

Nanotechnology-based biosensors: a typical analysis of materials, methods, and applications

Ashu Nayak 

*Corresponding Author. Assistant Professor, Department of CS & IT, Kalinga University, Raipur, India. E-mail address: ku.ashunayak@kalingauniversity.ac.in

Vasani Vaibhav Prakash 

Research Scholar, Department of CS & IT, Kalinga University, Raipur, India. E-mail address: vasani.vaibhav.prakash@kalingauniversity.ac.in

Abstract

Objective

Biosecurity, medical diagnostics, and environmental monitoring are just a few of the many areas that rely on biosensors (BSs). They can identify a wide variety of chemical and biological contaminants, including infectious diseases, pollutants, hazardous materials, and particular biomolecules. Biosensors can detect trace amounts of substances and are easy to use, scalable, inexpensive, and precise. Because of their low cost, user-friendliness, and adaptability, biosensors have become increasingly popular in the medical industry.

Results

Biosensors have been greatly improved with the incorporation of nanotechnology (NT), especially with regard to detection speed, selectivity, and sensitivity. In NT-based biosensors, nanomaterials (NMs) such nano-wires, Quantum Dots (QDs), Carbon Nanotubes (CNTs), and nano-rods are commonly utilized. Because of their large surface area, NMs improve sensitivity and enable more precise detection of compounds at low concentrations. As a result of their exceptional electrical and thermal conductivity, great carrying capacity, extraordinary durability, and changeable color, they provide an important role in the creation of reliable and efficient biosensors.

Conclusions

This paper delves into the integration of biosensors that are enabled by nanotechnology, namely

NT-enabled BSs. It examines the principles, designs, and materials utilized to make these sensors. There is an emphasis on the expanding role of NT-based biosensors in fields as diverse as healthcare and environmental monitoring. Developing next-generation diagnostic tools, environmental monitoring devices, and biosecurity instruments is made more feasible by combining nanotechnology with biosensors. Due to the special characteristics of nanomaterials, NT-based biosensors could completely change the way we detect substances. They would be able to detect a wide variety of substances much more quickly, accurately, and with a high level of sensitivity, which would be great for research and practical uses in many fields.

Keywords: Biosensors, nanotechnology, nanomaterials

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Introduction

Biosensing is a fundamental notion naturally found in several life forms, serving as a defense mechanism against attackers and challenging conditions from an evolutionary perspective (Song et al. 2022). Some types of algae have intrinsic biosensing that allows them to detect and react to poisons, sharks have electro-sensory skills, and dogs have naturally enhanced hunting instincts. A Biosensor (BS) is an instrument that detects chemical substances by utilizing a specific biochemical process mediated by antibodies, isolated digestive enzymes, organelle-like structures, or organs (Lei & Guo 2022). This detection is achieved by recognizing optical, heat, or electrical impulses.

Nanotechnology (NT) has applications in diverse scientific disciplines such as chemistry, physics, pharmaceutical research, material research, healthcare, and farming (Malik et al. 2023; Tülay Çağatay et al. 2021). On the other hand, nanotechnology is a multidisciplinary scientific

field that uses a set of tools and techniques derived from engineering, physics, chemistry and biology (Mohammadabadi et al. 2009; Heidarpour et al. 2011; Mohammadabadi & Mozafari 2018). Advances in nanoscience and nanotechnology have routinely enabled the fabrication and identification of submicron bioactive carriers. The delivery of bioactive substances to target sites in the body and their release behavior are directly affected by particle size (Mortazavi et al. 2005; Zarrabi et al. 2020). Compared to micrometer-sized carriers, nanocarriers provide more surface area and have the potential to increase solubility, increase bioavailability, improve controlled release, and enable precise targeting of entrapped substances (Heidarpour et al. 2011; Mohammadabadi and Mozafari, 2019). The favourable outcomes in other domains have created significant opportunities in the agricultural sector (Surendar et al. 2024). Precision Farming (PF) is a cultivating management approach that involves tracking and reacting to crop variations within and between fields (Radhika & Masood 2022; Mizik 2023). The goal is to create a system that supports decisions about managing the entire farm and maximizing output using accessible assets. NT is widely employed in contemporary farming to implement PF effectively. NT encompasses nanoparticles (NP) with diameters on the scale of 100 nm or smaller (Najahi-Missaoui et al. 2020). Nanomaterials (NM) are used in plant security, feeding, and management of farms due to their small dimensions, excellent surface-to-volume proportion, and distinctive optical features (Chen et al. 2020). There is a strong need to explore materials suitable for BSs to meet their specifications and investigate the ease of production. This phenomenon is widespread in BSs that rely on Liquid Crystal (LC) technology, as these BSs depend solely on the materials' properties (Deng et al. 2021; Mamdapur et al. 2017). The optical characteristics of LC-based BSs are significantly affected by the realignment of the linked particles, which is contingent upon the physical and chemical environment of the BS. LCs are frequently employed in the production of BSs. BSs have been developed to mitigate the drawbacks, utilizing nonbiological recognition components, such as transition metal oxides (Chia et al. 2021). These materials have recently gained significant attention as a consequence of their exceptional stability, strong selectivity, and excellent sensitivities. This review examines BSs that utilize NT, including the substances employed in constructing these nano sensors and their possible uses. This article provides a detailed analysis of the difficulties encountered in deploying BSs and their potential opportunities.

History of NT-based BS

NPs are incorporated into the manufacturing process, culminating in the creation of BSs known as NT-based BSs. NMs are extensively studied and analysed due to their diverse

bioanalytical capabilities in bio-imaging, testing, drug delivery, and therapeutic applications. An amperometry apparatus has been employed to evaluate enzyme-based responses. Fluorescence Quantum Dots (QD) gadgets are now utilized to quantify the effectiveness of binding and immunolabeling techniques that make use of attached NPs to examine biomolecular connections (García De Arquer et al. 2021). NPs possess inherent optical characteristics and have an opportunity to be linked to fluorescent indicators, which renders them highly intriguing BSs. Electro examinations, fluorescent-based examinations, and biologically Field-Effect Transistor (FET) examinations can result in the production of Carbon Nanotubes (CNTs) and other related carbon-based nanostructures such as Reducing Graphene Oxide (rGO) graphite and graphene films (Ozyilmaz & Bayram 2023; Norizan et al. 2020). Fluorescent-based tests are often identified by observing the quenching properties of graphite. Carbon NMs can exhibit different configurations according to the employed measuring technique. QDs offer a diverse range of applications in sensors and imaging thanks to their fluorescent properties, which are determined by their shape and size. Modifying QDs using polymers like carbohydrates is necessary to achieve targeted recognition (Alaghmandfard et al. 2021). QDs offer numerous advantages compared to traditional dyes. These include better molar attenuation and quantum factor yields, a broader absorption spectrum, a shorter spectrum of emission, higher durability against photo-bleaching, and so on. They are commonly used in FET applications and sandwich tests (Cheng et al. 2022). Several discrete nano-based BSs can be employed for various applications. Unconventional uses of NT in BS include the creation of glucose sensors for individuals with diabetes, the detection of antibodies, the tracking of microbial bioburden in urinary system infections, and the creation of tests for cancer diagnosis. NT-based BSs are undeniably valuable instruments in tissue study, serving diagnostic and therapeutic purposes (Shen et al. 2021).

Nanostructures can be chemically manufactured using several methods, with the sol-gel approach and reverse micelles creation being particularly notable. Both bottom-up and top-down techniques can generate NM. The bottom-up strategy involves reducing the size of substance building blocks by self-assembly to create nanostructures. QDs and NPs are synthesized from colloid dispersion using these methods (Ding et al. 2022). Due to their reduced rate of failure and more consistent chemical structure, these procedures are a feasible alternative. The top-down approach includes starting with a predetermined nanostructure and meticulously planning the fabrication of larger-scale structures—several instances of ball milling, severe plastic deformation, and Inductively Connected Plasma (ICP) etching (Racka-Szmidt et al. 2021). A significant drawback of these approaches is the presence of many faults in the surface architecture. The summary of the literature survey is demonstrated in Table 1.

Table 1. Summary of the literature survey

Concept	Details
NPs in Manufacturing	Integrated into the production process, resulting in the development of NT-based BSs.
NMs in Bioanalytics	Thoroughly researched for the purposes of bio-imaging, testing, drug delivery, and therapeutic applications.
Amperometry Apparatus	Hired to assess reactions involving enzymes.
Fluorescence QDs	Used to measure the efficiency of binding and immunolabeling methods by employing NPs to study biomolecular interactions.
NPs Optical Characteristics	These BSs possess inherent optical features that are connected to fluorescent indicators, which make them fascinating.
Electro and Fluorescent Tests	Electrochemical and fluorescence-based analyses, and FET analyses, can generate CNTs, rGO, graphite, and graphene films.
Fluorescent-Based Tests	Graphite was identified by the observation of its quenching properties.
QDs in Sensors and Imaging	QDs have a wide range of uses in sensors and imaging because of their fluorescence qualities, determined by their form and size.
Modification of QDs	It is essential to utilize polymers such as carbohydrates for specific recognition purposes.
Advantages of QDs Over Traditional Dyes	Enhance molar attenuation, increase quantum factor production, broaden absorption spectrum, shorten emission spectrum, improve durability against photo-bleaching, and so on.
Applications of QDs	Mostly employed in FET devices and sandwich tests.
Nano-Based BSs Applications	These are used for glucose sensors, detecting antibodies, monitoring microbial bioburden in urine infections, and diagnosing cancer.
NT-based BSs	Precious instruments utilized in the examination of tissues for the goal of diagnosis and treatment.
NPs Chemical Manufacturing	Produced by techniques such as the sol-gel process and the synthesis of reverse micelles.
Bottom-Up Strategy	The process entails the spontaneous organization of NPs and QDs, which are produced through the dispersion of colloidal particles.
Top-Down Approach	The process entails initiating with a nanostructure and designing structures on a bigger scale. Illustrative methods encompass ball milling, extreme plastic deformation, and ICP etching.

NMs for BSs

BS study has attracted significant attention from researchers owing to its possible uses in various industrial and scientific areas, such as bioinformatics, biotechnology, gadgets, materials research, medical care, and health sciences. A BS is an instrument capable of detecting a biological component in touch with a substance being analysed and converting the biological reaction into a suitable signal using a transducer. However, Developing BSs has numerous obstacles, including sensitivity, reaction time, consistency, and low thresholds for detection.

Graphene BSs: Due to its exceptional physicochemical properties, NT lauds graphene as a substance. Graphene possesses desirable features such as excellent conductivity, minimal charge carrier opposition, and a large surface-to-volume ratio, making it highly suitable for transducing material. Graphene is a 2D substance since it has a thickness of only one atom. Graphene can be produced using several methods. The development of procedures for making large quantities of graphene needs to be improved. This hinders its use for numerous prospective purposes. Graphene Oxide (GO) is produced by oxidizing graphene using various methods. The reduction process can then further transform GO into rGO (Jiang et al. 2020). Several researchers have developed an extremely sensitive graphene opto BS to identify live tumor cells responding to the chemotherapeutic paclitaxel after drug administration. The researchers have employed a unique optical approach to detect fluctuations in the Refractive Incidence (RI) with the added benefit of sensing living cells without labelling. This technology offers advantages regarding non-destructive examinations and dynamical cell surveillance that are not affected by electromagnetic transmission or contamination from the surface.

Gold NPs in BSs: Gold NPs (GNPs) provide a highly effective platform for BS due to their distinctive colorimetric belongings, which are determined by their shape, dimensions, and level of aggregation when exposed to analytes (Hua et al. 2021). The transition of GNPs from a uniform distribution to a clustered condition in a liquid media causes a noticeable change in hue, shifting from red to blue. GNPs have a diameter ranging from 1 to 100 nm, resulting in a high surface-to-volume proportion and elevated surface energies. Several researchers have successfully integrated GNPs into developing micro-cantilever-based BSs for protein detection. They used a method of creating a small enclosed space at the tip of the cantilever to enable a specific biological response, which helps achieve a high accuracy level in identification. Scientists developed a BS from GNP incorporating a unique dual-sensing technique. This BS can detect spikes of the virus using saliva from people. The created method successfully identified spike antigens using electrochemical and colorimetric techniques. The colorimetric test utilized an antibody-antigen connection to

detect peaks. This contact caused the formation of GNPs, resulting in a colour change from reddish to lavender. The method had a Limit of Detection (LOD) of 42 ng/mL.

Carbon Nanotubes in BSs: Carbon, when in its allotropic form, is referred to as CNT and is renowned for its exceptional mechanical, electrical, electrocatalytic, and thermodynamic characteristics (Ferrier & Honeychurch 2021). The structure can be described as a sheet of graphene rolled upwards; the number of constituent walls influences its characteristics. The unique geometry of CNT has garnered significant interest for its possible uses in the BS sector. CNTs have enhanced biosensing characteristics when infused with polyaniline (PANI). PANI exhibits enhanced redox action that, when paired with CNT, can produce an increased signal output in biological BSs. The CNT-based PANI nanohybrid exhibits a distinctive flower-like morphology, which offers a substantial surface region and has been tested for the identification of Mycobacterium Tuberculosis (MTB) at a microscopic level (Joshi et al. 2022). The nanohybrid can provide extremely high sensitivity for detecting MTB, with a LOD of 0.31 femtomoles. The electrostatic attributes of CNT have been utilized to detect lactase in human sweat specimens. CNTs have proven helpful in cutaneous biosensing, allowing for affordable health surveillance without invasive surgeries. Researchers have developed a BS for thermal injuries using a composite material of Polylactic Acid (PLA) and CNT integrated into a Microneedle Array (MNA) (Rezapour Sarabi et al. 2022). The micro-needle matrix composed of PLA has exceptional mechanical characteristics, enabling painless and non-bleeding skin permeability while serving as an in-situ component in electrostatic BSs.

QD-based BSs: QDs, known as luminescent semiconductor nanocrystals, are NPs with sizes smaller than 10 nm. The cutting-edge biological sensing technologies have garnered considerable attention (Ding et al. 2022). Investigators extensively use QD remarkable optical, electrical, and size-dependent QDs in sensing applications. QDs have been demonstrated to possess a significant surface-to-volume proportion and exceptional charge carrier transport capabilities, potentially enhancing a BS's efficiency. Carbon QDs (CQDs) have gained attention in cutting-edge sensing studies due to their remarkable characteristics, including reduced toxicity, enhanced solubility, chemical resistance, and adaptability (Molaei 2020). The fluorescent characteristic of CQDs and the intense attraction between single-stranded DNA and acrylamide were employed to detect AM in dough layers in real-time, achieving a LOD of 2.32×10^{-8} M. BSs using Zinc Oxide (ZnO) based QDs for the precise identification of cysteine in liquid solutions. They devised an innovative approach to creating a luminous probe using melamine-modified ZnO-based QDs.

Cell-based BSs: Cell-based BSs (CBBS) have garnered significant attention as analytical instruments in several fields, such as healthcare, food bio-processing, businesses, and environmental surveillance (Do et al. 2020). These BSs are small and offer an elevated substrate for biological processes. As analyzers, CBBS employ bioactive molecules, including enzymes, microbes, algae, molds, bacteria, and plant tissue. These analysers are equipped with suitable transducers. The most reported detectors rely on microbes, specifically yeast and bacteria. The sensor intentionally exhibits binary behavior, providing a definitive "yes" or "no" response to the existence of Cu(II) in the analyte. The detector produces colorimetric feedback when combined with the betaxanthin visual characteristics. When combined with 2-phenylethanol, the detector can produce olfactory signals using formaldehyde. The betaxanthin-based colorimetric test demonstrated a remarkable sensitivity in detecting Cu(II), with a limit of determination as low as 0.32 ppm. The presence of mercury (Hg^{2+}) in water at a small scale was evaluated using a sensor that relies on bioluminescence in *Escherichia coli*. The bacteria were inserted into a photon-sensitive, compact silicon photomultiplier optical detector. When the sensor detects the presence of Hg^{2+} ions, it triggers the luciferase proteins in bacteria to generate photons, resulting in bioluminescence emission rapidly.

Other NMs in BSs: Transition metal oxides have recently undergone extensive investigation for their unique electrochemical characteristics and ability to exist in several oxidation states, making them very suitable for BS purposes. They have gained a reputation for being highly cost-effective, and the framework influences their reaction. The presence of oxygen atoms attached to the change in metal resulted in many polymorphs with varying stoichiometry. The exceptional electrocatalytic action, tolerance with living organisms, and large surface region of Co_3O_4 have been utilized to develop a BS for detecting glucose (Su et al. 2020). The Co_3O_4 crystals with a cubic structure were used as ink to screen-print the circuit of the BS device. The chip demonstrated a notable sensitivity to fructose, with a detecting limit of 12 μM and a broad range spanning from 10 to 500 μM . Titanium Dioxide (TiO_2), a very adaptable metal oxide, has proven to be highly successful in constructing BSs due to its exceptional photoelectrochemical characteristics (Bertel et al. 2021). The TiO_2 nanotube panels are combined with QDs to identify asulam, an herbicide, in actual water samples from the surroundings. The artificially created sensor exhibited a significant linear spectrum ranging from 0.01–3.5 ng/ml with a detection limit of 3.8 pg/ml. The ZnO nanorods cultivated on a silicon substrate exhibited excellent sensitivity toward phosphate. The created FET-based BS achieved a sensitivity level of 79.12 $\mu\text{AmM}^{-1}\text{cm}^{-2}$. It could detect concentrations ranging from 1 to 6000 μM , with a detection limit of approximately 0.8 μM .

Challenges and Prospects: NT-based BSs have become an essential research component due to the challenges of transferring in vitro systems to in vivo environments (Zhu et al. 2021). The interdependence of the system's variables significantly impacts the manifestation of various analytes, necessitating systematic real-time surveillance. Multiple industries are capitalizing on recent advancements in NT-based BSs because of their exceptional magnetic, electrochemical, acoustic, piezoelectric devices and optical characteristics. The area of tissue science still needs to successfully integrate these sensors due to a critical hurdle. Applying Machine Learning (ML) is one of the most recent innovations, which has addressed these limitations (Cui et al. 2020). When evaluating the setup of BSs, ML can be regarded as an algorithmic approach to analyze sensor data and extract meaningful information using statistical techniques. Various scholars have explored profound insights into utilizing ML techniques for biosensing purposes and their data manipulation. The NT-based BSs can make use of their advanced recognizing patterns skills and ML techniques to extract valuable insights from unprocessed information. Biomarker approaches will explore the increasing potential for developing precise treatments, diagnostic tools, and medical equipment (Karaboğa & Sezgentürk 2022). There is potential for revolutionary transformation in the methods used to collect human specimens. Through surgery, embedded BSs can significantly expedite the advancement of personalized therapies. Wearable technologies, specifically smart wristbands, can monitor various samples without causing any harm or invasion. These samples comprise saliva, exhaled condensing respiration, blood, and interstitial fluids gathered in a more invasive manner. Another potential option involves using wearable BSs in combination with ML for health surveillance (Song et al. 2023). Due to their significant capacity to assess the human body without the need for invasive procedures, wearable BSs have attracted considerable interest. Wearable BSs aim to continuously track biomarkers by incorporating a series of detectors on flexible coverings. The size of the specimens required for training ML algorithms can be significantly decreased by utilizing manual overrides. This emphasizes the crucial need to incorporate interpretable ML in the domain of mobile devices in clinical applications and associated medical interventions.

Conclusions: The preceding sections comprehensively discussed using NT-based BS technologies. ML approaches can improve the accuracy of predicting the amounts of trace substances and successfully differentiate between complex overlapping patterns. Convolutional Neural Networks (CNNs) and Recurring Neural Networks (RNNs) are increasingly used in sensory input analysis. Conventional regression study necessitates using a distinct formula for determining the dependent parameters of the sample. To overcome the limitation in data transfer between ML and BSs, scholars can employ multiplexed or high-throughput biological materials

detectors, such as microarrays and multichannel fluidic circuits. BSs are extensively utilized in the medical field and offer numerous advantages to patients and doctors. They play a crucial role in illness prevention, administration, medical evaluation, therapy, health data access, and treatment results assessment. BSs are now experiencing widespread utilization in the development of NM. The main objective of clinical healthcare is to categorize patients into distinct groups utilizing uncomplicated BSs. Several investigations have identified LC interface ideas, which can be used to develop stimuli-responsive materials for highly accurate BSs. The selection of target atoms, immobilization techniques, and catalysts will determine the success level achieved in this sector. Various intelligent NT-based methods could be used to enhance the sensing capabilities of the LC-based BS, specifically its ability to detect low levels and its superior sensitivity. These sensors are cost-effective as they can be readily manufactured without sophisticated supplies. They consume minimal power to operate and exhibit consistent and reproducible sensing outcomes, regardless of the testing on distinct samples. The researchers are dedicated to conducting additional research on utilizing these sensors for sickness detection, food security, and pandemic management. Due to their favorable sensing capabilities, NT-enabled LC-based BSs can detect many biological chemicals effectively.

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حسگرهای زیستی مبتنی بر فناوری نانو: تجزیه و تحلیل معمولی از مواد، روش‌ها و کاربردها

اشو نایاک  ID

*نویسنده مسئول: استادیار، گروه علوم کامپیوتر و فناوری اطلاعات، دانشگاه کالینگا، رایپور، هند. آدرس پست الکترونیکی:

ku.ashunayak@kalingauniversity.ac.in

واسانی ویبهاو پراکاش  ID

پژوهشگر، گروه علوم کامپیوتر و فناوری اطلاعات، دانشگاه کالینگا، رایپور، هند. آدرس پست الکترونیکی:

vasani.vaibhav.prakash@kalingauniversity.ac.in

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چکیده

هدف: امنیت زیستی، تشخیص پزشکی، و نظارت بر محیط زیست تنها تعدادی از حوزه‌هایی هستند که بر حسگرهای زیستی (BSs) متکی هستند. آن‌ها می‌توانند طیف گسترده‌ای از آلاینده‌های شیمیایی و بیولوژیکی، از جمله بیماری‌های عفونی، آلاینده‌ها، مواد خطرناک و مولکول‌های زیستی خاص را شناسایی کنند. حسگرهای زیستی می‌توانند مقادیر کمی از مواد را تشخیص دهند و استفاده از آن‌ها آسان است، مقیاس پذیر، ارزان و دقیق هستند. به دلیل هزینه کم، کاربر پسند بودن و سازگاری، حسگرهای زیستی به طور فزاینده‌ای در صنعت پزشکی محبوب شده‌اند.

نتایج: حسگرهای زیستی با ادغام فناوری نانو (NT)، به ویژه با توجه به سرعت تشخیص، گزینش پذیری و حساسیت، بسیار بهبود یافته‌اند. در حسگرهای زیستی مبتنی بر NT، نانومواد (NMs) مانند نانوسیم‌ها، نقاط کوانتومی (QD)، نانولوله‌های کربنی (CNTs)، و نانو میله‌ها معمولاً استفاده می‌شوند. به دلیل مساحت سطح بزرگشان، NMها حساسیت را بهبود می‌بخشند و تشخیص دقیق‌تر ترکیبات را در غلظت‌های پایین امکان پذیر می‌کنند. در نتیجه هدایت الکتریکی و حرارتی استثنایی، ظرفیت حمل عالی، دوام فوق العاده و رنگ قابل تغییر، نقش مهمی در ایجاد حسگرهای زیستی قابل اعتماد و کارآمد ایفا می‌کنند.

نتیجه گیری: این مطالعه به ادغام حسگرهای زیستی که توسط فناوری نانو فعال شده‌اند، یعنی BSهای فعال شده با فناوری نانو می‌پردازد. اصول، طرح‌ها و مواد مورد استفاده برای ساخت این حسگرها را بررسی می‌کند. تاکید بر نقش رو به گسترش حسگرهای زیستی مبتنی بر NT در زمینه‌های متنوعی مانند مراقبت‌های بهداشتی و نظارت بر محیط‌زیست وجود دارد. توسعه نسل بعدی ابزارهای تشخیصی، دستگاه‌های نظارت بر محیط زیست و ابزارهای امنیت زیستی با ترکیب نانوتکنولوژی با حسگرهای زیستی امکان پذیرتر می‌شود. با توجه به ویژگی‌های خاص نانومواد، حسگرهای زیستی مبتنی بر NT می‌توانند نحوه تشخیص مواد را کاملاً تغییر دهند. آنها قادر خواهند بود طیف گسترده‌ای از مواد را بسیار سریعتر، دقیق‌تر و با سطح بالایی از حساسیت تشخیص دهند، که برای تحقیقات و کاربردهای عملی در بسیاری از زمینه‌ها عالی خواهد بود.

واژه‌های کلیدی: حسگرهای زیستی، نانوتکنولوژی، نانومواد

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