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Role of nanostructured silicon in revolutionizing biosensors

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Abstract

Biosensors, a remarkable fusion of bioreceptors, transducers, and amplifiers, stand as versatile analytical tools capable of detecting a wide spectrum of analytes including heavy metal ions, carbohydrates, amino acids, gases, and disease-associated substances. This comprehensive review underscores the diverse types, classifications, and applications of biosensors. This review summarizes the leading advancements in porous silicon (PSi) based biosensors, achieved over the past few years. The cost-effective fabrication process, the high internal surface area, the tunable pore size, and the photonic properties made the PSi an appealing transducing substrate for biosensing purposes, with applications in different research fields. Different optical PSi biosensors are reviewed and different biorecognition elements immobilized on the surface of the transducing material. The adoption of these nanomaterials in biosensors capitalizes on their inherent attributes of heightened sensitivity, selectivity, reproducibility, and stability. Nanobiosensors, borne from the convergence of nanotechnology, biotechnology, and sensor engineering, are primed to revolutionize the healthcare and diagnostics.

Keywords: Biosensor, porous silicon, nanomaterials, nanosensor

Introduction

Nanotechnology is the study of the control of matter on an atomic and molecular scale. It generally involves development of materials and devices of the size 1-100 nanometers (nm). Dimensions upto few tens of nanometers are known as the nanoscale, where unique phenomena enable novel applications. Nanotechnology involves imaging, measuring, modeling, and manipulating matter at this length scale. A single gold atom is about a third of a nanometer in diameter. Unusual physical, chemical, and biological properties can emerge in materials at nanoscale. These properties may differ from those of bulk materials and single atoms or molecules [1].

Nanotechnology has the potential to create many new materials and devices with a vast range of applications such as in medicine, electronics and energy production. On the other hand, nanotechnology raises same issues as with any new technology, including concerns about the toxicity and environmental impact of nanomaterials. Many areas of biomedicine are expected to be benefited from the produce of nanotechnology such as sensors for use in laboratory, clinic, and human body; new formulations and routes for drug delivery; and biocompatible high performance materials for use in implants. Nanomedicine refers to future developments in medicine that will be based on the ability to build nanorobots. In future these nanorobots could actually be programmed to repair specific diseased cells, functioning in a way similar to antibodies in our natural healing processes. Nanotechnology may increase the capabilities of electronics devices by reducing their weight and power consumption. It may hold the key to making space-flight more practical. Advancements in nanomaterials may lead to the development of lightweight solar sails and cable for the space elevator. By significantly reducing the amount of rocket fuel required, these advances could lower the cost of reaching orbit and traveling in space. It is having an impact on several aspects of food science, from how food is grown to how it is packaged. Companies are developing nanomaterials that will make a difference not only in the taste of food, but also in food safety, and the health benefits that food delivers. Nanotechnology is being utilized to reduce the cost of catalysts used in fuel cells to produce hydrogen ions from fuel such as methanol and to improve the efficiency of membranes used in fuel cells to separate hydrogen ions from other gases such as oxygen. This technology plays an important role in developing nanotech solar cells that can be manufactured at significantly lower cost than conventional solar cells. Companies are currently developing batteries using nanomaterials which can be recharged significantly faster than conventional batteries. Nanotechnology can address the shortage of fossil fuels such as diesel and gasoline by making the production of fuels from low grade economical raw materials, increasing the mileage of engines. It can improve the performance of catalysts used to transform hazardous vapors escaping from cars or industrial plants into harmless gases. This is because catalysts made from nanoparticles have a greater surface area to interact with the reacting chemicals than catalysts made from larger particles. Nanotechnology is being used to develop solutions to three very different problems in water quality. One challenge is the removal of industrial wastes such as a cleaning solvent called Trichloroethylene (TCE) from groundwater. Nanoparticles can be used to convert the contaminating chemical through a chemical reaction to make it harmless. Studies have shown that this method can be used successfully to reach contaminates dispersed in underground ponds and at much lower cost than the methods that require pumping out the underground water for treatment. Nanotechnology can enable sensors to detect very small amounts of chemical vapors. Various types of detecting elements such as carbon nanotubes, zinc oxide nanowires or palladium nanoparticles can be used in nanotechnology-based sensors. Because of the small size of nanotubes, nanowires, or nanoparticles, a few gas molecules are sufficient to change the electrical properties of the sensing elements. This allows the detection of a very low concentration of chemical vapours [2,3,4]

An interdisciplinary research, recent advances in instrumentation and methods for applying nanotechnology to various areas in biology and medicine have led to a new generation of nanodevices that make it possible to characterize the chemical, mechanical, and other molecular properties, as well as discover novel phenomena and biological processes occurring at the molecular level. These advances provide science with a wide range of tools for biomedical applications in therapeutic, diagnostic, and preventive medicine. This emerging field plays an important role in the development and use of nanobiosensors with various analytical techniques for the detection and monitoring of specific biomolecules.

Nanotechnology is playing an increasingly important role in the development of nanobiosensors. The biosensors are defined as analytical devices incorporating a biological material such as tissue, microorganisms, organelles, cell receptors, enzymes, antibodies, nucleic acids, natural products, etc., a biologically derived material such as recombinant antibodies, engineered proteins, aptamers, etc or a biomimic such as synthetic catalysts, combinatorial ligands intimately associated with or integrated within a physicochemical transducer or transducing microsystem, which may be optical, electrochemical, thermometric, piezoelectric, magnetic or micromechanical. Biosensors usually yield a digital electronic signal which is proportional to the concentration of a specific analyte or group of analytes. While the signal may in principle be continuous, devices can be configured to yield single measurements to meet specific requirements. Biosensors have been applied to a wide variety of analytical problems including those of medicine, drug discovery, environment, food processing industries, security, and defence. The emerging field of bioelectronics seeks to exploit biology in conjunction with electronics in a wider context encompassing, for example, biological fuel cells and biomaterials for information processing, information storage, electronic components and actuators [5].

Biosensors are a special class of sensing devices which use a biological mechanism to recognise a test species in a mixture. According to IUPAC definition, a biosensor is precisely defined as a self-containing integrated device, capable of providing specific quantitative or semi-quantitative analytical information using a biological recognition element which is in contact with a transduction element. Biosensors are basically made up of three elements: (i) the selector, (ii) the transducer and (iii) the detector. Selector is the biological component creating the recognition event when in contact with the substance to be detected, transducer transforms the interaction between the selector and the analyte in a physically measurable signal and the detector allows to process and display the physical chemical signal in a suitable form. Figure 1 shows the components of a typical biosensor [6].

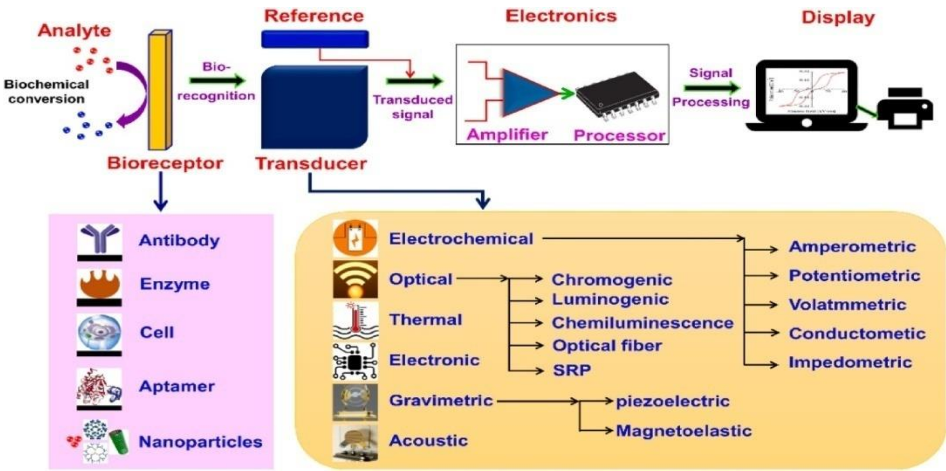

Figure 1. Biosensors and their components (reprinted from Ref. no. [6], copyright 2021, MDPI).

Biosensors in general are classified on the basis of the nature of the transduction method where one can distinguish amongst the electrochemical biosensors, amperometric biosensor, interferometric biosensor and so on. Another classification can also be made on the basis of the nature of the biological element such as enzymatic biosensors, geneosensors, immunosensors, etc. The main parameters characterizing the performances of a biosensor are selectivity, sensitivity, reproducibility, time response, stability and life time. Some of them depend upon the choice of the biological element used as selector, system geometry, working and storage conditions. Selectivity is the ability of a device to recognise a specific element in a mixture without interfering in the device performances deriving from addition of other substances. This property is strictly connected with the selectivity of the biological element used as selector, for example enzymatic biosensors have in general a high selectivity, deriving from the selectivity of enzymes. Sensitivity, reproducibility and time response depend on the biological element, the geometry of the system and the detection methods.

Sensitivity and other attributes of biosensors can be improved by using nanomaterials in their construction. Nanomaterials, or matrices with at least one of their dimensions ranging in scale from 1 to 100 nm, display unique physical and chemical features because of effects such as the quantum size effect, mini size effect, surface effect and macro-quantum tunnel effect. The living organisms have various nanoscale structural and functional units, ranging between 1 and 100 nm where nanotechnology research is focused. These units are then orgainzed into higher-order structures. Nanotechnology is playing an increasingly important role in the development of biosensors. Advancements in nanotechnology, biotechnology, and materials science are driving the development of increasingly sophisticated biosensors. [2,7,8,9]. Some emerging trends include:

- **Wearable Biosensors:** These can continuously monitor health parameters like heart rate, blood pressure, and glucose levels.
- **Implantable Biosensors:** These can provide real-time information on internal bodily functions.
- **Lab-on-a-Chip Devices:** These integrate multiple biosensors onto a single chip, enabling rapid and simultaneous detection of multiple analytes.

Silicon is the second most abundant element in Earth's crust, and it is considered one of the most important materials for the world. Crystalline silicon has continued to serve as the foundational building block for the microelectronic industry, and new forms of silicon materials have promised an even brighter future with emerging applications from optoelectronic devices, energy and environment technologies and new therapeutics [4,10,11]. Silicon biosensors are a type of biosensor that utilizes silicon as the sensing material. They are designed to detect and measure various biological analytes, such as DNA, proteins, and other biomolecules. These devices have gained significant attention due to their high sensitivity, selectivity, and potential for miniaturization. The basic principle behind silicon biosensors is their ability to convert biological interactions into measurable electrical signals. This is typically achieved through a combination of:

1. **Silicon Substrate:** The foundation of the biosensor is a silicon substrate, which provides a stable and well-defined platform for the integration of other components.
2. **Bioreceptor Layer:** A bioreceptor layer, such as antibodies, aptamers, or nucleic acid probes, is immobilized onto the silicon surface. This layer specifically binds to the target analyte of interest.
3. **Transduction Mechanism:** When the target analyte binds to the bioreceptor, it triggers a change in the physical or chemical properties of the silicon substrate. This change can be detected through various transduction mechanisms, including:

- **Electrochemical Transduction:** The binding event alters the electrical conductivity or impedance of the silicon substrate, generating a measurable signal.
- **Optical Transduction:** The binding event changes the optical properties of the silicon substrate, such as refractive index or fluorescence intensity, which can be detected using optical techniques.
- **Mass-Sensitive Transduction:** The binding event increases the mass of the silicon substrate, leading to a change in its resonant frequency, which can be measured.

Use of nanomaterials in biosensors allows the use of many new signal transduction technologies in their manufacture. Because of their submicron size, nanosensors, nanoprobes and other nanosystems are revolutionizing the fields of chemical and biological analysis, to enable rapid analysis of multiple substances

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in vivo. At the new frontiers of nanostructure silicon research, biomedical applications are very appealing because silicon is highly biocompatible. With the small sized silicon materials suitable for these applications, two distinct structures are porous silicon, and silicon nanocrystals which are also called quantum dots. Porous silicon is a form of crystalline silicon where the surface is embedded with nanometer sized pores, while silicon quantum dots are ultra small crystals of only a few nanometers in size. They both exhibit unique optical features suitable for sensing and imaging, which can be tuned via comparable surface engineering methods. For this reason, this review combines the two subjects in one article, with the scope of advancing the fields through a comparative approach. Since both porous silicon and silicon quantum dots have been actively researched in the past two decades and multiple excellent reviews have been published, this paper will only highlight recent progresses in the past several years [12-16].

Nanoparticles are integrated during fabrication and the resulting biosensors are called nano-biosensors. Nanomaterials are always the most investigated and examined of these because of the wide range of bioanalytical activities they provide in fields such as bioimaging, diagnostics, medication administration, and the treatments [17-19]. An important nanostructure material that has been studied extensively for nanosensing applications is nanocrystalline silicon, often referred to as porous silicon. Porous silicon (PSi) was discovered by Uhlir and others at Bell labs in the 1950s when a reddish-brown colour appeared on silicon during attempts at electropolishing. Initially attributed to a suboxide species, PSi attracted very little scientific attention until two key discoveries by Canham and co-workers. The first in 1990 was the prediction and then demonstration of room temperature photoluminescence from the material that was easily tunable making PSi a promising material for optoelectronics. Since the discovery of its strong visible luminescence at room temperature, porous silicon has attracted considerable interest in its possible use in construction of biosensors. Its ability to emit light is due to its tiny pores that range from less than 2 nm to micrometer dimensions. In addition, porous silicon possesses a high surface to volume ratio (as much as 500 m^2 cm^{-3}) and it can be fabricated easily using some of the established processes of the usual silicon technology [20-22].

Porous silicon has been used as an optical interferometric transducer for detecting small organic molecules (biotin and digoxigenin), 16-nucleotide DNA oligomers, and proteins (streptavidin and antibodies) at pico- and femtomolar analyte concentrations. Microcavity resonators made of porous silicon have been used in biosensors. These resonators possess the unique characteristics of line narrowing and luminescence enhancement. Chan et al. (2000) fabricated a DNA biosensor based on a porous silicon microcavity structure. The microcavity structure was highly sensitive and any slight change in the effective optical thickness modified its reflectivity spectrum, causing a spectral shift in the interference peaks. Potentiometric biosensors based on porous silicon have been described. The enzymes penicillinase and lipase were separately I mmobilized on the surface of PSi to detect penicillin and triglycerides. The hydrolysis reactions caused a change in the pH of the solution. The enzyme solution-oxidized porous silicon-crystalline silicon structure was used to detect the changes in pH during hydrolysis as a shift in the capacitance–voltage (C–V) characteristics [23-28].

The concept of interferometric biosensing takes advantage of the difference in the phase of light reflected at the top surface and base of a thin film whereby its reflectance spectrum shows an interference pattern that depends on the optical thickness of the PSi thin film. Binding of analytes to receptors immobilized on the pore walls results in an increase in the average refractive index of the material and hence an increase

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in the optical thickness. This increase in optical thickness is detected as a shift of the interference pattern towards higher wavelengths (red-shift). With suitable surface passivation, researchers have detected biomolecules by red-shifts in Fabry–Perot fringes for a range of analytes including complementary DNA, proteins and small molecules. Novel built-in control systems and advances in chemical passivation strategies, should allow for continued progress with Psi Fabry–Perot optical materials in biosensing [29-32].

The refractive index of PSi is dependent on its porosity (volume ratio of air to silicon), which in turn is a function of the current density applied during formation. The duration of the current pulses during fabrication determine the layer thickness. Thus, by periodically altering the current density during anodisation, it becomes possible to produce one dimensional photonic crystals with a periodically varying refractive index normal to the surface. Optical resonant microcavities represent a second class of photonic crystals that were produced in PSi and these have received considerably more attention for biosensing applications. The luminescent property also makes porous silicon an attractive biomaterial in bioimaging. Luminescent porous silicon nanoparticles with emission on 650–900 nm range, fabricated by lifting off porous silicon film and sonication, are suitable candidates for *in vivo* imaging, as like silicon quantum dots, they can be easily degraded in aqueous solutions into non-toxic orthosilicic acid [33,34].

For nanostructured porous silicon devices to effectively transduce a biorecognition event the following criteria must be met: (1) the porous silicon scaffold must be protected from degradation, (2) the surface must prevent false-positives from non-specific interactions with interfering species in a complex biological sample and (3) a specific recognition moiety must be provided to bind the analyte. The past two decades have seen remarkable progress in using crystalline silicon micro and nanostructures in biosensing and bioimaging applications. This article tends to provide a tutorial typed guide to the frontiers using two representative structures of porous silicon and silicon quantum dots. In light of the remarkable optical properties, porous silicon offers a good prospect for bio-applications. The recent advances in establishing better biological recognition interfaces, enhancing signal processing, developing new sensing strategies and adopting novel optical structures have shown promises in achieving high-sensitivity sensing performance on porous silicon. Especially, the integration of other materials or sensing techniques into porous silicon to form hybrid structure with dual or multiple properties has expanded the potential with porous silicon. Due to the chemical nature of silicon, the interfacial property of particle surface chemistry is particularly influential over their optical properties. We can conclude that the new frontiers brought by the two types of nanostructures will open new opportunities in using these materials for more application in nanomedicine.

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