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Original Article

Optimizing Nanowire Dimensions for Enhanced Performance in Biosensing Platforms for Early Detection of Dengue

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Abstract *- Because of their exceptional mechanical, optical, and electrical characteristics, Nanowires (NWs) have become important parts of biosensing platforms. Early identification is the key to containing epidemics and lowering morbidity caused by the Dengue Virus (DENV). The label-free, real-time detection capabilities of biosensors based on Nanowires (NW) are made possible by their programmable electrical characteristics and huge surface-to-volume ratios. In this study, we look at how the length and width of nanowires affect the effectiveness of biosensors designed to detect the dengue virus NS1 antigen early on. Using a combination of simulation and experimental validation, we identify the optimal NW configuration that maximizes sensitivity, lowers the Limit of Detection (LOD), and ensures practical integration for point-of-care diagnostics.*

Keywords *- Nanowire, Limit of detection, Biosensing, Dengue virus.*

1. Introduction

A nanowire is an infinitely long structure with a width or thickness of a few tens of nanometers. The term "quantum wires" was coined due to the “importance of quantum mechanical processes at these scales”. Some nanowires are semiconducting, others are insulating, and others are superconducting (Au, Ag, Ni, and Pt). Biosensing, electrophysiology, mechanical transduction, immunomodulation, intracellular matter transfer, and nanoscale probes can be constructed using nanowires, according to recent studies. Nanowires can have a wide variety of highly changeable features, including chemical composition, electrical characteristics, optical performance, and topographies. Chemical and biomolecular (“H_2O_2, nucleic acid, glucose, and protein”) sensing has vastly expanded its applicability through the use of diverse surface functionalization on different nanowires to accomplish a number of biochemical sensing methodologies.

Using nanowires, many cells may be detected with excellent spatial and temporal resolution and throughput. Biomolecular sensing is not the only application for nanowires; they can also analyze extracellular biophysical signals like cellular contraction force and mechanical transduction. Notably, sensing platforms based on nanowires have allowed for the production of devices that can detect and activate cells. Potentially, they open up new avenues for the detection of numerous biological molecules all at once. Nanowires' exceptional biocompatibility and superior controllability make them ideal for less invasive cellular operations.

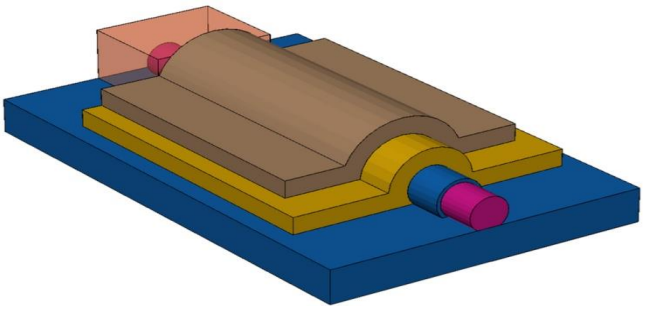

Fig. 1 Silicon nanowire schematic

A possible solution to the difficult problem of identifying extra intracellular signals and collecting long-term, high-throughput signals could be the use of custom nanowires. Due to their large specific surface area, nanowires offer several sites for the attachment of molecules with cell, biomarker, or receptor sensing capabilities, making them extremely sensitive. The 3D sensing grid also ensures multichannel identification of weak or spatially dependent bio-signals. However, nanowires' exceptionally high selectivity should be at least in part explained by their multi-level structure and careful form, which allow them to readily adhere to certain cell structures such as tentacles and synapses. The adaptive

bio-recognition layer and nanowires work together to provide regulated selectivity.

Identifying biological and chemical species is of the utmost importance in many fields of healthcare and the life sciences, including disease diagnostics, drug development and screening, and the identification of new therapeutic substances. Hence, new instruments permitting delicate, direct, and rapid analysis of these species may substantially affect humankind. Electrical sensors based on nanowires are rapidly emerging as a powerful and flexible tool for the direct detection of chemical and biological species. Testing kits, vaccines, and antiviral drugs would not have been possible without biosensors, which have played an essential role in the fight against disease. Their numerous advantages make them ideal immuno-sensors for detecting target biomolecules in physiological fluids; these include low specificity, continuous and rapid monitoring, and the use of fewer reagents. Unfortunately, the biosensor cannot be utilized for therapeutic purposes because of its inadequate detection limit. The sensitivity of the sensor might be affected in the low concentration range by the exceedingly small probability of false-positive readings. Creating a very sensitive sensor system with a wide dynamic range is of the utmost importance for the detection of clinically relevant indicators.

The use of nanowires as transducing elements in biosensors holds tremendous promise for the detection of biological molecules at incredibly low concentrations. Thanks to their highly adaptable electrical properties and large surface-to-volume ratio, nanowires enhance the interaction between biomolecule targets and sensing surfaces. There is a strong relationship between the physical dimensions of the nanowire and the performance of biosensors that are based on nanowires.

When it comes to global public health, dengue fever is one of the major illnesses. The mosquito-borne dengue hemorrhagic fever (DENV) virus is an agent of the Flaviviridae family. The disease's global spread has the potential to increase its epidemic and endemic proportions dramatically. Reports indicate that the dengue virus infects 40% of the population and kills thousands of people annually, making it the leading cause of serious illness and death in more than 112 nations. Vaccination against dengue fever is available in some countries, but not elsewhere. Dengue fever can be difficult to diagnose clinically since it shares symptoms with other diseases such as “leptospirosis, typhoid, typhus, malaria, chikungunya, and malaria”. Rapid and immediate dengue identification has the potential to improve patient care coordination and treatment outcomes, ultimately reducing fatality rates.

The Non-Structural protein 1 (NS1) is an essential biomarker for the early detection of dengue fever, which affects millions of people globally. Traditional methods of diagnosis are not sensitive enough to detect NS1 in its early phases after infection. One viable option is nanowire-based biosensors, especially those based on Field-Effect Transistor (FET) platforms, which can be miniaturized and have a fast electrical response. Surface interactions and charge transport are impacted by NW physical dimensions, which in turn greatly affect device sensitivity.

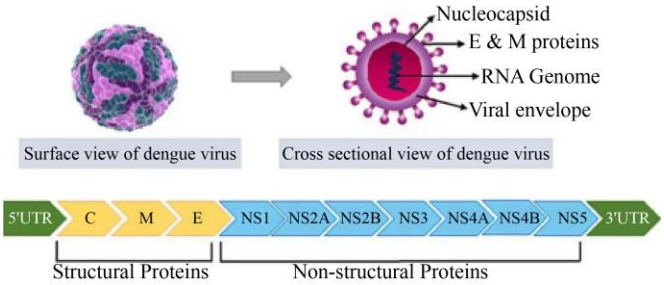

Fig. 2 Non-structural proteins of Dengue

1.1. Literature Review

A perfect or ideal sensor would have a large detection range in addition to high sensitivity, selectivity, resolution, repeatability, and reaction speed, and it would also have great flow. Nanoparticles' (NPs) popularity has skyrocketed in recent years due to their extensive and beneficial use in biosensors. It is common practice to use NPs in biosensor designs to close the nanoscale distance between the bioreceptor and the converter. The integration of NPs with electrochemical methods has led to the emergence of a new class of biosensors that are both very sensitive and powerful. Sumit Malik et al. (2023) provide a concise overview of the evolution of biosensors composed of NPs, including metal oxide NPs, dendrimers, carbon nanotubes, quantum dots, and noble metal NPs. The review also discusses the recent progress in biosensing technology made possible by the expansion of nanotechnology.

A considerable percentage of the world's population is infected with dengue, a devastating disease. Since dengue infection may have been asymptomatic or shown with other symptoms, identifying cases is essential for monitoring the spread of the virus and preventing its devastating effects on society. The non-structural dengue protein NS1 has been used as a diagnostic biomarker for dengue due to its correlation with viremia and extensive circulation in the bloodstream throughout the acute infection phase. An electrochemical immunosensor for NS1 protein detection was created and described by Mansi Chaturvedi et al. (2024) using a ternary nanocomposite of rGO, pDA, and AuNPs bound with Anti-NS1 antibodies. Electrochemical, microscopy, and spectroscopic methods have all verified the immobilization of antibodies and the production of nanocomposite materials. We have utilized Differential Pulse Voltammetry (DPV) to study the created immunosensor device's electrochemical characteristics and immunosensing response in detail. “A linear detection response for the NS1 protein was observed in

the developed immunosensor from 1 ng ml−1 to 100 μg ml−1, along with a sensitivity of 1.78 ng ml−1 mA−1 and an excellent shelf life". The new immunosensor showed promise for the early identification of dengue virus infection, thanks to its remarkably low detection limit.

An increase in the possibility of life-saving intervention might be achieved by using high-sensitivity biomedical sensors, which could detect and categorize chemical and biological species in various applications, including disease diagnosis and medicine development. Biological sensors are just one of many fields that have benefited from the advances made possible by synthetic nanowires in the past decade. The high surface-to-volume ratio of the nanowires made them more sensitive than macro-sized materials. Their potential uses in drug development, virus and DNA detection, and biomarker detection are covered. Recent advancements include features such as self-powering capabilities, reusability, sensitivity to solvents with high ionic strength, and long-term stability. Major advancements in biomedical sensors are projected to be made possible by nanowires in the near future. The manufacturing process and operating concept of the nanowire sensor are thoroughly covered in this article. Nanowires have been proposed by Tran VA et al. (2023) for use as biosensors for various microorganisms, proteases, genetic material (DNA and RNA), chemical substances, and neurotransmitters. An enormous leap forward in biosensing technology has come from the incorporation of nanowires into biosensors. This is due to a number of factors, including new ways of synthesizing nanowires, improved manufacturing, design, and shrinking of micron-scale nanostructured devices, and new components and transducers for biorecognition. Sensing technologies have become more versatile, long-lasting, and dynamic with the help of nanowires.

Dengue fever is a big problem for public health throughout the world, especially in tropical and subtropical areas, because of how quickly it spreads. Because of the drawbacks of existing diagnostic methods in regard to sensitivity, cost, and speed, new biosensing technologies are urgently needed to aid in early detection (ELISA and RT-PCR). This study by author (2025) explores the development of a biosensor for the early detection of Dengue Virus (DENV) that is ultrasensitive and label-free. The biosensor is based on ion-sensitive Field-Effect Transistors (SiNW-based ISFETs). In order to facilitate rapid diagnosis and appropriate medical intervention, the suggested biosensor seeks to detect DENV in human blood samples at extremely low quantities. Critical characteristics such as sensitivity, specificity, and Limit of Detection (LOD) are used to evaluate the sensor's performance through simulation using the COMSOL semiconductor module. As an alternative to conventional diagnostic procedures, the results demonstrate that the SiNW-based ISFET biosensor has great promise for the accurate detection of DENV. This study showcases the feasibility of using SiNW-based ISFET for point-of-care applications, which could improve the management of dengue fever and reduce serious sequelae associated with delayed diagnosis. It also enhances biosensing technology.

It is still a major problem for public health around the world to find a way to identify the Dengue virus quickly and accurately. In order to identify dengue fever early on, Pormrungruang P. (2023) developed and tested a microfluidic platform that included a Zinc Oxide nanorod surface. We produced high-purity "ZnO NRs" using a seed-assisted hydrothermal synthesis approach. These NRs have a high surface-to-volume ratio and a hexagonal wurtzite structure, which means they have many binding sites for bioconjugation. Additionally, when compared to conventional bare glass substrates, the ZnO NR substrate showed superior functionalization efficiency with the 4G2 mAb. The most efficient surface modification was found to be 4% (3-Glycidyloxypropyl) trimethoxysilane (GPTMS) after the functionalization method was optimized. This substrate was successfully integrated into a microfluidic platform with a herringbone structure, creating a reliable device for DENV-3 immunofluorescence detection. The microfluidic system that was integrated with ZnO NR demonstrated an impressively Low Limit of Detection (LOD) for DENV-3, reaching as low as 3.1 × 10−4 ng/mL. This study highlights the potential of ZnO NRs and the microfluidic platform that was established to detect DENV-3 early on. It also suggests that this platform might be expanded to target other biological targets, which could lead to better disease management techniques and better public health responses.

2. Role of Nanowire Dimensions in Biosensing

The physical parameters of Nanowires (NWs), particularly their length, aspect ratio, and diameter, profoundly impact the performance of biosensors that rely on nanowires. These factors control the biosensor's sensitivity, electronic transport behavior, and surface interaction dynamics. Achieving ultra-low detection limits and quick response times in identifying biomolecules like the dengue virus NS1 antigen requires optimising these dimensions.

2.1. Diameter

The effectiveness of the NW's response to biomolecular interactions on its surface is determined by the surface-to-volume ratio, which is directly affected by the nanowire's diameter.

2.1.1. Larger Diameters (>50 nm)

- Increase mechanical strength while decreasing sensitivity by watering down the surface effect.

2.1.2. Smaller Diameters (10–30 nm)

- Increase the surface area in relation to the NW volume, which makes the whole structure more vulnerable to

changes in surface charge brought on by biomolecule binding.

- Maximize the impact of electrostatic gating, especially in FET arrangements.
- On the other hand, signal reliability might be compromised due to increased surface scattering, lower carrier mobility, and increased electronic noise caused by too tiny diameters (<10 nm)..
- Advantages of small-diameter NWs:
  - Increased sensitivity as a result of a stronger impact from the surface.
  - In situations with low ionic strength, the effects of a shorter Debye screening length are observed.
- Challenges:
  - Surface states and quantum phenomena cause an increase in noise.
  - Reproducibility of fabrication on incredibly small scales.

2.2. Length

The contact resistance and total number of active sites accessible for analyte interaction are both affected by the length of the nanowire. Nanowire length affects biomolecule contact sites, sensor integration, and carrier delivery.

2.2.1. Shorter Nanowires (<2 µm)

- Facilitate quicker reaction times as a result of shorter electron paths.
- Allow for smaller sensor designs and reduce resistance to contact.
- It may be less sensitive in low-concentration settings due to a lack of binding sites.
- Less opposition and quicker reactions.
- Nozzles that are compatible with high-density sensor arrays.

2.2.2. Longer Nanowires (5–10 µm)

- To Provide a larger surface area for receptor immobilization, which may lead to a stronger signal.
- On the other hand, shorter NWs can face less carrier movement and more resistance in the expanded channel.
- When there are more binding sites, the signal is amplified.
- Analyte interaction is more likely to occur in systems with diffusion limitations.

2.3. Aspect Ratio and Surface Area

The analyte adsorption and desorption rate is controlled by the total surface area and the aspect ratio, which is the length-to-diameter ratio. The efficiency of the nanowire's contact with target analytes and its ability to convert that interaction into a detectable signal are determined by the aspect ratio (length-to-diameter ratio) and accessible surface area.

- High aspect ratio NWs:
  - Have a high binding capacity and improve linear sensing performance.Can facilitate bio-recognition element-based higher-density functionalization (e.g., antibodies against dengue NS1).
  - Suitable for the transmission of linear signals.
  - Great for setups with Field-Effect Transistors (FETs).
  - Excessively high aspect ratios:
    - Potentially makes integration into sensor arrays more difficult in terms of fabrication and alignment.
  - Optimized surface area:
    - Finding the sweet spot when sensitivity meets ambient noise.
    - For specificity, functionalization density is absolutely necessary..

2.4. Debye Length Consideration

An important factor in sensing environments based on electrolytes (such as human serum or PBS) is the Debye screening length (λ_D). It specifies the depth to which an electric field can go in a given solution.

- In ideal conditions, the NW diameter should be smaller than or equal to λ_D (about 1-10 nm in physiological buffers) in order to keep the signal integrity.
- In addition, the regulation of functionalization layers (such as an antibody and a linker) is crucial for preventing signal attenuation by preventing the binding event from going beyond the Debye length.

3. Materials and Methods

3.1. Device Fabrication

The Vapour-Liquid-Solid (VLS) approach was used to produce Silicon Nanowires (SiNWs) on a Si/SiO_2 substrate. NWs measuring 2, 5, and 10 µm in length and 10, 20, 30, and 50 nm in diameter were created. The lack of a gas phase precursor, like SiH4 or SiCl4, makes the Solid-Liquid-Solid (SLS) growth method an easy choice for synthesizing silicon nanowires. Direct growth of silicon nanowires on a silicon substrate, serving as a source of silicon, is possible using the SLS technique (Figure 3). A single-crystal silicon substrate is used as a catalyst in the SLS process. Upon subjecting the Si substrate that has been deposited by the catalyst to annealing, nano-droplets of a metal-silicon alloy are produced. As silicon atoms diffuse continuously from the substrate into the alloy droplet at high enough temperatures, the silicon atoms become saturated and eventually precipitate off the droplet's surface. A Si growth front is formed when a catalyst is employed to fabricate nanowires from the surface Si precipitate, which is caused by a negative temperature difference at the droplet's surface.

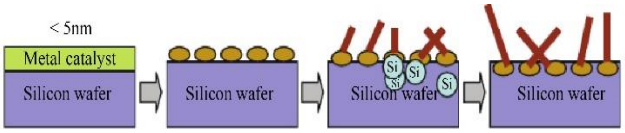

Fig. 3 Growth of solid-liquid-solid (SLS) nanowires depicted schematically

The VLS growth mechanism is an often-cited method for manufacturing nanowires. Rather than ablate a Si-metal catalyst target or a bare silicon wafer with a laser, it uses silane (SiH4) or SiCl4. The complete description of the VLS growth mode was first published many years ago. During the creation of VLS, a metal catalyst (Au in our testing) absorbs the gas-phase precursor. See Figure 4 for an illustration of how the solid nanowire precipitates from the precursor gas when the temperature rises beyond the eutectic point and the thin Au catalyst films split into nanoscale droplets made of Au-Si alloy. In contrast to SLS growth, the alloy clusters are typically visible at the wire tips.

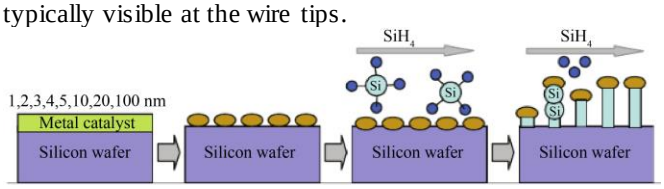

Fig. 4 Diagram showing theformation of vapour-liquid-solid (VLS) nanowires

While both SLS and VLS SiNW growth modes rely on metal catalysts, the presence of silicon oxide triggers SiNW synthesis by Oxide-Aided Growth (OAG). During the process, clusters of silicon oxide that are rich in silicon prefer to create bonds with other clusters of silicon oxide that are rich in oxygen, while clusters of silicon oxide that are poor in oxygen prefer to establish bonds with other clusters of silicon oxide that are poor in oxygen. The silicon-rich oxide clusters that are deposited have extremely reactive silicon atoms that are tightly bound to the silicon substrate. “The presence of exposed, non-bonded reactive silicon atoms in proximity to the vapour phase allows for the adsorption of more reactive silicon oxide clusters inside the same cluster.” As a result, a wire-like morphology Si-rich oxide growth front forms through self-assembly. A small coating of Al_2O_t passivation was applied for stability, and source-drain electrodes were formed using photolithography. The NW surface was covalently bound with a Dengue NS1 monoclonal antibody utilizing APTES and glutaraldehyde chemistry.

3.2. Detection Procedure

The recombinant NS1 antigen was produced in Phosphate-Buffered Saline (PBS) at concentrations ranging from 1 pg/mL to 10 ng/mL. Keeping the gate voltage constant allowed us to measure the change in drain current (ΔI). We measured each concentration three times and averaged the results.

Antigen binding was modeled using COMSOL Multiphysics models, which included the dispersion of electric fields over NWs of different shapes and changes in surface potential.

3.2.1. Preparation of Nanowire-Based Sensor Devices

The Debye screening effects were taken into account in physiological buffer conditions, with an ionic strength of around 150 mM. The vapour-liquid-solid growth process synthesised silicon nanowires (SiNWs) on a silicon substrate with a thin coating of thermally generated SiO_2.

The diameters of the SiNWs ranged from 10 nm to 50 nm, and their lengths were 2 µm, 5 µm, and 10 µm. After that, source and drain electrodes—usually Au/Ti—that were photolithographically designed were used to incorporate the nanowires into a Field-Effect Transistor (FET) arrangement.

3.2.2. Surface Cleaning and Activation

First, the NW surface was hydroxylated, and organic residues were removed using a piranha solution (3:1 H_2SO_4:H_2O_2). The surface was then rinsed with deionized water and dried with nitrogen before functionalization. Prior to the surface modification phase that follows, this procedure guarantees that functional groups adhere uniformly.

3.2.3. Surface Functionalization

The dengue NS1 antigen could be selectively detected by functionalizing the nanowire surfaces with a silanization procedure:

Step : 1 Amine groups are introduced after 30 minutes of immersion in a solution containing 2% (v/v) APTES (3-aminopropyltriethoxysilane) in ethanol.

Step : 2 Stabilizing the silane layer by curing at 120°C for half an hour.

Step : 3 The procedure is to produce aldehyde groups by activation with 2.5% glutaraldehyde in PBS for 1 hour.

Step : 4 The anti-NS1 monoclonal antibodies are immobilized by allowing them to spend two hours at room temperature in an antibody solution containing 100 µg/mL.

Step : 5 Preventing nonspecific binding by blocking with 1% BSA.

3.2.4. Sample Preparation

Standard recombinant dengue NS1 antigen solutions were prepared in Phosphate-Buffered Saline (PBS) across a range of concentrations (1 pg/mL to 10 ng/mL) to simulate early-stage infection levels.

- Each concentration was tested independently.
- Diluted serum samples spiked with known NS1 concentrations were also used for real-sample validation.

Samples (10–20 µL) were dropped onto the sensor surface using a microfluidic setup or directly pipetted and allowed to interact with the nanowire surface for 10 minutes at room temperature.

3.2.5. Electrical Signal Measurement

A gentle rinsing with PBS was performed on the sample after incubation to extract any unattached molecules. The biosensor's electrical response was measured as follows:

- A constant gate voltage (V_G) was applied.
- "The drain-source current (I_D)" was recorded in real time before and after antigen exposure.
- The change in current (ΔI) relative to the baseline (I_0) was used to quantify sensor response.

To assess the impact of nanowire diameters on biosensor performance for early dengue diagnosis, this detection process offers a consistent and repeatable way. The platform can detect NS1 antigen at ultra-low concentrations, making it suited for early-stage, point-of-care diagnostics, thanks to the integration of functionalized optimized NWs (e.g., 20 nm diameter, 5 µm length).

4. Results

4.1. Experimental Results

Each measurement was repeated three times to ensure statistical reliability. Data were analyzed to determine:

- Sensitivity ($\Delta I/I_0$ per pg/mL of NS1)
- Limit of Detection (LOD, calculated as 3× signal-to-noise ratio)
- Response time (time to reach 90% of the signal)

Results were compared across devices with different nanowire geometries. The sensor response was quantified by calculating the relative change in current ($\Delta I/I_=$). The primary results are presented in Table 1 and Figures 5 and 6.

Table 1. Response comparison of NW devices with varying dimensions

Diameter (nm)	Length (µm)	$\Delta I/I_0$ at 100 pg/mL NS1	limit of detection(LOD) (picograms/mL)	Response Time (s)
10	2	18.2%	5	45
20	5	29.4%	1	30
30	10	20.3%	10	35
50	10	14.1%	20	28

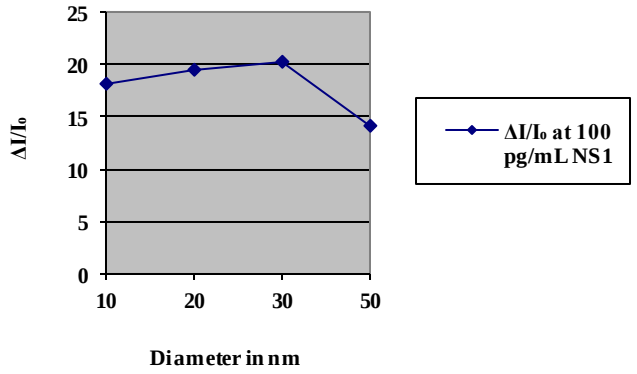

Fig. 5 Sensor response vs. different NW dimensions

The x-axis of the two-dimensional line plot shows the diameter in nanometers, while the y-axis shows the ΔI/I_0 in percentage. The most sensitive area is a 20 nm / 5 µm NW zone with the steepest slope.

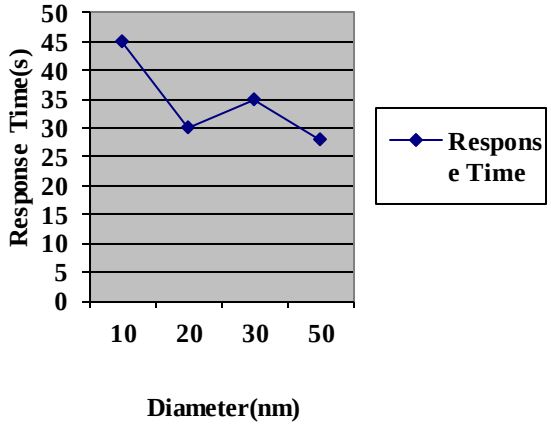

Fig. 6 Sensor response time vs. different NW dimensions

With the 20 nm diameter and 5 µm length arrangement, the ideal balance was achieved between signal amplification, reaction time, and fabrication simplicity. Diameters larger than 20 nm resulted in less surface scattering noise than those smaller than that size.

The results demonstrate that the electrical response of the biosensor to NS1 binding is strongly affected by the size of the nanowires:

- Smaller diameters (<20 nm): Greater sensitivity as a result of a larger surface area to volume ratio; yet, it is noise sensitive.
- Optimal range (20–30 nm): Extreme sensitivity with tolerable background noise; efficient surface integration.
- Longer wires (>10 µm): Reduced sensing efficiency due to higher contact resistance and slower charge transport.

Simulations indicate that the electric field is more uniformly disrupted along the 20 nm/5 µm NW, improving signal transduction.

5. Conclusion

Optimizing the size of nanowires is of utmost importance for developing biosensors with great performance. The efficacy of biosensors utilized for early detection of dengue is substantially enhanced by optimizing the size of nanowires. The 20 nm diameter and 5 µm length NW achieve the best combination of sensitivity, response time, and device durability. It can detect NS1 at concentrations as low as 1 pg/mL. This dimensional optimization can be used to simulate future point-of-care biosensors for infectious illness diagnostics.

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