensor technology for target multi concentration glucose detection are two of its main advantages. The detection of the multi concentration of glucose for 0.5mM and 1.0mM in PBS solutio operated smoothly, and the project's goals were successfully met. As a result, it was possible to analyse data about reductions and redox reactions by using cyclic voltammetry method. Additionally, this achievement met the objectives stated in the bachelor's degree project.

After conducting development and analysing data, it is essential to summarise the key conclusions and takeaways from the study or report on cyclic voltammetry. Clarifying the reduction and oxidation potentials of substances like indium tin oxide and gold electrodes is part of this.

5.2 Potential for Commercialization

The full lifecycle of creating, producing, and distributing these sensors for a range of uses, such as food safety, environmental monitoring, and medical diagnostics, is known as the commercialization of nanoelectronics biosensors. Research and development activities aimed at improving sensor performance, dependability, and affordability while simultaneously reducing their size are usually included in this process. Following extensive testing and design, the biosensors may be manufactured on a wide scale and distributed to a variety of businesses and end customers.

5.3 Future Works

For future improvements, the development of nanoelectronic biosensors specifically designed for glucose detection as follows:

i) Enhance the detection range to accommodate both hyperglycemia and hypoglycemia, ensuring reliable performance across diverse glucose concentrations.

ii) Develop multi-analyte biosensors capable of detecting glucose along with other metabolic markers, such as lactate or cholesterol.

iii) Optimize surface functionalization techniques, such as polymer coatings or self-assembled monolayers, to enhance biocompatibility, anti-fouling properties, and selective glucose detection.

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