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Nanobiosensors: Next Generation Point-of-Care Biomedical Devices for Personalized Diagnosis

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Imagine an era where patients will be able to tell the doctor that they themselves have detected the target molecule (*e.g.*, antigen, proteins, chemical molecule, *etc.*) related to a disease using a personalized diagnostic tools (*e.g.,* glucose for diabetes, *Salmonella typhi* for typhoid, bilirubin for anemia). This may help the clinicians to quickly design the adequate therapeutic strategies for patients. A biosensor based diagnostic technology promises to do just that-quick onsite diagnosis. Biosensors in general are stand alone miniature portable devices that can detect range of analytes quickly with the help of transducers that converts the biological response into measurable analytical signals. It represents a rapidly expanding field currently and is expected to reach $22.68 billion market by 2020. Moving this proof-of-concept device for everyday analysis of biological or chemical samples has involved tremendous development in biosensors research [1]. Therefore, many such diagnostic devices are available in the global market for various medical purpose such as; malaria testing kit [(CareStart™ Malaria HRP2/PLDH; Access Bio, United States) (Maleriscan® Malaria Pf/PAN; Bhat Bio-Tech (P) Ltd., India)], hCG based pregnancy testing kits [(Pregnosis®; Hoffmann-La Roche Ltd., Montreal), (Velocit®; Dr.Reddy's India)], and portable glucometers [(CareStart™ G6PD, Access Bio, United States)] *etc.* Although these miniaturized devices are extensively fabricated and possess good market potential, research to improvise the existing designs in terms of relativity, sensitivity, detection time, and point-of-care diagnosis are still underway [2].

Research and development to design biosensor prototypes has been rapid and ever expanding. To overcome the challenges related to sensitivity in detecting and capturing target molecules, introduction of "nanotechnology" has been found to be extensively useful. The advances in nanotechnology offers sensitive and specific detection of analyte by: (i) integrating new novel microfluidic/nanofluidics technologies to design small, and easy-to-use devices [3], (ii) surface functionalization of biomaterials on nanocomposites, and (iii) new signal amplification strategies using various nanomaterials [4,5]. The developments in nanotechnology and changes in electronic, thermal, and, optical property of nanoscale materials have brought new detection methods in biosensing [6-8]. Research and development in the field of nanobiosensors is wide and multidisciplinary, spanning knowledge of researchers from diverse backgrounds such as biological science, medical science, material science, physics, chemistry, electronics, mechanical engineering, and other engineering sciences to develop various types of nanobiosensor prototypes [7,9-11]. Tremendous work has been done on next generation fabrication of [12], semi-synthetic [13] and synthetic ligands [14], plastic antibodies [15], catalytic electrodes [16], bioinspired nanotechnologies for sensing, therapy, and controlled surface for cellular interaction [17], *in vivo* [18] and *in vitro* [19,20] devices for regenerative medicine, arrays, biomimetics and tele-interfaces for digital health [21]. These platforms may help to design commercially viable nanobiosensor for various biomedical applications. Among the available nanobiosensor types, electrochemical readout system is considered to be most powerful due to its high sensitivity and ability to be miniaturized for fast bimolecular analysis [22], thereby helping in designing therapeutic strategies quickly to overcome patients stress [20,23].

Researchers have developed a highly sensitive and interference-free endotoxin detection system using new nanobiomaterials and nanobioconjugated paper/plastic settings. Prototypes for immunosensors [24], lateral flow based biosensors [25], microfluidic sensor system [26], enzyme sensor [23], paper inkjet sensor [27] *etc.* for detection of various clinically important target molecules including parasite, hormones, cancer biomarkers, heavy metal ions, cancer cells, and bacteria have been developed. In current years, aptamers has been extensively studied in diagnostics and therapeutics to design novel nanobiosensors. Aptamers have been used to design single-disposable nanobiosensors that can integrate multiple biophysical and biochemical processes even at low concentrations with high sensitivity. In a recent report a "real-time aptamer based biosensor" has been developed [28] that continuously measure specific biomolecules directly in living animals. Recent reports demonstrates the ability of aptamers to diagnose pancreatic ductal adenocarcinoma for *in vivo* imaging and clinical tissue recognition [29] and detection of human liver cancer cells [30]. Electrochemically tuned nanostructures has also been applied to design new nanobiosensor prototypes [31,32]. Researchers have reported tuned molecular probe / surface for ultrasensitive biomolecular detection of virus [33], circulating nucleic acids [31], and circulating cancer cells [34].

Currently smartphones because of its handy, well equipped, and classy features such as: advanced processors, increased memory, high-resolution camera, high-end security *via* fingerprinting, and a variety of built-in sensors has been used to design nanobiosensor prototypes. Based on the idea to design personalised nanobiosensor settings, extensive work has been done on portable detection system using high resolution smartphone cameras [35]. Notable work using this technology has been done in *in-vitro* and real-time monitoring of clinical condition. The data produced by smartphone based *in vitro* diagnostics can be added with spatial and temporal information, which can be used for monitoring and management in critical situations [36]. Research on smartphone based nanobiosensor prototypes such as: lateral flow assays (LFA), microscopy, electrochemical sensing, immunoassays, surface plasmon resonance-based biosensing, flow cytometry, and optical detection has been reported [37]. Examples

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of few commercialized smartphone based prototypes are iHealth, AliveCor, GENTAG, Mobile Assay, and CellScope *etc.*

Though the reports mentioned above clearly show tremendous promise in nanobiosensor research and its continuous development, still there is incredible scope to design new sensing strategies and improve the known sensing strategies. The future work should be directed towards the development of new, sensitive, selective, quick, and personalized diagnosis strategies for bimolecular analysis.

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