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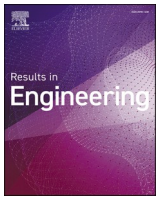

Review article

Application of Nanobiosensor engineering in the diagnosis of neurodegenerative disorders

Thikra S. Dhahi [a], Alaa Kamal Yousif Dafhalla [b], A. Wesam Al-Mufti [h], Mohamed Elshaikh Elobaid [c], Tijjani Adam [c,d,f,*], Subash C.B. Gopinath [e,g,i,j]

[a] Health and Medical Technicals College, Southern Technical University, Basrah, Iraq
[b] Department of Computer Engineering, College of Computer Science and Engineering, University of Ha'il, KSA, Saudi Arabia
[c] Faculty of Electronic Engineering & Technology, Universiti Malaysia Perlis, 02600 Arau Perlis, Malaysia
[d] Institute of Nano Electronic Engineering, Universiti Malaysia Perlis, 01000, Kangar, Perlis, Malaysia
[e] Center for Global Health Research, Saveetha Medical College & Hospital, Saveetha Institute of Medical and Technical Sciences (SIMATS), Thandalam, Chennai 602 105, Tamil Nadu, India
[f] Micro System Technology, Centre of Excellence (CoE), Universiti Malaysia Perlis (UniMAP), Perlis, Malaysia
[g] Department of Technical Sciences, Western Caspian University, Baku AZ 1075, Azerbaijan
[h] Department of Medical Physics, College of Science, Al-Karkh University of Science Al-Hadi University College, Baghdad, 10011, Iraq
[i] Faculty of Chemical Engineering & Technology, Universiti Malaysia Perlis (UniMAP), 02600 Arau, Perlis, Malaysia
[j] Department of Computer Science and Engineering, Faculty of Science and Information Technology, Daffodil International University, Daffodil Smart City, Birulia, Savar, Dhaka 1216, Bangladesh

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ABSTRACT

Neurodegenerative diseases like Alzheimer's disease and Parkinson's disease are hard to diagnose and treat early. They are characterised by progressive loss of neuronal function and structure leading to crippling cognitive, motor and psychiatric impairments. In recent years, nanobiosensor engineering has emerged as a promising way to address the limitations of traditional diagnostic methods for neurodegenerative diseases. Nanobiosensors which combine nanotechnology and biosensing principles can detect disease specific biomarkers with high sensitivity and specificity to enable early and accurate diagnosis. One of the key advantages of nanobiosensors in diagnosing neurodegenerative diseases is their ability to detect and quantify specific proteins or molecules that are biomarkers for these conditions. For example, accumulation of amyloid beta peptides and hyperphosphorylation of tau protein are hallmarks of Alzheimer's disease. Nanobiosensors can be designed to selectively bind to these biomarkers providing rapid and non-invasive method for early disease detection. This enables more targeted and personalized treatment approaches. Furthermore, nanomaterials have shown potential in biosensing applications due to their unique physical, optical, and electrical properties. Their small size, large surface-to-volume ratio, and tunable properties enable them to interact with biological molecules in remarkable ways. One notable property is their ability to be functionalized with molecular beacons, reporter molecules, pacification layers, and targeting biomolecules, creating highly sensitive and specific biofunctional nanoprobes. This review aims to explore the promising role of nanobiosensor engineering in the early diagnosis and management of neurodegenerative disorders.

1. Introduction

Neurodegenerative disorders are a group of conditions. They impact central nervous system. These disorders lead to gradual decline. The decline is of nerve cells [1]. The gradual onset and progression of neurodegenerative disorders make early diagnosis challenging [2]. The subtle initial symptoms often mimic other conditions. Lack of definitive diagnostic tools exacerbates the problem. Patients and doctors both may misinterpret early warning signs. Misdiagnosed or undiagnosed patients lose valuable treatment time. Early intervention can slow disease progression. Research focuses on identifying biomarkers [3]. Neurodegenerative diseases, such as Alzheimer's and Parkinson's continue to rise

* Corresponding author. Faculty of Electronic Engineering & Technology, Universiti Malaysia Perlis, 02600 Arau Perlis, Malaysia
E-mail address: tijjani@unimap.edu.my (T. Adam).

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[3]. This trend highlights urgency of early detection efforts. Moreover, the burden on healthcare systems becomes substantial [4]. An integrated approach could significantly enhance outcomes. Furthermore, the development of nanobiosensors for the diagnosis of neurodegenerative disorders is active area of research [5]. This field holds promise for early detection of ailments such as Alzheimer's and Parkinson's disease. Nanobiosensors employ nanotechnology to detect biological markers [6]. They do with remarkable sensitivity. Specificity is also achieved. Researchers are exploring their potential [7]. These tools could revolutionize healthcare. Enabling timely and accurate diagnoses is crucial In the future. These advancements could lead to more effective treatments. Identifying diseases at earlier stages is essential [8]. It may become possible to slow or even halt progression. Enhancing patient outcomes is key goal of this cutting-edge research. The use of nanobiosensors that utilize nanotechnology is being explored as promising method for diagnosing diseases of the central nervous system. Nanobiosensors are designed to detect specific biomarkers [9]. These biomarkers are associated with neurological conditions. The central nervous system presents unique challenges for diagnosis. Nanobiosensors offer a potential for earlier detection [10]. Early detection can significantly improve patient outcomes. Traditional diagnostic methods are often invasive [11]. They can also be expensive and less accurate. Nanobiosensors could provide a non-invasive and cost-effective alternative [12]. Their development is still in the early stages. More research is necessary to fully understand their capabilities and limitations. There are ethical considerations to take into account. Nanoparticle-based biosensors have also demonstrated improved biocompatibility and reduced toxicity compared to traditional sensors [13]. Researchers are using nanobiosensors to enhance detection of neurodegenerative disorders [14]. Research in neurodegenerative disorders aims to identify genetic and environmental risk factors linked to Alzheimer's and Parkinson's disease development [15]. Genetic studies reveal gene mutations and variations [16]. These increase individual's susceptibility to certain diseases. Environmental factors like toxins and pollutants are suggested to contribute to disease onset [17]. Nanobiosensors represent cutting-edge technology in medical diagnostics [18]. They offer high sensitivity and specificity for detecting biomarkers of neurodegenerative diseases. These diseases such as Alzheimer's and Parkinson's, present significant challenges for early diagnosis [19]. Biomarkers are often present in low concentrations in body fluids due to their complex nature, high dynamic range of protein concentrations, diverse post-translational modifications, and biological variability in human samples [20]. This makes detection difficult with conventional methods. To overcome these challenges, highly selective protein enrichment and separation techniques, such as affinity-based capture methods and advanced liquid chromatography-mass spectrometry methods, can be implemented [21]. Using a panel of biomarkers instead of a single biomarker can increase the sensitivity and specificity of the assay, as different biomarkers may provide complementary information about the disease or physiological state being investigated [22]. Biosensors and other advanced detection technologies can also help overcome matrix interference and enhance the specificity of biomarker measurements in physiological fluids [23]. Nanobiosensors exploit unique properties of nanomaterials. These properties include increased surface area and reactivity [24]. They enhance interactions between biomarkers and the sensor's surface. This leads to improved detection limits. Therefore enabling earlier diagnosis. The fundamental principle behind nanobiosensors involves the use of biorecognition elements [25]. These elements can include antibodies, aptamers or enzymes. They specifically bind to target biomarkers. Once binding occurs, a transducer converts this event into a measurable signal. This signal can be electrical optical, or mechanical. Different types of nanobiosensors are being explored. These include electrochemical optical and piezoelectric sensors [26]. Each type offers distinct advantages. For example, electrochemical sensors are highly sensitive and can be miniaturized [27]. Optical sensors provide real-time monitoring. Piezoelectric sensors are known for high accuracy [28]. Recent advancements in nanotechnology have led to integration of nanoparticles with traditional biosensors [29]. Nanoparticles can improve sensor performance [30]. They can also allow for multiplexed detection of multiple biomarkers simultaneously. This is crucial for comprehensive diagnostic assessment. Challenges remain in the field. These include ensuring the stability and reproducibility of nanobiosensors [31]. Additionally the complexity of biological samples can interfere with detection. Nanobiosensors hold promise for revolutionizing the detection of neurodegenerative diseases [32]. Their enhanced sensitivity and specificity can lead to earlier diagnosis and better patient outcomes. Ongoing research aims to overcome current limitations. This will pave way for widespread clinical adoption in near future. This review explores applications of nanobiosensor engineering in neurodegenerative disorder diagnosis. This review aims to explore applications of nanobiosensor for the diagnosis of Alzheimer's disease. It also examines the use of nanobiosensors in diagnosing Parkinson's disease. As Alzheimer's disease and diagnosing Parkinson's disease are most closely related to aging they represent two critical areas of study within the field of neurology [33]. Both disorders have unique sets of symptoms. Alzheimer's disease primarily affects memory and cognitive function [34]. Parkinson's disease mainly impacts motor skills [35]. Alzheimer's disease is characterized by the accumulation of amyloid plaques in the brain [36]. This leads to neuronal death. Patients often experience difficulties with language disorientation, mood swings and behavioral issues. In contrast Parkinson's disease is primarily marked by depletion of dopamine in brain [37]. Motor symptoms such as tremors, rigidity and bradykinesia are typical. Early diagnosis can dramatically improve the quality of life for patients. Nanobiosensors offer a promising approach for early detection due to their high sensitivity and specificity [38]. The conventional diagnostic techniques have low sensitivity and specificity. They also may not detect the disease at an early stage. Conventional diagnostic techniques often suffer from limited sensitivity and specificity, resulting in a high rate of false-positive and false-negative results. For example, the detection limit of enzyme-linked immunosorbent assay for cancer biomarkers such as prostate-specific antigen is typically in the range of 1–10 ng/mL [39]. In contrast, nanobiosensors incorporating quantum dots, carbon nanotubes, or gold nanoparticles have reported detection limits as low as 10 pg/mL for the same biomarkers, demonstrating the potential for significantly improved sensitivity using nanomaterial-based approaches [40]. However, the construction of nanobiosensors involves complex processes [41]. First the choice of nanomaterial is critical. It determines the sensor's sensitivity and efficacy. Next, the biological element must be carefully selected to ensure specificity. Lastly the functionalization process attaches the biological element to the nanomaterial. This step is vital to maintaining the bioactivity of the sensor. Table 1 presents a nanobiosensor designed for the detection of neurodegenerative diseases. The sensitivity, specificity, and accessibility of nanobiosensor-based diagnostic platforms could be further improved by integration with cutting-edge technologies like photonic crystal [42], microfluidic [43], and wearable [44]. These devices find applications in disease diagnosis, environmental monitoring, and drug discovery [45]. Optical microscopy can be considered as one of the available techniques for developing the biosensors. Although optical microscopy alone cannot measure the size of individual bioparticles, but combination of nanoparticle tracking analysis with surface-sensitive optical imaging allows anyone to quantify the size of biological particles attached to lipid bi-layers [43]. Also, particle size, shape and orientation can be determined by measuring optical cross-sections of nanoparticles in wide field extinction microscopy for different light wavelengths and excitation polarization. It has been mentioned that electrochemical catalysis is improved by strengthening the electrodes with carbon nanotubes and silver nanoparticles, leading to remarkable detection limits in the micromolar range for both compounds as well as outstanding selectivity and sensitivity [46]. The integration of cutting-edge technologies, such as photonic crystals, microfluidics, and wearable systems, can significantly enhance

Table 1
Nanobiosensor for neurodegenerative diseases detection.

Sensor probe	Type of sensor	Limit of detection	sensitivity	specificity	Ref.
Polysaccharide	Optical sensor	70 nM	–	–	[47]
Chemical	Microcantilever array	6 ng	–	–	[48]
Aptamer	Electrochemical sensor	10 pM	–	–	[49]
Antibody	ELISA	1 ng/mL	–	–	[50]
Sample (Peptide)	Surface plasmon resonance dased response	–	–	–	[51]
Sample (Antibody)	Conjugation technology approach	13057.0 pg/mL	–	–	[52]
(sample Antibody	Graphical plot analysis	Derive from gut	–	–	[53]
Indirect	Ultrasonication method	Cerebrospinal fluid	–	–	[54]
Antibody	ELISA	Plasma	–	–	[55]
Aptamer	Colorimetric	1 nM	–	–	[56]
Aptamer	Surface plasmon resonance	0.64 fM	–	–	[57]
Antibody	Voltammetry	10 aM	–	–	[58]

the sensitivity, specificity, and accessibility of nanobiosensor-based diagnostic platforms. Malmir's (2022) [182] research on the characterization of nanoparticles with optical fluidic cavities underscores the potential of microfluidic technology in achieving precise control and manipulation of nanoparticles, thereby improving the accuracy and efficiency of biosensing processes. Additionally, the 2023 study published in *BioMedical Engineering OnLine* [183] highlights the role of AI-based technologies in optimizing diagnostic platforms, allowing for real-time data analysis and improved decision-making. By combining these advanced technologies, nanobiosensors can be designed to offer superior diagnostic capabilities, with higher sensitivity and specificity, while remaining accessible for practical applications, such as wearable diagnostics. This multidisciplinary approach paves the way for more accurate and user-friendly diagnostic tools that can be widely implemented in various healthcare settings.

1.1. Alzheimer's disease

Alzheimer's disease a progressive neurodegenerative disorder, is characterized by cognitive decline and memory impairment [59]. This disorder affects communication skills reasoning abilities and other vital functions. Early signs include difficulty remembering recent events or conversations, challenges in problem-solving and confusion about dates or places [60]. As Alzheimer's progresses, symptoms intensify, including memory loss and deteriorating language skills, making it difficult for patients to find the right words [61]. Behavioral changes can also occur ranging from mood swings to agitation or aggression [62]. The root causes of Alzheimer's disease are complex [63]. Genetic, environmental and lifestyle factors intertwine leading to the hallmark amyloid plaques and tau tangles in the brain [64]. These abnormalities disrupt neuron function and trigger a cascade of cellular damage. The hippocampus, an area critical for memory formation is severely affected. Age remains the most significant risk factor. Most individuals diagnosed with Alzheimer's are over 65 [65]. However, early-onset Alzheimer's occurring in people younger than 65, is not uncommon. Other risk factors include family history and medical conditions such as cardiovascular disease or diabetes [66]. Diagnosis involves comprehensive evaluation. Physicians conduct physical and neurological exams mental status tests and brain imaging to rule out other conditions. Biomarkers in cerebrospinal fluid are emerging as diagnostic tools, enhancing accuracy [67]. Currently there is no cure for Alzheimer's disease. Treatments focus on alleviating symptoms and improving quality of life. Medications like cholinesterase inhibitors and memantine can temporarily boost cognitive function. Non-drug approaches, including cognitive therapy and social engagement are equally important. The cause of Alzheimer's disease is not yet known but experts deliberate that mix of genetic, environmental and lifestyle factors play a role in its onset [68]. Researchers have been conducting extensive studies to identify the primary risk factors. Genetic predisposition for instance, has been highlighted as a significant element [34]. Family history of the illness increases one's chance of developing the disease. Beyond genetics environmental influences are also being closely examined. Ultimately, the interplay between these various risk factors remains complex. Medical professionals need more research to form a comprehensive understanding. Nevertheless increasing awareness about these factors can help in early detection and management. Oxidative stress is a critical player in the pathogenesis of Alzheimer's disease [69]. It occurs when there is an imbalance between the production of reactive oxygen species (ROS) and the body's ability to detoxify these reactive intermediates or repair the resulting damage. The brain, with its high oxygen consumption and lipid-rich environment is particularly vulnerable to oxidative damage [70]. Proteins, lipids and DNA in brain cells can be damaged by ROS leading to neuronal dysfunction and cell death [71]. Synaptic dysfunction is another hallmark of Alzheimer's disease. Synapses are the connections between neurons that allow them to communicate [72]. In Alzheimer's, the loss of synaptic function precedes neuron death and is thought to underlie the cognitive decline observed in patients [73]. Oxidative stress contributes to synaptic dysfunction. Through various mechanisms it impairs the proteins and pathways critical for synaptic health. Recent studies suggest a bidirectional relationship between oxidative stress and synaptic dysfunction [74]. For example oxidative stress can lead to synaptic dysfunction [75]. Conversely, synaptic dysfunction can exacerbate oxidative stress. This creates a vicious cycle that accelerates disease progression. Understanding the interplay between oxidative stress and synaptic dysfunction could offer new therapeutic targets. Antioxidants are compounds that inhibit oxidation and can neutralize ROS [76]. They have been researched as potential treatments for Alzheimer's disease. Some studies have shown that antioxidants can reduce oxidative damage. However clinical trials have yielded inconsistent results. One reason might be that oxidative stress is not the only factor driving the disease. Multimodal approaches that target different aspects of the disease may be more effective. At present there are around 50 million AD patients worldwide [36]. This number is projected to double every 5 years. It will increase to reach 152 million by 2050. AD burden affects individuals, their families and the economy. The estimated global costs are US$1 trillion annually. At present there is no cure for Alzheimer's disease [77]. Fig. 1 depicts the physiological structure of the brain and neurons in healthy and Alzheimer's disease brains [78]. While the focus on amyloid-beta as a key biomarker has been well-established, there are other promising biomarkers that could potentially be detected using nanobiosensor technology. One such candidate is the tau protein, a microtubule-associated protein that plays a crucial role in the pathogenesis of Alzheimer's disease [79]. Abnormal tau protein aggregation and hyperphosphorylation lead to the formation of neurofibrillary tangles, a hallmark pathological feature of the disease [80]. Measuring tau levels in the cerebrospinal fluid or through neuroimaging techniques could provide valuable insights into the disease process and potentially serve as an early diagnostic tool. In addition to tau, neuroinflammatory markers may also hold promise for nanobiosensor detection in Alzheimer's disease [81]. Neuroinflammation is increasingly recognized as a key player in the pathogenesis of the disease, with elevated levels of inflammatory cytokines and activated microglia observed in the brains

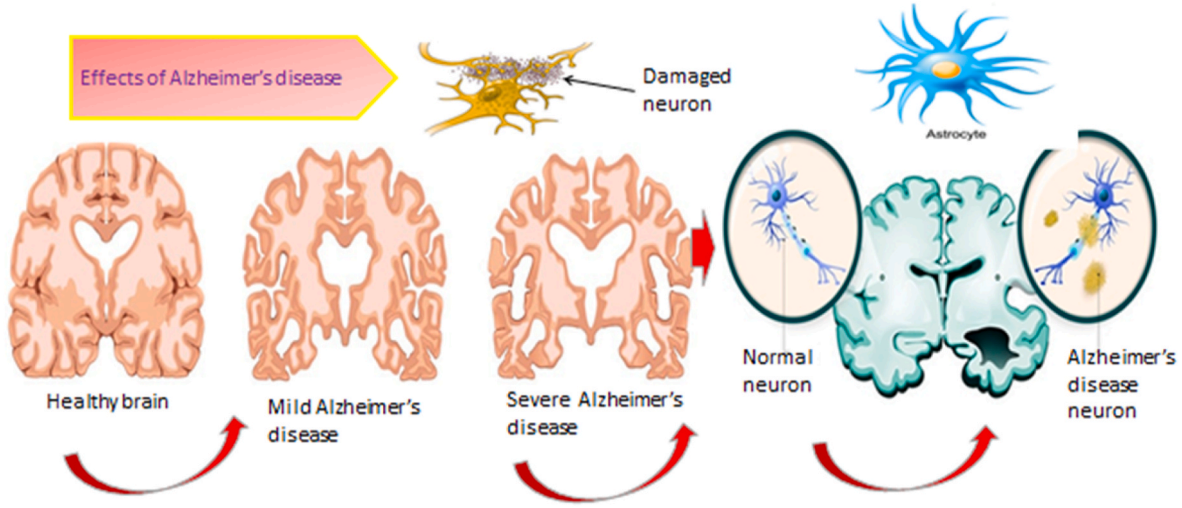

Fig. 1. The physiological structure of the brain and neurons in healthy brain and Alzheimer's disease brain.

of Alzheimer's patients [82]. Hence, the study of alternative biomarkers like tau protein and neuroinflammatory markers could enhance our understanding of Alzheimer's disease, potentially leading to the creation of more sensitive diagnostic tools.

1.2. Parkinson's disease

Parkinson's disease worsens as dopaminergic neurons in brain decrease [83]. The primary cause is still unclear but researchers point towards loss of these neurons. Researchers believe multiple factors contribute to the development of Parkinson's disease [84]. Both genetic predispositions and environmental exposures play a role [85]. Certain gene mutations appear to increase the risk [86]. However not everyone with these mutations develops the disease. Environmental factors such as exposure to pesticides and heavy metals also seem to increase risk [87]. Age is another critical factor. Risk increases significantly with age. Individuals over 60 Parkinson's disease is highly susceptible to various factors, including chronic inflammation, which can damage neurons over time, leading to progressive degeneration and worsening Parkinson's disease as dopaminergic neurons decrease [88]. The primary cause is still unclear. The aggregation of alpha-synuclein protein within neurons forms Lewy bodies which are commonly found in the brains of patients with Parkinson's disease [89]. Environmental factors like pesticides or heavy metals may increase Parkinson's disease risk, causing symptoms like tremors, rigidity bradykinesia, and postural instability, which typically require clinical evaluation and medical history examination [90]. There is no single test to confirm the presence of the disease. Neurologists often rely on symptoms and physical examinations. They may use imaging tests such as MRI or CT scans to rule out other conditions. Dopamine transporter scans can also provide supportive evidence for diagnosis. Early detection of Parkinson's disease is crucial for effective management and treatment, as symptoms often appear subtle and gradual, with patients often reporting handwriting changes, decreased facial expressions, or slight tremors [91]. Once diagnosed, treatment options focus on managing symptoms. There currently is no cure for Parkinson's disease. Medications aim to increase or substitute for dopamine. Common drugs include Levodopa and dopamine agonists. These can help manage motor symptoms. Physical therapy is also an important component of treatment. It helps to maintain mobility and flexibility. In severe cases surgical options such as deep brain stimulation might be considered. Living with Parkinson's disease requires comprehensive care. Patients benefit from multidisciplinary approaches that include neurologists, therapists and support groups. Increasingly researchers are focusing on identifying biomarkers for disease diagnosis and progression. Biomarkers can help distinguish PD from other neurodegenerative disorders [92]. One category of biomarkers involves imaging techniques. Positron emission tomography (PET) and magnetic resonance imaging (MRI) have been utilized [93]. They help in visualizing brain changes. These imaging techniques specifically target dopamine system. Dopamine is neurotransmitter closely associated with PD. Another important category includes biochemical biomarkers. For instance, cerebrospinal fluid (CSF) analysis can reveal protein abnormalities [94]. These proteins can include alpha-synuclein. Elevated levels of alpha-synuclein are often found in PD patients [95]. Genetic markers also hold promise. Certain genetic mutations are associated with PD. Genetic testing can identify mutations in genes like LRRK2 and PARK7, which are key to Parkinson's disease [96]. Early diagnosis can be achieved by identifying these mutations, which can be aided by clinical biomarkers. Tremors rigidity and bradykinesia are key indicators. Non-motor symptoms should not be ignored. These can include sleep disorders and olfactory dysfunction. Ultimately, understanding biomarkers advances PD research. It allows clinicians to create more sophisticated treatment. Fig. 2 illustrates Parkinson's disease, a brain disorder characterized by neuron death, resulting in a deficiency in dopamine production, a crucial neurotransmitter, originating from the ventral tegmental area [97].

Parkinson's disease is a neurodegenerative disorder affecting motor function, primarily due to the progressive death of dopaminergic neurons in the substantia nigra pars compacta [98]. This leads to substantial reductions in dopamine levels in the striatum. However the precise molecular mechanisms underlying PD remain complex and multifaceted. One pivotal hallmark of Parkinson's disease is the presence of intracellular protein aggregates called Lewy bodies [99]. These inclusions primarily contain alpha-synuclein, a 140-amino acid protein. Under physiological conditions alpha-synuclein is essential for synaptic vesicle regulation [100]. However, in PD this protein undergoes misfolding and subsequent aggregation (Fig. 3) [101]. This results in the formation of toxic oligomers and fibrils. These aggregates are believed to impair normal cellular functions and promote neuronal death. The pathological aggregation of alpha-synuclein involves several stages, including nucleation, elongation, and fragmentation [102]. Each step is influenced by various genetic and environmental factors. Mutations in the SNCA gene which encodes alpha-synuclein, have been directly linked to familial forms of PD [103]. Moreover several post-translational modifications, such as phosphorylation and ubiquitination have been implicated in its aggregation. It is hypothesized that mitochondrial dysfunction, oxidative stress and cellular trafficking defects contribute to the pathogenesis of the disease. The spread of alpha-synuclein

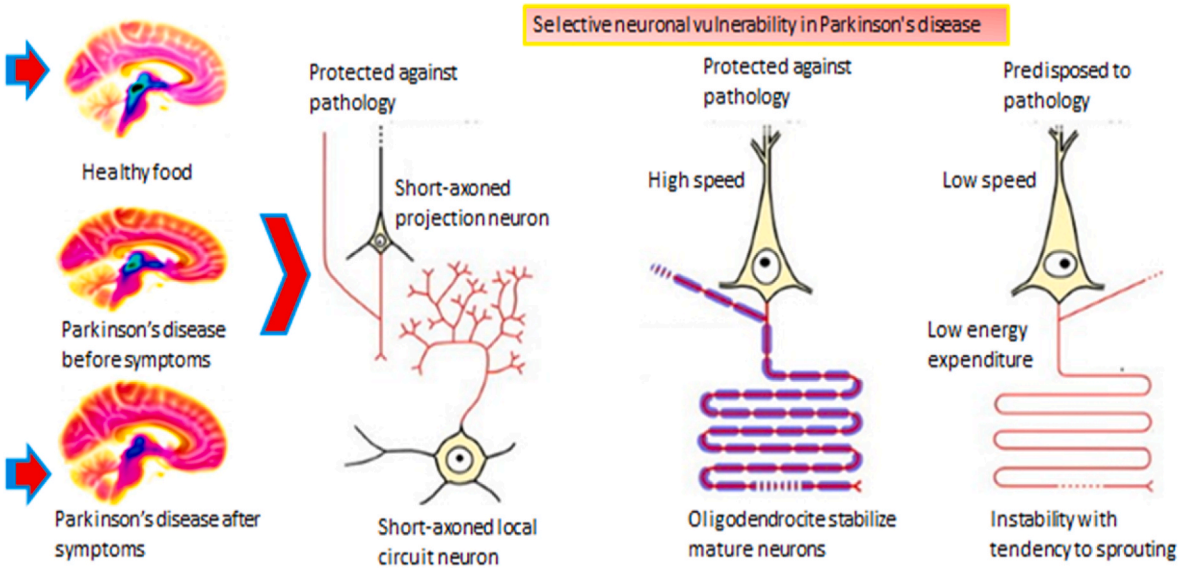

Fig. 2. Parkinson's disease causes dopamine loss due to neuron death and alpha-synuclein aggregation in the brain.

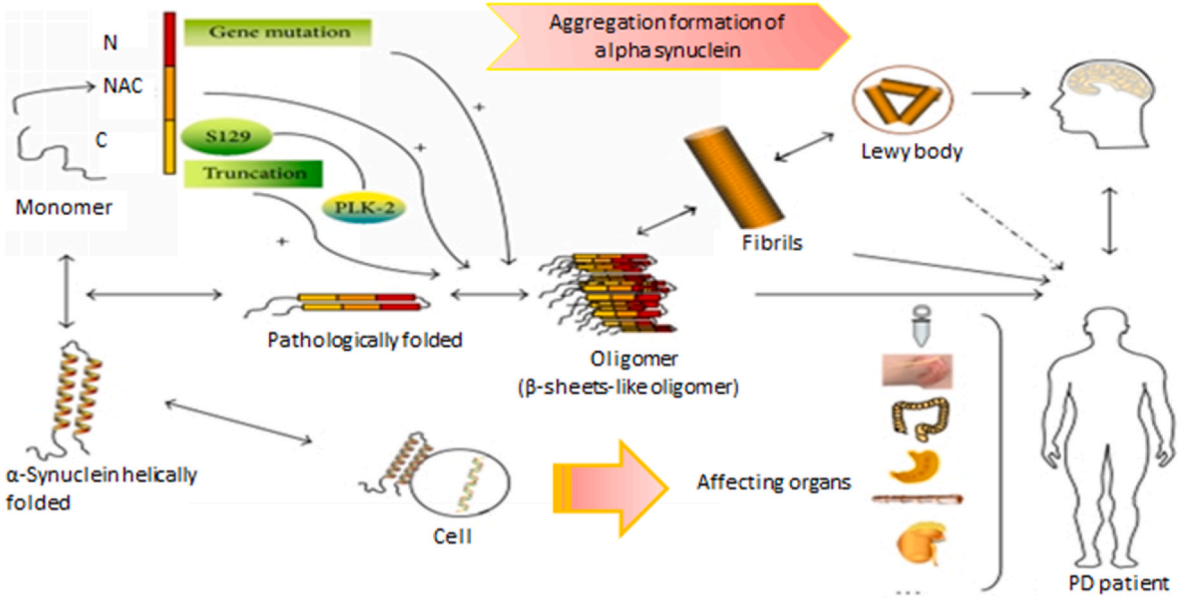

Fig. 3. Alpha-synuclein aggregation disrupts cellular function, leading to neuronal death and driving Parkinson's disease progression.

pathology is another crucial aspect (Fig. 3) [104]. The protein may propagate in a prion-like manner. It transfers from one neuron to another. The ability to detect and monitor the various pathological forms of alpha-synuclein is crucial for understanding the progression of Parkinson's disease and developing effective therapeutic interventions. Conventional methods for detecting alpha-synuclein aggregation, such as immunohistochemistry and Western blotting, have limitations in sensitivity and specificity, particularly when it comes to distinguishing between different structural forms of the protein [105]. This is where nanobiosensors have emerged as a promising approach to address this challenge. Nanobiosensors are analytical devices that utilize nanoscale materials, such as nanoparticles, nanowires, or carbon nanotubes, to detect and monitor biomolecular interactions with high sensitivity and specificity [106]. In the context of Parkinson's disease, nanobiosensors have been developed to target and detect different forms of alpha-synuclein, including oligomers, protofibrils, and amyloid fibrils [107]. These nanobiosensors often incorporate specific antibodies or aptamers that can recognize and bind to the various structural forms of alpha-synuclein, enabling the sensitive and selective detection of these proteins in biological samples.

1.3. Nanobiosensor

A sensor is a tool that can both identify and measure the presence of analyte in a sample [108]. The sensor is made up of transducer readout system and a detection system known as a receptor. The same method is used to develop a biosensor. A biosensor senses biological reactions and converts them into electrical signals. "Biosensor" simply means a biological sensor. It is a device used for the examination and detection of chemical substances involved in biological reactions in enzymes. It also detects reactions in tissues, microbes cells, amino acids etc. The transducer converts the biological response. This response comes from the bio elements' interaction with the test analyte into electrical signal. The method by which the bioreceptor layer (biological component) is

mounted on the transducer has significant impact on the success of biosensors. The major objective is to maintain the stability of the biological element. It must also establish a close contact between it and the sensory surface. Hence, nanobiosensors are advanced technology that combine nanotechnology with biology, operating on a small scale, using nanomaterials' unique properties to detect biological elements, enhancing precision and sensitivity [109]. Nanobiosensors have significant applications in medical diagnostics, environmental monitoring, and food safety [110]. They can identify biomarkers for diseases early, enabling timely intervention and improved patient outcomes, demonstrating remarkable potential in this field. In addition the small size of nanobiosensors allows for minimally invasive procedures [111]. This is particularly beneficial in scenarios requiring regular monitoring. Nanobiosensors are crucial for environmental monitoring due to their ability to detect pollutants and toxins at low concentrations, enabling immediate corrective actions and addressing environmental pollution concerns [112]. This helps in maintaining the ecological balance. Nanobiosensors are revolutionizing food safety by identifying contaminants like pathogens and pesticides, offering a quicker and more efficient alternative to traditional methods, thereby ensuring the safety of food products for consumption [113]. Nanobiosensors involve attaching analyte to biological substance as shown in Fig. 4 [24]. These sensors contain three main components: a bioreceptor transducer and an electronic system. Nanobiosensors are highly sensitive and specific bioreceptors that interact with target molecules, converting these interactions into measurable signals. They are valuable in medical diagnostics, environmental monitoring, food safety, and security. Nanobiosensor technology is characterized by miniaturization, portability, and real-time data tracking [114]. Advances in nanomaterials enhance sensor performance, making them ideal for personal healthcare and disease management [115]. Their potential to revolutionize disease management is immense, with expanding uses in various fields. The biosensor, as depicted in Fig. 4, involves attaching an analyte to a biological substance, generating a measurable electrical response using electrochemical biosensors to measure changes in electric current, ionic, and conductance [116]. Biosensors offer advantages such as specificity and sensitivity, as their biological recognition element differentiates between different biomolecules and only binds to the target molecule [117]. The biosensor can be developed using advanced nanotechnology and electrochemical processes. This innovation occurred on cutting-edge platform [118]. It employs sophisticated materials to enable highly sensitive detection mechanisms. This allows it to identify even minimal concentrations of target substances. The sensitivity and specificity of the biosensor are unparalleled. Its operational efficiency is optimal for medical and environmental applications. Furthermore, nanobiosensors have emerged as a promising alternative to traditional diagnostic techniques like neuroimaging and cerebrospinal fluid analysis, offering a range of unique capabilities that can significantly enhance the field of healthcare [119]. One of the primary advantages of nanobiosensors is their remarkable sensitivity and specificity, which can be attributed to the incorporation of nanoscale components [120]. The use of nanoparticles and nanostructures in the design of biosensors has enabled the immobilisation and reuse of expensive enzymes, leading to improved testing processes and cost-effectiveness [121]. Additionally, the integration of nanotechnology, such as NEMS and MEMS, has further enhanced the overall performance of nanobiosensors, making them more reliable, faster, and more comfortable for diagnosis [122]. Advances in the development of molecular biosensors and biomarker discovery have also provided a deeper understanding of diseases like cancer, enabling earlier detection and the use of more targeted treatments [123]. Nanobiosensors have also demonstrated their potential in the diagnosis of various chronic conditions, including kidney disease and tuberculosis, with the incorporation of nanoscale environments leading to more accurate and reliable results [124]. Additionally, the label-free nature of certain nanobiosensors allows for the detection of molecules that are difficult to tag or label, expanding the range of applications in the medical and healthcare fields [125]. Nanobiosensor technology has significantly improved molecular diagnostics by enabling more sensitive, accurate, and rapid detection of various biomarkers [126]. Nanomaterials like nanoparticles and nanostructures have been widely incorporated into biosensor platforms, enhancing their performance and broadening their applications [127]. One notable development is the emergence of multiplexed nanobiosensor platforms, which allow for the simultaneous detection of multiple analytes in a single sample, providing a more comprehensive and reliable assessment of the patient's condition. This multiplexing capability is achieved by leveraging the unique properties of nanomaterials, such as high surface-to-volume ratios and the ability to functionalize with various biomolecules. Examples of multiplexed nanobiosensor platforms include gold nanoparticles functionalized with different antibodies, each targeting a specific biomarker, enabling simultaneous detection of multiple analytes with high sensitivity [128]. Carbon-based nanomaterials, such as carbon nanotubes and graphene, can be modified to target different biomolecules, demonstrating the ability to detect various cancer biomarkers, infectious disease markers, and other clinically relevant analytes with improved sensitivity and specificity [129]. The development

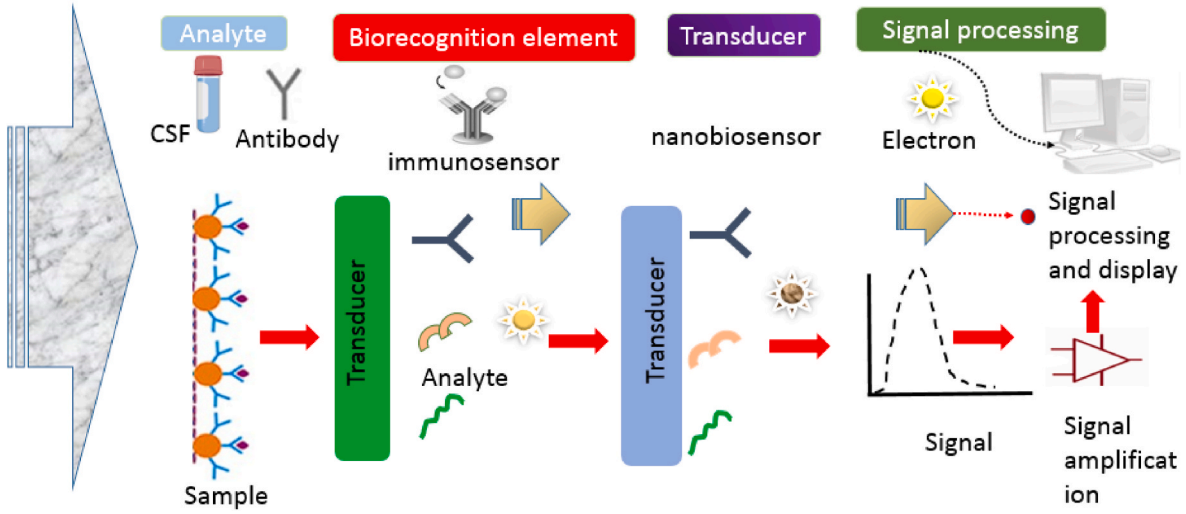

Fig. 4. The biosensor's working principle involves attaching an analyte to a biological substance, forming a bound analyte that generates a measurable electrical response using electrochemical biosensors, which measure electric current, ionic, and conductance changes.

of microfluidic and lab-on-a-chip technologies has further advanced the capabilities of multiplexed nanobiosensor platforms [130]. By integrating microfluidics with nanobiosensors, researchers have created miniaturized, portable devices capable of performing rapid, automated, and highly sensitive analyses. In addition, one of the key advantages of nanobiosensor-based assays is their ability to provide more accurate and reliable results compared to traditional diagnostic techniques [131]. Furthermore, the integration of nanoparticles and microarray/biochip technology has made the testing process more comfortable, faster, and cost-effective [132]. However, the widespread adoption of nanobiosensor-based assays has been hindered by their relatively high cost compared to conventional diagnostic methods [133]. Addressing this challenge is crucial to ensure that the benefits of this technology are accessible to a wider population, especially in resource-limited settings. Several strategies can be explored to make nanobiosensor-based assays more affordable and widely available. One approach is to optimize the manufacturing processes and explore alternative materials to reduce the overall production cost [12]. Additionally, the development of label-free nanobiosensors can eliminate the need for expensive labeling compounds, further reducing the cost of the assays [134]. Furthermore, the integration of nanobiosensors with smartphone-based platforms or other portable devices can help decentralize diagnostic services and make them more accessible to patients [135]. One key application of nanobiosensors is their ability to identify and quantify the signals generated by specific bioanalysis interactions [9]. During a bioanalysis process, the interaction between a target analyte and a recognition element (e.g., an antibody or DNA probe) generates a detectable signal, which can be optical, electrochemical, or mass-based (Fig. 4). Nanobiosensors are designed to transduce these signals into a measurable output, such as a change in light intensity, electrical current, or resonance frequency, that can be correlated to the concentration of the target analyte. In addition, as a nanosensor, nanowires are also a promising solution for improving electrical conductivity and enhancing detection processes due to their unique properties, such as high surface-to-volume ratio and exceptional electronic characteristics [136]. Their high aspect ratio and reduced dimensionality enable efficient electron transport, leading to enhanced electrical conductivity. The high surface area of nanowires allows for increased interaction with target analytes, resulting in a more sensitive detection process [137]. The improved sensitivity of nanowire arrays is due to their ability to transduce small changes in the presence of target biomolecules into measurable electrical signals [138]. The increased surface area and electron transport capabilities of nanowires amplify the signal, allowing for the detection of even trace amounts of the analyte. Incorporating nanowires into electrochemical sensors has further enhanced the sensitivity and selectivity of these devices [139]. The incorporation of nanomaterials, such as metal nanoparticles, carbon nanotubes, and graphene, has been shown to improve the electrical conductivity and electrocatalytic properties of the working electrodes, resulting in greater sensitivity and faster response times [140]. Furthermore, Immunosensors, a unique and innovative class of biosensors, have garnered significant attention in the scientific community due to their remarkable potential in various applications, particularly in the realm of nanobiosensors (Table 2). These hybrid devices, which seamlessly integrate the specificity and sensitivity of biological recognition elements, typically antibodies or antigens, with the advanced capabilities of nanomaterials, have paved the way for unprecedented advancements in diverse fields such as environmental monitoring, early disease detection, and point-of-care diagnostics. Table 2 presents a comprehensive overview of immunosensors, a unique class of biosensors utilizing nanomaterials. These sensors can be classified into nonlabeled types, including potentiometry, reflectometry, elipsometry, SPR, acoustic wave, labeled, amperometry, fluorometry, and electrochemiluminescence. They can be used for various applications such as detection of antibodies, ion sensors, and detecting capillary fill devices.

Table 2
Immunosensors, a unique class of biosensors, with nanomaterials.

Type of immunosensor	Measuring principle	Sensor construction	Reference
Nonlabeled	Potentiometry	Electrode/antibody membrane, electrode/antibody electrode, antibody gate/FET, electrode/antibody, ionophore membrane	[141]
	Reflectometry	Antibody/Si	[142]
	Elipsometry	Antige/SiO2	[143]
	SPR	Antibody/Au thin layer/optical guide	[144]
	Acoustic wave	Antibody/quartz	[145]
Labeled	Potentiometry	Immobilized antibody/ion sensor	[146]
	Amperometry	Antibody membrane/O2 electrode Immobilized antibody/electrode	[147]
	Fluorometry	Antibody/optical fibercore Antibody/optical wave guide Capillary fill device Integrated	[148]
	Chemiluminescence	Antibody (antigen)/optical fiber Antibody (antigen)/optical guide	[149]
	Electrochemiluminescence	Labeled antibody/optical fiber electrode	[150]

1.4. Diagnosis of neurodegenerative diseases using nanobiosensors

Nanobiosensors are crucial in clinical settings for sensing tasks, recording electrical signals generated by detection materials [25]. They are widely used in various domains, particularly in medicine. Understanding biosensing is essential for developing nanobiosensors, which are single devices that combine biological detection elements, sensor systems, and transducers. They are particularly important in medicine processes. This combination gives it higher selectivity and sensitivity than other diagnostic tools. Nanobiosensors are especially helpful when diagnosing clinical problems such as Parkinson's disease. Kalinke et al. suggest sensors that increase the precision of Parkinson's disease diagnosis [151]. These can be made possible by nanofabrication. Numerous methods based on nanotechnology have been applied to the detection of dopamine. This is crucial to diagnose Parkinson's disease. Anionik and Karbon [152] describe one technique that uses carbon paste electrode to detect ascorbic acid and dopamine at the same time. Electrochemical catalysis is improved by strengthening the electrodes with carbon nanotubes and silver nanoparticles. This leads to remarkable detection limits in the micromolar range for both compounds. The method also offers outstanding selectivity and sensitivity. Furthermore. Zhang et al. [153] have produced zinc oxide (ZnO) nanowire array in three dimensions for graphene foam. Differential pulse voltammetry is technique that can detect ascorbic acid. It can also detect uric acid and dopamine in Parkinson's disease. By using nanowires the electrical conductivity and sensitivity of the array are improved and the uric acid and dopamine detection limits are lowered to 1 nanomol. Uric acid levels are lower in Parkinson's disease patients than in healthy people. This suggests that uric acid may be utilized as a biomarker to identify the condition. Parkinson's disease is also associated with mitochondrial dysfunction. Aptasensors have been developed utilizing colorimetry and electrochemical impedance spectroscopy to specifically identify alpha synuclein oligomers in Parkinson's disease [154]. The EIS detection limits of 1 pM, 8 pM and 10 nM were determined. The suitability of

serum for research of alpha synuclein oligomer in biological materials was confirmed by analysis [155]. For early identification of Parkinson's disease, a precise electrochemical sensor was developed [156]. The sensor can detect the clustering of alpha synuclein. In human blood serum, the sensor is able to identify alpha synuclein oligomers. Its detection limit is 0. 64 fM and its detection range is 1 fM to 1 nM. The sensor is a promising tool for Parkinson's disease early diagnosis. This is due to its stability and reproducibility. Specifically an electrochemical biosensor based on molecular fingerprint polymers has been developed to detect alpha synuclein in Parkinson's disease [157]. Electrochemical impedance spectroscopy tests revealed that the suggested sensor had exceptional analytical performance. It excelled in the detection of alpha synuclein. Its linear range is between 1 fM and 10 pM. Furthermore, biomarker concentrations linked with Parkinson's disease in humans have been measured using immunosensors [158]. The linear range according to voltammetric data, is 3.5 10-5 mol L-1 to 80 10-4 mol L-1. It has a detection limit of 5.1 10-6 mol L-1. Parkinson's disease protein 7 (PARK7/DJ-1) was successfully detected by electrochemical impedance spectroscopy. This was achieved by functionalizing the electrode with particular anti-PARK7/DJ-1 antibodies. Researchers have developed an electrochemical immunosensor using self-assembled monolayer electrodes, which can detect synuclein without the need for labels [159]. Changes in the quantity of alpha synuclein connected to the immunosensor probe caused changes in the redox reaction's current and charge transfer resistance (Rct). The immunosensor successfully detected alpha synuclein in diluted human blood samples, demonstrating outstanding consistency and resistance to interference. Alpha synuclein may be recognized by the proposed immunological sensor. This allows for early diagnosis of Parkinson's disease. It might also be extended to find additional significant body biomarkers. The effects of dopamine in Parkinson's disease-related cell solutions have been investigated using impedance analysis (Yalcin & Luttge 2021). The results demonstrate the importance of measuring impedance during cell immobilisation. This is because it provides information on how cell medium reacts electrically to frequency. Graphene-coupled gold nanoparticles have been used develop a novel immunoassay [160]. This is for detection of alpha synuclein in human plasma samples. The material's electrochemical activity is increased through the interaction of graphene with gold nanoparticles (AuNPs). The sensitivity of the sensing layer is enhanced. Its detection limit is decreased by augmenting the substrate's surface area and conductivity. To investigate the effect of levodopa on Parkinson's disease voltammetric assay was created. It employed a screen-printed carbon sensor modified with mesoporous carbon. When cyclic voltammetry data were compared to FTIR measurements, no discernible differences were found. A carbon fiber electrode has been developed to detect dopamine in Parkinson's disease using fast-scan cyclic voltammetry [161]. A novel biosensor with high sensitivity and selectivity has been developed to identify miR 133b biomarker. The tube electrodes are appropriate for in vivo detection. They can precisely identify dopamine in vitro. They function like CFMEs. Chandra & Adeloju, 2020. The sensor uses a complementary ss-DNA sequence. It is affixed to a gold electrode surface. It is labeled with methylene blue redox marker. Under ideal circumstances the sensors' linear concentration range is 10 fM to 520 pM, their detection limit is 168 aM. Their sensitivity is 0.3 nA pM-1. Additionally their ability to distinguish between matched and mismatched miR sequences suggests that they may find application in laboratory settings. Furthermore, the sensitivity and electrical conductivity of nanowire-enhanced nanobiosensors have allowed dopamine and uric acid to be detected at single nanomole [162]. Patients with Parkinson's disease had lower uric acid levels This suggests uric acid may be used as biomarker for diagnosis. It has been determined that alpha synuclein is an essential neuronal protein for the diagnosis of Parkinson's disease. For non-destructive and real-time molecular measurement electrochemical techniques are widely used in industry These include healthcare and the environment. An example is electrochemical impedance spectroscopy (EIS) (Ameer et al., 2023). Furthermore, EIS does not require any special reagents. This makes it perfect for label-free applications. When compared to alternative approaches this not only lowers costs It also facilitates performance. Parkinson's disease was identified using EIS [163]. The results show that when frequency varies. The impedance measured during cell immobilisation represents the electrical behaviour of the cell environment. Immunosensory evaluations using electrochemical impedance spectroscopy (EIS) have been used to find biomarkers for Parkinson's disease [164]. The immunological sensor has been recommended. It has been used to gauge the body's biomarker levels for Parkinson's disease. They have shown to be beneficial. It serves as a different method for diagnosing this illness. Furthermore, EIS investigations with amplitudes of 5 mV have been carried out to find biomarkers for Parkinson's disease within the frequency range of 0.1 Hz–100 kHz [165]. This innovative sensor interface allows the detection of several biomarkers in bodily fluids. Very sensitive sensor for detecting entacapone a Parkinson's disease medicine, was created by electropolymerizing glycine on a carbon paste electrode to add gold nanoparticles and sodium dodecyl sulphate [166]. Several voltammetric techniques were used. Electrochemical impedance spectroscopy (EIS) and scanning electron microscopy (SEM) were also utilized to test the redesigned electrode. The sensor responded linearly in the range of 4. 1107 to 05103 mol-1 with a correlation value of 0. 9990. It was discovered that 2. 82 x 10^{-9} mol^{-1} was the lower detection limit. In actual samples, the sensor was able to detect NE Furthermore. Positive results were found while testing with Stalevo tablets containing Levodopa LD and Carbidopa CD. Dhinesh Kumar et al. used EIS to detect Parkinson's disease sensitivity biomarker PARK7/DJ-1, a biomarker closely linked to the AuNP/PPy immunosensor [167]. The microchip, based on a redox cycle, detected dopamine within a sensing range of 0.1–50 M, with a limit of detection (LOD) of 0.15 M. A microfabricated array with gold-doped TiO2 nanotubes was developed for photoelectrochemically detecting alpha synuclein [168]. This sensor maintains stability of the primary antibody and has low detection limits, making it a useful biomarker for early detection of Parkinson's disease, detecting aggregation. The detection was performed with high sensitivity and selectivity by an EIS-based aptasensor. A silica probe with gold nanourchin is used to diagnose Parkinson's disease using current-voltage measurement on a split-finger interdigital electrode surface, as part of research into biosensors for disease diagnosis and treatment [98]. Within the linear detection range the current-voltage response grew continuously from 100 fM to 1 nM. A linear curve was used to plot the detection limits. Sensitivity and signal-to-noise ratio was n = 3 (y = 0. 081x + 1. 593 R2 = 0. 9983) One part per million is the detection limit measured. Even in samples with serum added. The sensor performed well in differentiating between various indicators of neurodegenerative disorders. It demonstrated its repeatability. Parkinson's disease diagnosis is aided by this technique. A nano-biosensor has been developed for the sensitive detection of Alzheimer's disease, using advanced methods like surface plasmon resonance [169]. This label-free approach quantifies even the smallest molecular structures in CSF and blood samples, overcoming the limitations of early detection techniquesEarly detection is critical for timely intervention and management of Alzheimer's disease and Parkinson's disease. Researchers are developing blood and cerebrospinal fluid tests, non-invasive saliva and urine tests, and other diagnostic tools. The ultimate goal is to create point-of-care diagnostic tools that are accessible, affordable, and deliver quick results. A new electrochemical nanobiosensor has been developed for early detection of Parkinson's disease (PD) using the quantification of circulating biomarker miR-195 [170]. The sensor uses exfoliated graphene oxide and gold nanowires to modify surface of screen-printed carbon electrode. A single-strand thiolated probe is designed for specific hybridization with target miRNA (miR-195) and doxorubicin is used as an electrochemical indicator. This indicator is employed for differential pulse voltammetry measurements. The analytical performance of the nanobiosensor showed high sensitivity. It had a detection limit of 2.9 fM and a dynamic range of

10.0–900.0 fM. The biosensor also achieved good selectivity for target miRNA over non-specific oligonucleotides. Real human serum analysis showed no interference in biosensor's function. The miR-195 electrochemical nanobiosensor could be suggested for clinicians in PD medical diagnosis. The working principle of the nanobiosensor involves the specific binding of alpha-synuclein aggregates to designed nanoprobes (Fig. 5) [171]. This interaction generates measurable electrical signals. These can then be analyzed to determine the concentration of alpha-synuclein aggregates. Moreover, these sensors can be adapted for real-time on-site analysis, providing a significant advantage over traditional methods. One of the key advantages of nanobiosensor platforms is their potential for early detection of neurodegenerative diseases [172]. By targeting specific biomarkers, these sensors can identify the presence of pathological changes in the brain before the onset of overt clinical symptoms. Furthermore, nanobiosensors can provide continuous monitoring of disease progression, allowing for more accurate assessment of treatment response and disease trajectory. Despite the promising preclinical data, the clinical validation and head-to-head comparison of nanobiosensor platforms for neurodegenerative disease diagnosis have been limited. However, a few studies have begun to explore the clinical utility of these novel diagnostic tools. In a recent study, researchers developed a nanobiosensor platform capable of detecting specific protein aggregates associated with Alzheimer's disease [173]. The sensor was able to accurately diagnose Alzheimer's disease in a cohort of patients, with a sensitivity and specificity comparable to established diagnostic methods, such as cerebrospinal fluid analysis and neuroimaging. Another study focused on the use of nanobiosensors for the early detection of Parkinson's disease [174]. The researchers demonstrated that their nanobiosensor platform could identify specific biomarkers associated with Parkinson's disease, such as alpha-synuclein, with high sensitivity and specificity, even in the pre-symptomatic stage of the disease. These preliminary findings suggest that nanobiosensor platforms have the potential to revolutionize the diagnosis and monitoring of neurodegenerative diseases.

1.5. Limitations and challenges of nanobiosensor

Nanobiosensors are emerging as promising tools for a wide array of applications in medical diagnostics and environmental monitoring. However they face several limitations and challenges [175]. These issues must be addressed before their widespread adoption can be realized. One of the main challenges is the sensitivity of nanobiosensors [176]. While they can be incredibly sensitive to specific biomarkers under ideal conditions, their performance can deteriorate in complex biological samples. This is particularly true where there are many interfering substances present. This issue becomes more pronounced when detecting low-abundance targets. Researchers must develop strategies to enhance selectivity. One of the primary concerns is standardization and reproducibility, as the unique properties of nanomaterials can lead to significant variability in performance. Ensuring consistent and reliable sensor performance is crucial for successful deployment in critical applications like environmental monitoring, medical diagnostics, and food safety. Another potential limitation is the long-term stability and durability of nanomaterials-based sensing devices. Many nanomaterials, such as carbon nanotubes and metal nanoparticles, can undergo degradation or agglomeration under certain environmental conditions, leading to a loss of sensitivity and reliability over time. Developing strategies to improve the stability and shelf-life of nanobiosensors is an active area of research. Lastly, the potential toxicity and environmental impact of nanomaterials used in biosensors are important considerations. Careful evaluation of their safety and potential adverse effects on human health and the environment is crucial for their successful integration into various applications. The fabrication processes of nanobiosensors can vary often leading to batch-to-batch variations [177]. These inconsistencies can result in unreliable measurements. Standardization of the manufacturing processes is essential to mitigate this problem. Nanobiosensors also suffer from stability issues [178]. Many of the biorecognition elements used in these devices are susceptible to denaturation and degradation. This reduces the usability of the sensors over time. There is a pressing need for more stable biorecognition elements. The integration into existing systems poses another hurdle. Many current diagnostic platforms are not designed to incorporate nanobiosensors [26]. Adaptation or redesign of these systems is needed. Only then can they accommodate the new technology seamlessly. Regulatory approval processes present additional challenges. Nanobiosensors often incorporate materials and mechanisms that are novel and not yet fully understood. Regulatory bodies require comprehensive testing and validation. This can be time-consuming and expensive. Furthermore commercialization of nanobiosensors is hindered by high production costs [179]. The materials and technologies required for their manufacture are often expensive. This makes large-scale production economically unfeasible. Additionally, there are potential ethical and privacy concerns [180]. Manufacturing costs are high. Scale-up from laboratory to clinical settings is complex.

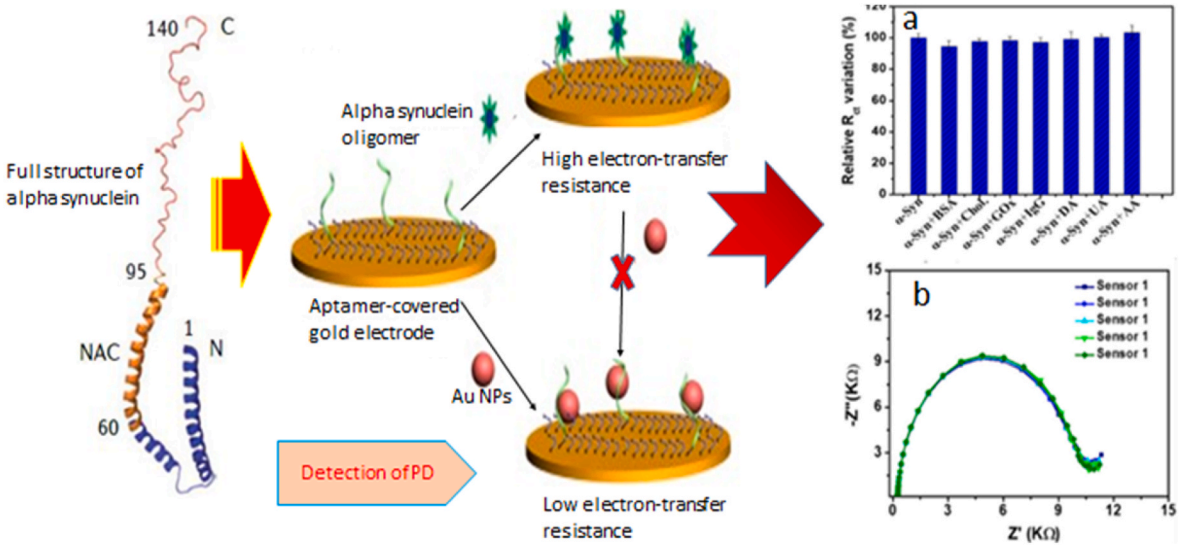

Fig. 5. The possibility for precise diagnosis was demonstrated by the electrochemical detection of α-synuclein using a nanobiosensor as a biomarker for Parkinson's disease. Early diagnosis is made possible by the sensor's superior performance, great selectivity, and low detection limits.

Regulatory approval processes are rigorous [181]. Addressing these issues is crucial. Collaborations between scientists, engineers and healthcare professionals are essential.

1.6. Future perspective

Neurodegenerative diseases represent one of the main challenges in modern medicine. These conditions characterized by gradual neuronal loss, include Alzheimer's disease Parkinson's disease, Huntington's disease and amyotrophic lateral sclerosis (ALS). Early diagnosis is crucial for effective management. Conventional diagnostic methods however, often lack precision and sensitivity. Recent advances in nanotechnology promise to revolutionize this field. Nanobiosensors which combine nanomaterials with biological sensing elements, offer a new frontier for disease diagnosis. They exhibit high sensitivity specificity and the potential for miniaturization. These characteristics make them suitable for early detection of neurodegenerative diseases. Nanobiosensors can detect biomarkers at molecular levels. They enable early diagnosis before clinical symptoms appear. Efforts to improve the functionality and application of nanobiosensors are ongoing. Various types of nanomaterials, such as nanoparticles nanotubes and nanowires, have been employed to enhance sensor performance. Each type offers distinct advantages. For instance gold nanoparticles are known for biocompatibility. Carbon nanotubes, on the other hand provide high electrical conductivity. Advances in material science continue to drive progress in nanobiosensor technology. Integration with microfluidics is another promising development. Microfluidic platforms allow precise control of small fluid volumes. This enables efficient sample handling and reduces reagent consumption. When coupled with nanobiosensors, microfluidics can offer a powerful tool for point-of-care diagnostics. Such integration paves the way for portable user-friendly devices. This is important for healthcare in remote or resource-limited settings. Despite the potential advantages, challenges remain. The production costs of nanobiosensors can be high. Additionally translating laboratory success to clinical applications requires rigorous validation. Regulatory approvals also pose hurdles to timely market introduction.Clinical trials play an essential role in this process. They assess the safety, efficacy and reliability of new diagnostic tools. Collaboration among researchers clinicians and industry is crucial. Together, they can address technical and regulatory challenges. Their combined efforts could lead to the widespread adoption of nanobiosensors. Continuous research and development are needed. Overcoming existing challenges will be key to their successful implementation. The future of neurodegenerative disease diagnosis could be significantly improved with these innovative technologies. The integration of wearable devices and point-of-care testing in healthcare presents a promising future for personalized, continuous, and accessible medical data. However, it faces several technical hurdles. One is ensuring seamless interoperability between wearable devices and existing hospital information systems, which may not be easily processed due to lack of data standards or compatible interfaces. Standardized data formats and communication protocols are needed to facilitate the smooth exchange of information between wearables and electronic health records. Another challenge is improving the accuracy and reliability of wearable sensor data, as the data collected can be prone to errors or inconsistencies. Advancements in sensor design, calibration techniques, and signal processing algorithms are essential for enhancing the precision and trustworthiness of wearable health data. The long-term safety and biocompatibility of wearable devices in close contact with the human body must be rigorously evaluated, considering potential risks such as skin irritation or interference with other medical devices. Addressing patient privacy and data security concerns is crucial for widespread adoption of integrated wearable and point-of-care systems, requiring robust encryption, data anonymization, and user-controlled access mechanisms to protect sensitive health information and build trust among patients and healthcare providers. Nanobiosensors have shown promise in diagnosing diseases like cancer, chronic kidney disease, and tuberculosis due to their enhanced characteristics. However, converting these platforms from research to clinical use is a complex challenge. Key milestones include demonstrating their performance and reliability in controlled clinical settings, which requires rigorous testing and validation. Additionally, developing scalable manufacturing processes that consistently produce nanobiosensors at a cost-effective level is crucial. This involves optimizing fabrication techniques, streamlining quality control measures, and establishing reliable supply chains for materials and components. These milestones are essential for successful commercialization of nanobiosensors.

2. Conclusion

The implementation of nanobiosensors offers a promising avenue for the diagnosis of neurodegenerative diseases. Traditional diagnostic methods are often invasive. They also lack the necessary sensitivity and specificity. This makes early detection difficult. Nanobiosensors equipped with exceptional sensitivity, can detect biomarkers at low concentrations. These devices can provide real-time monitoring. Such capabilities significantly enhance early diagnosis. Nanobiosensors use various nanomaterials such as gold nanoparticles, carbon nanotubes and quantum dots. These substances have unique properties. The properties can be fine-tuned. This enables precise detection of disease-specific biomarkers. Coupled with advancements in microfluidics and data analytics the potential for portable, cost-effective and highly accurate diagnostic tools is on the horizon. However there are challenges. The fabrication of nanobiosensors requires precise control over nanomaterial properties. Ensuring biocompatibility is also crucial. Moreover, regulatory hurdles can delay the commercialization of these technologies. Researchers are actively addressing these issues. Innovations in material science and engineering bring us closer to reliable nanobiosensors. One more consideration is data interpretation. The wealth of data generated by these sensors necessitates robust algorithms. These algorithms should minimize false positives and negatives. Artificial intelligence (AI) and machine learning algorithms play a significant role in this aspect. Their integration into nanobiosensor systems can automate data analysis. They provide accurate diagnostics much faster. Nanobiosensors are gaining attention due to their potential to enable personalized medicine. These devices, which use nanomaterials and nanodevices, offer enhanced sensitivity, specificity, and response time compared to traditional biosensors. They are well-suited for detecting and monitoring various biomarkers and health indicators. One example is in cardiac health monitoring, where nanobiosensors can continuously monitor an individual's biomarkers, such as troponin or natriuretic peptides, which indicate myocardial injury or heart failure. This allows healthcare providers to adjust treatment plans and optimize drug dosages and interventions. Similarly, nanobiosensors could be used for early detection of cancer by monitoring specific biomarkers. This increased sensitivity and specificity could enable early cancer identification and real-time insights into the patient's response to treatment, allowing for timely adjustments and personalized care.

CRediT authorship contribution statement

Thikra S. Dhahi: Writing – review & editing, Resources, Formal analysis. **Alaa Kamal Yousif Dafhalla:** Writing – review & editing, Resources, Conceptualization. **A. Wesam Al-Mufti:** Writing – review & editing, Resources. **Mohamed Elshaikh Elobaid:** Writing – review & editing, Software, Resources, Conceptualization. **Tijjani Adam:** Writing – review & editing, Writing – original draft, Software, Resources, Conceptualization. **Subash C.B. Gopinath:** Writing – review & editing, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial

interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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