Enhancing the Dispersity and Electrochemical Properties of Chitosan-Coated Carbon Nanotubes for Manufacturing High-Sensitivity Biosensors with Optimal Electrical Conductivity

Dong Sup Kim , Abdus Sobhan , Jun-Hyun Oh , Jinyoung Lee *

Posted Date: 8 May 2024

doi: 10.20944/preprints202405.0519.v1

Keywords: Dispersity; Biosensor; Single-walled carbon nanotube; Electrical Conductivity; Sensitivity

Article

Enhancing the Dispersity and Electrochemical Properties of Chitosan-Coated Carbon Nanotubes for Manufacturing High-Sensitivity Biosensors with Optimal Electrical Conductivity

Dong Sup Kim [1], Abdus Sobhan [2,3], Jun-Hyun Oh [4] and Jinyoung Lee [1,*]

[1] Department of Green Chemical Engineering, Sangmyung University, 31 Sangmyungdae-Gil, Dongnam-Gu, Cheonan, Chungnam 31066, Republic of Korea
[2] Department of Agriculture and Applied Science, Alcorn State University, Mississippi, USA
[3] Department of Agricultural Engineering, South Dakota State University, Brookings, USA
[4] Department of Plant and Food Sciences, Sangmyung University, 31 Sangmyungdae-Gil, Dongnam-Gu, Cheonan, Chungnam 31066, Republic of Korea
* Correspondence: dorgly@smu.ac.kr

Abstract: Recent developments in high-performance electrode materials have been pivotal for real-time monitoring biosensors, necessitating compatibility with biomaterials and robust electrochemi-cal properties. This study explores the development of electrode materials using single-walled carbon nanotubes (SWCNTs) and multi-walled carbon nanotubes (MWCNTs), with a primary fo-cus on assessing their dispersion and electrochemical properties. Various solvents, including N N-Dimethylformamide (DMF), deionized water, ethanol, and acetone, were used for dispersion analysis by employing ultrasonic waves. The results showed that SWCNTs exhibited well-dispersed characteristics without precipitation when introduced to a DMF solution. It found that resistance values decreased as the concentration of SWCNTs increased over the range of 0.025 to 0.4 g/L, with a considerable electrical conductivity reached at concentrations ranging from 0.2 g/L to 0.4 g/L in DMF. The biosensor platform was evaluated with 1-pyrenebutanoic acid succin-imidyl este (PBSE) as the linker and glucose oxidase (Gox) and chitosan as the binding substrate. The binding of Gox with glucose resulted in a significant decrease in resistance value of the biosensor with rising their concentrations ranged from 0.001 to 0.1 M. Though this research provides founda-tional insights for the advancement of SWCNT-based high-performance electrode materials, it will pave the way for the next generation of efficient and reliable biosensors.

Keywords: dispersity; biosensor; single-walled carbon nanotube; electrical conductivity; sensitivity

1. Introduction

The development of high-sensitivity biosensors relies heavily on the optimization of carbon nanotubes (CNTs), specifically focusing on enhancing their dispersity and electrochemical properties while maintaining proper electrical conductivity [1,2]. Achieving well-dispersed CNTs is essential to prevent agglomeration, ensuring uniform coverage and accessibility of the nanotube surface for biomolecule attachment [3]. Biosensors developed with well dispersed and optimized CNTs have the potential to detect biomolecules with enhanced sensitivity and rapidity. Diabetes mellitus is a chronic metabolic disorder affecting millions of people worldwide [4–6]. Non-invasive glucose monitoring has emerged as a highly sought-after alternative to blood-based measurements, offering continuous monitoring without the need for repeated finger pricks [7]. The development of reliable biosensors capable of non-invasive detecting glucose in sweat is of significant interest for diabetes management [8].

Carbon nanotubes (CNTs) have attracted significant attention due to their exceptional physical and chemical properties that has prompted increasing number of researchers for the construction of

 doi:10.20944/preprints202405.0519.v1

an analytical device to detect biomolecules ranging from glucose, nucleic acids, and small proteins, and prokaryotic and eukaryotic bacterial cells [9]. They have a tubular structure composed of monomer graphene deposed either in a single sheet (single-walled carbon nanotube, SWCNT) or in multiple sheets of graphene (multi-walled carbon nanotube, MWCNT) [10].

Single-walled carbon nanotubes (SWCNTs) have emerged as a versatile nanomaterial for biosensing applications, owing to their exceptional electrical, mechanical, and chemical properties [11]. SWCNTs possess high electrical conductivity, a large surface area, and excellent biocompatibility, making them ideal candidates for glucose sensing [11,12]. These nanotubes have a diameter typically in the order of nanometers, with lengths ranging from micrometers to millimeters that lead to a wide range of potential new research applications [13]. The discovery of SWCNTs, along with their multi-walled counterparts (MWCNTs), has opened new avenues for innovation and applications in nanotechnology [12]. Multi-walled carbon nanotubes (MWCNTs) have garnered significant attention in the field of biosensor research due to their unique properties including electrical conductivity, increased surface area, and biocompatibility [14]. Unlike SWCNTs, MWCNTs consist of several nanotubes nested within one another, with the number of layers typically ranging from two to a few dozen [15]. This unique structure imparts distinctive properties to MWCNTs, making them valuable across a wide range of applications in various scientific and industrial fields.

By leveraging the specific interaction between glucose and enzymes immobilized on SWCNT surfaces, the detection of D-glucose can be achieved with remarkable sensitivity and selectivity [12]. The proposed SWCNT-based biosensor offers several advantages for non-invasive glucose monitoring in sweat [13]. Firstly, the high electrical conductivity of SWCNTs enables efficient charge transfer, facilitating sensitive and rapid glucose detection. Secondly, the large surface area of SWCNTs provides ample sites for enzyme immobilization, enhancing the biosensor's sensitivity and detection limits [8]. Moreover, the biocompatibility of SWCNTs ensures long-term stability and compatibility with sweat constituents, enabling reliable and accurate glucose measurements [14].

Furthermore, the unique mechanical properties of SWCNTs make them suitable for the development of miniaturized biosensor devices, which are highly desirable for point-of-care diagnostics [12]. In this research paper, we highlighted the development and characterization of a SWCNT-based biosensor for D-glucose detection in sweat. The fabrication process involves the functionalization of SWCNTs, followed by the immobilization of glucose oxidase (GOx) as the sensing element [15]. The performance of the biosensor is systematically evaluated using standard glucose solutions, as well as sweat samples collected from healthy individuals. The objectives of this study are to determine the dispersity of CNTs into the solvents for biosensor or sensor development; optimize various parameters, including enzyme loading, pH, and temperature, and enhance the biosensor's performance; and assess or evaluate response of the biosensor to potential glucose interferents with rapidity and sensitivity.

In addition to the remarkable properties of carbon nanotubes, the use of chitosan, a natural polymer, has been gaining traction in the field of biosensing due to its excellent film-forming ability and biocompatibility [16]. Chitosan offers a favorable microenvironment for enzyme immobilization, significantly affecting the stability and activity of the immobilized enzymes such as glucose oxidase (GOx) [17]. The integration of chitosan with carbon nanotubes has been shown to enhance the dispersion of CNTs further and prevent their agglomeration, thereby maintaining the high surface-to-volume ratio crucial for enzyme attachment and biosensor sensitivity [18].

Furthermore, chitosan's cationic nature under acidic conditions facilitates a strong electrostatic interaction with negatively charged biomolecules and enzymes. This interaction not only helps in the immobilization of enzymes on the biosensor's surface but also stabilizes the immobilized enzymes, maintaining their bioactivity over a longer period [19]. This innovative approach of combining chitosan with CNTs for enzyme immobilization can lead to the development of biosensors with enhanced performance, higher sensitivity, and greater stability.

Moreover, chitosan is known for its non-toxicity, biodegradability, and biocompatibility, making it an excellent material for applications in biosensors, particularly those intended for medical and food industry applications. The presence of chitosan in the matrix of carbon nanotubes-based

 doi:10.20944/preprints202405.0519.v1

biosensors can significantly improve the adherence and uniformity of enzyme layers, resulting in more reproducible and reliable glucose detection [20].

2. Materials and Methods

2.1. Chemicals

SWCNT and MWCNT (called CNTs) were supplied by (Sigma Aldrich, Seoul Korea) and their purity was greater than 95%. The solvents, namely N, N-Dimethylformamide (DMF), Acetone, Di-water, and ethanol were obtained from (Sigma Aldrich, Seoul Korea). The glucose substrate (ng/mL, naturally purified and prepared in) and glucose oxidase enzyme against glucose were procured from Inc. (Sigma Aldrich, Seoul Korea). A 10% (v/v) phosphate buffer saline (PBS, 0.1 M, pH 7.4, 0.8% NaCl) was purchased from Life Technologies (Seoul Korea) and was prepared by mixing with purified water. Glucose substrate was diluted for use in 10% PBS. All other chemicals were of analytical reagent grade and were used without further purification.

2.2. Solvent suspension and Dispersion of CNTs

In this study, the commonly used solvents for preparing spinning solutions included dimethylformamide (DMF), acetone, ethanol, and deionized water (Di-water). The dispersion of the CNTs (SWCNTs or MWCNTs) were performed by mixing CNTs with DMF, acetone, ethanol, and DI-water, individually, at the concentration of 0.5 g/L and sonicated for 2 h for preparing CNTs' spinning solutions using ultrasonic waves (write the equipment details). After that, the physical properties of dispersed CNTs' solution like concentration measurement using high UV-spectrophotometer were performed to confirm their effective chemical interaction and high reproducibility with the applied reactant spinning solvents.

The dispersion of CNTs were primarily assessed through sedimentation process by following the previous procedure with minor modifications [16]. The sediment CNTs in the sonicated solution were captured and monitored with hand-held smart photometer after one day, one week and a month to observe the long-term stability of the dispersions. UV-spectroscopy analysis was performed using a SHIMADZU instrument at 100.0 kV. Additionally, to further understand the interactions between the nanotubes and solvents, UV measurements were conducted. These measurements were used to determine the surface charge of the nanotubes in different solvents, which is a critical factor in understanding their dispersion and stability [16]. The comprehensive analysis offered valuable data optimizing solvent choice and processing conditions for MWCNT applications in various fields, including sensor technology, nanocomposites, and electronic devices.

2.3. Biosensor Development with SWCNTs

Biosensor was developed with SWCNTs by following procedure with slight modification [17]. Firstly, different concentrations of SWCNTs (0.025, 0.05, 0.1, 0.2, 0.4 g/L) were dispersed in DMF solution and sonicated for at least 2 h. Following sonication, each sonicated SWCNTs with an aliquot of 10 µl was applied to the sensor plate and annealed for 15 min into incubator at 80 ^{o}C to bind the SWCNTs on the sensor plate. After annealed, the biosensor plates were washed with deionized water to eliminate unbound SWCNTs and dried with N_2 gas. Following this, electrical resistance of the biosensor with respect to each concentration was measured using a multi-meter tester to evaluate the impact of SWCNT concentrations on conductivity.

To optimize PBSE, the developed SWCNT-based biosensor was functionalized with different concentrations of a PBSE linker (1.0, 2.0, 4.0, 6.0, 8.0 g/L) to investigate how the linker concentration affects the overall conductivity and stability of the dispersion. Each concentration was thoroughly tested to determine the most effective ratio of linkers for enhancing the electrical properties of the biosensor. In addition, to optimize glucose oxidase (Gox) as a binding substrate, the linker functionalized biosensor was carefully immobilized with Gox at varying concentrations (0.01, 0.05, 0.1, 0.2, 0.5 g/L) and studied its effect on the electrical properties of the composite material. The immobilization of Gox at different concentrations was crucial for determining the optimal amount

 doi:10.20944/preprints202405.0519.v1

required to achieve the best sensor performance. To further enhance enzyme immobilization, a solution mixing method was employed, where chitosan was dissolved with the enzyme solution before applying to the SWCNT-based biosensor, ensuring a uniform and stable attachment of glucose oxidase onto the biosensor surface [21]. The immobilization of Gox at different concentrations was crucial for determining the optimal amount required to achieve the best sensor performance.

2.4. Detection of Glucose by the Fabricated Biosensor

The Gox immobilized biosensor was tested with 80 µL of diluted glucose solution over the range of 0.2 – 0.9 g/L at room temperature using a detection time of 30 min to allow for the Gox-glucose reaction to occur. After the reaction, the applied biosensor was washed with DI water to remove any unbound glucose molecule from the sensor surface, and the resistance of the sensor electrode was measured using a potentiostat. A change in resistance confirmed the attachment of glucose onto the Gox and this change in resistance was only observed for glucose concentration. In this study, linear sweep voltammetry (LSV) measurements were performed at each step using a potentiostat device (DY2013, EG Technology, Seoul, South Korea) at room temperature to measure resistance.

3. Results and Discussion

3.1. Dispersion Characteristics of CNTs in Various Solvents

Figure 1 presents the experimental scheme for the dispersion of CNTs in various solutions, followed by the measurement of dispersion and electrical resistance. The process initiates with the preparation of CNTs suspensions in selected solvents, acetone, DMF, Di-water, and ethanol under ultrasonication to achieve optimal dispersion. The degree of dispersion is then quantitatively assessed using UV-Vi's spectroscopy, where absorbance patterns provide insight into the uniformity and stability of the CNTs within the solvents. Subsequently, the electrical resistance of the dispersed CNTs is measured, offering a functional evaluation that correlates the quality of dispersion with the electrical properties vital for biosensor applications. This schematic illustration encapsulates the critical steps undertaken to ensure the effective integration of CNTs for enhanced performance in biosensor devices.

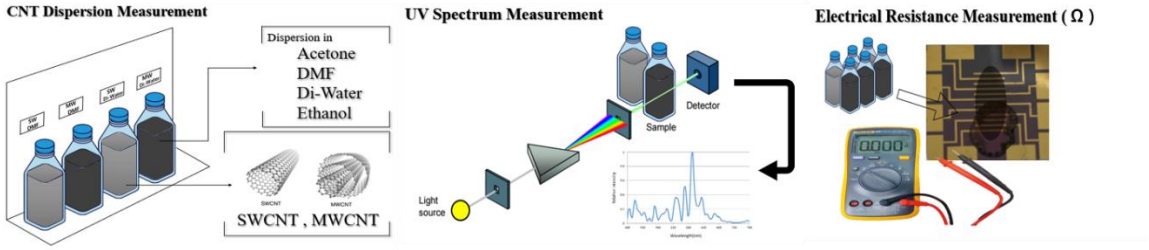

Figure 1. Experimental scheme of the CNTs dispersion in various solvents (DMF, acetone, DI-water, and ethanol) and degree of dispersion measured with UV-Vis and electro resistance.

3.2. Dispersion Analysis of CNTs in Various Solvents

Functionalization of nanomaterials involves altering their chemical and physical properties through chemical reactions [18,22,23]. Optimal interfaces contact between nanomaterials and reactants is essential for functionalization to ensure effective chemical interaction and high reproducibility of reaction products. Solvents are employed to create a spinning solution that can dissolve the specified polymer materials. However, not all solvents are universally suitable due to their varying abilities to dissolve polymers. Beyond dissolving polymers, solvents play additional roles in the electrospinning process. They aid in maintaining the viscosity of the spinning solution and facilitate the integration of polymer materials with carbon nanotubes (CNTs) during electrospinning [24]. Therefore, commonly used solvents for preparing spinning solutions include dimethylformamide (DMF), acetone, ethanol, and deionized water (Di-water).

 doi:10.20944/preprints202405.0519.v1

As can be seen in Figure 2, the suspension of SWCNTs shows a uniform and stable dispersion without any visible settling, indicating excellent solubility and stability of SWCNTs in DMF, which can be attributed to the strong interaction between the solvent molecules and the nanotubes [25]. Whereas a similarly homogeneous dispersion of MWCNTs was observed in DMF, with the dark coloration suggesting a high concentration of well-dispersed nanotubes [26]. A slight sedimentation at the bottom of the vial indicates a moderate dispersion of SWCNTs in ethanol, reflecting partial compatibility between the solvent and the nanotubes. There is evidence of partial sedimentation; however, the dispersion is notably more homogeneous compared to SWCNTs, suggesting that MWCNTs have a somewhat enhanced interaction with ethanol. Substantial sedimentation into water was observed, indicative of poor dispersion. The lack of stabilization agents in water for SWCNTs leads to significant aggregation. The stark layer separation with sediment at the bottom of the vial confirms the hydrophobic nature of MWCNTs, which do not disperse well in water. The presence of some aggregates amidst a moderately dispersed solution suggests that while acetone can disperse SWCNTs to a certain extent, it is not as effective as DMF. The dispersion is relatively better than that of SWCNTs in the same solvent, which may be due to the larger dimensions and different surface chemistry of MWCNTs, affecting their interaction with acetone. The visual assessment of the suspensions post-ultrasonication provides essential insights into the solubility and stability of carbon nanotubes in various solvents. The observed dispersion levels are crucial for determining the potential application of these nanotube suspensions in the development of biosensors, with DMF being identified as the most suitable solvent for achieving a homogenous dispersion of both types of CNTs.

Figure 2. The visual outcomes of the dispersion experiments for single-walled carbon nanotubes (SWCNTs) and multi-walled carbon nanotubes (MWCNTs) following a 2-hour ultrasonication process in different solvents: DMF, ethanol, deionized water (Di-water), and acetone.

3.3. UV-Visible Spectral Analysis of CNTs Dispersions

The UV-Visible spectral data for dispersions of SWCNTs and MWCNTs in N, N-dimethylformamide (DMF) and deionized water (DW) are presented in Figure For SWCNTs in DMF, the spectrum exhibited a progressive increase in absorbance with a rising concentration, indicative of a stable and uniform dispersion. The consistency of the data points suggests effective interaction between the DMF molecules and SWCNTs, facilitating a reliable dispersion suitable for subsequent applications [27]. In contrast, the MWCNTs in DMF showed a similar trend with a slightly increased variability in absorbance, potentially due to the more complex morphology of MWCNTs affecting the uniformity of the dispersion. The SWCNT dispersions in deionized water revealed a less steep increase in absorbance, accompanied by greater data dispersion. This outcome suggests that without the aid of surfactants or stabilizing agents, deionized water alone does not provide sufficient dispersal capacity for SWCNTs. MWCNT dispersions in deionized water also exhibited an upward trend in absorbance, but the slope was less marked compared to SWCNTs, reflecting the inherent difficulty in achieving homogeneous dispersion in a polar solvent like water for these hydrophobic nanomaterials. The spectral analysis underscores the significant influence of solvent choice on the dispersion quality of CNTs. DMF proved to be a superior dispersant for both SWCNTs and MWCNTs, as evidenced by the higher and more consistent absorbance values. This finding is critical for the preparation of CNT-based materials where dispersion quality directly impacts the performance, particularly in sensor technology and nanocomposite fabrication [27,28].

 doi:10.20944/preprints202405.0519.v1

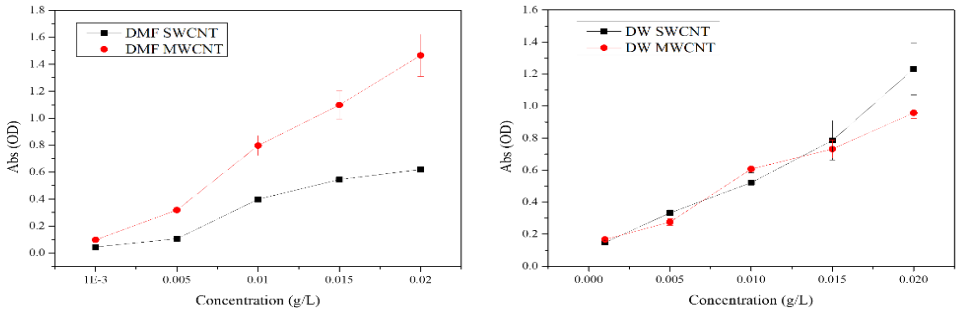

Figure 3. UV–Vi's spectrum of DMF and DW aqueous dispersions of the SWCNT and MWCNT.

3.4. Quantitative Analysis of Electrical Resistance in CNT Dispersions

Figure 4 delineates the variation in electrical resistance as a function of SWCNTs concentration. The SWCNT solutions were prepared at concentrations of 0.025 g/L, 0.05 g/L, 0.1 g/L, 0.2 g/L, and 0.4 g/L, and their corresponding electrical resistances were meticulously measured. The data manifest a clear inverse relationship between the concentration of SWCNTs and electrical resistance; as the concentration of the SWCNT solution was augmented, a concomitant decrease in resistance was observed [29,30]. This trend reinforces the assertion that SWCNTs exhibit high electrical conductivity, and that an increase in the concentration of these nanotubes facilitates a more efficient electron flow. Notably, the graph illustrates a tapering in the rate of decrease in electrical resistance at concentrations exceeding 0.4 g/L. This concentration suggests an onset of particle-particle interactions where the proximity of SWCNT particles at higher concentrations leads to a saturation point beyond which the resistance reduction is no longer substantial. The phenomena observed postulate the presence of an optimal concentration range wherein the conductive pathways are maximized before the effects of aggregation or inter-tube resistance become dominant. These findings are instrumental in delineating the concentration-resistance profile of SWCNT solutions and have significant implications for their application in nanoelectronics. The results elucidate the potential for tailoring the electrical properties of SWCNT-based materials by controlling their concentration, which is crucial for the development of nanoelectronics devices and circuits. The optimal concentration of SWCNTs for electrical conductivity appears to be at or slightly below 0.4 g/L. At this concentration, the SWCNT dispersion achieves a balance between maximizing conductivity and preventing the onset of counterproductive particle aggregation. Beyond this concentration, the incremental benefits in conductivity diminish, indicating a threshold where further increases in SWCNT concentration do not significantly enhance the electron flow. Thus, for applications requiring high conductivity without the drawbacks of excessive nanotube aggregation, maintaining the SWCNT concentration around 0.1 to 0.4 g/L is advisable.

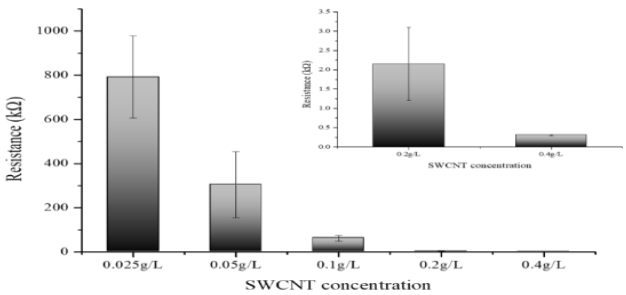

Figure 4. Electrical resistance measurement of different SWCNT concentrations (0.025, 0.05, 0.1, 0.2, and 0.4 g/L).

 doi:10.20944/preprints202405.0519.v1

3.5. Quantitative Analysis of Electrical Resistance in CNT Dispersions

Figure 5 illustrates the electrical resistance profile of SWCNT-based biosensor as a function of varying concentrations of a PBSE linker. The biosensor's resistance was systematically measured across a series of PBSE linker concentrations: 1.0, 2.0, 4.0, 6.0, and 8.0 g/L. The results demonstrate a discernible increase in resistance with escalating concentrations of the PBSE linker. At the lowest concentration (1.0 g/L), the biosensor exhibited the lowest resistance, suggesting a minimal barrier to electron flow within the SWCNT network. As the concentration of the PBSE linker was increased to 2.0 g/L and 4.0 g/L, a gradual increase in resistance was observed, which may be attributed to the increased density of the linker molecules within the biosensor matrix, possibly leading to more hindered electron mobility. Interestingly, at higher concentrations of 6.0 g/L and 8.0 g/L, the resistance values show a more pronounced escalation, indicating that the PBSE linker concentration has surpassed an optimal threshold for electron transport. This could be due to the formation of a more congested network, where the PBSE linkers introduce additional scattering points for electrons, thus raising the biosensor's overall resistance [31,32]. These findings elucidate the impact of PBSE linker concentration on the electrical properties of SWCNT-based biosensors. The observed trend highlights the importance of optimizing the concentration of PBSE linkers to achieve desired electrical performance, which is crucial for the sensitivity and specificity of the biosensor applications. The optimal concentration of the PBSE linker appears to lie below 4.0 g/L, where the resistance values begin to rise sharply, suggesting that concentrations above this level might compromise the electrical conductivity of the biosensor.

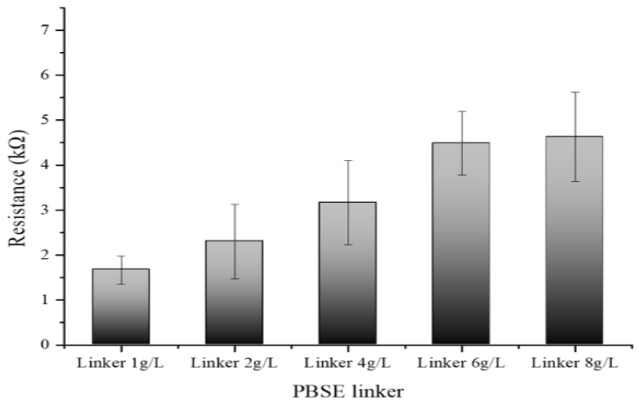

Figure 5. Resistance of SWCNT –based biosensor reacted with different PBSE linker concentration (1.0, 2.0, 4.0, 6.0, and 8.0 g/L).

3.6. Optimization of Gox Concentration with Developed Biosensors

Figure 6 provides significant insights into the optimization of glucose oxidase (Gox) concentration for SWCNT-PBSE biosensors. The experimental data depicted a clear trend in electrical resistance associated with varying levels of Gox concentration. Initially, an increase in Gox concentration from 0.01 g/L to 0.1 g/L corresponded to a rise in electrical resistance. This increment may be due to the insulating properties of Gox, which when in higher quantity could hinder the electron transfer across the SWCNT network. Interestingly, a peak resistance was observed at 0.1 g/L, after which the resistance began to decrease at concentrations of 0.2 g/L and further reduced at 0.5 g/L. This phenomenon suggests that there is a critical concentration threshold, where the catalytic activity of Gox begins to outweigh its insulating effects, thus enhancing the overall conductivity of the biosensor. The decrease in resistance at higher Gox concentrations could be indicative of more efficient enzymatic turnover leading to improved charge transfer within the biosensor matrix [32,33]. Therefore, the results from this study suggest that the concentration of Gox plays a pivotal role in the electrical behavior of SWCNT-PBSE biosensors. For applications requiring precise electrical

 doi:10.20944/preprints202405.0519.v1

performance, careful calibration of Gox concentration is essential. The optimal concentration for Gox appears to be beyond 0.1 g/L, where the biosensor system benefits from the enzymatic activity without significant compromise to conductivity. These findings have substantial implications for the design and development of biosensors, particularly in the field of bioelectronics where sensor sensitivity and specificity are paramount.

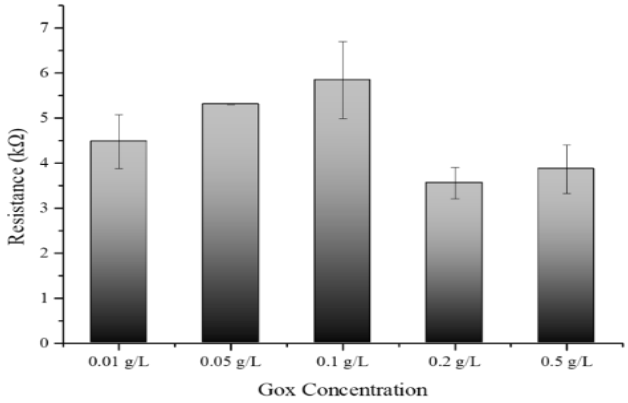

Figure 6. Resistance of SWCNT–PBSE biosensor reacted with different concentration Gox (0.01, 0.05, 0.1, 0.2, and 0.5 g/L).

3.7. Glucose concentration Impact on Electrical Resistance in the Developed Biosensors

Figure 7 demonstrates the relationship between glucose concentration and the electrical resistance of SWCNT-based biosensor. The biosensor's sensitivity to varying glucose concentrations (0.01, 0.05, 0.1, 0.5, and 1.0 M) was quantitatively assessed through resistance measurements. The experimental findings reveal a distinct correlation where the electrical resistance decreases as glucose concentration increases from 0.01 M to 0.1 M. This decrease in resistance likely results from the enzymatic activity of glucose oxidase, which facilitates electron transfer processes in the presence of glucose, thereby enhancing the conductivity of the SWCNT network. However, at higher glucose concentrations of 0.05 M and 0.1 M, the resistance begins to plateau and then increase, suggesting a saturation point in the biosensor's response. This saturation could be attributed to the enzymatic reaction approaching its maximum rate, beyond which additional glucose does not correspond to an increase in electron transfer rate. This trend indicates that the SWCNT-based biosensor possesses an optimal detection range for glucose, which is crucial for its application in medical diagnostics, particularly for blood glucose monitoring in diabetic patients [33]. The data from this study suggest that the biosensor maintains high sensitivity and specificity within the lower concentration range (0.01 to 0.1 M), which is within the physiologically relevant range for glucose in human blood. The understanding of this concentration-dependent response is vital for the design of SWCNT-based biosensors, ensuring that they operate within their most responsive range for accurate and reliable glucose detection [33]. These results underscore the potential of SWCNT-based biosensors to serve as effective tools for glucose monitoring, with significant implications for the management of diabetes and other conditions characterized by alterations in blood glucose levels.

 doi:10.20944/preprints202405.0519.v1

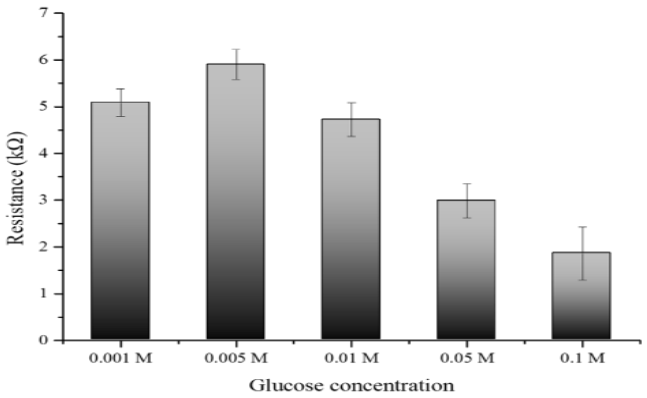

Figure 7. Measurement of electrical resistance sensing different glucose concentration (0.01, 0.05, 0.01, 0.05, and 0.1 M).

4. Conclusions

This study has investigated the dispersion characteristics of CNTs in various solvents, their interaction with PBSE linkers, the optimization of glucose oxidase (Gox) concentration, and the consequent impact on electrical resistance in biosensor applications. The optimal dispersion of CNTs was achieved in DMF, which exhibited the most stable and uniform nanotube suspension, as visually confirmed and quantitatively supported by UV-Vis spectral analysis. The electrical resistance measurements further validated that DMF is the solvent of choice for SWCNT-based biosensors due to its favorable interaction with the carbon nanotubes. The interaction with PBSE linkers and Gox concentration offered a concentration-dependent electrical resistance, which peaked and then plateaued, indicating optimal ranges for biosensor performance. For glucose detection, the SWCNT-based biosensor exhibited enhanced sensitivity at lower concentrations, suggesting its efficacy for blood glucose monitoring within the physiological range. This research underscores the importance of fine-tuning SWCNT, PBSE, and Gox concentrations to achieve biosensors with optimal electrical properties for medical diagnostics. This study features the SWCNT-based biosensor's potential for accurate and reliable blood glucose monitoring, which is essential for diabetes management. The controlling concentration of SWCNTs, PBSE linkers, and Gox is critical for optimizing the electrical properties of SWCNT-based biosensors. These insights pave the way for the design of highly sensitive and specific biosensors, which are of paramount importance in the fields of medical diagnostics and bioelectronics.

Author Contributions: Dong Sup Kim: Conceptualization, Formal analysis, Investigation, writing original draft, writing review & editing **Abdus Sobhan:** Conceptualization, Formal analysis, writing draft, review & editing **Jun-Hyun Oh:** Conceptualization, Formal analysis **Jinyoung Lee:** Conceptualization, Writing – review & editing. All authors have read and approved the final manuscript.

Declaration of competing interest: The author declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper

Acknowledgements: This research was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (MSIP; No. 2021R1F1A1055676).

References

1. [1] M. Lotfy, J. Adeghate, H. Kalasz, J. Singh, E. Adeghate, Chronic Complications of Diabetes Mellitus: A Mini Review, Curr Diabetes Rev. 13 (1) (2017) 3-10. https://doi.org/10.2174/1573399812666151016101622.
2. [2] Diabetes Care in the Hospital: Standards of Medical Care in Diabetes, Diabetes Care. 44, supplement 1 S211-S220. https://doi.org/10.2337/dc21-S015.

3. [3] M. Erbach, G. Freckmann, R. Hinzmann, B. Kulzer, R. Ziegler, L. Heinemann, and O. Schnell, Interferences and Limitations in Blood Glucose Self-Testing, J Diabetes Sci Technol. 10 (2016) 1161-1168.
4. [4] F. Gao, C. Liu, L. Zhang, T. Liu, Z. Wang, Z. Song, H. Cai, Z. Fang, J. Chen, J. Wang, M. Han, J. Wang, K. Lin, R. Wang, M. Li, Q. Mei, X. Ma, S. Liang, G. Gou & N. Xue, Wearable and flexible electrochemical sensors for sweat analysis: a review, Microsystems & Nanoengineering. 9 (2023) 1. https://doi.org/10.1038/s41378-022-00443-6.
5. [5] M. Younus Wani, N.A. Ganie, K.A. Dar, S.Q. Dar, A. Husain Khan, N. A. Khan, S. Zahmatkesh, M. Saood Manzar, R. Banerjee, Nanotechnology future in food using carbohydrate macromolecules: A state-of-the-art review, Int. J. Biol. Macromol. 239 (2023) 124350. https://doi.org/10.1016/j.ijbiomac.2023.124350.
6. [6] A. Sobhan, J. H. Oh, P. Mi-Kyung, L. Jinyoung, Reusability of a single-walled carbon nanotube-based biosensor for detecting peanut allergens and Y. enterocolitica, Microelectronic Engineering. 225 (2020) 111281. https://doi.org/10.1016/j.mee.2020.111281.
7. [7] A. Hina W. Saadeh, Noninvasive Blood Glucose Monitoring Systems Using Near-Infrared Technology—A Review, Sensors. 22 (2022) 485. https://doi.org/10.3390/s22134855.
8. [8] S. D. Psoma, C. Kanthou, Wearable Insulin Biosensors for Diabetes Management: Advances and Challenges, Biosensors, 13 (2023) 719. https://doi.org/10.3390/bios13070719.
9. [9] A. Sobhan, L. Jinyoung, P. Mi-Kyung, O. Jun-Hyun, Rapid detection of Yersinia enterocolitica using a single–walled carbon nanotube-based biosensor for Kimchi product, Lwt. 108 (2019) 48-54. https://doi.org/10.1016/j.lwt.2019.03.037.
10. [10] W. Joseph, Carbon-Nanotube Based Electrochemical Biosensors: A Review, Electroanalysis. 17(1) (2005) 7-14. https://doi.org/10.1002/elan.200403113.
11. [11] M. Sireesha,V. Jagadeesh Babu, A. Sandeep Kranthi Kiran & S. Ramakrishna, A review on carbon nanotubes in biosensor devices and their applications in medicine, Nanocomposites. 4 (2018) 2. https://doi.org/10.1080/20550324.2018.1478765.
12. [12] J. Janssen, M. Lambeta, P. White.A. Byagowi, Carbon Nanotube-Based Electrochemical Biosensor for Label-Free Protein Detection, Biosensors. 9 (2019) 4 144. https://doi.org/10.3390/bios9040144. [13] P. Liu, Y. Jiao, X. Chai, Y. Ma, S. Liu, X. Fang, F. Fan, L. Xue, J. Han, Q. Liu, High-performance electric and optical biosensors based on single-walled carbon nanotubes, Journal of Luminescence. 250 (2022) 119084. https://doi.org/10.1016/j.jlumin.2022.119084.
13. [14] R. Nißler, J. Ackermann, C. Ma, & S. Kruss, Prospects of fluorescent single-chirality carbon nanotube-based biosensors. Analytical Chemistry. 94(28) (2022) 9941-9951. https://doi.org/10.1021/acs.analchem.2c01321.
14. [15] C. Alatzoglou, E. I. Tzianni, M. Patila, M. G. Trachioti, M. I. Prodromidis, H. Stamatis, Nanomaterials.14 (2024) 85. https://doi.org/10.3390/nano14010085.
15. [16] Y. Hyungsub, T. Russ, H. Byungil, Colloids Interface Sci. 52 (2023) 100686. https://doi.org/10.1016/j.colcom.2022.100686.
16. [17] L. Jinyoung, Carbon Nanotube-Based Biosensors Using Fusion Technologies with Biologicals & Chemicals for Food Assessment. Biosensors, 13(2) (2023) 183. https://doi.org/10.3390/bios13020183.
17. [18] Y. Gao, J. Luo, Z. Li, F. Teng, J. Zhang, S. Gao, M. Ma, X. Zhou and X. Tao, Dispersion of carbon nanotubes in aqueous cementitious materials: A review, Nanotechnology Reviews. 12 (2023) 20220560. https://doi.org/10.1515/ntrev-2022-0560.
18. [19] Q.Pan, Q. Wu, Q. Sun, X. Zhou, L. Cheng, S. Zang,Y. Yuan, Z. Zhang, J. Ma, Y. Zhang, B. Zhu, Biomolecule-friendly conducting PEDOT interface for long-term bioelectronic devices, Sensors and Actuators B: Chemical, 373 (2022). https://doi.org/10.1016/j.snb.2022.132703
19. [20] A. Z. Hameed, S. A. Raj, J. Kandasamy, M. A. Baghdadi and M. A. Shahzad, Chitosan: A Sustainable Material for Multifarious Applications, polymers, 14 (2022) 2335 https://doi.org/10.3390/polym14122335
20. [21] D. S. Kim, X. Yang, J.H. Lee, H. Y. Yoo, C. Park,S. W. Kim, and J. Lee, Development of GO/Co/Chitosan-Based Nano-Biosensor for Real-Time Detection of D-Glucose, biosensors, 12 (2022) 464 https://doi.org/10.3390/bios12070464
21. [22] M. Rizvi, H. Gerengi, and P. Gupta, Functionalization of Nanomaterials: Synthesis and Characterization, ACS Publications. 1 (2022) 1-26. https://doi.org/10.1021/bk-2022-1418.ch001.
22. [23] N. Kumar & S. Sinha Ray, Synthesis and Functionalization of Nanomaterials, Processing of Polymer-based Nanocomposites. 277 (2018) 15-55. https://doi.org/10.1007/978-3-319-97779-9_2.
23. [24] X. Yang, Y. Chen, C. Zhang, G. Duan, S. Jiang, Electrospun carbon nanofibers and their reinforced composites: Preparation, modification, applications, and perspectives, Composites Part B: Engineering. 249 (2022) 110386. https://doi.org/10.1016/j.compositesb.2022.110386.
24. [25] D. Devi Thongam, H. Chaturvedi, Functionalization of Pristine, Metallic, and Semiconducting-SWCNTs by ZnO for Efficient Charge Carrier ransfer: Analysis through Critical Coagulation Concentration, ACS OMEGA. 7 (2022) 14784-14796. https://doi.org/10.1021/acsomega.2c00193.

25. [26] Y. Hyungsub, T. Russ, H. Byungil, Dispersibility study of carbon nanotubes using multiple light scattering: A mini-review, Colloid and Interface Science Communications. 52 (2023) 100686. https://doi.org/10.1016/j.colcom.2022.100686.
26. [27] R. Chamorro, L. de Juan-Fernández, B. Nieto-Ortega, Maria J. Mayoral, S. Casado, L. Ruiz-González, Emilio M. Pérez and D. González-Rodríguez, Reversible dispersion and release of carbon nanotubes via cooperative clamping interactions with hydrogen-bonded nanorings, Chem. Sci. 17 (2018) 4176-4184. https://doi.org/10.1039/c8sc00843d.
27. [28] F. Daneshvar, H. Chen, K. Noh, H. J. Sue, Critical challenges and advances in the carbon nanotube–metal interface for next-generation electronics. Nanoscale Adv. 3 (2021) 942-962. https://doi.org/10.1039/D0NA00822B.
28. [29] G. Stando, S. Han, B. Kumanek, D. Łukowiec, and D. Janas, Tuning wettability and electrical conductivity of single-walled carbon nanotubes by the modified Hummers method. Sci Rep. 12 (2022) 4358. https://doi.org/10.1038/s41598-022-08343-5.
29. [30] A. Krasulina, Y. Myasnikova, V. Saik, M. Predtechensky, and S. N. Smirnov, Improved Characterization of Aqueous Single-Walled Carbon Nanotube Dispersions Using Dynamic Light Scattering and Analytical Centrifuge Methods, ACS OMEGA. 8 (2023) 39233-39241. https://doi.org/10.1021/acsomega.3c04639
30. [31] F. K. Metze, S. Sant, Z. Meng, H. A. Klok, and K. Kaur, Swelling-Activated, Soft Mechanochemistry in Polymer Materials, Langmuir. 39 (2023) 10 3546-3557. https://doi.org/10.1021/acs.langmuir.2c02801.
31. [32] N. Hoang Hiep, L. Sun Hyeok, L. Ui Jin, F. D. Cesar, K. Moonil, Immobilized Enzymes in Biosensor Applications, Materials. 12 (2019) 121. https://doi.org/10.3390/ma12010121.
32. [33] D. K. Manish, Z. Andleeb, A. Mohd, M. Mukesh, A. Laxmi, S. Siddhartha, S. Shruti, U. S. Ram, M. B. Ruben, B. K. Vivek, Improvement Strategies, Cost Effective Production, and Potential Applications of Fungal Glucose Oxidase (GOD): Current Updates, Sec. Food Microbiology. 8 (2017) 1032. https://doi.org/10.3389/fmicb.2017.01032.