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Size-Dependent Sensitivity of Biosensor Based on Carbon Nanotubes

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Abstract
In this work, a biosensor was designed and assembled from carbon nanotubes (CNTs) structure for biomedical applications. The characteristics of this biosensor were determined after the optimization of the performance parameters on synthetic species. In practical use, the sensitivity of the biosensor was determined as a function of the CNTs size and it was found to decrease exponentially with increasing the size of CNTs.

Keywords: Carbon nanotubes; Biosensors; Functional materials; Biomedical applications
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1. Introduction

Carbon nanotubes (CNTs) have emerged as one of the most promising nanomaterials in the field of biosensing due to their exceptional mechanical, electrical, and chemical properties. Their high surface area, excellent electrical conductivity, and ability to interact with biomolecules at the nanoscale make them ideal candidates for enhancing the sensitivity and functionality of biosensors. This article explores the design principles of CNT-based biosensors, evaluates their performance characteristics, and highlights their diverse applications [1-3].

Biosensors are analytical devices that convert a biological response into an electrical signal. A typical biosensor comprises a bioreceptor (such as an enzyme, antibody, or DNA probe), a transducer, and a signal processor [4,5]. CNTs can serve as the transducer material or as a platform for immobilizing bioreceptors, significantly improving the sensor's sensitivity, response time, and limit of detection [6].

CNTs are categorized as single-walled (SWCNTs) or multi-walled (MWCNTs) based on the number of graphene layers rolled into cylinders. Both types have been extensively explored in biosensing, with SWCNTs offering better electronic properties and MWCNTs providing greater surface area and ease of functionalization [7-9].

To interact with biological molecules, CNTs must be functionalized, either covalently or non-covalently. Covalent functionalization involves attaching functional groups directly to the CNT surface via chemical reactions (e.g., oxidation to introduce carboxyl groups). This provides strong binding sites but can disrupt the CNT's electronic structure. While non-covalent functionalization utilizes π–π stacking, van der Waals forces, or hydrophobic interactions to bind biomolecules, preserving the CNT's electrical properties [10-12].

The versatility of CNTs has led to their application in numerous fields. In medical diagnostics, glucose monitoring and enzyme-based sensors using CNTs for diabetic glucose control offer real-time, highly sensitive readings [13]. For cancer biomarkers, CNT-FET sensors detect specific cancer markers such as PSA (prostate-specific antigen) or CEA (carcinoembryonic antigen) at ultralow concentrations [14]. For infectious diseases, CNT immunosensors detect viral or bacterial pathogens like HIV, H1N1, or SARS-CoV-2 quickly and accurately [15]. In the environmental monitoring, CNT biosensors are used to detect environmental toxins, heavy metals (like lead or mercury), and pesticides with high sensitivity, aiding in pollution control and public health protection [16]. In food safety, pathogen detection can be performed by identifying bacteria such as *E. coli* or *Salmonella* in food products [17]. Toxin monitoring can be carried out by detecting aflatoxins or other chemical residues in agricultural produce [18]. In biowarfare and security, CNT-based biosensors can be engineered to detect biological warfare agents like anthrax spores or nerve agents, providing rapid alerts in military or public safety scenarios [19]. In wearable and implantable devices, the integration of CNT sensors into flexible substrates and textiles enables real-time health monitoring in wearable devices. CNTs' biocompatibility also opens the door to implantable biosensors for long-term physiological tracking [20].

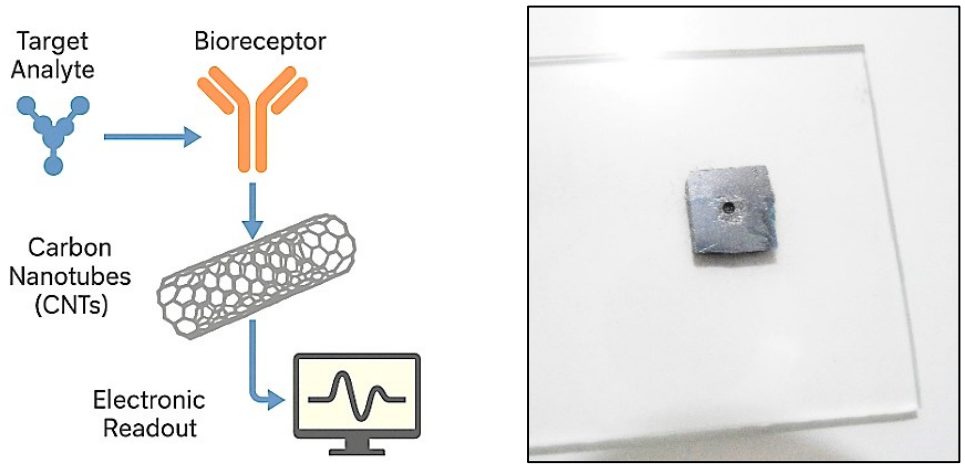
CNT-based biosensors outperform many traditional sensors due to parameters such as the sensitivity as CNTs provide a large surface area-to-volume ratio and superior electron transport, enabling the detection of extremely low concentrations of analytes—often down to femtomolar levels. Second parameter is the selectivity where the use of highly specific bioreceptors (e.g., antibodies, aptamers) ensures strong selectivity [21]. Additionally, surface modifications and nanocomposites (e.g., CNT-metal nanoparticles) can further enhance specificity. Third parameter is the response time as the fast electron transfer and nanoscale proximity of the recognition element to the transducer result in rapid detection, often within seconds to minutes. Stability and reusability are important because CNT biosensors are stable over a wide range of temperatures and pH conditions. However, long-term stability and reusability depend on the bioreceptor's durability and the sensor's anti-fouling characteristics. Owing to their nanoscale dimensions, CNT biosensors can be miniaturized for integration into portable or wearable devices, facilitating point-of-care testing and continuous monitoring [22].

Despite their potential, CNT-based biosensors face several challenges. Toxicity and biocompatibility, while CNTs are generally biocompatible, their safety profile depends on size, purity, and functionalization. Long-term effects in vivo remain under investigation. Manufacturing scalability as producing uniform and defect-free CNTs at industrial scale is still a technical bottleneck. Sensor reproducibility because ensuring consistent performance across batches is difficult due to variability in CNT properties. However, ongoing research in nanofabrication, surface chemistry, and machine learning for signal processing is rapidly advancing the field. Hybrid materials—such as CNTs combined with graphene, polymers, or metal-organic frameworks (MOFs)—offer promising avenues for multifunctional and multiplexed sensing platforms [23].

2. Experimental Part

Depending on the target analyte, CNT biosensors incorporate various bioreceptors such as enzymes used in glucose and urea sensors, antibodies used for detecting pathogens or proteins (immunosensors), nucleic acids employed in detecting DNA/RNA sequences and mutations, and aptamers synthetic oligonucleotides offering high affinity for a broad range of targets. Figure (1) schematically and photographically explains the contents of a CNTs-based biosensor.

CNTs enable multiple modes of signal transduction. Electrochemical is the most common method, measuring changes in current, potential, or impedance. Field-effect transistors (FETs) where CNTs act as the semiconducting channel; changes in conductivity occur upon binding of the analyte. Optical fluorescence or Raman signals are modulated by interactions with analytes. Piezoelectric detects mass change upon analyte binding (less common for CNTs).



(a) (b)

Fig. (1) (a) Schematic explanation, and (b) a photograph of the fabricated CNTs-based biosensor

3. Results and Discussion

Figure (2) illustrates the relationship between the sensitivity of a biosensor and the size of Carbon Nanotubes (CNTs) used within it. A clear downward trend is seen, which indicates an inverse relationship: as the CNTs size increases, the biosensor sensitivity decreases. The most striking observation is the clear inverse relationship between CNTs size and biosensor sensitivity. This means smaller CNTs lead to higher sensitivity, and larger CNTs lead to lower sensitivity. While the overall trend

is decreasing, the curve appears to be somewhat non-linear. The initial drop in sensitivity (from ~5 nm to ~10 nm) seems steeper than the subsequent drops (from ~15 nm to ~25 nm). This suggests that the impact of increasing CNTs size might be more pronounced at smaller sizes. The sensitivity ranges from approximately 90% for the smallest CNTs (~5 nm) down to about 60% for the largest CNTs (~25 nm). This substantial variation highlights the critical role of CNTs size in optimizing biosensor performance. The observed trend can be attributed to several fundamental properties of CNTs and their interaction with the biosensor components and target analytes. As the size (diameter or length, depending on what "size" refers to specifically in this context, but typically diameter for single-walled CNTs or multi-walled CNTs) of CNTs decreases, their surface area-to-volume ratio increases significantly. A larger surface area provides more sites for immobilization of biorecognition elements such as enzymes, antibodies, DNA probes, or other biological recognition elements those can be more densely packed onto the surface of smaller CNTs. This increases the probability of binding with the target analyte. More surface area allows for greater interaction with the target molecules, leading to a stronger and more detectable signal. CNTs are known for their excellent electrical conductivity. A larger surface area can facilitate more efficient electron transfer between the biorecognition element, the target analyte, and the transducer, which is crucial for electrochemical biosensors.

Quantum Confinement Effects: For very small CNTs, quantum confinement effects can become more pronounced, potentially altering their electronic band structure and enhancing their conductivity or semi-conducting properties. These changes might lead to more efficient signal transduction. Defects and Edge Sites: Smaller CNTs might have a higher density of edge sites or defects (depending on their synthesis and purification), which can act as active sites for electron transfer reactions or binding, further contributing to sensitivity.

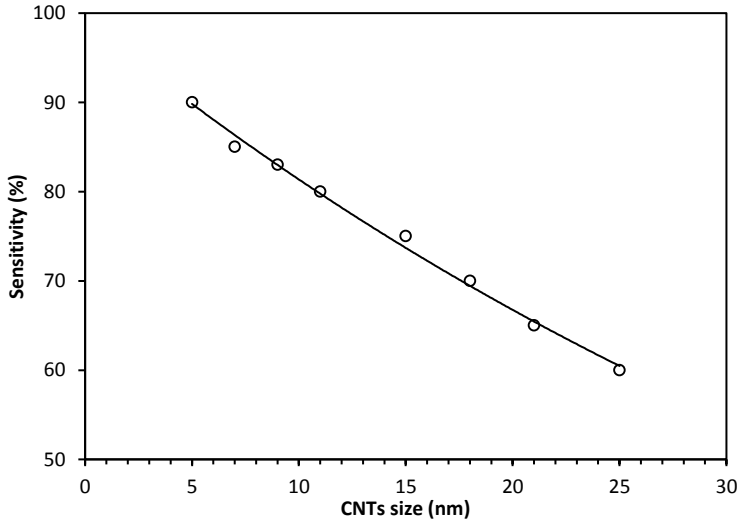


Fig. (2) Variation of biosensor sensitivity with CNTs size

In a biosensor, the target analyte needs to diffuse to the active sites on the CNTs. Smaller CNTs, potentially forming a more porous and accessible network (if they are integrated into a film or composite), might allow for faster and more efficient diffusion of analytes to the binding sites. Larger CNTs might create a less permeable or more tortuous path for analytes. While not directly observable from this graph, the surface properties related to size can also influence biocompatibility. Smaller, more dispersed CNTs might present a more favorable environment for biomolecule immobilization without excessive denaturation, leading to better functional activity. Larger CNTs might aggregate more easily, reducing effective surface area and potentially causing steric hindrance for biorecognition events.

This figure strongly suggests that for this specific biosensor application, using smaller CNTs (in the ~5-10 nm range) is crucial for achieving high sensitivity. There might be an optimal point where sensitivity peaks, and further reduction in size might not yield significant improvements or could introduce other challenges (e.g., synthesis difficulty, purification, aggregation). While smaller CNTs offer higher sensitivity, practical considerations exist. Producing uniform, very small CNTs with high purity can be more challenging and expensive. Smaller CNTs tend to aggregate more readily due to van der Waals forces, making their uniform dispersion in a biosensor matrix difficult, which can reduce their

effective surface area. Although generally considered safe at low concentrations, the biological impact of extremely small nanoparticles is an ongoing area of research. Researchers and engineers designing biosensors based on CNTs must weigh the benefits of enhanced sensitivity from smaller CNTs against the practicalities of their synthesis, integration, and cost.

To gain an even deeper understanding, one would ideally need more information, such as type of CNTs, single-walled (SWCNTs) or multi-walled (MWCNTs) as their properties differ. The type of biosensor is important whether it is electrochemical, optical, or mass-sensitive because the mechanism of signal transduction influences how CNTs size impacts sensitivity. The functionalization method should be considered as well to determine how were the CNTs functionalized (e.g., covalent, non-covalent). The functionalization can significantly impact their interaction with biorecognition elements and analytes. The purity and defect density of the CNTs can also play a role. Both stability and reproducibility are also considered to show how the CNTs size affects the long-term stability and reproducibility of the biosensor.

Figure (2) unequivocally demonstrates that reducing CNTs size is an effective strategy for enhancing biosensor sensitivity. This is primarily attributed to the increased surface area, improved electronic properties, and better mass transport kinetics associated with smaller nanomaterials. This insight is vital for the rational design and optimization of high-performance CNT-based biosensors.

4. Conclusion

Carbon nanotubes have revolutionized the design and capabilities of modern biosensors. Their unique physicochemical properties allow for the development of highly sensitive, selective, and compact sensing devices that span a wide range of applications from healthcare to environmental monitoring. As fabrication techniques improve and biocompatibility is better understood, CNT-based biosensors are poised to become integral to next-generation diagnostic and analytical tools.

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