The Role of Nanomaterials in the Recent Development of Electrochemical Biosensors

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Abstract
Medical forensics and homeland security have been focusing on the food and beverage industries, for water quality remote sensing, drug residue determination in food, etc. NT is playing a growing role in BS development. NT-based BS, also known as NBS technology, are reshaping the medical field. They are used in metabolite measurement, diabetes monitoring, and other applications, such as environmental protection. Pesticide and heavy metal ions detection in river water, as well as genomes sequencing the use of NM in BS design have increased their sensitivity and ability to also develop NP special properties, such as high electrical conductivity, improved shock resistance, sensitive response and flexibility. These advances result from the confluence of NP characteristics, allowing for the presentation of numerous modern flag transduction innovations in BS, such as the development of devices, and forms for manufacturing them and enhancing their measurement capability. Imaging the nanoscale objects has improved sensors connected with tiny atoms. Many mechanical devices, optical resonators and bi-functional architecture based on NBS have been developed. BS have also been discussed in this research, in order to highlight their critical applications in a variety of fields. This study discusses the various types of BS that depend on multiple types of NM, as well as their biological and implicational factors and analytical techniques, such as amperometric, CV potentiometric optical techniques, and other measurements methods that use enzyme and non-enzymatic BS.

Keywords: NT application, NBS, BS analytical techniques, enzyme BS and nanoenzymatic sensors**.**

Introduction•

NT might be a modern and vital technology throughout the twenty-first century. It may be a department of science and innovation that makes materials from single particles. It examines the properties and applications of materials with structures that range in size from 0.1 to 100 nm. Du to NT fast advancement, it is nowadays broadly

• The abbreviations list is in pages 216-217.

used in therapeutics and materials science, gadgets, vitality industry, and in a series of other disciplines and areas [1, 2].

NM have solid action within distinctive nanounits. This characteristic enables NM to have interesting impacts, such as quantum expanse surface vitality and measurement abilities allowed by its range, and interface effects, due to the fast increment of the surface nuclear proportion [3, 4]. Because of NM properties, combined with the continuous enhancement of atomic science innovation, new fabric innovation and cutting edge therapeutic investigation, NT has been naturally incorporated, particularly within the study and treatment of illnesses [5]. NM, like many other technological segments, have illustrated their usefulness for biosensing applications, with expanded sensitivities and lower LOD in a few orders of size. One expected advantage of all NM is their tall particular surface zone, which allows for the immobilization of a wider number of bio receptor units. One of the continuous challenges is the immobilization methodology used to conjugate the bio specific substance with such NM. As such, one of the critical factors for developing enzyme immobilization approaches consist in the techniques used for this procedure. A dependable BS review summarizes effective methods for biofunctionalizing NM [6].

NT has gone through a colossal advancement amidst the final decades, due to the changed applications of metallic NM in several areas, such as science, nourishment, horticulture, designing, gadgets, makeup, pharmaceutics, nutrition, biology and medicine. MtNP have gained a pivotal position, due to their unique physicochemical properties and critical biotechnological applications [7, 8]. According to a showcase report worldwide, MtNP generation is valued at 13.7 billion US dollars, with an anticipated increment of 50 billion US dollars by 2026. MtNP wide employment has essentially contributed to a significant improvement in the macroeconomic industry. The request for MtNP is high in three locals around the world: Western Europe, Pacific Asia and North America [9]. Over the final decade, numerous analysts have synthesized MtNP, resourcing to conventional chemical and physical strategies, since the biological approach is still too costly. Essentially, chemical strategies are not safe, as they use unsafe materials that impact negatively MtNP biomedical applications. Therefore, investigations have moved towards MtNP that use cost-effective, biocompatible and non-toxic natural materials [10, 11].

Right now, NT is holding colossal prospects for elective diabetes administration procedures [12]. Attractive NP imaging of resistant cell mass and movement, as well as QD empowered gas sensors, may open up new roads for early sensing. Discrete sensors with progressed affectability and effectiveness for glucose have been made conceivable by MCNT, GNC and QD. Cell treatments backed by nanofiber-based frameworks or safe choice films, as well as glucose-responsive nanogels and nanovesicles, offer novel approaches to discharge control, by regulating proper dosages. Glucose administration using these frameworks inside a worthy run has been reported to happen, at best, 70% of the time. Therefore, superior diabetes administration apparatuses are still required. Later propels in NT have appeared to guarantee an exhaustive run of restorative conditions [13-15].

Two primary types of NP

Organic and inorganic NP are the foremost common sorts of these materials. While organic NP are made up of C, the inorganic ones include magnetic and semiconductor NM, such as ZnO and TiO_2, and noble metals like Ag and Au, since they have started being used as catalysts [16], optoelectronic materials and BS [17].

To name a few applications, medicine encapsulation and contrast agents have received a lot of attention. Furthermore, as inorganic biomass NP (Ag and Au NP) cater for higher-quality fabric properties with utilitarian adaptability, their formation is gaining popularity.

Metallic NP have a significant biomedical potential. Fe-Ag-Ti-Al, Zn-Au and Cu-C alloys, Pd and Ti fullerenes have all been applied to make NP. In the 16th century, AuNP were used for both medical and staining purposes [18].

NT applications

BS

BS are organically inferred expository gadgets used in conjunction with interpreters for acknowledgment units and flag changing over frameworks, in order to distinguish different illnesses and disorders [19, 20]. They can assess the accuracy of particular analyses through sensing by natural fabrics, such as enzymes, genomes and antibodies [21, 22].

Organic materials work with such sensing components, and can join a physicochemical locator, creating a quantifiable flag of which concentrated shifts depend on the analytic course [23, 24].

BS must give quick, particular and delicate biochemical flag transduction [24, 25]. BS are a device able to create a flag from a natural reaction [26]. BS comprise three fundamental components: a transducer, a bio receptor and a locator, and they are employed to identify essential metabolites, immunological atoms and an assortment of other substances [26, 27]. Their fruitful integration of organic and electronic components, so as to produce a flag amid any examination, for optimized execution, is one of their major qualities, such as it is the bio receptor capacity to remain stable in a nanobiologic environment.

BS can be classified according to their transduction and organic sensing components, which incorporate piezoelectric [28] and potentiometric techniques, with transduction and antibodies organelles containing chemicals bio determination [26, 29, 30].

Furthermore, BS characteristics required for proficiency may incorporate affectability, reaction time and specificity [31].

NM in BS development

To be developed in large quantities, BS materials must be biocompatible, accurate and reproducible. Most recently developed BS materials exhibit improved stability, sensitivity, chemical and mechanical intensity, for any practical application [56]. NM main feature is that they have, at least, one external dimension in the range from 1 to

100 nm. Structures with zero to three dimensions can be individual or combined, single or sporadic.
For BS immobilization purposes, there are several metallic NM, such as Au, Cu and Ag. Non-metallic NP, such as C compounds, e.g. Gr nanotubes and G, have also been used [32].
NP are used in heavy-metal sensors, for pre concentration and isolation systems [33, 34]. Their immobilization action raises the surface to volume ratio, as well as the access to the active surface [35, 36].
Several industries have been using NM to create BS with improved sensitivity, selectivity and specificity [52-54]. Therapeutic, nourishment, electronic, enzymatic and other industries have widespread BS adoption. BS several applications are ahead discussed, based on the distributions volume through logical databases (Table 1) [54, 55].

Table 1. Different applications for NM based BS.

NM	Applications	Reference
AgNP	Antibacterial	[54]
AgNP	Antifungal	[55]
AgNP	Cytotoxicity	[56]
AuNBP	Impedimetry	[57]
AuNP	Electrochemical	[58]
AuNP	Fluorescent	[59]
Au/CdS QD	Electrochemical	[60]
Cerium oxide	Suppress myocardial inflammatory process	[61]
Cerium oxide	Suppress retinal degenerative process	[62]
CuO/LIG	Amperometry	[63]
CuNP/ZnO NRA	Glc BS	[64]
Cu@TiC/C	Glc BS	[65]
MNP PAMAM PtNP/RGO-CMC	Food	[66]
MnO2 modified MWCNT	Biomedical	[67]
Pt-CuO/RGO	Glc BS	[68]
PtNP/NPG PBS	Glc BS	[69]
ZnO nanosheets	Electrochemical	[70]
ZnS QD	Photoluminescence	[71]
ZnO thin films	Electrochemical	[72]

Types of analytical electrochemical techniques for BS

CV technique

CV is a flexible electrochemical method for analyzing redox status, in a variety of mechanical and investigative settings. Its typical applications include drugs performance assessment in pharmaceuticals [36, 37], biological samples label measurements and bio-molecules discovery, such as hormones [38, 39].
Traditional CV estimations require cell arrangements that incorporate WE, CE and RE, respectively. The WE was used to calculate I response to a clearing voltage E connected to the specimen. CV was able to detect the location of lower molecular weight compounds [40].

Amperometric technique

In the amperometric method, the current is measured at constant E, to show a logarithmic response. However, the voltammetric method is a subclass of the former, whereby the applied E of the electrode changes, when I is measured, causing the analyte oxidation or reduction [41].

The electrochemical cell assembly includes the active anode (WE), the reference cathode (RE) and the counter cathode (CE) [42]. In the electrochemical response that consumes or generates electrons, the WE potential is controlled towards the RE. This approach has a high sensitivity and selectivity towards the target analytes in the test solution. The resulting I between the CE and WE is measured, being associated with the target species concentration [43].

Potentiometric technique

This method comprises two electrodes: an indicator (WE) and a RE. The WE E changes as a response to the target sample, while the RE E is fixed, being independent of the target analyte properties. The E difference (at constant I) is measured when both electrodes are immersed in an electrochemical cell containing the solution, in the potentiometric measurement. The possible changes are proportionate to the particular analyte concentration in the solution. Different species can be measured by this technique, such as hydron, ammonium cation, etc. However, the PH meter probe and glass membrane are the commonly potentiometric electrodes used [44].

BS categories

BS based on light

Fiber active probes have enzymes and dyes on the tip (often fluorescent). Light comes into contact with reagents that disclose the optical fiber information. After the interaction, light comes back with a concentration that is measured. It shows the sum of analytes present, e.g. an optic lactate sensor that uses lactate monooxygenase and oxygen. [45]

Enzymatic BS

The enzyme is a familiar biocatalyst that expands organic responses rates. The enzymatic BS mechanism is based on the catalyst response and capability to distinguish the target analytes [46]. The analytes recognition process involves several possible mechanisms: the analyte metabolization through the enzyme and the chemical concentration are evaluated by estimating the catalyst effect on the former through the latter. The enzyme is restrained or enhanced by the catalyst, so that the measured concentration is related to the diminished enzymatic arrangement, and the changes in enzymatic properties [47, 48]. Because of the lengthy research on this kind of sensors, different BS based on enzymatic specificity can be produced. Due to the enzymatic structure susceptibility, improving its sensitivity, stability and adaptability is costly and complicated [48]. Electrochemical transducers are the most common type used in EBS. The more widespread EBS are glucose and urea. Fully developed and assessed, AuNP, amperometric, enzymatic and glucose based BS have been employed for glucose detection (in vitro real time) within the brain [49].

Non-EBS

Despite their selectivity and effectiveness, enzymes have some drawbacks, such as incapacitation difficulty [50]. As a result, numerous essays have been conducted to create non-EBS, using appropriately altered electrodes. Recently, several researches have proposed inorganic nanocomposites for non-EBS made of Glc.

The $SrPdO_3$ (cubic) perovskite/AuNP modified Gr electrode had a lower discovery restrain of 10 m, and a high Glc specificity. Non-enzymatic sensing strategy depended on Glc chemisorption onto the electrode surface, following GDL arrangement from a dehydrogenation response and, finally, the latter changed to gluconate, through its reaction with hydroxide particles [51].

Conclusion

NT might be the most promising science field, and it is a modern approach. Evermore, current NM will be created and used as NT advances, in order to promote medicine breakthroughs, bring forward modern ideas and produce commitments towards disease diagnosis and management. NP are used in various applications, such drugs conveyance, cancer treatment and DNA examination, antibacterial variables, BS enhanced responses, isolation science and magnetic resonance imaging. Due to the required BS reasonable stable output response, NM have become essential components in BS devices, with better sensitivity, stability, reproducibility and selectivity. NM have allowed BS common sense enforcement in medicinal, healthcare (Glc and lactose levels measurement in the body, and folic acid, biotin, vitamin B12 and pantothenic acid analytical monitoring), nourishment, microbiological and pharmaceuticals areas, as an alternative to the molecular markers diagnosis of actual samples. Additionally, they give an estimate of buildups in healthcare, such as antibiotics and development regulators, especially in nutritional, drug invention and modern compound bioactivities of environmental (e.g. BOD) BS that detect water contamination.

Authors' contributions

Saif Kareem Abdulhussein: collected data; organized research idea; contributed to the paper writing. **Fatin Fadhel Mohammed Al-Kazazz**: collected data; organized research idea; contributed to the paper writing. **Ahmed Mahdi Rheima**: collected data; organized research idea; contributed to the paper writing.

Abbreviations

AuNBP: gold nanobipyramids
BOD: biochemical oxygen demand
BS: biosensor
CdS: cadmium sulfide

CE: counter electrode
CMC: carboxymethyl cellulose
CV: cyclic voltammetry
E: electric potential
EBS: enzymatic biosensor
G: graphene
GDL: glucone-decta-latone or gluconolactone
Glc: glucose
GNC: graphene nanocomposites
Gr: graphite
I: electric current
LOD: limit of detection
MNP: magnetic nanoparticles
MtNP: metallic nanoparticles
MWCNT: multiwall carbon nanotubes
NB: nanotechnology
NBS: nanobiosensor
NM: nanomaterials
NP: nanoparticles
NPG: nanoporous gold
NRA: nanorod arrays
PAMAM: polyamidoamine
PbS: lead sulfide
QD: quantum dots
Redox: reduction oxidation reaction
RE: reference electrode
RGO: reduced graphene oxide
TiO_2: titanium oxide
WE: working electrode
ZnO: zinc oxide

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