Biomaterials for Biosensing Applications

Alisha Prasad[1], Kuldeep Mahato[1], Pawan Kumar Maurya[2] and Pranjal Chandra[1]*

[1]Department of Biosciences and Bioengineering, Indian Institute of Technology Guwahati, Guwahati-781 039, Assam, India

[2]Interdisciplinary Laboratory for Clinical Neuroscience (LiNC), Department of Psychiatry, Universidade Federal de Sao Paulo - UNIFESP, Sao Paulo, Brazil

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 voltameteric [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 grapheme [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_3O_4) nanoparticles [32]. Synonymous work has been done using cobalt oxide (Co_3O_4)-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

*Corresponding author: Pranjal Chandra, Department of Biosciences and Bioengineering, Indian Institute of Technology Guwahati, Guwahati-781 039, Assam, India, Tel: +91(0)-361-258-3207; Fax: 0361-258-2249; E-mail: pranjalmicro13@gmail.com/pchandra13@iitg.ernet.in

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.

Acknowledgements

References

1. Brooks SL, Ashby RE, Turner APF, Calder MR, Clarke DJ (1988) Development of an on-line glucose sensor for fermentation monitoring. Biosensors 3: 45-56.

2. Yager P, Domingo GJ, Gerdes J (2008) Point-of-care diagnostics for global health. Annu Rev Biomed Eng 10: 107-144.

3. Barsan MM, Ghica ME, Brett CM (2015) Electrochemical sensors and biosensors based on redox polymer/carbon nanotube modified electrodes: a review. Anal Chim Acta 881: 1-23.

4. Yadav SK, Chandra P, Goyal RN, Shim YB (2013) A review on determination of steroids in biological samples exploiting nanobio-electroanalytical methods. Anal Chim Acta 762: 14-24.

5. Sakamoto H, Watanabe K, Koto A, Koizumi G, Satomura T, et al. (2015) A bienzyme electrochemical biosensor for the detection of collagen l-hydroxyproline. Sensing and Bio-Sensing Research 4: 37-39.

6. Linardy EM, Erskine SM, Lima NE, Lonergan T, Mokany E, et al. (2016) EzyAmp signal amplification cascade enables isothermal detection of nucleic acid and protein targets. Biosens Bioelectron 75: 59-66.

7. Zhu Y, Chandra P, Shim YB (2013) Ultrasensitive and selective electrochemical diagnosis of breast cancer based on a hydrazine-Au nanoparticle-aptamer bioconjugate. Anal Chem 85: 1058-1064.

8. Zhu Y, Chandra P, Ban C, Shim YB (2012) Electrochemical evaluation of binding affinity for aptamer selection using the microarray chip. Electroanalysis 24: 1057-1064.

9. Chandra P, Noh HB, Shim YB (2013) Cancer cell detection based on the interaction between an anticancer drug and cell membrane components. Chem Commun (Camb) 49: 1900-1902.

10. Baaske MD, Foreman MR, Vollmer F (2014) Single-molecule nucleic acid interactions monitored on a label-free microcavity biosensor platform. Nat Nanotechnol 9: 933-939.

11. Halstead JM, Lionnet T, Wilbertz JH, Wippich F, Ephrussi A, et al. (2015) Translation. An RNA biosensor for imaging the first round of translation from single cells to living animals. Science 347: 1367-1671.

12. Ding C, Tian Y (2015) Gold nanocluster-based fluorescence biosensor for targeted imaging in cancer cells and ratiometric determination of intracellular pH. Biosens Bioelectron 65: 183-190.

13. Noh H-B, Lee K-S, Chandra P, Won M-S, Shim YB, et al. (2012) Application of a Cu-Co alloy dendrite on glucose and hydrogen peroxide sensors. Electrochimica Acta 61: 36-43.

14. Koh WC, Chandra P, Kim DM, Shim YB (2011) Electropolymerized self-assembled layer on gold nanoparticles: detection of inducible nitric oxide synthase in neuronal cell culture. Anal Chem 83: 6177-6183.

15. Chandra P, Zaidi SA, Noh H-B, Shim YB (2011) Separation and simultaneous detection of anticancer drugs in a microfluidic device with an amperometric biosensor. Biosensors and Bioelectronics 28: 326-332.

16. Zhu Y, Chandra P, Song KM, Ban C, Shim YB (2012) Label-free detection of kanamycin based on the aptamer-functionalized conducting polymer/gold nanocomposite. Biosens Bioelectron 36: 29-34.

17. Chandra P, Noh HB, Won MS, Shim YB (2011) Detection of daunomycin using phosphatidylserine and aptamer co-immobilized on Au nanoparticles deposited conducting polymer. Biosens Bioelectron 26: 4442-4449.

18. Chandra P, Son NX, Noh HB, Goyal RN, Shim YB (2013) Investigation on the downregulation of dopamine by acetaminophen administration based on their simultaneous determination in urine. Biosens Bioelectron 39: 139-144.

19. Jolly P, Tamboli V, Harniman RL, Estrela P, Allender CJ, et al. (2016) Aptamer-MIP hybrid receptor for highly sensitive electrochemical detection of prostate specific antigen. Biosens Bioelectron 75: 188-195.

20. Yuen JM, Shah NC, Walsh Jr JT, Glucksberg MR, Van Duyne RP, et al. (2010) Transcutaneous glucose sensing by surface-enhanced spatially offset Raman spectroscopy in a rat model. Analytical chemistry 82: 8382-8385.

21. Noh HB, Chandra P, Moon JO, Shim YB (2012) In vivo detection of glutathione disulfide and oxidative stress monitoring using a biosensor. Biomaterials 33: 2600-2607.

22. Yadav SK, Agrawal B, Chandra P, Goyal RN (2014) In vitro chloramphenicol detection in a Haemophilus influenza model using an aptamer-polymer based electrochemical biosensor. Biosensors and Bioelectronics 55: 337-342.

23. Maxwell T, Banu T, Price E, Tharkur J, Campos MGN, et al. (2015) Non-Cytotoxic Quantum Dot–Chitosan Nanogel Biosensing Probe for Potential Cancer Targeting Agent. Nanomaterials 5: 2359-2379.

24. Li J, Mei H, Zheng W, Pan P, Sun XJ, et al. (2014) A novel hydrogen peroxide biosensor based on hemoglobin-collagen-CNTs composite nanofibers. Colloids Surf B Biointerfaces 118: 77-82.

25. Pradhan D, Niroui F, Leung K (2010) High-performance, flexible enzymatic glucose biosensor based on ZnO nanowires supported on a gold-coated polyester substrate. ACS applied materials & interfaces 2: 2409-2412.

26. Sengiz C, Congur G, Eksin E, Erdem A (2015) Multiwalled Carbon Nanotubes-Chitosan Modified Single-Use Biosensors for Electrochemical Monitoring of Drug-DNA Interactions. Electroanalysis 27: 1855-1863.

27. Agrawal B, Chandra P, Goyal RN, Shim YB (2013) Detection of norfloxacin and monitoring its effect on caffeine catabolism in urine samples. Biosens Bioelectron 47: 307-312.

28. Chandra P, Das D, Abdelwahab AA (2010) Gold Nanoparticles in Molecular Diagnostics and Therapeutics. Digest Journal of Nanomaterials & Biostructures 5: 363-367.

29. Zhang R, Chen W (2014) Nitrogen-doped carbon quantum dots: facile synthesis and application as a "turn-off" fluorescent probe for detection of Hg2+ ions. Biosens Bioelectron 55: 83-90.

30. Cai B, Wang S, Huang L, Ning Y, Zhang Z, et al. (2014) Ultrasensitive label-free detection of PNA-DNA hybridization by reduced graphene oxide field-effect transistor biosensor. ACS Nano 8: 2632-2638.

31. Han E, Yang Y, He Z, Cai J, Zhang X, et al. (2015) Development of tyrosinase biosensor based on quantum dots/chitosan nanocomposite for detection of phenolic compounds. Anal Biochem 486: 102-106.

32. Zhang W, Li X, Zou R, Wu H, Shi H, et al. (2015) Multifunctional glucose biosensors from Fe$_3$O$_4$ nanoparticles modified chitosan/graphene nanocomposites. Sci Rep 5: 11129.

33. Ali A, Israr-Qadir M, Wazir Z, Tufail M, Ibupoto ZH, et al. (2015) Cobalt oxide magnetic nanoparticles-chitosan nanocomposite based electrochemical urea biosensor. Indian Journal of Physics 89: 331-336.

34. Solanki PR, Patel MK, Ali MA, Malhotra B (2015) A chitosan modified nickel oxide platform for biosensing applications. Journal of Materials Chemistry B 3: 6698-6708.

35. Zong S, Cao Y, Zhou Y, Ju H (2006) Zirconia nanoparticles enhanced grafted collagen tri-helix scaffold for unmediated biosensing of hydrogen peroxide. Langmuir 22: 8915-8919.