Optimization of Surface Charge Density for Measuring Stability in a Cortisol Sensor using Nanomaterials With Comsol Multiphysics

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Abstract: Cortisol is a vital stress-associated hormone. An efficient technology that provides cortisol detection is important for stress management and wearable devices. While nanomaterial-based electrochemical biosensors offer quick response times and have demonstrated excellent sensitivity, they face long-term performance issues due to charge transfer instability at the electrode surface. In this paper, we used COMSOL Multiphysics to perform comparative numerical analyses of graphene, zinc oxide (ZnO), and carbon nanotube (CNT) cortisol electrochemical biosensors. A two-dimensional axisymmetric geometry integrated electroanalytical modelling with Butler-Volmer electrode kinetics to evaluate responses in current density and surface charge density across different electrodes. From the results, we show that surface charge density and electrochemical current output are strongly related, suggesting that surface charge density is a determinant of performance. Among the three materials, graphene had the highest surface charge density, yielding the most stable response. In comparison, both ZnO and CNTs had lower levels of charge accumulation. The results support the idea that surface charge density not only improves sensitivity but also offers a more meaningful measure of the electrochemical cortisol biosensor. The findings of this study are useful for the development of wearable and point-of-care electrochemical cortisol biosensors by optimizing surface charge density

Keywords: Electrochemical biosensor; Cortisol sensing; Surface charge density; Nanomaterials; COMSOL Multiphysics; Wearable sensors

Introduction

Cortisol is one of the primary hormones released during the body's stress response, helping it modulate its response to stress, maintain circadian rhythms, and perform other functions, such as metabolism and immune system function. The stress, mood, endocrine, and heart and blood vessel (cardiovascular) systems of the body have imbalances linked to cortisol secretion. Understanding such imbalances is important from both clinical and physiological perspectives.

The imbalances indicate the potential presence of chronic stress and related endocrine, cardiovascular, and mental health (psychiatric) issues (Gibson, 2015; Trusso Sfrazzetto & Santonocito, 2022). As a result, considerable attention is being paid to developing small, sensitive, and stress-free methods for measuring cortisol levels in the body.

For cortisol sensing, the electrochemical biosensor is the best choice. The factors that have increased interest in these biosensors are their improved efficiency, lower energy requirements, and compatibility with a stress-free, wearable monitoring system. The detection of cortisol using biosensors that are made of nanomaterials such as graphene, carbon nanotubes (CNTs), and ZnO nanorods and have a surface modified with a molecularly imprinted polymer and an aptamer is being carried out in sweat, saliva, and other biosamples (Singh et al., 2014; Upasham et al., 2018; Zubarev et al., 2022). Biosensors used for analytical testing in clinical diagnostic laboratories have low detection limits and wide linear detection ranges. As a result, the biosensors can be used for monitoring health from a distance (point-of-care monitoring) and continuous monitoring (on-body monitoring).

Even with recent improvements, most cortisol biosensors focus on short-term performance. Operational long-term stability is still lacking. Continuous sensors, especially wearables, are prone to signal drift, baseline changes, and sensor performance degradation. This occurs due to electrode material ageing and interactions between biosignals and the electrode-electrolyte interface (Gibson, 2015; Gao et al., 2023). This is an important sensor reliability issue and a real-world deployment challenge, even with high sensitivity.

Surface charge phenomena and interfacial charge transport are both very important for the stability of the electrochemical signal. Surface charge density variations affect the double-layer capacitance, charge transfer resistance, and current, especially for high aspect ratio nanostructured electrodes (Ferrier & Honeychurch, 2021; Lacatus et al., 2015). Surface charge density variation has rarely been used to quantitatively assess evaporative biosensor stability. Most studies focus on instantaneous current-concentration relations, which do not consider charge redistribution over time or across cumulative sensing events (Singh et al., 2014; Trusso Sfrazzetto & Santonocito, 2022).

The COMSOL Multiphysics simulation model is an excellent option for analyzing interfacial phenomena in a structured manner. Gordic (2008) and Al-Dairy et al. (2021) and Wangare et al. (2024) have used finite element analysis to model nanomaterials-based electrochemical biosensors (glucose, oestrogen, and cortisol biosensors) to develop controlled models for the analysis of the materials and structures, and their electrochemical characteristics. However, there is a lack of comparative studies of surface charge stability with varying nanomaterials.

This research presents surface charge density for the first time as a performance metric focused on stability for evaluating electrochemical cortisol sensors based on nanomaterials. Within the same electrochemical environment, a comparative analysis of COMSOL Multiphysics for ZnO, CNT, and Graphene is conducted. By moving the assessment away from metrics dominated by sensitivity, this research aims to provide a significant framework for selecting electrode materials that will deliver stable, reproducible performance for wearable biosensors for cortisol measurement.

Nanomaterials for the Stability of the Cortisol Sensor

While measuring cortisol sensors' electrochemical readings, long-term stability is not only determined by sensitivity but also by the charge-transport properties of the interface the sensor maintains under the same operating conditions. Stability, in the context of electrochemical sensors, is the ability to produce the same reading when the same stimulus is presented. Such reading consistency is of utmost importance in applications where sensors must be worn for extended periods. (Gibson, 2015; Ferrier & Honeychurch, 2021). The aforementioned properties indicate how long sensors can be used before they begin to give varied readings.

The electronic properties, along with the surface, charge, and physical properties of the nanoparticles, also enhance the stability of the electrodes. Additionally, the surface area of nanoparticles raises the level of electrochemical stimulation. On the other hand, it also increases the charge accumulation on the surface, leading to the formation of a stable system (Chen & Chatterjee, 2019; Malik et al., 2013). Therefore, even when subjected to the same electrochemical environment, various nanomaterials behave differently.

The unique π-π conjugation and interlayer charge delocalization, which form a two-dimensional lattice structure, enable extensive charge transport and binding interactions, contributing to the enhanced electrical stability of graphene-based electrodes (Ren, 2022; Zubarev et al., 2022). Defect density and intrinsic characteristics of graphene ensure a homogeneous charge distribution on the material surface and mitigate charge trapping, thereby reducing baseline drift in electrochemical cycling. Stabilization effects of multilayer graphene systems are derived from the electrochemical double-layer capacitance and multiple pathways for charge transport, explaining the reduced impact of transient charge in the electrochemical double-layer on offset fluctuations from analyte binding events (Lacatus et al., 2015). These effects are increasingly reported for the use of graphene in cortisolsensitive systems intended for prolonged or continuous use (Trusso Sfrazzetto & Santonocito, 2022).

In comparison, carbon nanotubes (CNTs) achieve fast electron transfer rates due to their onedimensional conductive pathways and high aspect ratios. While CNT-modified electrodes demonstrate fast response times and heightened sensitivity, stability issues due to localised charge build-up at tube junctions and defect sites, may arise (Ferrier & Honeychurch, 2021). During prolonged use, charge density that is uneven and localised due to bundling and heterogeneous functionalisation at the surface, can cause signal drift (Malik et al., 2013). From an overall stability perspective, CNTs are signalretaining effective; however, graphene performs better in this regard.

Moderate electrical conductivity and chemical stability characterize ZnO nanostructures, the semiconducting alternative. Due to a wide bandgap and low bias charge, ZnO nanowires and nanorods show steady electrochemical response with low charge leakage (Al-Dairy et al., 2021; Li et al., 2022). Even so, surface-state and oxygen-vacancy issues create recombination centres that reduce charge persistence at the electrode-electrolyte interface. Therefore, in terms of uniformity of charge distribution, the stability of ZnO-based cortisol sensors is intermediate, superior to CNT systems and inferior to graphene-based platforms (Trusso Sfrazzetto & Santonocito, 2022).

The electrode materials should be evaluated from the perspective of electrochemical stability to understand the interrelation between the surface charge density behaviour and the intrinsic electrical properties of the defined nanomaterials. Graphene promotes uniform charge storage and reassignment, while ZnO enables charge moderation according to surface- and material-dependent properties, and CNTs favour more rapid electron transfer, although their control is limited. These properties should be considered when evaluating electrode compositions beyond sensitivity to understand their electrochemical stability.

COMSOL Multiphysics Flow

This section explains the entire workflow in COMSOL Multiphysics for simulating the electrochemical cortisol sensor. The aim here is to provide clarity and consistency in the modelling process by detailing the modelling steps, the coupling of different types of physics, and the different approaches taken to solve the model. To aid readers, a summary of the entire workflow is provided in a schematic flow diagram in Figure X, which illustrates the various workflow steps and the simulation steps.

3.1 Model Dimensionality and Geometry Selection

For the electrochemical sensor structure, a two-dimensional axisymmetric geometry was chosen. This is the best way to retain the physical accuracy for shapes that are circular or radially symmetric, which is common for the electrodes in electrochemical biosensor devices, and manage the computational cost. Axisymmetric modelling is common in biosensor studies that use COMSOL because of the ability to efficiently model the diffuse fields, the electric potential distributions, and the various aspects of the electrochemistry at the interfaces, while reducing the computational expense of using a complete three-dimensional model (Gordic et al., 2020; Al-Dairy et al., 2021).

The geometry being modelled comprises an electrode domain in contact with an electrolyte domain containing the cortisol analyte. The nanomaterials (ZnO, CNTs, or graphene) are modelled using the electrochemical attributes of the respective materials, rather than nanoscale geometries, which is a common and accepted approach in finite element biosensor modelling (Wangare et al., 2024; Lacatus et al., 2015).

3.2 Physics Interface Selection: Electroanalysis Module

Using COMSOL Multiphysics, electrochemical behaviour was analysed using the Electroanalysis interface. This physics interface helps integrate the solution of species transport, distribution of the electric potential, and electrode kinetics. The Electroanalysis module has been used extensively to model hormone and biomolecule sensors because of its incorporation of diffusion-controlled transport and non-linear electrode reactions (Wangare et al., 2024; Yamaguchi et al., 2021).

In this module, cortisol transport in the electrolyte was modelled using Fickian diffusion, and the electrostatic potential field governed charge transport. The interface between the electrode and the electrolyte was defined by electrode reaction nodes, which were used to obtain the current density from the given kinetic equations.

3.3 Electrode Kinetics and Boundary Conditions

Butler-Volmer kinetics describes electrode reactions and provides a meaningful representation of electron transfer at the electrode surface. This equation is useful for comparing different nanomaterials and describes behaviour that depends on the material, which can be characterized by the exchange current density and transfer coefficients (Al-Dairy et al., 2021; Wang, 2006).

To ensure the simulation yields reliable results while meeting the physics-based goals, appropriate boundary conditions were applied. The surface of the working electrode was specified as the boundary of an active electrochemical process, while the boundaries of the surfaces that insulate the electrodes were defined as zero-flux boundaries for both active species transport and the electric current flow. The outer boundaries of the domain were defined as the bulk reservoir boundaries to simulate the conditions of the sensor used in the experiments (Gordic et al., 2020).

3.4 Meshing Strategy

To capture the steep gradients of concentration, electric potential, and surface charge density, an extra-fine mesh was used in the electrolyte/electrode interface. In the regions of interest where interfacial electrochemical processes occur, particularly for generating surface-related quantities such as current density and surface charge (COMSOL AB, 2019), finer meshes are critical. In the bulk electrolyte regions, coarser meshes were used to achieve greater computational efficiency while preserving simulation accuracy.

3.5 Study Type and Solution Strategy

All simulations utilized a stationary study. This method assumes a steady state, which is appropriate for evaluating sensor performance, considering the surface charge density and current density at a constant analyte concentration. When the primary focus is not on transient effects, stationary studies are typically used in modelling electrochemical biosensors and in studying materialdependent behavior under the same operating conditions (Wangare et al., 2024; Al-Dairy et al., 2021).

The coupled electrochemical physics nonlinear system of equations was solved by COMSOL’s fully coupled solver with automatic damping for convergence.

3.6 Surface Charge Density Extraction

From the perspective of the interfacial electrochemical sensing, surface charge density (SCD) is one of the primary descriptors. SCD is a measure of charge accumulation and redistribution at the sensing interface, making it a direct descriptor of electrochemical behaviour across different nanomaterials and a means to evaluate performance with respect to certain stability (Lacatus et al., 2015; Gordic et al., 2020).

The average and localized SCD values across the electrode edge were calculated and postprocessed with surface integration operators. These values were extracted for comparative and sensitivity analyses to support the consistency across the different simulated material configurations.

Figure 1 demonstrates COMSOL Multiphysics classifies and analyses nanomaterials-based electrochemical cortisol sensors. Initially, the sensor geometry and material parameters are defined. Next, parameters of the electrochemical sheath are defined using the Electroanalysis interface. For electrode-electrolyte interfaces, a combination of diffusion-controlled transport and Butler-Volmer will be utilized. Interfacial phenomena will be resolved using an extra-fine mesh. Steady-state electrochemical responses will be retrieved via stationary simulations, from which average current density and surface charge density will be obtained. Finally, the response will be assessed to evaluate the sensor's stability and sensitivity, and to compare the electrodes made of ZnO, CNT, and graphene.

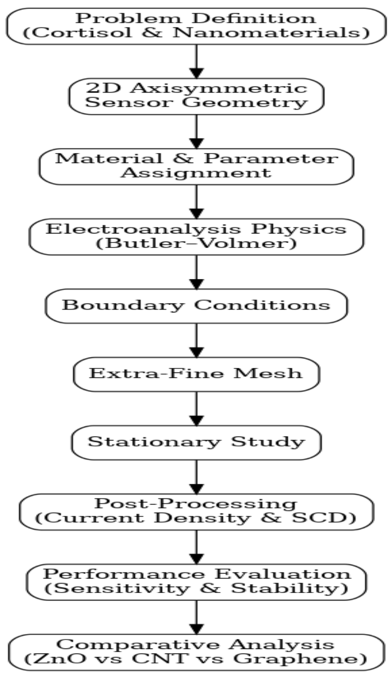

Figure 1. Flow diagram illustrating the COMSOL Multiphysics workflow for modeling nanomaterial-based electrochemical cortisol sensors, including geometry definition, physics coupling, numerical solution, and stability evaluation using surface charge density

Design of Sensor in COMSOL

4.1 Sensor Geometry and Dimensionality

We designed the electrochemical cortisol sensor using 2D axisymmetric geometry. We modelled the sensor as a circular working electrode submerged in an electrolyte. The electrochemical biosensor design exhibits structural symmetry that has been employed and validated in numerous previous computational studies aimed at detecting hormones and biomolecules. Axisymmetric design captures behaviours in radial diffusion, electric potential, and interfacial charge distributions, while being less computationally intensive than a full 3D design.

Prior studies conducted in COMSOL demonstrated that electrochemical biosensors with a 2D axisymmetric design reproduce electrochemical responses in a steady state. These responses include the current densities and charge balances, provided that the electrode design maintains radial symmetry. Such designs lend themselves well to analyses focused on stability, where the primary variable alters the interfacial charge distribution rather than small structural changes. (Gordic, 2008; Lacatus et al., 2015).

The sensor comprises two functional regions within the sensor domain. The first region, the electrode surface, acts as the electrochemically active boundary, and the second region, the surrounding electrolyte, includes the cortisol species. The geometric design was executed to provide sufficient diffusion length while minimizing boundary effects, utilizing modelling practices from prior electrochemical sensor simulations.

4.2 Assigning Properties to Nanomaterials

Four distinct configurations incorporating nanomaterials in electrodes were studied: graphene; carbon nanotubes (CNTs); and zinc oxide (ZnO). Instead of directly quantifying nanoscale surface characteristics, a nanoscale-specific approach utilizing electrochemical parameters such as: electrical conductivity, charge transfer area, W, and interfacial charge responsiveness, ΔQ, was applied. Across multiple studies, this approach has been successfully utilized in finite element analysis of nanostructured biosensors, enabling comparative analysis of disparate materials with consistent geometrical parameters.

In biosensor models, graphene is commonly represented as an electrode material that is highly and uniformly conductive due to delocalized charge. This representation has been validated in the biosensor simulations of Ren (2022) and Zubarev et al. (2022). High charge transport capability is characteristic of CNT electrodes, and in consideration of surface charge transport heterogeneity, an adjustment of ZnO electrodes was made regarding charge transport and surface state effect characterizations, thus ZnO continues to be represented as a semiconductor material of moderate charge transport (Li et al. 2022), with this representation being consistent in the modelling of ZnO nanorod-based biosensors.

Identical geometric and boundary conditions across the three configurations enable the distinctions in the electrochemical response to be attributable to the intrinsic characteristics of the constituent materials, rather than to attributable numeric artefacts.

4.3. Meshing Strategy

Different geometries require unique mesh strategies. A mesh should be constructed that allows for the resolution of the interfacial electrochemical phenomena. When designing the mesh, one must pay attention to the large electric potential, steep gradients of charge, the concentration at the surface, and the concentration of the electrolyte. Therefore, the boundary of the electrodes is where the finest mesh is required to capture the localised phenomena.

When refining mesh to electrochemical interfaces during the modelling of biosensors in COMSOL, the mesh must be fine enough to effectively portray changes in current density and surface charge. A mesh that is too fine will increase computational time and cost, which is exactly what was done in the bulk of the electrolyte where the gradients are smooth and the electric field is less complicated. The hybrid mesh that was employed follows the COMSOL modelling guideline for electrochemical sensors nanomaterials (COMSOL AB, 2019, and Wangare et al., 2024).

Preliminary simulations were conducted to check mesh independence and to ensure that quantities of electrochemical phenomena were not affected by further mesh refinement.

4.4 The Stability Analysis Scope Using 2D Axisymmetric Modelling

The main goal in this case is examining the electrochemical stability via the surface charge density behaviour in steady-state. In this analysis, spatial charge distribution, uniformity, and material properties focused cannot be influenced as well as 3D localised phenomena. Thus, 2D axisymmetric modelling is more than satisfactory as it gives the opportunity for the analytical evaluation of several nanomaterials.

Previous research in the electrochemical biosensor stability and materials selection suggests that axisymmetric finite-element models, in a more rigorous sense, capture almost all the phenomena related to interfacial charge redistribution and electrostatics concerning the sensor (Lacatus et al, 2015; Gordic, 2008). These features of the models also improve reproducibility; the lesser the numerical complexity, the more reproducible the study becomes, and in turn, it allows for more extensive parametric studies than most other models, which adds to the models' usefulness.

These provided sensor design parameters outline a solid and optimal design for most computationally inexpensive proof of concept for evaluating stability metrics (in the nanomaterial sense) in electrochemical cortisol sensing.

Results and Discussion

5.1 Time-Dependent Current Density Response

The decline and eventual stabilisation of the average global current density was investigated for a fixed free cortisol concentration of 5.4 $mol \cdot m^{-3}$. The electrodes were simulated in the presence of graphene, ZnO, and Carbon Nanotubes (CNTs), while all other conditions (geometry, kinetics, boundaries) were kept the same.

With the graphene-based electrode, current density demonstrated a sharp increase within the first minute followed by a decline and subsequent stabilisation for the remainder of the time. In comparison, the electrode based on ZnO displayed a lower and slower response in peak current density. The electrode based on CNTs exhibited an absence of an initial transient peak and demonstrated a monotonic ascent in current density over time, showing the stabilisation of charge transport pathways.

The current response at the interface of the sensor is clearly influenced by different materials provided in the interface layer.

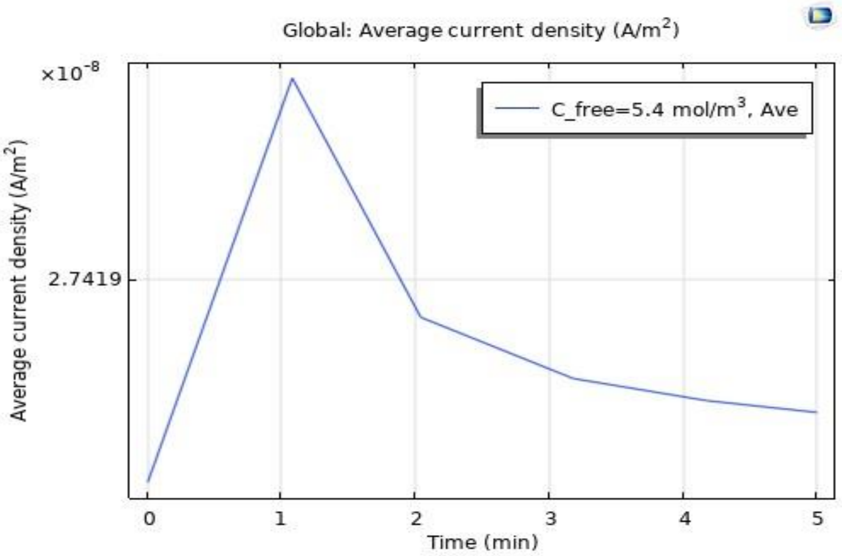

Figure 5.1. Time-dependent global average current density response of the graphene-based electrode at a cortisol concentration of 5.4 mol·m⁻³

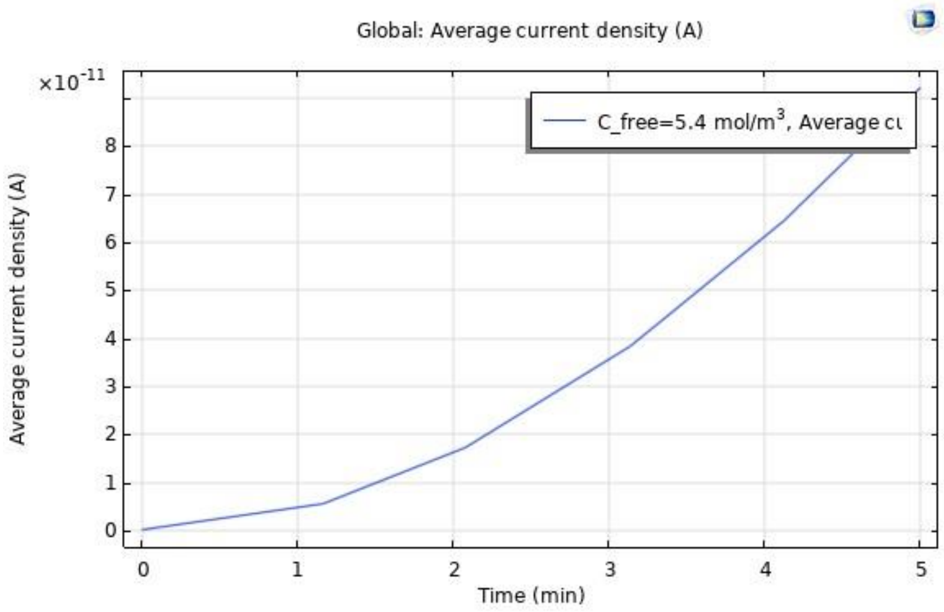

Figure 5.2. Time-dependent global average current density response of the ZnO-based electrode at a cortisol concentration of 5.4 mol·m⁻³

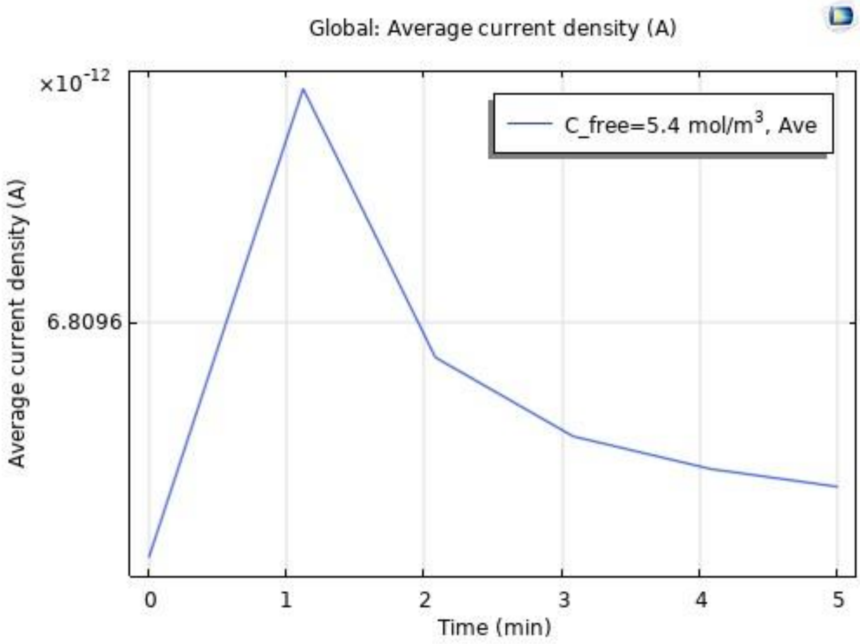

Figure 5.3. Time-dependent global average current density response of the CNT-based electrode at a cortisol concentration of 5.4 mol·m⁻³

5.2 Surface Charge Density of Nanomaterial-Modified Electrodes

In order to measure the electrostatic properties of the sensing interface, the surface charge densities from the COMSOL simulations for each of the nanomaterials were retrieved. Table 2 summarises the average surface charge density values obtained from the calculations.

Among the nanomaterials tested, Graphene had the highest surface charge density, which was listed above ZnO and the CNTs. The range of values illustrates the varying degree of the influence of interfacial charge incorporation on the nanomaterials.

Table 2. Surface charge density of different nanomaterials used in the cortisol sensor model.

Sr. No	Nanomaterial	Surface Charge Density (C/m^2)
1	Graphene	4.01699×10^{-8}
2	ZnO	1.36632×10^{-10}
3	Carbon nanotubes (CNTs)	1.04179×10^{-11}

5.3 Relationship Between Surface Charge Density and Current Output

The output current density was directly related to the surface charge density. With the same cortisol concentration and electrochemical conditions, nanomaterials with greater surface charge density produced greater average current densities.

Graphene exhibited the greatest surface charge density and therefore the most pronounced current-density response, as well as the most notable transient response. The electrodes based on ZnO and CNT exhibited progressively lower surface charge density and thus lower current output.

It is evident that surface charge density is one of the main factors that control the electrochemical signal produced in nanomaterial cortisol sensors.

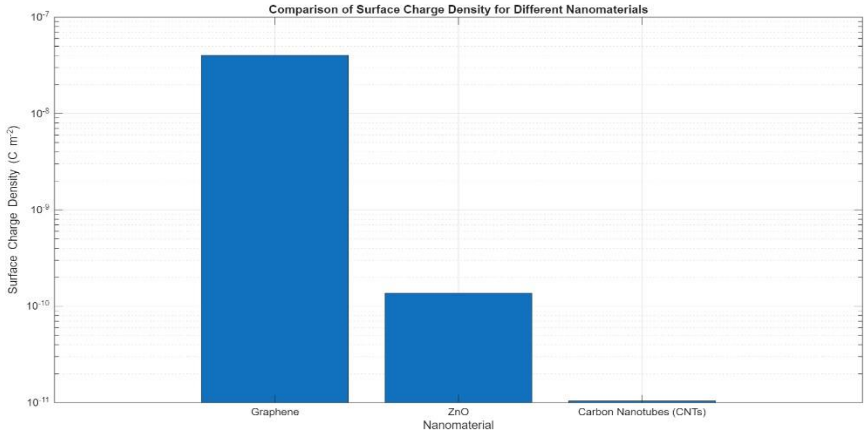

Figure 5.4. Comparison of surface charge density for graphene, ZnO, and CNT-based electrodes

5.4 Comparative Performance Across Nanomaterials

Performance assessments for all simulations showed the same ranking for the nanomaterials for both charge density and current density under the same operating conditions. Electrodes with graphene exhibited the most superior electrochemical response. The next ranking was for electrodes based on ZnO and CNT.

The same order was found for both transient current density plots and steady-state surface charge density values, confirming the robustness of the comparative modelling framework.

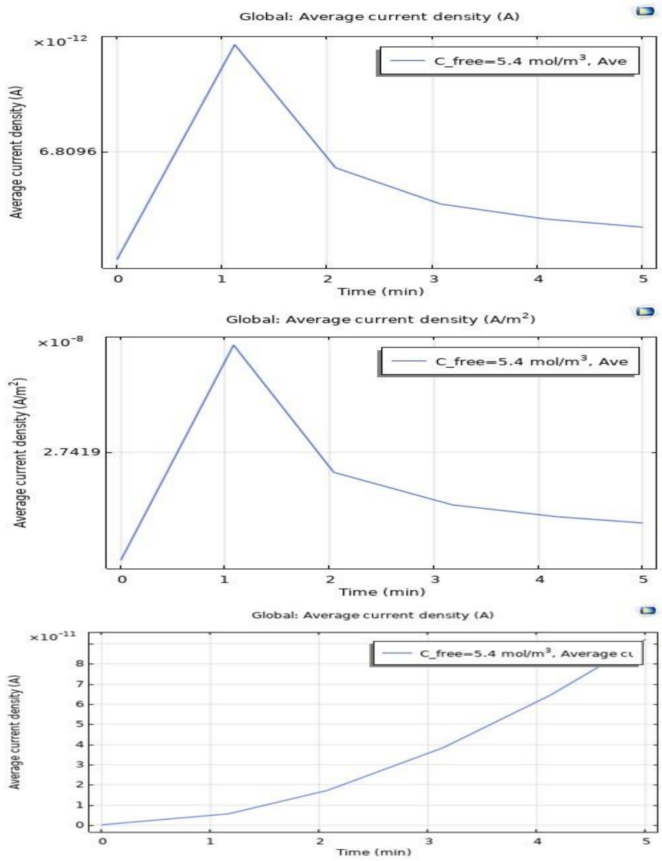

Figure 5.5. Overlay comparison of time-dependent current density responses for graphene, ZnO, and CNT-based electrodes

5.5 Reproducibility of Simulated Results

Repetitive modelling with the same set of parameters validated the consistency of the identified trends. Although small numerical differences in total current density were attributed to solver convergence and mesh discretization, the performance of the nanomaterials relative to one another remained the same.

This steady performance affirms the dependability of the COMSOL-based numerical framework for assessing nanomaterial-modified cortisol sensors in comparison.

Discussion

The reasons for the different electrochemical performance of electrodes made of graphene, ZnO, and CNT are based mainly on their differences in surface charge density, conductivity, and electrochemical interfacial kinetics. Table 2 summarises graphene's charge surface charge density of 4.02×10^{-8} C m^{-2} which is almost two levels higher than ZnO, and 3 levels higher than CNT. This immense difference directly correlates to double layers formed, as well as the number of available active sites for electrochemical-advancing interactions, causing electrochemical-advancing conditions to be more effective and enhancing current densities.

The height of graphene's charge density indicates its thinness as a material, high mobility, and electro-optical structures that facilitate the free movement of electrons at the interfaces of (electrode/electrolyte). Ren and others (Ref, 2022) found similar things. A majority of CNT and metal oxides are supplemented with graphite to enhance charge transfer, while graphene retains most of those CNT and metal oxides properties and retains more than a hundred times the charges than those composites. A similar current density was found for all simulated concentrations of cortisol with all aggregates composed primarily of CNT or metal oxides.

ZnO-based electrodes also exhibit varying levels of efficiency that are not yet fully optimized for electrochemical systems. As an example, ZnO nanorods have an isoelectric point that is higher than most and have a surface chemistry that is more favourable for the adsorption of hormones, which allows for higher surface affinity and analyte adhesion (Li et al. 2022). While this adjustment is favourable for the binding of cortisol, the electrical conductivity of ZnO (which is less than that of graphene and more so than that of a supposed ideal conductor) leads to fewer free electrons and a decreased current density. In previous COMSOL based sensor models, the sensitivity of the biosensor was shown to be reliant upon the surface area of the ZnO nanostructures, an area that was still semiconducting despite increasing the surface area (Al-Dairy et al. 2021, Wangare et al. 2024).

In the study conducted, CNT-based electrodes exhibited the weakest electrochemical responses and lacked surface charge density. They provide sufficient conductive pathways and are strong mechanically, but the active surface area that can be effectively altered is strongly dependent on the areas of the aligned and functionalized electrodes. In idealized geometric environments for certain simulation-based studies, CNT electrodes are likely to underperform relative to graphene that does provide a continuous charge distribution that is of high density and that is for structural support (Ferrier and Honeychurch 2021). In previous modelling studies concerning biosensors that are of a steroid hormone based CNT, the increase of current is dependent upon extensive surface functionalization (Wangare et al. 2024).

The time-resolved current density profiles provide more evidence of different kinetic characteristics of the nanomaterials. After an initial increase in current, graphene shows current stabilization, indicative of efficient charge redistribution and interfacial polarization, which are of minimal concern. ZnO shows an electrode with a delayed peak response, typical of diffusion-limited transport coupled with slower charge transfer. In CNT, current responses increase over longer time scales, indicative of the progressive adsorption of the target analyte and the concomitant charge carrier limitation. These results apply to the fundamentals of electrochemical biosensing and the previous comparative analyses of nanomaterial-modified electrodes (Grieshaber et al., 2008; Singh et al., 2014).

The obtained sensitivity values, from a sensing performance perspective, fall within the performance of wearable cortisol biosensors. CNT composites and graphene-based sensors, which are Carbon based composite materials, have shown achievement of nanomolar detection limits with a range of normalized sensitivity of the order of $\sim 1\ \mathrm{A\ m^{-2}\ \mu mol^{-1}\ L}$ particularly in applications involving sweat (Upasham et al., 2018; Wang et al., 2023). Likewise, Electrochemical immunosensors based on ZnO nanostructures have illustrated large detection ranges and low limits of detection, which highlight the importance of nanostructured surfaces in cortisol sensing (Yamaguchi et al., 2012; Li et al., 2022).

The analysis overall shows that due to the simulation's identical conditions, graphene, out of all the materials, presents the best degree of surface charge density, efficient electron transfer, and current consistency. ZnO shows acceptable results and has the benefit of being biocompatible, while CNTs still need better structural or chemical sensitivity. Therefore, these results prove graphene to be a top candidate for the flexible electrochemical cortisol biosensor and provide a reason for future optimisations for the sensors and the experimental validations.

6.1 Limitations of the Study

The current study, while providing a valued comparison, has some limitations. First, the study evaluates a numerical simulation using COMSOL Multiphysics, a simulation tool that optimises material characteristics, kinetic factors and boundary conditions; thus, real-world phenomena such as surface irregularities, defects in the electrodes due to the fabrication process, and biofouling and fouling of electrodes have not been simulated explicitly (Al-Dairy et al., 2021; Lacatus et al., 2015). Therefore, while results may not accurately replicate current density values observed in experiments, the relative performance among the materials is still valid.

Second, the model does not address the molecular-scale binding processes and enzymatic pathways involved in the redox processes, which is a common occurrence in cortisol biosensors, including immunosensors, aptasensors, or MIP-based systems (Grieshaber et al., 2008; Singh et al., 2014). Hence, the model concentrates on the electrochemical conversion and not on the biochemical specificity, which in future work needs to be addressed during experimental validation.

Lastly, unexplored in the present framework are the operational time aspects of drift, reusability, ageing, and sensor stability. These aspects are known to impact the cortisol sensors that are wearable and point of use the most, especially when they are operated for long and continuous periods (Gibson, 2011; Upasham et al., 2018). The next steps will focus on stability modelling and integration with experimental work to enhance the applicability of the proposed sensor architectures.

Conclusion

This research makes advances in the comparative analysis of nanomaterial-based electrochemical cortisol sensors with an emphasis on sensor interfaces over other metrics like sensor sensitivity. Evaluating the electrochemical behaviours of nanomaterials occurred in a singular framework (COMSOL Multiphysics) and unified simulation for the graphene, ZnO, and carbon nanotube (CNT) electrodes under the same geometry, kinetics, and concentration. The findings indicate that surface charge density (SCD) is the primary determinant of electrochemical consistency and overall electrochemical robustness in nanomaterials.

Among the tested materials, graphene demonstrated the highest overall SCD, along with the greatest current stability, attributed to its 2D structure and delocalised pi (π) electron system. The efficient charge redistribution at the electrode/electrolyte interface makes graphene an ideal candidate for stability-centred cortisol sensing, especially for continuous sensing or wearable applications. On the other hand, CNT electrodes presented low overall SCD, despite the good transport pathways for charge, supporting design criteria for stability. These electrodes would be most appropriate for the sensitivity-driven portion of the design, offering less long-term stability. ZnO electrodes demonstrated an intermediate position, with a polar surface and semiconducting charge transport.

One of the most important results of this research is the recognition of surface charge density as a meaningful design parameter for electrochemical biosensors. Unlike other design parameters that ignore performance in terms of sensitivity, SCD encompasses the phenomena of charge build-up and redistribution at interfaces, which affect signal reproducibility and drift. Since the SCD and current density relationship is valid for all materials in the simulations, it can be used as a guide for the selection of materials in the preliminary design of cortisol sensors.

These results indicate that future sensor designs may be best served by novel designs using CNTgraphene composites. Such composites can be expected to synergistically offer the high sensitivity of CNTs and the charge stability of graphene. As such, hybrid systems should be able to overcome the sensitivity and stability trade-off that plague most of today's wearable cortisol sensors.

This study is based on numerical simulations, yet it constructs a solid theoretical framework for comparing materials and optimising sensors. Experimental validation, integration of a biochemical recognition element, and testing for electrochemical (bio) recognition under realistic biofluids will be the focus of the next phase. The results of this study and the presented framework should facilitate the rational design of electrochemical cortisol sensors to meet critical, emerging real-world healthcare needs.

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