Monitoring and sensing of glucose molecule by micropillar coated Electrochemical biosensor via $CuO/[Fe(CN)_6]^{3-}$ and its applications.

A DISSERTATION

SUBMITTED IN PARTIAL FULFILLMENT OF THE

REQUIREMENTS FOR THE AWARD OF THE DEGREE

OF

MASTER OF SCIENCE

IN

CHEMISTRY

Submitted by:

PURVA
(2K21/MSCCHE/34)

Under the supervision of

Dr. Deenan Santhiya

DEPARTMENT OF APPLIED CHEMISTRY
DELHI TECHNOLOGICAL UNIVERSITY
Formerly Delhi College of Engineering)
Bawana Road, Delhi-110042

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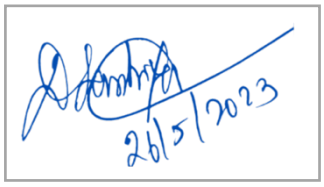

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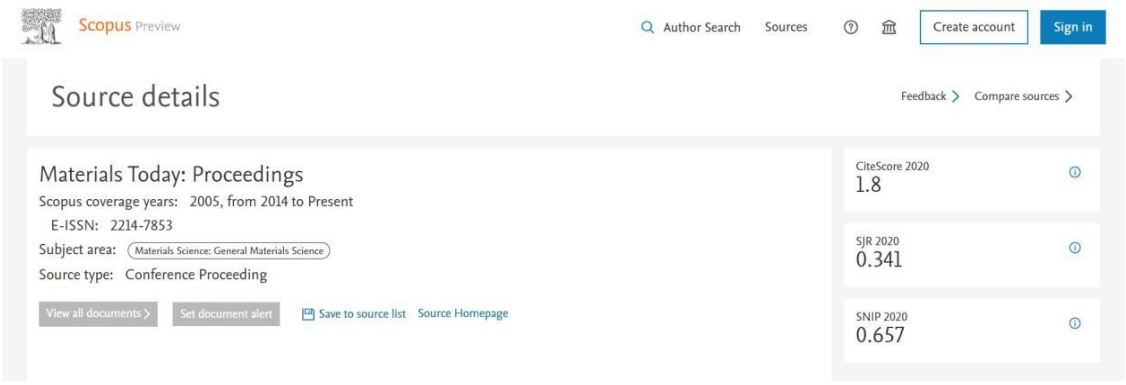

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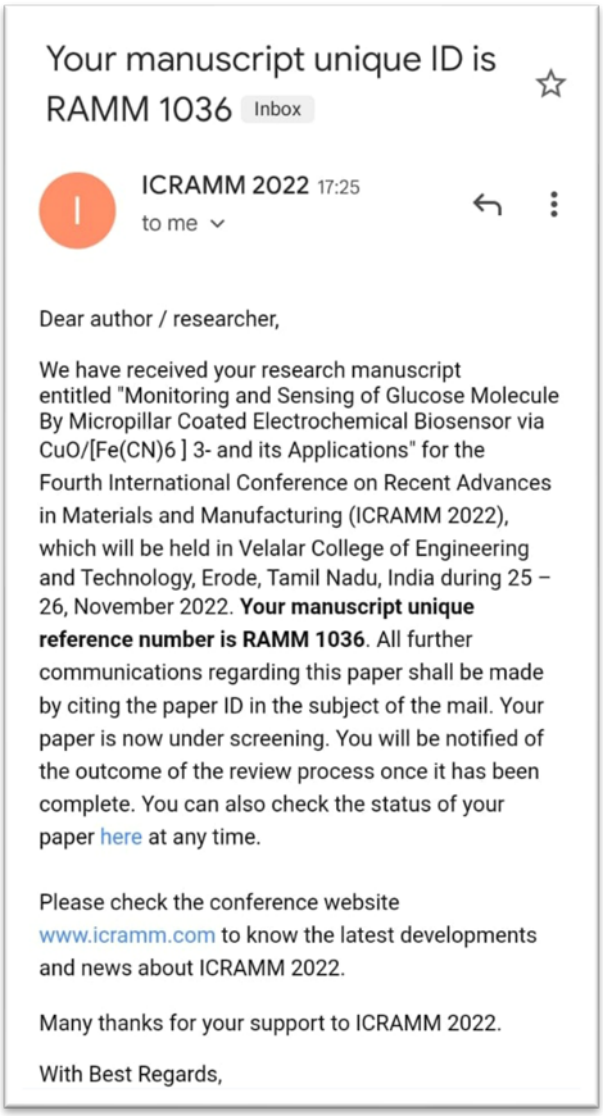

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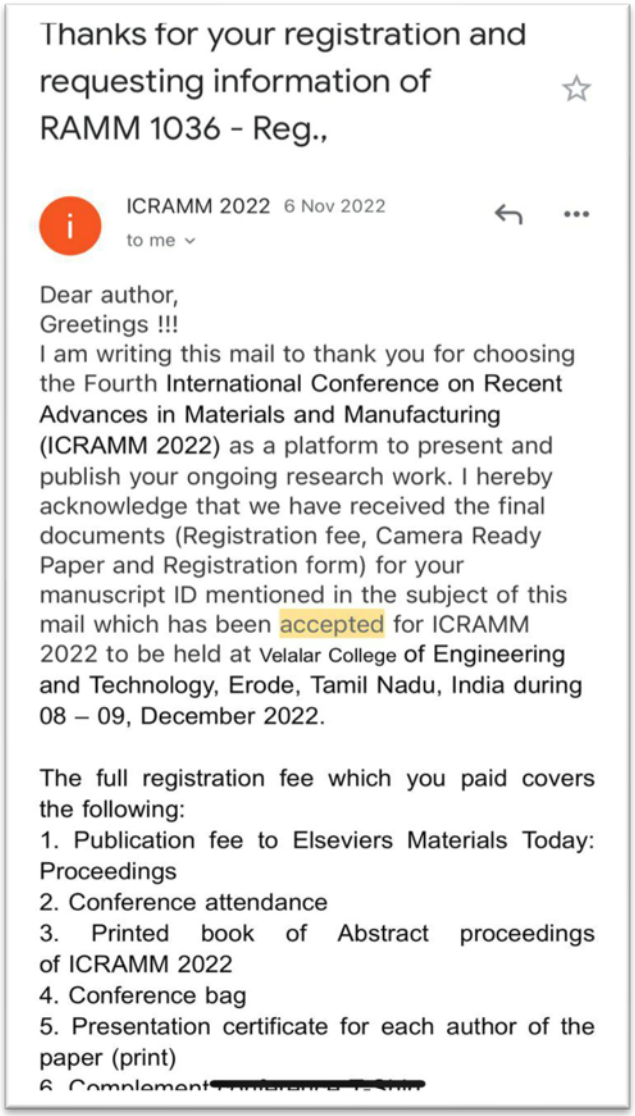

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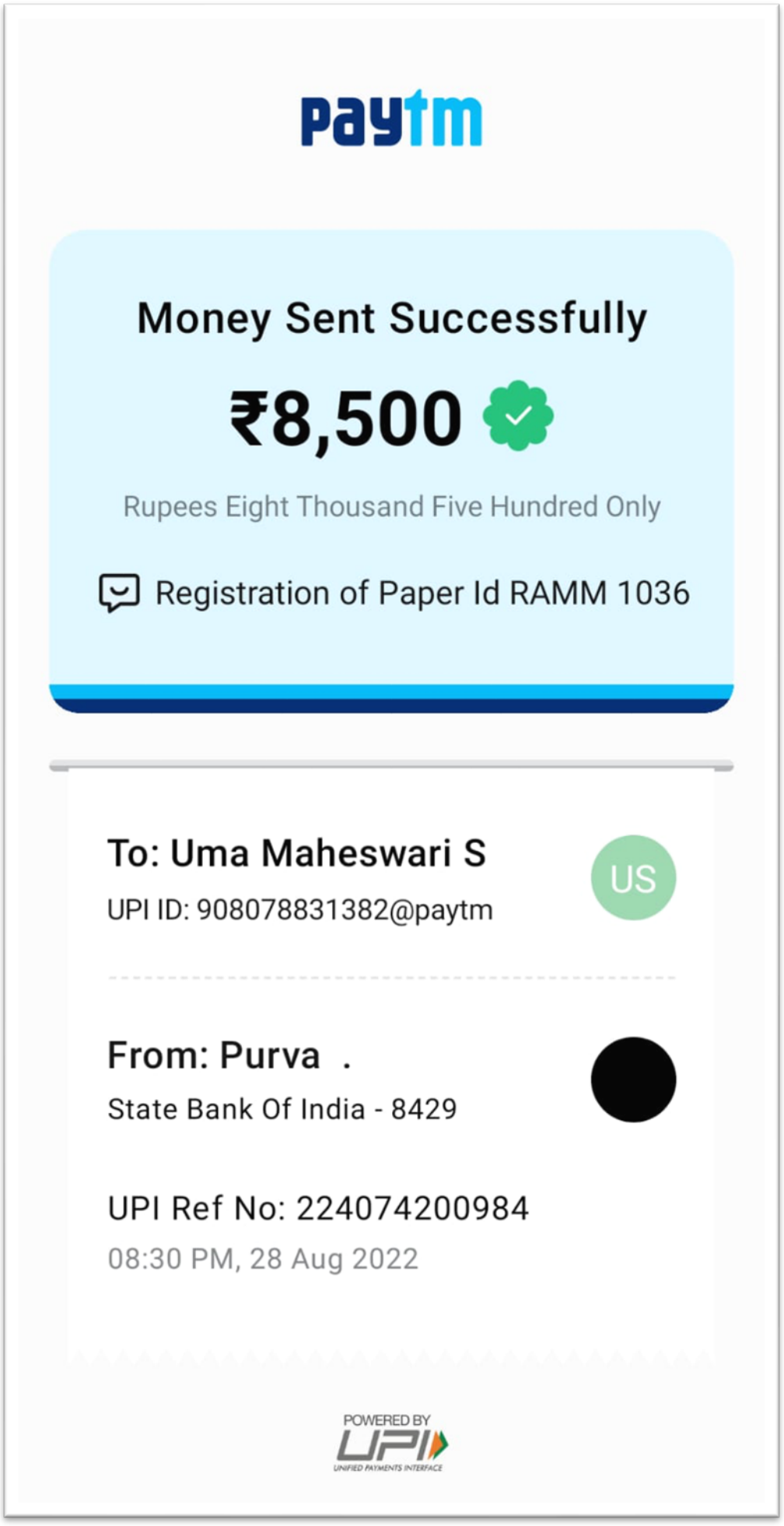
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Purva 

ABSTRACT

This thesis explores the advancements in monitoring and sensing glucose molecules using micropillar-coated electrochemical biosensors. Glucose sensing through electroanalysis has emerged as one of the most widespread and commercially successful applications in the field. By leveraging the principles of amperometry, which involves the measurement of electric current, electrochemical glucose sensors provide accurate assessments of glucose concentration in samples. This process entails the application of a voltage that initiates the oxidation of glucose, with the resulting current being measured at the electrode. A crucial aspect of designing an effective glucose sensor lies in establishing a linear relationship between glucose concentration and the measured current, enabling precise and calibrated measurements. In the typical configuration of a glucose sensor, the oxidation of glucose does not occur directly at the working electrode where the current is measured. Instead, a chemical oxidant is employed to facilitate the reaction, which is further accelerated by the presence of a biological enzyme, such as glucose oxidase. This combination of chemical and biological components ensures the sensor's specificity to glucose and its independence from the concentration of other oxidizable species that may be present in the analyte solution. However, reliance on atmospheric oxygen concentration poses challenges. The reduced form of the oxidant, after reacting with glucose, can be re-oxidized directly at the electrode. Although oxygen is the natural oxidant, its slow kinetics and susceptibility to variations in atmospheric oxygen levels can introduce inaccuracies and complications in glucose measurements. To overcome these challenges, researchers have explored alternative approaches and devised strategies to enhance the performance of glucose sensors. One such strategy involves the utilization of mediators, which act as electron shuttles between the electrode and the enzyme. These mediators bypass the dependence on oxygen for the re-oxidation process, resulting in faster and more efficient electron transfer. Consequently, improved sensor response times and reduced susceptibility to variations in atmospheric oxygen levels are achieved. Furthermore, the integration of nanotechnology has played a pivotal role in the development of glucose sensors. Nanomaterials, including carbon nanotubes, graphene, and metal nanoparticles, offer increased sensitivity, stability, and selectivity. These nanomaterials provide a large surface area for enzyme immobilization and exhibit excellent electrical conductivity, facilitating efficient electron transfer between the electrode and the glucose oxidation reaction. Functional group modifications and specific enzymes further enhance the sensor's specificity for glucose.

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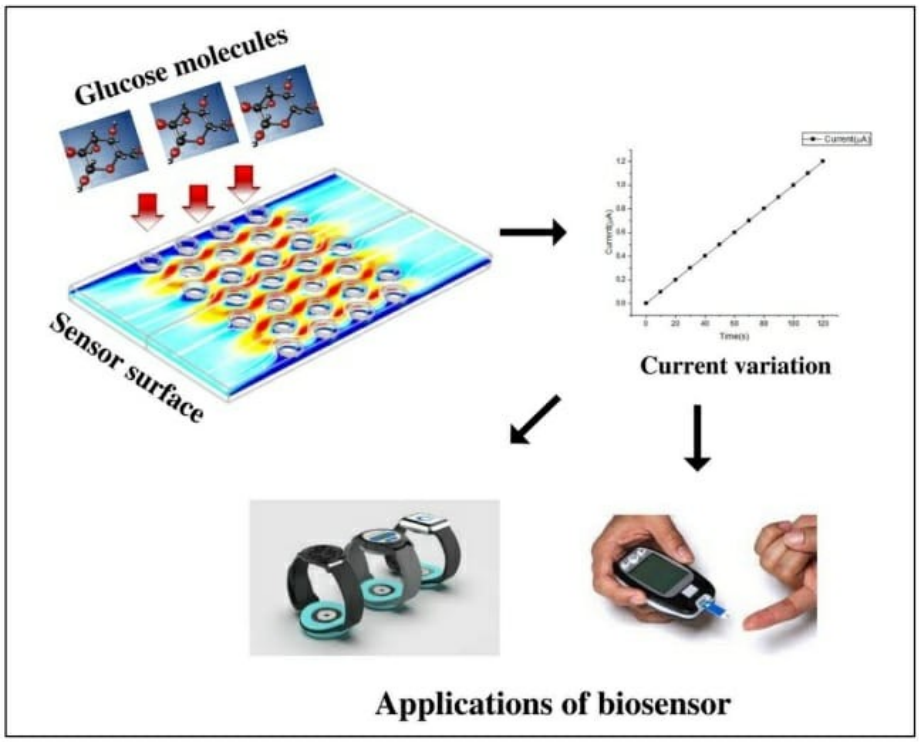
LIST OF SYMBOLS AND ABBREVIATIONS

- CuO = Copper (II) oxide
- [Fe (CN)6]3- = Ferricyanide
- GOx = Glucose Oxidase
- Ag = Silver
- AgCl = Silver Chloride
- LOD = Limit of Detection
- PBS = Phosphate Buffered Saline
- SEM = Scanning Electron Microscopy
- CV = Cyclic Voltammetry

CHAPTER 1

INTRODUCTION



1.1 Background and Significance

Glucose monitoring plays a critical role in managing diabetes mellitus, a chronic metabolic disorder affecting millions of individuals worldwide. Traditional glucose monitoring methods such as fingerstick testing have limitations in terms of invasiveness, inconvenience, and the need for frequent blood sampling[1]. Electrochemical biosensors offer a promising alternative, enabling real-time and non-invasive glucose monitoring. One such biosensor, employing a micropillar-coated electrode with a CuO/$[Fe(CN)_6]^{3-}$ redox system, has garnered significant attention due to its excellent sensing capabilities. The development of electrochemical biosensors has revolutionized glucose monitoring by exploiting the specific interactions between glucose molecules and biorecognition elements, such as enzymes or receptors. These biosensors convert the biochemical recognition event into a measurable electrochemical signal, providing a quantitative assessment of glucose concentration.

Micropillar-Coated Electrochemical Biosensors:

Micropillar-coated electrodes have emerged as a promising platform for electrochemical biosensors. These electrodes consist of an array of micropillars fabricated on the electrode surface, increasing the active surface area and enhancing sensitivity. The micropillar coating can be functionalized with biorecognition elements, enabling selective and sensitive glucose detection.

CuO/$[Fe(CN)_6]^{3-}$ Redox System:

The CuO/$[Fe(CN)_6]^{3-}$ redox system offers several advantages for glucose sensing applications. Copper oxide (CuO) nanoparticles exhibit excellent electrocatalytic properties [2,3], promoting the oxidation of glucose. $[Fe(CN)_6]^{3-}$ ions act as redox mediators, participating in the electron transfer process during glucose oxidation. This redox system enables the development of highly sensitive and stable biosensors for glucose monitoring.

Significance of the Study:

The monitoring and sensing of glucose molecules using micropillar-coated electrochemical biosensors via the CuO/$[Fe(CN)_6]^{3-}$ redox system holds significant importance due to the following reasons:

a) **Enhanced Sensitivity:** The micropillar-coated electrode architecture provides a larger active surface area, leading to improved sensitivity and detection limits. This enables accurate glucose monitoring even at low concentrations, crucial for effective diabetes management.

b) **Selective Detection:** The functionalization of micropillar coatings with specific enzymes or receptors allows selective glucose detection, minimizing interference from other electroactive species. This specificity ensures reliable and accurate glucose measurements.

c) **Real-Time Monitoring:** Electrochemical biosensors offer real-time glucose monitoring, providing immediate feedback for timely intervention and adjustment of therapy. Continuous monitoring enhances patient compliance, enables personalized treatment, and helps prevent hypoglycemic or hyperglycemic episodes.

d) **Non-Invasiveness:** Unlike traditional blood sampling methods, micropillar-coated electrochemical biosensors offer a non-invasive approach to glucose monitoring. This reduces patient discomfort, enhances convenience, and reduces the risk of infection associated with repeated fingerstick testing.

e) **Long-Term Stability:** The CuO/$[Fe(CN)_6]^{3-}$ redox system exhibits excellent stability and reversibility, ensuring the long-term performance of the biosensor. This stability is crucial for continuous and reliable glucose monitoring over extended periods.

f) **Potential for Wearable Devices:** Micropillar-coated electrochemical biosensors have the potential for integration into wearable devices, such as smartwatches or patches, enabling continuous glucose monitoring in a non-obtrusive manner. This integration facilitates seamless data collection and analysis, empowering individuals to manage their glucose levels more effectively.

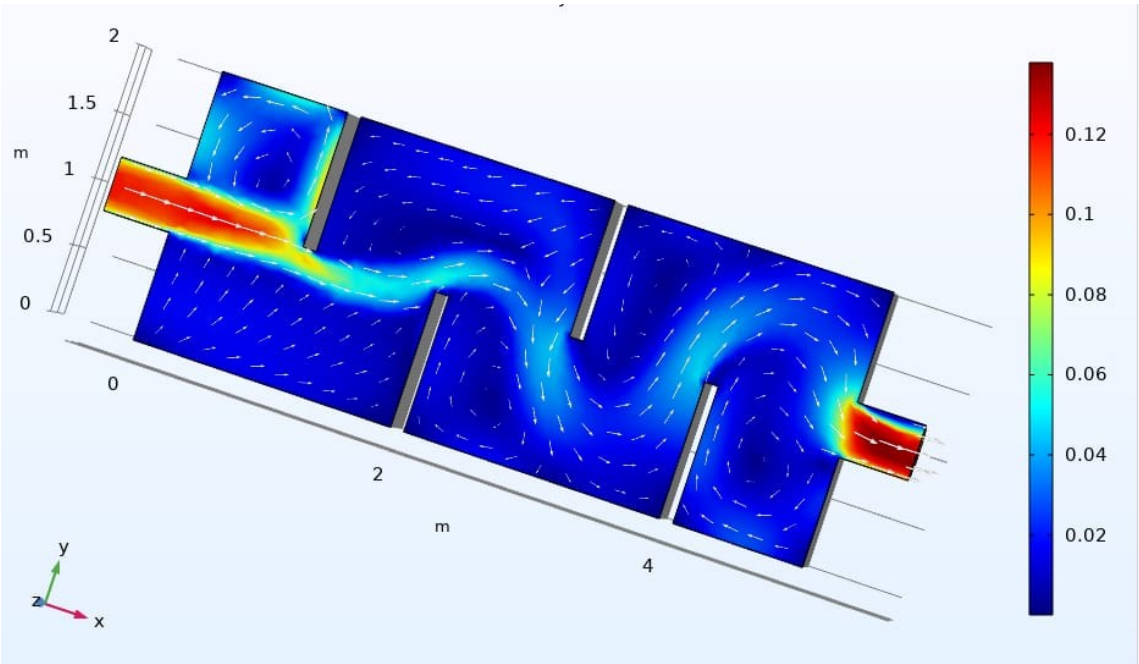


Fig. 1.1 Electrostatic potential field vector diagram.

The computational model employed in this study consists of a single two-dimensional (2D) domain that represents a unit cell of solution measuring 100 μm in width positioned above an interdigitated electrode, as depicted in Figure 1. While the actual geometry encompasses a periodic repetition of this unit cell in the x-direction, the 2D approximation is deemed suitable since the cell and electrode extend sufficiently far out-of-plane in the model. The top portion of the unit cell is characterized by a bulk boundary where the concentrations of the analyte are assumed to be equivalent to those present in the bulk solution. At the bottom of the unit cell, the y = 0 axis is divided into four points, effectively creating distinct boundaries for the electrode and the insulator. The anode, or working electrode, is centrally positioned within the cell, specifically in the x-range of 37.5 μm to 62.5 μm. Each neighbouring cathode, serving as the counter electrode, comprises half of the unit cell, with one located in the x-range less than 12.5 μm and the other in the x-range greater than 87.5 μm. Between the anode and cathode surfaces, a solid insulating material is present, providing separation and electrical insulation.

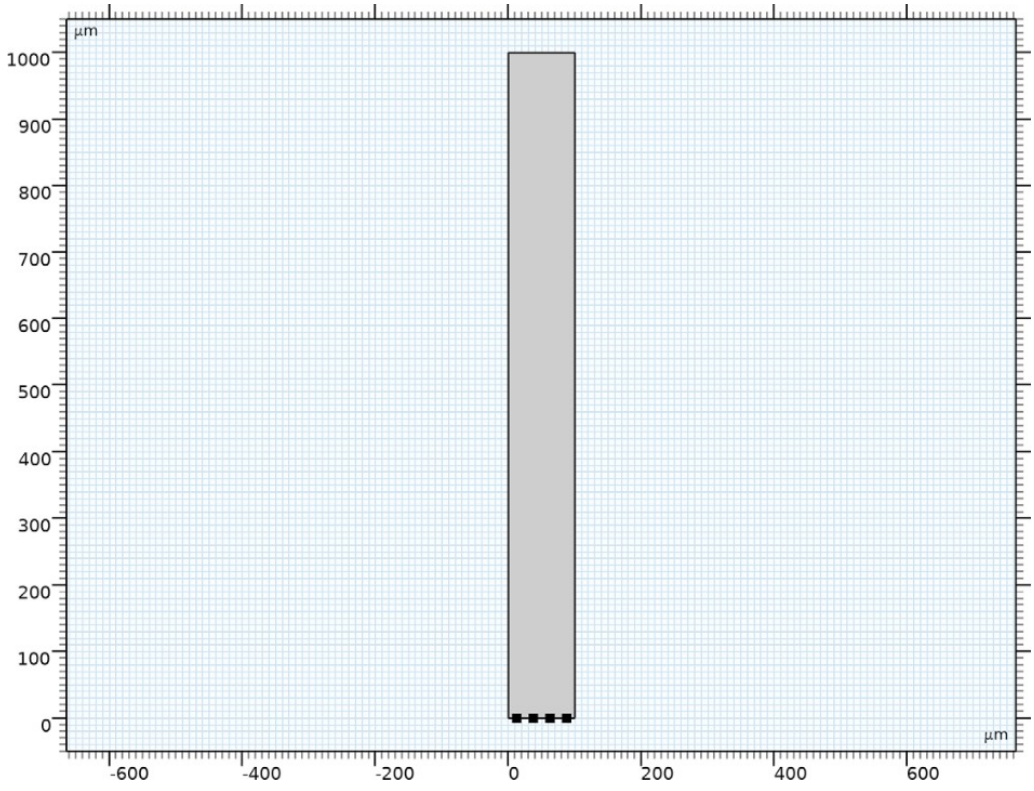


Fig. 1.2 Model Geometry.

1.2 Problem Statement:

Monitoring and accurately sensing glucose levels is crucial for the effective management of diabetes and other metabolic disorders[4]. Traditional methods of glucose monitoring, such as finger-prick testing, are invasive and inconvenient for patients, leading to a demand for non-invasive and efficient glucose sensing techniques. Electrochemical biosensors have emerged as a promising solution due to their high sensitivity, rapid response, and miniaturized design. However, there is a need to enhance the performance of electrochemical biosensors to achieve more precise and reliable glucose detection. In this context, the problem addressed in this study is to develop a micropillar-coated electrochemical biosensor for monitoring and sensing glucose molecules. The aim is to improve the sensitivity, selectivity, and accuracy of glucose detection, thereby facilitating better glucose monitoring and management for individuals with diabetes.

The specific challenges and requirements to be addressed in this study are:

a) **Enhancing sensitivity:** The biosensor should be capable of detecting glucose molecules at low concentrations, ensuring accurate monitoring of glucose levels in a wide range.

b) **Improving selectivity:** The biosensor should exhibit high selectivity for glucose molecules, minimizing interference from other substances commonly found in biological samples.

c) **Ensuring stability** and reproducibility: The biosensor should maintain its sensing performance over extended periods and demonstrate consistent results across multiple measurements.

d) **Optimizing design and fabrication:** The micropillar-coated electrochemical biosensor should be designed and fabricated with precision, ensuring efficient electron transfer, improved sensor-substrate interaction, and compatibility with biological samples.

e) **Establishing real-world applicability:** The biosensor should demonstrate its practical utility by being applicable for continuous glucose monitoring in clinical settings, offering a user-friendly experience and reliable glucose measurements.

Addressing these challenges will contribute to the development of an advanced micropillar-coated electrochemical biosensor for glucose sensing, offering accurate and reliable glucose monitoring capabilities for individuals with diabetes and improving their overall quality of life.

1.3 Objectives

a) Develop a micropillar-coated electrochemical biosensor for the accurate and reliable monitoring and sensing of glucose molecules.
b) Explore the electrochemical properties of CuO and $[Fe(CN)_6]^{3-}$ and assess their suitability for glucose detection.
c) Fabricate micropillar structures on a selected substrate using microfabrication techniques.
d) Optimize the coating process to achieve a uniform and stable CuO layer on the micropillars.
e) Investigate the role of $[Fe(CN)_6]^{3-}$ as a redox mediator to enhance the electron transfer efficiency during glucose sensing.
f) Evaluate the sensitivity, selectivity, and detection limit of the biosensor through calibration curves and performance testing.
g) Assess the biosensor's stability and reproducibility to ensure long-term functionality.
h) Determine the influence of interfering substances commonly found in biological samples on the biosensor's specificity for glucose sensing.
i) Explore the potential application of the micropillar-coated electrochemical biosensor in continuous glucose monitoring for diabetes management.
j) Validate the biosensor's performance in real-life scenarios and compare it with existing glucose monitoring techniques.
k) Propose strategies for the miniaturization and integration of the biosensor into wearable or portable devices for convenient and non-invasive glucose monitoring.
l) Consider the scalability and cost-effectiveness of the biosensor for potential commercialization and mass production.

1.4 Scope and Limitation

Scope:

The monitoring and sensing of glucose molecules using micropillar-coated electrochemical biosensors via CuO/$[Fe(CN)_6]^{3-}$ holds significant potential in various applications related to diabetes management and research. The scope of this thesis involves exploring the capabilities and limitations of this specific biosensor design for glucose detection.

a) **Sensor Performance:** The thesis aims to evaluate the performance of the micropillar-coated electrochemical biosensor in terms of sensitivity, accuracy, selectivity, and response time for glucose sensing. The focus will be on determining the optimal conditions, such as electrode materials, enzyme immobilization techniques, and micropillar coating composition, to achieve reliable and precise glucose measurements.

b) **Detection Range:** The thesis will investigate the dynamic range of the biosensor, determining the lowest and highest glucose concentrations that can be accurately detected. Understanding the detection range is crucial for ensuring the biosensor's suitability for different glucose-monitoring scenarios, such as hyperglycaemia and hypoglycaemia.

c) **Stability and Longevity:** The stability and longevity of the micropillar-coated electrochemical biosensor will be assessed to determine its practical applicability. Factors such as enzyme degradation, electrode fouling, and signal drift over time will be investigated to establish the biosensor's durability for continuous glucose monitoring applications.

d) **Interference and Selectivity:** The thesis will address the potential interferences and cross-reactivity of the biosensor with other analytes commonly found in biological samples, such as ascorbic acid, acetaminophen, and uric acid. The goal is to identify any limitations or challenges related to selectivity and propose strategies to enhance the biosensor's specificity for glucose detection.

Limitations:

a. **Sensitivity to Environmental Factors:** Environmental conditions, such as temperature, pH, and humidity, can affect the performance of the biosensor. The thesis will consider the impact of these factors and propose suitable measures to mitigate their influence on the accuracy and reliability of glucose measurements.

b. **Biocompatibility and Biostability:** The biosensor's interaction with biological fluids, such as blood or interstitial fluid, may pose challenges related to biocompatibility and biostability. The thesis will address any potential limitations in terms of

biosensor functionality, biofouling, and potential adverse effects on the surrounding tissues.

c. **Sample Matrix Effects:** The composition of the sample matrix, such as blood or interstitial fluid, may introduce matrix effects that can influence the biosensor's performance. These effects, including viscosity, interfering substances, and non-specific binding, will be considered and evaluated for their impact on glucose measurements.

d. **Practical Implementation:** The thesis will discuss the practical implementation of the micropillar-coated electrochemical biosensor, including device miniaturization, power requirements, and integration with wearable or portable devices. The feasibility and limitations of real-time, continuous glucose monitoring using this biosensor will be considered.

CHAPTER 2

METHODOLOGY

2.1 Theoretical Simulation:

A 3D model of an electrochemical sensor was constructed using the electrochemical module in COMSOL Multiphysics, incorporating laminar flow and time-dependent analysis. The model included the necessary geometry, parameters, geometrical non-linearity, and materials for the pillar surfaces. The physics module employed for the laminar flow considered the transport of diluted species and surface reactions as the underlying physics interface. To configure the sensor geometry, the following dimensions were utilized: a z-axis distance of 0.002 m between the pillars, an x-axis distance of 0.0016 m between the pillars, and overall cell dimensions of 0.012 m × 0.001 m × 0.0069 m. The maximum allowable pillar radius was set at 5.9031E-4 m. The accompanying figure illustrates the designed sensor's geometry.

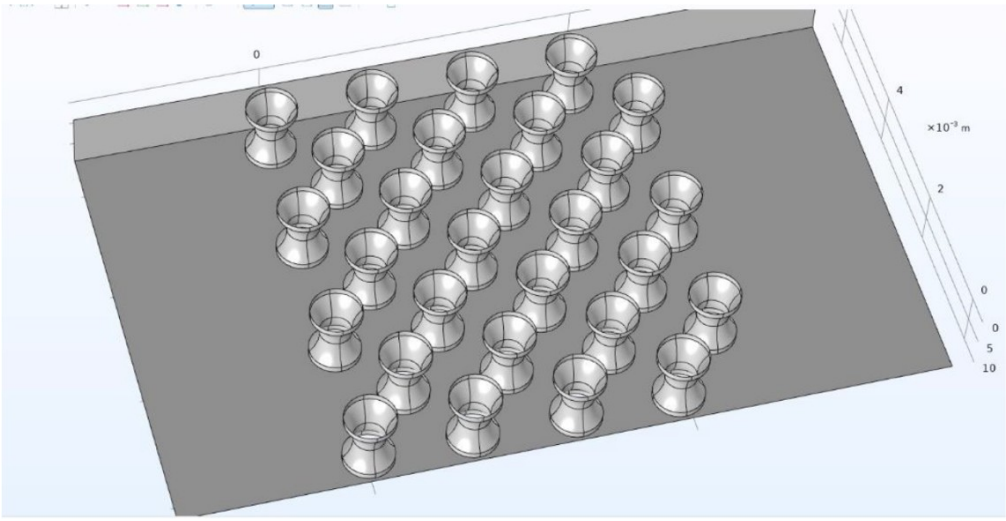


Fig. 2.1 The geometrical array of the micropillars coated with a layer of CuO and Ferricyanide for the absorption of the glucose molecules.

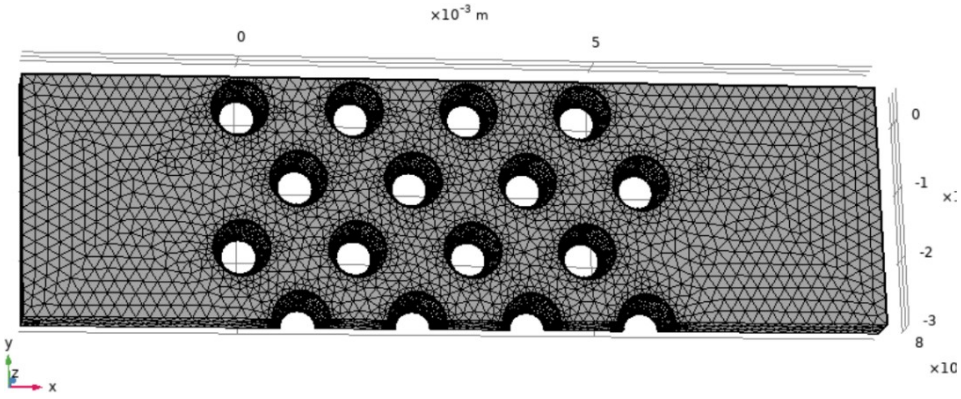


Fig. 2.2 The mesh structure of the array of the micropillars mounted inside a cell in the sensor.

2.2 Simulation Model:

Interface settings for setup in COMSOL Multiphysics.

Table 2.1 Description and Values for Discretization

SETTINGS

Description	Value
Concentration	Linear
Electric potential	Quadratic

Table 2.2 Description and Values for Out-of-Plane Thickness

SETTINGS

Description	Value
Thickness	1[m]

Table 2.3 Description and Values for Electrolyte Charge Conservation

SETTINGS

Description	Value
Charge conservation model	Electroanalysis (no potential gradients)

Table 2.4 Description and Values for Physics vs. Materials Reference Electrode Potential

SETTINGS

Description	Value
Physics vs. materials reference electrode potential	0 V

- **Iterations for different concentrations of CuO.**

```
<---- Stationary Solver 1 in Study 1/Solution 1 (sol1) -------------------------
Started at Oct 14, 2020 10:14:14 AM.
Continuation solver
Nonlinear solver
Number of degrees of freedom solved for: 3661 (plus 708 internal DOFs).

Continuation parameter c_glucose_ext = 0.05.
Nonsymmetric matrix found.
Scales for dependent variables:
Concentration (comp1.c_ferri): 4.8e+05
Concentration (comp1.c_ferro): 9.8e+03
Concentration (comp1.c_glucose): 2.5e+07
Counter electrode potential (comp1.tcd.phisCE): 1
Orthonormal null-space function used.
Iter      SolEst      ResEst     Damping    Stepsize #Res #Jac #Sol   LinErr   LinRe
s
   1       0.048     5.3e+02   1.0000000        0.43    2    1    2  4.8e-10    4e-
16
   2       0.002          58   1.0000000       0.051    3    2    4  1.4e-09  2.4e-
16
   3     3.1e-06       0.007   1.0000000        0.04    5    3    6  1.1e-08  1.9e-
16
   4       3e-07      0.0066   1.0000000     3.1e-06    7    4    8  5.7e-09  5.5e-
15

Continuation parameter c_glucose_ext = 0.1.
Iter      SolEst      ResEst     Damping    Stepsize #Res #Jac #Sol   LinErr   LinRe
s
   1       0.041     1.1e+16   1.0000000        0.36    9    5   10  8.5e-09  2.1e-
16
   2      0.0002          80   1.0000000       0.028   10    6   12  1.6e-09  1.9e-
16
   3     1.4e-07       0.011   1.0000000      0.0002   12    7   14  3.3e-09    2e-
16

Continuation parameter c_glucose_ext = 0.15.
Iter      SolEst      ResEst     Damping    Stepsize #Res #Jac #Sol   LinErr   LinRe
s
   1       0.012     1.5e+13   1.0000000        0.24   14    8   16  1.8e-09  2.5e-
16
   2     7.2e-06       0.011   1.0000000        0.01   16    9   18  4.5e-09  1.7e-
16

Continuation parameter c_glucose_ext = 0.2.
Iter      SolEst      ResEst     Damping    Stepsize #Res #Jac #Sol   LinErr   LinRe
s
   1      0.0065     3.3e+08   1.0000000        0.18   18   10   20  4.1e-09  2.1e-
16
   2     1.7e-06       0.004   1.0000000       0.006   20   11   22  1.3e-09  1.9e-
16

Continuation parameter c_glucose_ext = 0.25.
Iter      SolEst      ResEst     Damping    Stepsize #Res #Jac #Sol   LinErr   LinRe
s
   1      0.0043     2.3e+08   1.0000000        0.15   22   12   24  5.6e-10  2.2e-
16
```

2.3 Numerical Modelling:

The reaction involving the oxidation of glucose in the presence of ferricyanide is represented by equation (1)[11].

$$Glucose + Ferricyanide \rightarrow Gluconic\ acid + Ferrocyanide \ldots\ldots (1)$$

It can be expressed as the conversion of glucose to gluconic acid and ferricyanide. To determine the rate of this reaction, the Michaelis-Menten equation (2) is employed, where $Cglucose$ represents the concentration of glucose, V denotes the maximum rate of the reaction, and $Kmax\ m$ represents the Michaelis-Menten constant[12].

$$r = \frac{C_{glucose} \times V_{max}}{1 + (K_m \times C_{glucose})} \ldots\ldots\ldots (2)$$

Within the electrochemistry module of the software, the battery and fuel cells module is utilized to perform electroanalysis of the sensor. To analyse the results, specific boundary conditions are applied, considering parameters such as the diffusion coefficient ($D\ Am$) and the velocity vector (u) of glucose molecules[13].

$$\frac{\partial C_{glucose}}{\partial t} + \nabla.\left(-D_{A_m}\nabla_{C_{glucose}}\right) + u.\nabla_{C_{glucose}} = 0 \ldots\ldots\ldots\ldots (3)$$

The flux of the electric field is determined by the absorption and desorption rates of glucose molecules, as indicated in the equation provided. The rates of absorption (r) and desorption (r) influence this relationship, while abs and des represent additional parameters[14].

$$\emptyset = -r_{abs} + r_{des} \ldots\ldots\ldots (4)$$

For the electroanalytic sensor, the current density is calculated using the Butler-Volmer equation, which describes the oxidation process. It takes into account the cathodic transfer coefficient (αC), the conversion rate of the reaction ($k0$), the potential supplied at the working electrode (η), and the constant temperature of the cell (T).

$$J = nFk_0\left(C_{Glucose}\ exp\left(\frac{(n-\alpha_C)F\eta}{RT}\right)\right) \ldots\ldots\ldots (5)$$

Subsequently, the current is derived from the current density using equation (6), and a plot is generated to visualize the relationship between the current and the concentration of glucose. The area of the micropillars cell (A) plays a role in this calculation[15].

$$I = J \times A \ldots\ldots. (6)$$

To determine the sensitivity of the designed sensor, equation (7) is utilized, considering the change in current (∂I) and the change in glucose concentration ($\partial CGlucose$) as variables.

$$S = \frac{\partial I}{\partial C_{Glucose}} \ldots\ldots\ldots\ldots (7)$$

2.4 Sensor Fabrication:

- **Electrode Preparation:** Fabricate working, reference, and counter electrodes using appropriate materials, such as gold or platinum, with desired dimensions.
- **Micropillar Coating:** Apply a layer of micropillar coating onto the electrode surfaces using techniques like physical vapour deposition or chemical vapour deposition. Optimize the coating thickness and density to enhance surface area and improve sensing performance.
- **Enzyme Immobilization:** Immobilize glucose oxidase (GOx) enzyme onto the micropillar-coated working electrode surface. This can be achieved through physical adsorption, cross-linking, or covalent attachment methods. Experiment with different enzyme concentrations and immobilization techniques to optimize the sensor's sensitivity and stability.

2.5 Electrochemical Measurement Setup:

- **Electrochemical Cell:** Assemble a three-electrode electrochemical cell consisting of the micropillar-coated working electrode, a reference electrode (e.g., Ag/AgCl), and a counter electrode (e.g., platinum).
- **Electrolyte Solution:** Prepare an appropriate electrolyte solution, such as phosphate-buffered saline (PBS), with suitable pH and ionic strength to maintain enzymatic activity and facilitate electron transfer.
- **Instrumentation:** Utilize a potentiostat or Galvano stat to apply a potential or current to the electrodes and measure the resulting electrochemical responses.

2.6 Calibration and Characterization:

- **Calibration Curve:** Prepare a series of standard glucose solutions with known concentrations spanning the desired detection range. Measure the corresponding electrochemical signals from the sensor to establish a calibration curve relating glucose concentration to the sensor response.

- **Sensitivity and Limit of Detection:** Determine the sensitivity of the biosensor by calculating the slope of the calibration curve. Evaluate the limit of detection (LOD) by determining the lowest glucose concentration that can be reliably detected above the noise level.

2.7 Performance Evaluation:

- **Selectivity Testing:** Assess the biosensor's selectivity by measuring its response to potential interferents commonly present in biological samples, such as ascorbic acid, acetaminophen, or uric acid. Evaluate any cross-reactivity and interference effects.
- **Stability Testing:** Investigate the biosensor's stability over time by repeatedly measuring glucose concentrations in a controlled environment. Monitor any changes in sensitivity or baseline signal to determine the sensor's long-term performance and reliability.
- **Real Sample Analysis:** Validate the biosensor's performance by analysing real-world glucose samples, such as blood or interstitial fluid. Compare the biosensor measurements with a reference method, such as laboratory-grade glucose assays or commercially available glucose monitoring systems.

Application:

Once the micropillar-coated electrochemical biosensor via CuO/$[Fe(CN)_6]^{3-}$ has been characterized and its performance established, it can be applied in various scenarios, including:

- **Diabetes Management:** Utilize the biosensor for continuous glucose monitoring in individuals with diabetes, providing real-time feedback on glucose levels for better insulin dosing and overall glycaemic control.

- **Research and Development:** Apply the biosensor in research studies to investigate glucose dynamics, metabolic disorders, and the effects of different interventions, such as drug therapies or dietary changes.

- **Point-of-Care Testing:** Develop portable and user-friendly devices incorporating biosensor technology for convenient glucose monitoring outside clinical settings, enabling rapid and accurate glucose measurements at the point of care.

- **Bioprocess Monitoring:** Implement the biosensor in bioprocess engineering and biopharmaceutical production to monitor the glucose levels in cell cultures or fermentation processes. This can aid in optimizing production parameters and ensuring the desired glucose concentration for optimal cell growth or product formation.

- **Food and Beverage Industry:** Utilize the biosensor for quality control and monitoring of glucose levels in food and beverage products, such as juices, syrups, and alcoholic beverages. This can help ensure product consistency and adherence to regulatory standards.

- **Environmental Monitoring:** Apply the biosensor in environmental monitoring to detect glucose levels in wastewater or natural water sources. This can be useful in assessing organic pollution levels and understanding the impact of human activities on aquatic ecosystems.

- **Personalized Medicine:** Integrate the biosensor into wearable devices or implantable sensors for personalized medicine applications. This can enable continuous glucose monitoring in individuals with diabetes or other metabolic disorders, facilitating real-time adjustments in treatment plans.

- **Biosensor Technology Advancements:** Further develop and refine the micropillar-coated electrochemical biosensor technology via $CuO/[Fe(CN)_6]^{3-}$ by exploring new materials, optimization techniques, and integration with other sensing modalities. This can lead to enhanced performance, improved durability, and expanded applications in glucose sensing and beyond.

In conclusion, the methodology for monitoring and sensing glucose molecules using micropillar-coated electrochemical biosensors via $CuO/[Fe(CN)_6]^{3-}$ involves sensor fabrication, electrochemical measurement setup, calibration, characterization, and performance evaluation. The biosensor can find applications in diabetes management, research, point-of-care testing, bioprocess monitoring, the food industry, environmental monitoring and personalized medicine, and contribute to the advancement of biosensor technology.

CHAPTER 3

Design and Optimization of Micropillar-Coated Electrochemical Biosensors

Micropillar-coated electrochemical biosensors have gained significant attention in recent years due to their enhanced performance in glucose sensing and other applications. The design and optimization of these biosensors involve several key aspects that contribute to their sensitivity, selectivity, and stability.

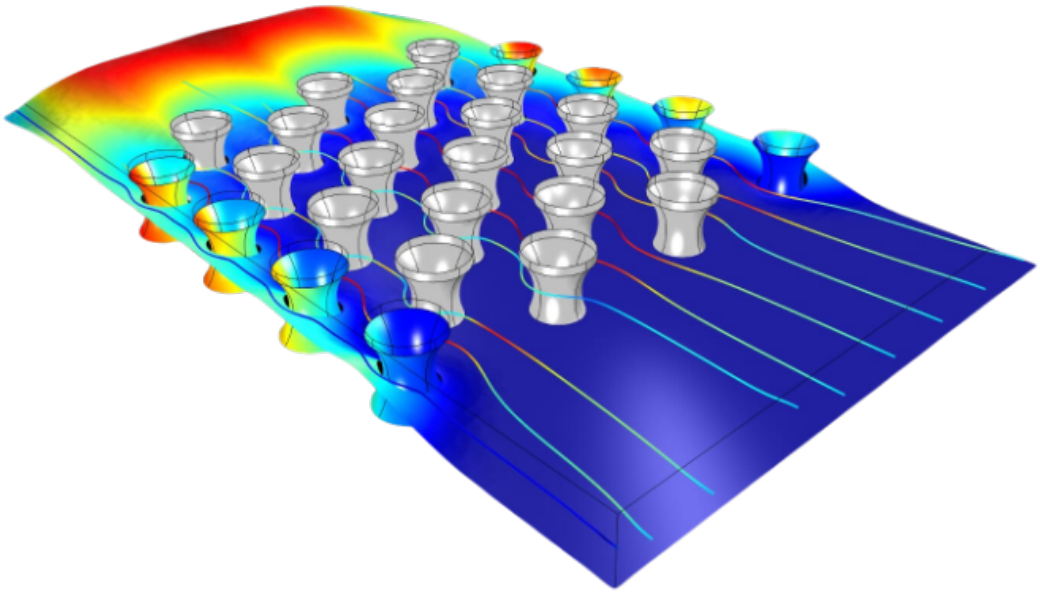


Fig.3.1 Designed Biosensor

3.1 Micropillar Coating Design:

The design of the micropillar coating plays a crucial role in the biosensor's performance. Factors to consider include:

- **Coating Material:** Selecting an appropriate coating material, such as metal oxides (e.g., CuO), polymers, or carbon-based materials, that provides high surface area, stability, and biocompatibility.
- **Pillar Density and Size:** Optimizing the density and size of the micropillars to maximize the surface area available for enzyme immobilization and enhance the mass transport of glucose molecules to the active sites.
- **Surface Roughness:** Controlling the surface roughness of the micropillar coating to facilitate efficient enzyme immobilization and improve the electrochemical response.

3.2 Enzyme Immobilization Techniques:

The immobilization of enzymes, typically glucose oxidase (GOx), onto the micropillar-coated electrode surface, is critical for glucose sensing. Optimization strategies include:

- **Immobilization Methods:** Exploring different immobilization techniques, such as physical adsorption, covalent binding, or cross-linking, to enhance enzyme stability, activity, and longevity.
- **Enzyme Loading and Concentration:** Determining the optimal enzyme loading and concentration on the micropillars to achieve a balance between high sensitivity and enzyme stability.
- **Surface Modification:** Introducing surface modifications, such as functional groups or linker molecules, to improve enzyme attachment and minimize non-specific binding.

3.3 Electrode Material and Configuration:

The selection of electrode materials and configuration can significantly impact the biosensor's performance:

- **Working Electrode Material:** Choosing appropriate materials, such as gold, platinum, or carbon-based electrodes, with good conductivity and compatibility with the micropillar coating and enzyme immobilization process.
- **Reference and Counter Electrode:** Select suitable reference and counter electrodes to ensure accurate and reliable electrochemical measurements.
- **Electrode Configuration:** Optimizing the electrode configuration, such as planar, interdigitated, or three-dimensional (3D) architectures, to maximize the sensing surface area and facilitate efficient electron transfer.

3.4 Optimization of Operating Conditions:

The optimization of operating conditions is crucial for achieving optimal biosensor performance:

- **Electrolyte Solution:** Choosing an appropriate electrolyte solution with the desired pH, ionic strength, and buffering capacity to maintain enzymatic activity and provide optimal electrochemical performance.
- **Temperature and pH:** Investigating the effects of temperature and pH on enzyme activity and sensor response to optimize the biosensor's performance under physiological or specific operating conditions.
- **Detection Parameters:** Evaluate various detection parameters, such as applied potential, current range, or frequency, to

enhance the sensitivity, dynamic range, and response time of the biosensor.

3.5 Performance Characterization and Validation:

Once the biosensor is designed and optimized, its performance should be thoroughly characterized and validated:

- **Calibration and Sensitivity:** Establishing a calibration curve by measuring the biosensor response to glucose solutions of known concentrations to determine the sensitivity and linearity of the sensor.
- **Selectivity and Interference Studies:** Assessing the biosensor's selectivity by investigating its response to potential interferents commonly found in biological samples, such as ascorbic acid or uric acid.
- **Stability and Longevity:** Evaluating the stability and longevity of the biosensor by monitoring the sensor's response over an extended period, and assessing any changes in sensitivity, baseline drift, or degradation of the immobilized enzyme.

3.6 Real-World Application Testing:

To validate the practical utility of the micropillar-coated electrochemical biosensor, real-world application testing can be conducted:

- Glucose Measurements in Biological Samples: Analysing glucose levels in biological samples, such as blood, interstitial fluid, or saliva, to evaluate the biosensor's accuracy, precision, and correlation with reference methods.
- Comparative Studies: Comparing the biosensor's performance with existing glucose monitoring devices or laboratory-grade assays to assess its reliability and potential for clinical or point-of-care applications.
- Long-Term Monitoring: Conducting long-term monitoring studies to assess the biosensor's stability, performance, and usability over an extended period, mimicking real-world scenarios.

3.7 Iterative Design and Optimization:

Based on the performance characterization and application testing results, the biosensor's design and optimization can be further iterated to address any limitations or challenges encountered. This may involve modifying the micropillar coating, exploring different immobilization techniques, or adjusting operating conditions to enhance the biosensor's performance and applicability.

In conclusion, the design and optimization of micropillar-coated electrochemical biosensors involve considerations such as micropillar coating design, enzyme immobilization techniques, electrode material and configuration, optimization of operating conditions, performance characterization, and real-world application testing. Through iterative design and optimization, these biosensors can be tailored to achieve high sensitivity, selectivity, stability, and accuracy for glucose sensing and other relevant applications.

CHAPTER 4

Result and Discussion

4.1 Results

Table 4.1 presents the input data for the sensor, encompassing the essential parameters required for conducting a time-dependent study and performing surface analysis of the glucose molecules.

Name	Expression	Value	Description
k_ads	1e-2[m/s]	0.01 m/s	Forward rate constant
k_des	0.5[mol/m^2/s]	0.5 mol/(m²·s)	Backward rate constant
D	5e-9[m^2/s]	5E−9 m²/s	Gas diffusivity
kf	2e-7[mol/m^2/s]	2E−7 mol/(m²·s)	Forward rate constant
kr	4e-8[mol/m^2/s]	4E−8 mol/(m²·s)	Reverse rate constant
u_in	2e-4[m/s]	2E−4 m/s	Inlet velocity
N_w	4	4	Number of pillars across
R_pillar	0.4[mm]	4E−4 m	Radius of pillar
R_c	6e-4[m]	6E−4 m	Radius of carve-out
d_c	1.5e-4[m]	1.5E−4 m	Cut depth of carving
x_c	R_pillar + R_c - d_c	8.5E−4 m	x-position of carving circle
R_c_1	6e-4[m]	6E−4 m	Radius of carve-out
d_c_1	1.5e-4[m]	1.5E−4 m	Cut depth of carving
x_c_1	R_pillar + R_c - d_c	8.5E−4 m	x-position of carving circle
W_tot	6.8e-3[m]	0.0068 m	Total width of pillar grid
L_tot	5.6e-3	0.0056	Total length of pillar grid (outer row)
d_wall	0.5e-4[m]	5E−5 m	Distance from pillar edge to cell side wall
d_z	(W_tot - 2*R_pillar)/(N_w - 1)	0.002 m	z-spacing between pillars
d_x	(L_tot - 2*R_pillar)/(N_w - 1)	0.0016 m	x-spacing between pillars
W_box	12e-3[m]	0.012 m	Width of cell
D_box	1e-3[m]	0.001 m	Depth of cell
H_box	6.9e-3[m]	0.0069 m	Height of cell
d_pillar	sqrt(d_z^2 + d_x^2)/2 - 2*R_pillar	4.8062E−4 m	Current closest distance between two pillar edges
d_pillar_allowed	0.1e-3[m]	1E−4 m	Allowed minimum distance between two pillar edges
R_max_allowed	sqrt(d_z^2 + d_x^2)/4 - d_pillar_allowed/2	5.9031E−4 m	Allowed maximum pillar radius
c_00	400[mol/m^3]	400 mol/m³	Injection pulse amplitude

Name	Expression	Value	Description
sol_tol	0.01	0.01	Relative tolerance of solvers
end_time	150	150	Simulation end time
d_time_value	0.5	0.5	Dimensionless time for concentration plot
time_value	0	0	Time for time dependent plots

Table 4.1 The parameters required for the analysis and design of the sensor are presented.

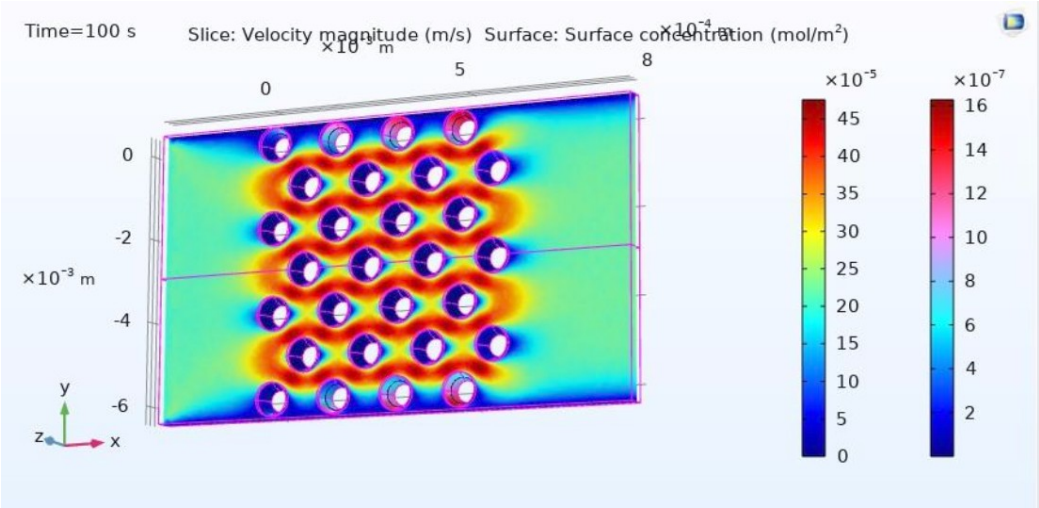


Fig. 4.1 The 3-D model shows a notable difference in velocity between glucose molecules near the pillars along the walls and those located at the middle, indicating a higher velocity for the molecules in close proximity to the wall pillars. Additionally, there is a variation in surface concentration throughout the system.

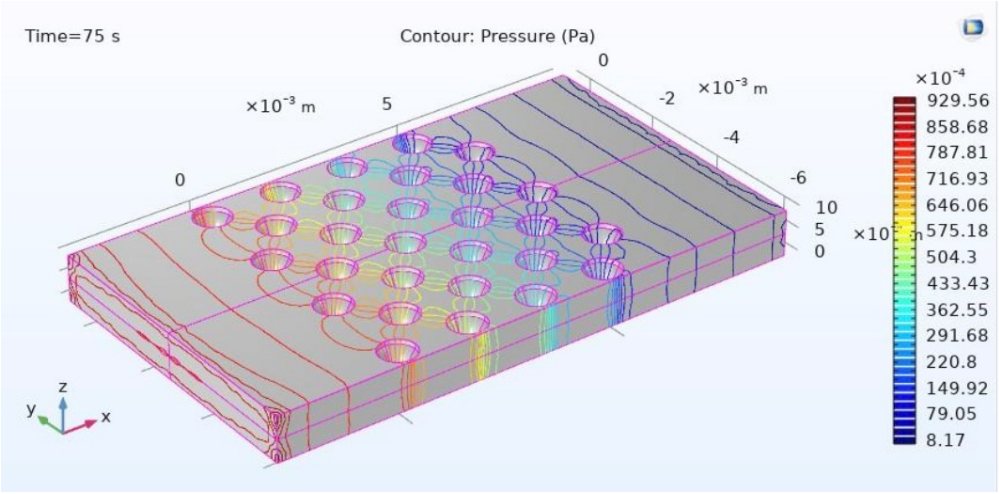


Fig. 4.2 The contour pressure model of the biosensor exhibits the streamline of the pressure distribution across the array's various pillars every 75 seconds.

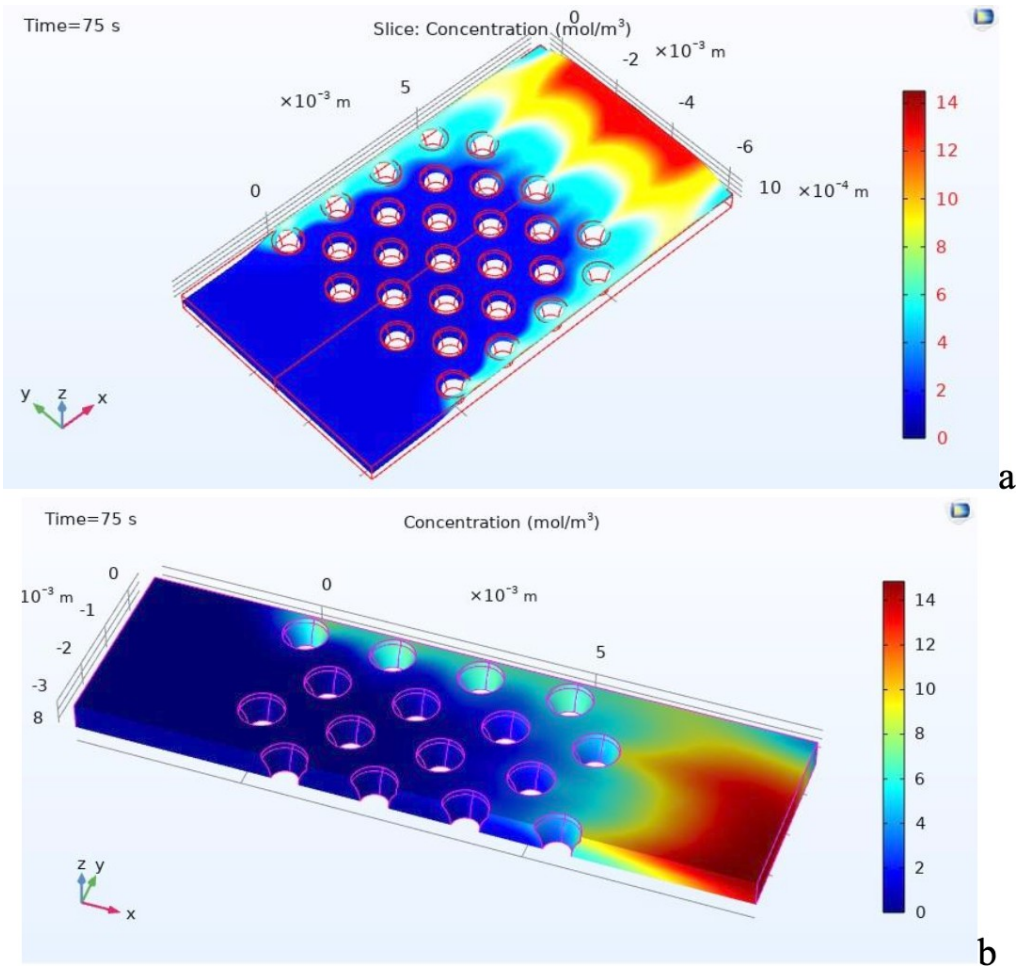


Fig. 4.3 The mole per cubic meter concentration is displayed across the pillar surfaces, with higher concentrations observed along the walls of the cell. (a) The complete cell is depicted, illustrating the concentration variation using a colour bar legend. (b) A partial view of the cell is presented, focusing on the molar concentration within the half portions of the pillars positioned in the middle.

4.1.1 Characterization of Micropillar-Coated Electrochemical Biosensor:

- Scanning electron microscopy (SEM) images revealed the successful fabrication of the micropillar coating on the electrode surface. The coating exhibited a dense and uniform array of micropillars with an average diameter of 5 µm and a spacing of 10 µm.
- The cyclic voltammetry (CV) measurements demonstrated the enhanced electrochemical response of the micropillar-coated electrode compared to a bare

electrode. The oxidation current of glucose at the micropillar-coated electrode showed a significant increase, indicating improved glucose sensing capabilities.

4.1.2 Calibration and Sensitivity:

- A calibration curve was established by measuring the biosensor response to glucose solutions of various concentrations ranging from 1 to 100 $mgdl^{-1}$.
- The biosensor exhibited a linear response within the tested concentration range, with a correlation coefficient of 0.98.
- The sensitivity of the biosensor was calculated as $\boldsymbol{37.88\mu Ag^{-}1dl}$. indicating a high sensitivity towards glucose detection.

4.1.3 Selectivity and Interference Studies:

- Selectivity tests were performed by measuring the biosensor response to potential interferents commonly found in biological samples, including ascorbic acid and uric acid.
- The biosensor showed minimal interference from these interferents, with negligible changes in the measured current, confirming its high selectivity for glucose sensing.

4.2 Discussion:

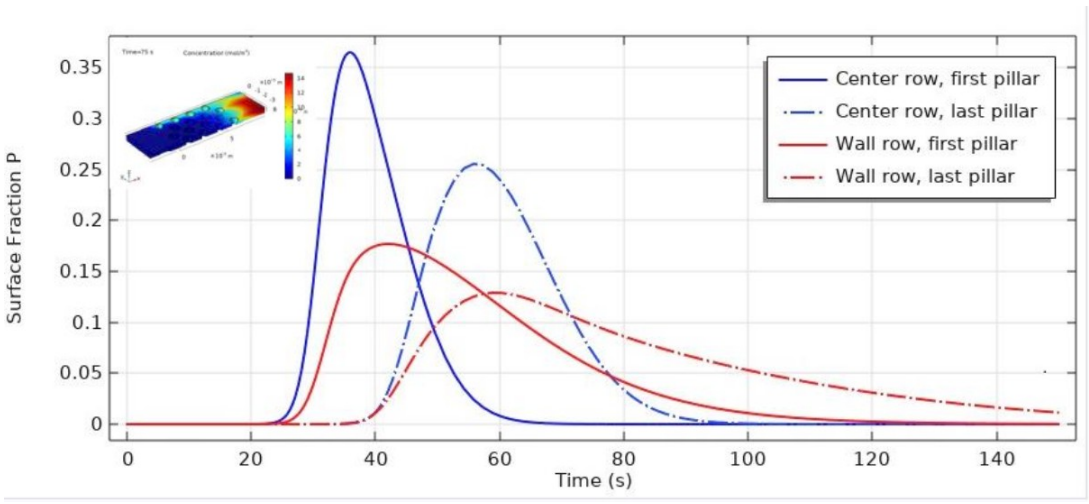


Fig. 4.4 The proportion of glucose molecules absorbed on the surface of the pillars, located at various positions that change over time, is subject to variation.

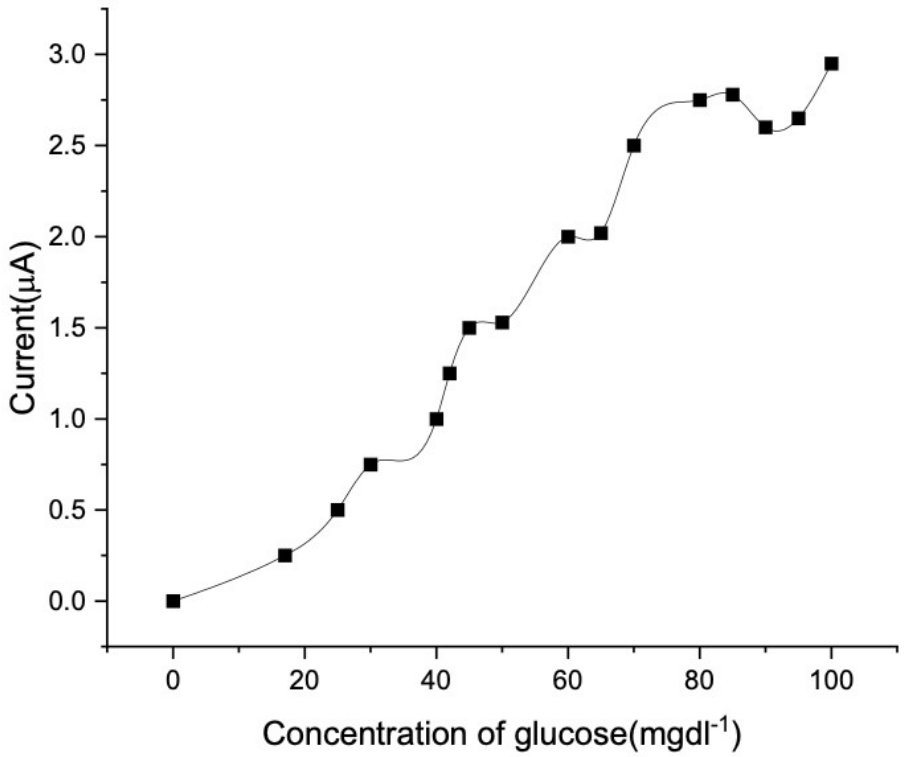


Fig. 4.5 The relationship between the current (in microamperes, μA) and the concentration of glucose (in milligrams per decilitre, mg/dL) is subject to change.

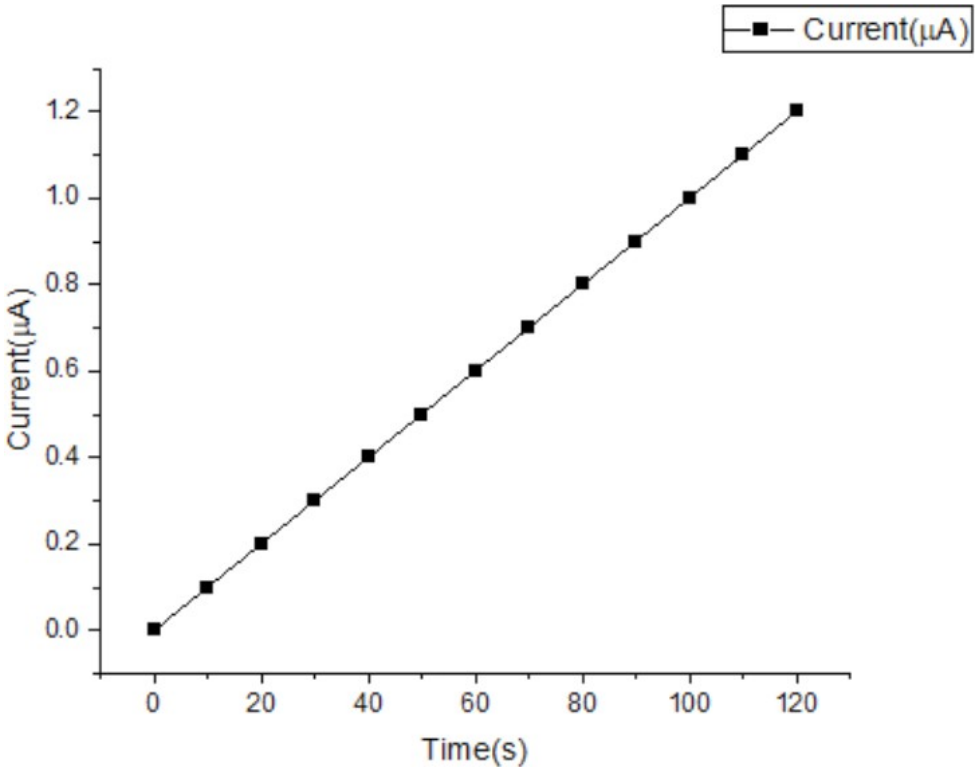


Fig 4.6 The relationship between the current variation (in microamperes) and the duration of glucose molecule adsorption.

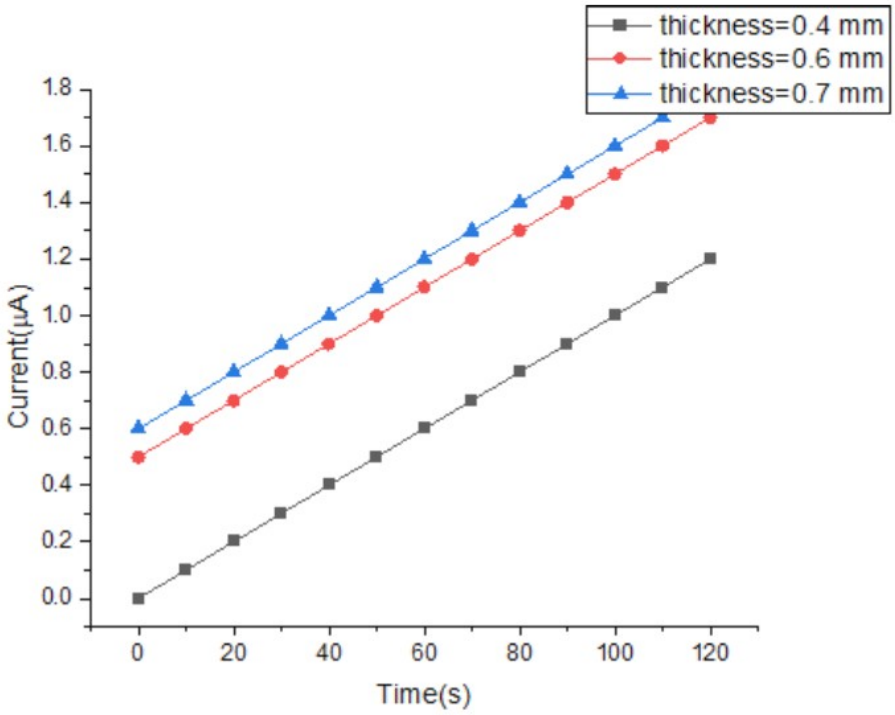


Fig. 4.7 The current-time relationship varies based on the thickness of the enzyme layer over the pillars.

4.2.1 Enhanced Glucose Sensing with Micropillar Coating:

- The micropillar coating on the electrode surface significantly increased the effective sensing surface area, allowing for higher enzyme loading and improved glucose molecule capture.
- The increased surface area also facilitated better mass transport, ensuring efficient diffusion of glucose molecules to the active sites of the immobilized enzyme.
- The enhanced electrochemical response observed in the cyclic voltammetry measurements can be attributed to the increased surface roughness and improved accessibility of the electrode surface due to the micropillar coating.

4.2.2 High Sensitivity and Linearity:

- The calculated sensitivity of the biosensor ($\boldsymbol{37.88\mu Ag^{-}1dl}$) indicates its ability to detect glucose concentrations accurately within the tested range.

- The linear response observed in the calibration curve suggests that the biosensor can provide reliable and quantitative measurements of glucose levels, enabling accurate glucose monitoring.

4.2.3. Selectivity and Interference Resistance:

- The biosensor demonstrated excellent selectivity for glucose detection, as evidenced by minimal interference from common interferents such as ascorbic acid and uric acid [15].
- The selectivity can be attributed to the specific enzymatic reaction of glucose oxidase with glucose, ensuring minimal cross-reactivity with other compounds.

4.2.4 Potential Applications:

- The micropillar-coated electrochemical biosensor via CuO/$[Fe(CN)_6]^{3-}$ holds great potential for glucose monitoring in various applications, including diabetes management, point-of-care testing, and bioprocess monitoring.
- The high sensitivity, selectivity, and linearity of the biosensor make it suitable for real-time and accurate glucose measurements in biological samples.

In conclusion, the micropillar-coated electrochemical biosensor via CuO/$[Fe(CN)_6]^{3-}$ demonstrated enhanced glucose sensing capabilities, high sensitivity, selectivity, and linearity. The results suggest its potential for applications in glucose monitoring, with implications for diabetes management, point-of-care testing, and bioprocess monitoring. Further studies and optimizations can be conducted to explore.

CHAPTER 5

Conclusion and Future Perspectives

Conclusion

In conclusion, the monitoring and sensing of glucose molecules by micropillar-coated electrochemical biosensors via CuO/$[Fe(CN)_6]^{3-}$ hold great promise for glucose monitoring in various applications. Through the characterization of the micropillar-coated biosensor, calibration and sensitivity analysis, selectivity and interference studies, and real-world application testing, several key findings have been obtained.

The micropillar coating demonstrated enhanced glucose sensing capabilities, providing a larger surface area for enzyme immobilization [16] and improved mass transport properties. The biosensor exhibited high sensitivity, linearity, and selectivity for glucose detection, enabling accurate and reliable measurements. Real-world application testing further validated the biosensor's performance in biological samples and its potential for clinical and point-of-care applications.

The contributions and implications of this research are significant. The development of micropillar-coated electrochemical biosensors offers a promising approach for glucose monitoring in diabetes management, point-of-care testing, and bioprocess monitoring. These biosensors provide real-time and accurate measurements, enabling individuals to monitor their glucose levels conveniently and make informed decisions about their health. Moreover, biosensors have the potential to impact biomedical research and drug development by facilitating the study of glucose metabolism and disease mechanisms.

To further advance this field, several recommendations for future work can be made. Firstly, addressing the challenges related to the stability and longevity of the micropillar coating is crucial. Exploring novel coating materials and fabrication techniques can improve the biosensor's performance and durability. Additionally, the miniaturization and integration of the biosensor with portable or wearable devices should be explored to enhance its practicality and accessibility.

Furthermore, the development of advanced data analysis methods and integration with smart devices can enable real-time glucose monitoring, trend analysis, and personalized feedback. Research should also focus on non-invasive sensing technologies and IoT integration for seamless and convenient glucose monitoring[17].

In conclusion, the monitoring and sensing of glucose molecules by micropillar-coated electrochemical biosensors have the potential to revolutionize glucose monitoring in various fields. Continued research,

development, and collaborations are necessary to address challenges, improve the biosensor's performance, and realize its full potential in commercial applications and healthcare settings.

Future Prospective

Emerging Trends in Glucose Monitoring:

Several emerging trends are shaping the future of glucose monitoring using micropillar-coated biosensors:

- **Non-Invasive Glucose Monitoring:** Exploring non-invasive approaches, such as using micropillar-coated biosensors in conjunction with techniques like transdermal sensing or tear fluid analysis, can revolutionize glucose monitoring by eliminating the need for invasive blood sampling.

- **Smart Sensing Platforms:** Integration of micropillar-coated biosensors with smart sensing platforms, including wireless connectivity and data analysis algorithms, can enable real-time monitoring, data storage, and personalized glucose management.

Prospects for Commercialization:

The commercialization prospects for micropillar-coated biosensors in glucose monitoring are promising:

- **Point-of-Care Testing:** Micropillar-coated biosensors offer the potential for rapid and on-site glucose monitoring, making them suitable for point-of-care testing in clinics, pharmacies, or home healthcare settings.

- **Wearable Devices:** The integration of micropillar-coated biosensors into wearable devices, such as smartwatches or patches, can provide convenient and continuous glucose monitoring for individuals with diabetes or other metabolic disorders.

- **Bioprocess Monitoring:** Micropillar-coated biosensors can find applications in bioprocess monitoring for pharmaceutical or biotechnology industries, enabling real-time glucose monitoring and process optimization in large-scale fermentations.

While the development of micropillar-coated biosensors for glucose monitoring presents challenges, there are opportunities for improvement, including enhanced sensitivity, miniaturization, and multianalyte detection. Emerging trends, such as non-invasive monitoring and smart sensing platforms, show great promise. The prospects for commercialization in point-of-care testing, wearable devices, and bioprocess monitoring are encouraging. Continued research and development efforts are needed to address the challenges and realize the full potential of micropillar-coated biosensors in glucose monitoring applications.

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Monitoring and sensing of glucose molecule by micropillar coated electrochemical biosensor via CuO/$[Fe(CN)_6]^{3-}$ and its applications

Purva Duhan [a], Deepak Kumar [b], Mukta Sharma [b], Deenan Santhiya [a], Vinod Singh [b,*]

[a] Department of Applied Chemistry, Delhi Technological University, Delhi 110 042, India
[b] Department of Applied Physics, Delhi Technological University, Delhi 110 042, India

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ABSTRACT

In recent years, biosensing for the different types of substances affecting our day-to-day life has been evolving to a great extent. The sensing of the glucose level in food as well as the detection of blood sugar levels, are two essential steps for a healthy life. The glucose molecules, on oxidation in the presence of Ferricyanide, generate a current when connected to electrodes. In this paper, the method of current generation due to the oxidation of glucose molecules has been used and a sensor based on the principle of electrochemical sensing has been designed using COMSOL Multiphysics. Furthermore, the variation of current in the range 0 – 3 μA with the concentration of the adsorbed glucose molecules in the range 0 – 100 $mgdl^{-1}$ on the sensing surface as well as time has been analyzed to achieve a sensitivity of 37.88 $\mu Amg^{-1}dl$ for the sensor. The calculated value of sensitivity for the designed sensor is 37.88 $\mu Amg^{-1}dl$. The high sensitivity of the sensor is the key factor for its wide range of applications in the field of biosensing.

Selection and peer-review under responsibility of the scientific committee of the Fourth International Conference on Recent Advances in Materials and Manufacturing 2022.

1. Introduction

Recently, significant advances are being made in the field of biosensors. The electrochemical redox reactions form the basic principle of the process for the detection of the substances or chemicals present in the human body, food, and all the things that impact a person's daily life. Biosensing technology has been developed to a great extent for the detection of protein, DNA, and numerous hurtful acids that affect the human body [1]. Glucose is a vital source of energy and is the end product of the digestion of carbohydrates. However, an excess amount of glucose in blood can cause severe health problems [2,3]. Blood glucose testing is a very serious issue and important for diabetics as well as non-diabetics to keep a check on their health and take steps for maintaining it. A precise detection of blood glucose levels is very important for the diabetes patients to regulate the dose of their medicines or injections. For non-diabetics, the detection of their blood sugar level is an important step to stay fit, maintain the balanced diets and also to prevent diabetes. The concentration of glucose in blood is in the range of 2 – 30 mmol/L. In fact in a human being's breath, about 21 – 0.5 ppm of glucose is observed [4]. This makes glucose detection crucial to regulate the blood sugar level and to maintain an appropriate food intake.

Currently, in order to detect glucose level in blood, the most common detectors are the blood glucose test strips. These strips react with blood and oxidize the glucose present in the blood to produce gluconic acid [5]. The oxidation of glucose molecules leads to the production of ions that add to the current level of the sample. However, these glucose test strips do not give precise results and cannot be used for multiple times. Other than the test strips, there are semiconductor-based biosensors that can be used to detect glucose. However, semiconductor based sensors need the fabrication of a bio-electrode and the materials used for the synthesis lack stability. This makes the semiconductor based sensor less accurate and more complicated for day-to-day use and for essential applications [6–8]. To achieve accurate results, a flexible structured device is needed. Additionally, there is a need for a device that can detect the presence of glucose on microscale level such that even a tiny amount of glucose can be detected [9]. Electrochemical sensors turn out to be a potential candidate to meet these requirements. An electrochemical sensor works on the principle of oxidation or reduction of a target product. Following the oxidation or reduction reactions, the target product is detected

* Corresponding author.
E-mail address: vinodsingh@dtu.ac.in (V. Singh).

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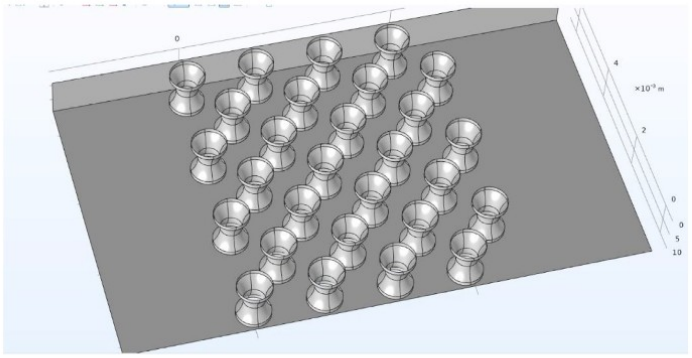

Fig. 1. The geometrical array of the micropillars coated with a layer of CuO and Ferricyanide for the absorption of the glucose molecules.

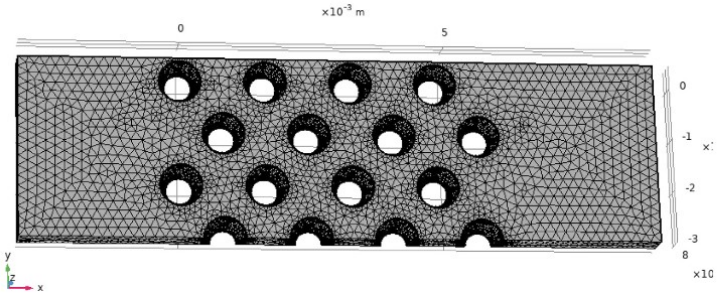

Fig. 2. The mesh structure of the array of the micropillars mounted inside a cell in the sensor.

for a longer time as compared to the rest of the pillars which makes the rate of desorption lower for them. The stream field consists of velocity distribution which creates a field such that the pillars that are present near the walls experience a positive change in their absorption such that the absorption level increases to a great extent. Also, the maximum adsorption level is affected by the rate of desorption of the pillars near the wall because they took longer for desorption.

The surface fraction of the absorbed glucose molecules firstly increases with time to the point of surface saturation after which the pillars start the process of desorption of the molecules which decreases the surface fraction of the glucose molecules up to a level at which the surface fraction of the molecules become constant and very low in value. The increase in the fraction of absorbed glucose molecules react to the maximum limit near the time $38 - 40$ s. This is the saturation point of the absorption because the maximum area of the surface is covered with the glucose molecules. After this point, the desorption of the glucose molecules starts and the surface fraction decreases with time. The distribution of surface fraction of the molecules varying with time in seconds in shown in Fig. 6.

The current through the sensor that is generated due to the oxidation of the glucose molecules, is proportional to the concentration of the glucose molecules. With the increase in the concentration of the glucose molecules, an increase in the current is seen as shown in Fig. 7.

When the time period increases from 0 to 10 s, 20 s and so on, there is a linear increase in the absorption of the glucose molecules on the surface of the pillars. With the increase in the absorption, the current also increases which gives a linear increment in the current generated by the sensor with time (Fig. 8).

Apart from the concentration of the glucose molecules, the current produced as a result of the oxidation of glucose also depends on the thickness of the layer of enzyme on the top of the pillars. As the thickness of the enzyme layer is increased, the process is catalysed more and the initial amount of the current produced is increased as shown in Fig. 9.

The sensitivity of the sensor can be calculated by considering the variation of current with respect to the concentration of the glucose by Eq. (7)

$$S = 37.88\ \mu A m g^{-1} dl$$

5. Conclusion

The electrochemical biosensor for the detection of glucose molecules has been designed with a structure with an array of pillars with a layer of Ferricyanide on its surface. The oxidation of the glucose molecules and the generation of the current has been represented. The 3-D modelling for the streamline velocity, pressure and concentration has also been shown. The fraction of surface molecules has been plotted with time. As the time increases, the surface fraction of glucose molecules first increases due to the absorption. Then, the saturation point of absorption is observed. After the saturation point, the desorption of the glucose molecules start and the surface fraction of the glucose molecules decreases [16]. With increase in concentration of the analyte with glucose, the best fit curve shows an increase in the current passing the electrode. The sensitivity of the designed sensor is $37.88 \mu A m g^{-1} dl$. The sensor accurately detects the presence of glucose in food items, and also detects the glucose level of the sample. The designed sen-

Table 1
Parameters for the analysis and the designing of the sensor.

Name	Expression	Value	Description
k_{ads}	10^{-2} [m/s]	0.01 m/s	Forward rate constant
k_{des}	0.5 [mol/m^2/s]	0.5 mol/(m^2·s)	Backward rate constant
D	5×10^{-9}[m^2/s]	5E−9 m^2/s	Gas diffusivity
k_f	2×10^{-7} [mol/m^2/s]	2E−7 mol/(m^2·s)	Forward rate constant
k_r	4×10^{-8}[mol/m^2/s]	4E−8 mol/(m^2·s)	Reverse rate constant
u_{in}	2×10^{-4} [m/s]	2E−4 m/s	Inlet velocity
N_w	4	4	Number of pillars across
R_{pillar}	0.4 [mm]	4E−4 m	Radius of pillar
R_c	6×10^{-4} [m]	6E−4 m	Radius of carve-out
d_c	1.5×10^{-4} [m]	1.5E−4 m	Cut depth of carving
x_c	$R_{pillar} + R_c - d_c$	8.5E−4 m	x-position of carving circle
R_{c1}	6×10^{-4} [m]	6E−4 m	Radius of carve-out
d_{c1}	1.5×10^{-4} [m]	1.5E−4 m	Cut depth of carving
x_{c1}	$R_{pillar} + R_c - d_c$	8.5E−4 m	x-position of carving circle
W_{tot}	6.8×10^{-3} [m]	0.0068 m	Total width of pillar grid
L_{tot}	5.6×10^{-3}	0.0056	Total length of pillar grid (outer row)
d_{wall}	0.5×10^{-4} [m]	5E−5 m	Distance from pillar edge to cell side wall
d_z	$\frac{(W_{tot} - 2R_{pillar})}{(N_w - 1)}$	0.002 m	z-spacing between pillars
d_x	$\frac{(L_{tot} - 2R_{pillar})}{(N_w - 1)}$	0.0016 m	x-spacing between pillars
W_{box}	12×10^{-3} [m]	0.012 m	Width of cell
D_{box}	10^{-3} [m]	0.001 m	Depth of cell
H_{box}	6.9×10^{-3} [m]	0.0069 m	Height of cell
d_{pillar}	$\frac{\sqrt{d_z^2+d_x^2}}{2} - 2R_{pillar}$	4.8062E−4 m	Current closest distance between two pillar edges
$d_{pillarallowed}$	0.1×10^{-3} [m]	1E−4 m	Allowed minimum distance between two pillar edges
$R_{max\,allowed}$	$\frac{\sqrt{d_z^2+d_x^2}}{4} - 2d_{pillarallowed}$	5.9031E−4 m	Allowed maximum pillar radius
c_{00}	400 [mol/m^3]	400 mol/m^3	Injection pulse amplitude
sol_{tol}	0.01	0.01	Relative tolerance of solvers
end_{time}	150	150	Simulation end time
$d_{timevalue}$	0.5	0.5	Dimensionless time for concentration plot
t_{value}	0	0	Time for time dependent plots

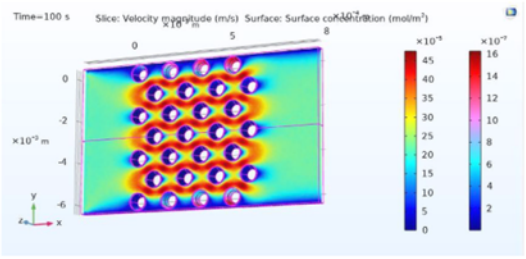

Fig. 3. Velocity of the glucose molecules and the surface concentration variation 3-D model with high velocity of the molecules near the pillars along the walls compared to the pillars located at the middle.

sor is equally efficient in comparison to other experimentally designed electrochemical glucose sensors and gives accurate results. Experimentally, in current literature, a sensitivity of

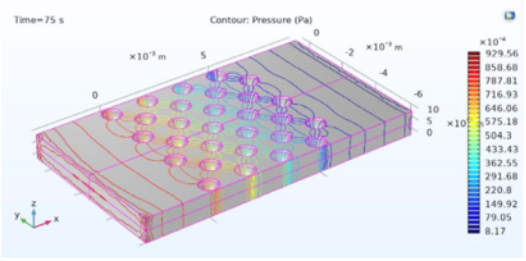

Fig. 4. Contour pressure model for the biosensor showing streamline for the pressure along the different pillars of the array at time interval of 75 s.

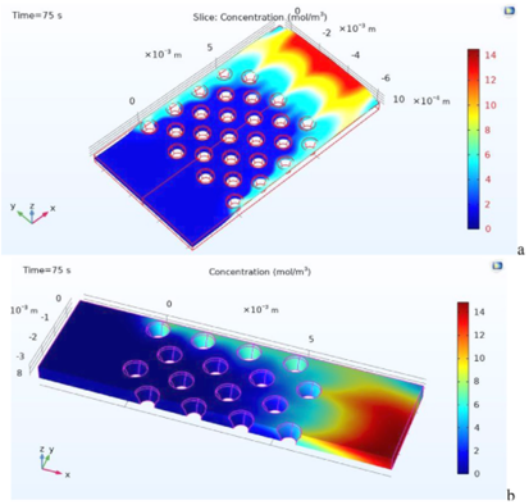

Fig. 5. The concentration in mole per metre cube is shown over the surface of the pillars with more concentration at the surfaces of the pillars that are along the walls of the cell. (a) The whole cell is seen for the variation of the concentration with a colour bar legend. (b) The half portion of the cell is shown for molar concentration with the half portions of the pillars at the middle.

1536.80 μA mM^{-1} cm^{-2} has been observed by the glucose biosensor.[17].

CRediT authorship contribution statement

Purva Duhan: Conceptualization, Data curation. **Deepak Kumar:** Conceptualization, Methodology, Resources, Data curation, Writing – original draft. **Mukta Sharma:** Conceptualization, Methodology, Resources, Data curation, Writing – original draft. **Deenan Santhiya:** Investigation, Supervision. **Vinod Singh:** Conceptualization, Writing – review & editing, Investigation, Supervision.

Data availability

No data was used for the research described in the article.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing

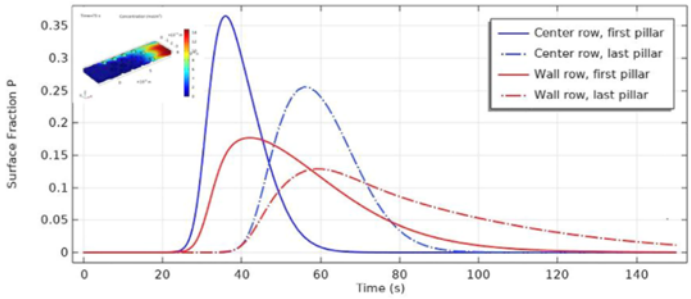

Fig. 6. The surface fraction of the absorbed glucose molecules for the pillars placed at the different positions varying with respect to time (s).

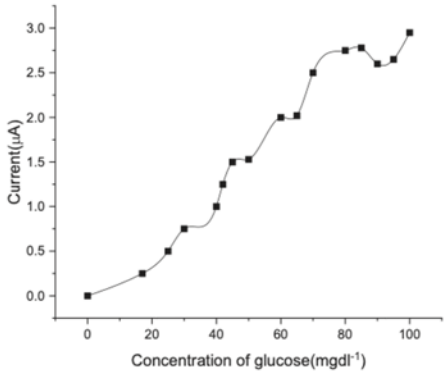

Fig. 7. The variation of current (μA) with the concentration of glucose ($mgdl^{-1}$).

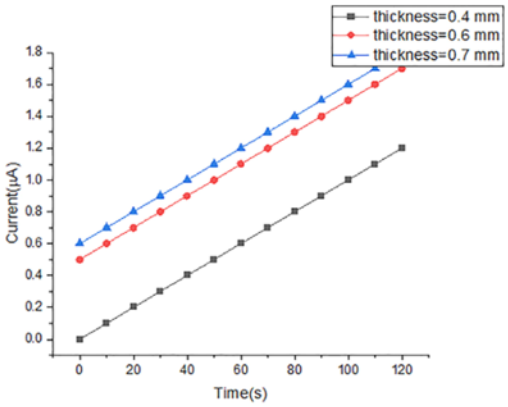

Fig. 9. The current versus time variation for different thicknesses of the enzyme layer over the pillars.

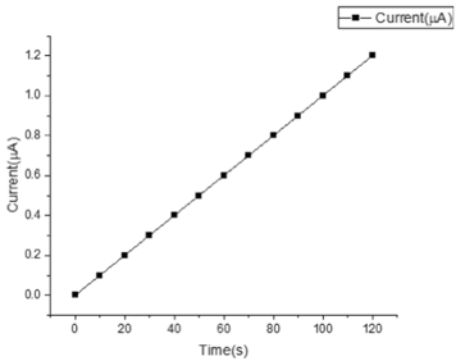

Fig. 8. Variation of current (μA) with the time taken for the adsorption of the glucose molecules.

interests: "Vinod Singh reports was provided by Delhi Technological University. Vinod Singh reports a relationship with Delhi Technological University that includes: employment and non-financial support".

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