

## Biomaterials for Biosensing Applications

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Biosensors are finding diverse applications and gradually becoming an integral part in a variety of analytical applications such as; clinical diagnosis, environmental monitoring, *etc.* since the introduction of glucose biosensors by Clark and Lyons in 1960 [1]. This was followed by the inception of the first enzyme-based glucose sensor developed by Updike and Hicks in 1967. Since then, extensive researches have been done towards biosensor designing due to its specificity, fast detection time, and high selectivity to detect analytes (DNA/RNA, proteins, cells), within the miniaturized settings [2]. A biosensor typically consists of a transducer in combination with a biologically active molecule that converts the biochemical response into a quantifiable signal. In general, a biosensor is comprised of three basic components *viz.* (i) a detector, (ii) a transducer, and (ii) a signal processor. The transducer can be electrochemical, optical, acoustic, or calorimetric type depending upon the diagnosis and the physiochemical character of the analyte [3]. Biosensors have been broadly studied based on various detection principles such as; conductometric, amperometric, potentiometric, and voltametric [4]. The selection of the biomaterial for designing a biosensing element is an important issue. Among these, enzymes [5], DNA/RNA [6], aptamers [7,8], antibodies [9], receptors [10], organelles [11] and animal cells/tissues [12] have been extensively utilized to develop various types of sensing systems. Studies have been reported on glucose biosensors [13], sensors for cancer detection [14,15], sensors for detection of various drugs such as kanamycin [16], daunomycin [17], and acetaminophen [18] using different types of biomaterials.

While designing a biosensor, the major considerations that should be followed are: (i) it should work in a wide range of pH and temperature conditions, (ii) it should involve facile fabrication steps, and (iii) it should have a wide dynamic range and high sensitivity [19]. The second step after selection of a biomaterial is its immobilization and its capability to retain its biological activity and detect the target molecules. Recently, the *in vivo* [20,21] and *in vitro* [7,22] design of biosensors to detect disease-specific biomarkers have earned great interest since it offers monitoring real-time biological signals.

The introduction of biosensors have emerged since it provides a miniaturized approach to solve the problems related to sensitivity, rapidity, selectivity, and high cost which the ELISA or the previously used genomic and proteomic based conventional methodologies involved. A major advantage of biosensor is to reduce the complexities faced by a common man offering them a point-of-care medical device for personalised diagnosis.

Over the years, remarkable efforts have been done to develop various types of personalized biosensing prototypes. These include natural biomaterials such as chitosan [23], collagen [24], and synthetic materials such as metal oxides [25], carbon nanotubes (CNT) [26,27], and various polymer composites [28] comprising quantum dots [29], and graphene [30].

The design of biosensors using various biomaterials involves an interdisciplinary approach from a variety of scientific fields. Due to this

reason, in last few decades tremendous researches have been done using different biomaterials to develop even more efficient diagnostic systems. Natural biopolymeric materials such as; chitosan have been widely used to develop biosensors by protein immobilization. This has been possible because of the positive charge of chitosan and its special properties such as excellent film forming ability and good biocompatibility [31]. A group of researchers from Zhejiang Foundation, China have reported a simple but efficient way to prepare novel water dispersible modified chitosan-graphene multifunctional glucose biosensors using a one-step ball milling technique. The multifunctional approach was achieved by introducing magnetic iron oxide (Fe<sub>3</sub>O<sub>4</sub>) nanoparticles [32]. Synonymous work has been done using cobalt oxide (Co<sub>3</sub>O<sub>4</sub>)-chitosan nanocomposites to develop a potentiometric urea biosensor. The incorporation of these nanoparticles have added promising features such biocompatibility, strong super paramagnetic property, low-toxicity, for applications in diverse biomedical areas such as drug delivery, hyperthermia treatment, cell separation, and as efficient biosensors. Biomaterials have been extensively used as polymeric fibres, polymer composites coupled with conducting materials to design efficient biosensing prototypes [33]. For example, studies have been reported using chitosan nanogel composites along with quantum dots as a biosensing probe for cancer cell detection. In another work, a design of amperometric biosensors using CdS quantum dots-chitosan nanocomposite for detection of phenols has been reported. Chitosan has also been coupled along with nickel oxide for the detection of environmental and clinically important pathogens like *Escherichia coli*, *Salmonella typhi* and other pathogens [34]. Based on the promising advantages that hybrid materials offer, researchers have also designed a reagentless amperometric glucose biosensor combining zirconia nanoparticles-collagen composite to prepare a tri-helix scaffold on graphite electrode [35]. The collagen grafted biosensor was found to be biocompatible, thermally steady, and highly sensitive and had improved selectivity.

Apart from using natural biomaterials for designing biosensors, studies on commercially available biomaterials (e.g., Collagen Type I, Sigma-Aldrich) have been reported to be more prominent and effective. This is due to the fact that the synthetic materials can be functionalized to design biosensors with high stability and sensitivity. Among these notable works have been done incorporating carbon nanotube to

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design biosensors. For example, researchers have developed a hydrogen peroxide biosensor using CNTs and electrospun collagen polymer [24]. The electrospun nanofibres helped design biosensors with good biocompatibility and high specificity due to the integration of collagen fibres and CNTs, respectively.

Despite of the fact that the studies mentioned above clearly indicates that extensive research have been done and are still on-going in designing nanobiosensors using various biomaterials. The available biosensors are extremely powerful; however, there are still chances to improve them in terms of selectivity, biocompatibility, for *in vivo* and *in vitro* diagnostics. Hence, the future work should be directed towards exploration of various types of natural and synthetic biomaterials for diverse biomedical applications.

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