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Review **Article**

NANOWIRES IN DIAGNOSIS OF ALZHEIMER'S DISEASE

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ABSTRACT
Alzheimer's disease (AD) is a progressive neurodegenerative disorder marked by the accumulation to improving therapeutic outcomes, yet current diagnostic tools are often invasive, expensive, and lack sufficient sensitivity for early-stage detection. Recent advancements of amyloid-beta plaques and tau tangles, leading to cognitive decline and neuronal loss. Early diagnosis is critical in nanotechnologyparticularly the application of nanowireshave opened promising avenues for the development of highly sensitive, non-invasive diagnostic tools for AD. Nanowires, owing to their unique one-dimensional structure, high surface-to-volume ratio, and tunable electrical and optical properties, serve as powerful platforms for biomarker detection. Various types of nanowires, including gold, silicon, carbon, and conducting polymer nanowires, have been engineered to detect AD-related biomarkers such as amyloid-beta and tau proteins through electrochemical sensing, field-effect transistor (FET) configurations, fluorescence, and surface-enhanced Raman spectroscopy (SERS). Despite significant progress, challenges remain in ensuring biocompatibility, reproducibility, and clinical scalability. This review highlights the mechanisms, materials, and sensing strategies used in nanowire-based diagnostics for Alzheimer's, emphasizing their potential to revolutionize early detection and enable more effective disease management.

Key words: Alzheimer's disease, Biomarkers, Gold Nanowires, Silicon Nanowires, Carbon Nanowires.

INTRODUCTION
Alzheimer's disease (AD) is a progressive neurodegenerative disorder that primarily affects memory, thinking, and behavior. It is characterized by the accumulation of amyloid plaques and tau tangles in the brain, which leads to the dysfunction and death of neurons[12]. Early detection of Alzheimer's is critical for effective intervention and therapy, but current diagnostic techniques, such as neuroimaging and cerebrospinal fluid (CSF) biomarkers, remain costly, invasive, and lack the sensitivity needed for early-stage diagnosis [8].
Recent advancements in nanotechnology, particularly the use of nanowires, are offering innovative, non-invasive, and highly sensitive methods for detecting biomarkers associated with Alzheimer's[1]. The applications of nanowires in the diagnosis of Alzheimer's focus on their unique properties, detection mechanisms, and potential clinical applications.

NANOWIRES AND THEIR ROLE IN ALZHEIMER'S DIAGNOSIS
Nanowires are one-dimensional structures with diameters in the nanometer range, typically in the range of 1–100 nm, and they exhibit distinct physical, chemical, and optical properties compared to bulk materials[18]. These properties make nanowires particularly useful in bio-sensing and diagnostic applications.

BIOMARKER DETECTION:
Nanowires can be functionalized to bind specifically to amyloid-beta (Aβ) peptides, tau proteins, or other biomarkers associated with Alzheimer's pathology[3]. Their high surface-to-volume ratio and electrical properties enable them to detect these biomarkers at extremely low concentrations, even in complex biological samples like blood, CSF, or saliva [5].

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Electrochemical Sensing:
Nanowires can be integrated into electrochemical sensors that detect changes in the current or voltage when they interact with biomarkers[2]. The binding of amyloid-beta peptides to functionalized nanowires induces measurable changes in the electrical properties of the nanowires, enabling sensitive detection of early-stage Alzheimer's[11].
Surface-Enhanced Raman Spectroscopy (SERS):
When coupled with SERS, nanowires can significantly enhance the Raman signals from biomolecules, allowing for the detection of Alzheimer's-related proteins with high sensitivity and specificity[7]. This method could allow for non-invasive detection from samples like blood or saliva[14].
Fluorescence-Based Detection:
Nanowires can be designed to emit specific fluorescence signals when they bind to Alzheimer's-related biomarkers[10]. This fluorescence can then be detected by specialized imaging systems, providing a quick and non-invasive diagnostic tool[12].

TYPES OF NANOWIRES USED IN ALZHEIMER'S DIAGNOSIS

Gold Nanowires (AuNWs):
Properties: Gold is biocompatible, stable, and easy to functionalize, making gold nanowires an ideal candidate for biosensing[1].
Applications: Gold nanowires have been widely used in electrochemical and optical sensors for detecting amyloid-beta peptides and tau proteins[2]. Their high conductivity allows for sensitive electrical measurements when biomolecules interact with the nanowire surface[7].
Silicon Nanowires (SiNWs):
Properties: Silicon nanowires have excellent mechanical properties, are easily synthesized, and are cost-effective [3].
Applications: SiNWs are used for their high surface area and ease of functionalization[5]. They are commonly used in field-effect transistors (FETs) for real-time biomarker detection in Alzheimer's diagnostics[13].
Carbon Nanowires (C-NWs):
Properties: Carbon-based nanowires are chemically stable, flexible, and electrically conductive[16].
Applications: Carbon nanowires are often used in sensors and biosensors for detecting Alzheimer's-related biomarkers, especially in combination with carbon nanotubes (CNTs) for enhanced performance [17].
Conducting Polymer Nanowires:
Properties: These nanowires combine the conductivity of metals and the versatility of polymers, offering excellent sensitivity to environmental changes[12].
Applications: Conducting polymer nanowires have been utilized for their ability to undergo significant changes in electrical conductivity upon binding with specific proteins, enabling highly sensitive detection of Alzheimer's-related biomarkers[13].

NANOWIRE-BASED SENSING PLATFORMS FOR ALZHEIMER'S DIAGNOSIS

Field-Effect Transistor (FET)-based Sensors:
Field-effect transistors (FETs) built using nanowires have gained significant attention for Alzheimer's diagnosis [5]. In this configuration, the nanowires serve as the channel of the transistor, and the binding of Alzheimer's-related proteins (such as amyloid-beta) to the nanowire surface results in a change in the electrical current, which is then detected and analyzed[3]. These sensors have demonstrated impressive sensitivity, with detection limits reaching picomolar concentrations of biomarkers[13].
Optical and Fluorescence-based Sensors:
Nanowires, particularly those made of gold or silver, exhibit surface plasmon resonance (SPR), which can be leveraged for the detection of Alzheimer's biomarkers[6]. When functionalized with antibodies specific to amyloid-beta or tau, these nanowires can detect the presence of these proteins in blood or CSF samples by monitoring changes in light scattering or fluorescence intensity[10].
Impedance-based Biosensors:
Nanowire-based impedance sensors are another promising diagnostic tool for Alzheimer's[11]. The impedance (resistance to electrical flow) of the nanowires changes when they interact with specific Alzheimer's biomarkers, enabling highly sensitive detection in real-time[12].

CHALLENGES AND FUTURE DIRECTIONS

Biocompatibility and Toxicity:
Although nanowires offer great potential in diagnostics, their biocompatibility and potential toxicity remain concerns[19]. Careful consideration must be given to the materials used in nanowire synthesis and their interaction with biological systems, as certain types of nanowires may cause toxicity or inflammation if not properly functionalized[15].
Standardization and Reproducibility:
The reproducibility and standardization of nanowire-based diagnostic platforms are key challenges[8]. Variations in nanowire synthesis and functionalization can lead to inconsistent results, affecting the reliability of diagnostic tests[13].

Integration with Existing Diagnostic Methods:

The integration of nanowire-based sensors with existing diagnostic techniques such as neuroimaging and biomarker assays will be crucial for achieving accurate, reliable, and non-invasive Alzheimer's diagnostics[12]. Combining these technologies could provide a holistic approach to early detection, ensuring that Alzheimer's is diagnosed at the earliest and most treatable stage[9].

Scalability for Clinical Use:

While nanowire-based sensors have shown promise in laboratory settings, scaling these technologies for widespread clinical use remains a significant hurdle[6]. Mass production of high-quality nanowires, the development of user-friendly devices, and regulatory approval are essential for the successful clinical translation of these technologies[8].

CONCLUSION

Nanowire-based sensors represent a cutting-edge technology for the diagnosis of Alzheimer's disease[1]. Their unique properties, such as high surface area, sensitivity, and ease of functionalization, allow for the development of highly sensitive and non-invasive diagnostic platforms[5]. While challenges remain, particularly regarding biocompatibility and standardization, the continued progress in nanotechnology and biosensing holds promise for transforming Alzheimer's diagnosis, potentially enabling early detection and improving patient outcomes[13]. Future research will likely focus on improving the sensitivity and specificity of these sensors, as well as their integration into real-world clinical settings[10].

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