ABSTRACT

Research activity and applications of biosensors for measurement of analytes has been of clinical interest over the last decade. Nanotechnology has been applied to improve performance of biosensors using electrochemical, optical, mechanical and physical modes of transduction and to allow arrays of biosensors to be constructed for parallel sensing. Biosensor measurements have been proposed for biomarkers for detection of cancer, cardiac issues, infectious diseases; DNA analysis etc. Novel applications of biosensors include measurements in alternate sample types such as urea and saliva. Biosensors based on immobilized whole cells have found new applications, for example to monitor the response of cancer cells to chemotherapeutic agents. This will drive to decrease the cost of health care, to shift some of the analytical tests from centralized facilities to “frontline” physicians and nurses, and to obtain more precise information more quickly about the health status of a patient.

The greatest impact of biosensors will be felt at point-of-care testing locations without laboratory support. Integration of biosensors into reliable, easy-to-use and rugged instrumentation will be required to assure success of biosensor-based systems at the point-of-care.

Translation of basic research findings to clinical applications within regulatory compliance is required for personalized medicine to become the new foundation for practice of medicine. Deploying even a few of the thousands of potential diagnostic biomarkers identified each year as part of personalized treatment workflows requires clinically efficient biosensor technologies to monitor multiple biomarkers in patients in real time. The recent advances in the field of biosensors, focusing on enzymes, aptamers, antibodies, and phages are applied more in clinical testing and cell analysis.

As the number of hazardous materials and pathogens in our environment and food increases, the development of highly selective and sensitive monitoring devices is ever more important. Despite significant progress, detection instruments are bulky and require qualified personnel and large amounts of reagents. In this context, the field of biosensing strives to develop devices that are sensitive, specific and yet miniature, and simple to operate.
In clinical laboratories, normally the method of drawing blood will be through the skin with conventional puncture and quantity drawn is usually 1-5 ml for testing purposes. However, in the minimally invasive systems, the quantity of blood needed for analysis is a drop of blood by finger pricking.

Early work involved abrasion of the skin, but a more sophisticated approach was adopted in the mid-1990s, which was based on electrochemical measurement. The designed device is intended for detecting trend and tracking patterns in glucose levels in human beings with diabetes. The instrument was proposed to use at home and in healthcare facilities to supplement information obtained from standard blood glucose monitoring devices. The attractive feature of the new device was the frequency of the automatic and noninvasive measurements, which offered the potential to provide previously unavailable information about blood glucose, including automatic and frequent measurements, and alerts for high and low glucose levels.

Miniaturized Sensors are used to sense and collect data from various devices to assist in system identification and health monitoring. The field of smart sensors, materials and structures is an important concept which incorporates human creativity and innovative ideas to serve public or the society for such tasks as biomedical, food, agriculture, defense or pharmaceutical applications. Furthermore, smart sensors help to control the environment better and to increase the energy efficiency of the devices. With the invention of nano technology, it is now possible to fabricate conducting polymer-based sensors and sensors with built-in flexible electronics resulting in high throughput devices and systems that are flexible, lighter, biocompatible and much less expensive to produce.

The performance of the conducting polymer nano materials in recent days are investigated to trace the factors which control the morphology of the nano materials and further the sensor film is subjected to detailed characterization to study the importance of the sensor in biological instruments. Conducting polymers and nanomaterials are generally used in bio-tech based sensors, smart systems and electronic devices. This in turn can be applied for health monitoring of human and complex systems in engineering and medicine.

The research on biosensors using conducting polymers and nanocomposites with sensor technology enables in future where billions of people can regularly access applications in global network as their daily routine.
In recent years, people and the society are bothered and scared about the disease “cancer” that is “Leukemia” which is creating panic in the hearts of most of the people in this world. For this disease, white blood corpuscles (WBC) count plays a vital role. The normal WBC count varies from 4000 to 11000 in cubic ml of blood and sometimes up to 30000 in case of any infection/allergy. If the WBC count exceeds 11000, further medical diagnosis is required to ascertain whether it is due to infection/allergy/leukemia.

Many investigators have worked in the area of glucose biosensors to miniaturize the sensor design which requires only 10 micro liters of blood sample. However no attempt has been made to determine leukocyte counts for leukemia. Hence there is a need to investigate biosensors for biological real time applications. The present work is focused on the design, synthesis, characterization and testing of sensor for biological real time applications.

In chapter 1, a brief introduction about biosensors, polymers and conducting polymers are discussed. The significance of nanocomposites required for the sensor design in biomedical applications is included. Further novel signal conditioning and processing electronics system required to condition and process the biosignals accessed from the sensors are presented. The classification and applications of biosensor are included and the compressive reviews of the current literature related to this work are presented.

In chapter 2, it has been clearly brought out that there is a need to design the biosensor for biological real time applications. The aim of the present work can be briefly stated as follows:

- It is proposed to design, synthesize and characterize the sensor for biological real time applications using conducting polymer, polyaniline (PANI) and gold nanocomposites.
- It is proposed to test the electrical I-V characteristics, by applying glucose oxidase, GO\textsubscript{X} on the fabricated sensor by two-probe technique for different enzyme concentrations.
- It is proposed to investigate the electrical I-V characteristics, by two probe techniques, by applying GO\textsubscript{X} on the fabricated sensor for various blood concentrations by adding deionized water.
• It is proposed to probe the electrical I-V characteristics, by two probe technique, to determine WBC count (leukocyte count) in the real time blood sample for different enzyme and its concentrations.

• It is proposed to study the surface morphology and thickness of the fabricated sensor by atomic force microscope (AFM) and optical profilometer technique.

• It is proposed to design and develop the novel signal conditioning and processing electronic system for biosensor output signals.

In chapter 3, the experimental synthesis and characterization of biosensors for different types I, II, III, IV and V are presented. In chapter 4, design, simulation, development and testing of nano and pico amperes signal conditioning electronic systems are discussed.

The results of sensor design, synthesis and characterization for type I (sensor design with PANI, gold nanoparticles, indium tin oxide and aluminum electrodes), type II (sensor design with PANI, gold nanoparticles, indium tin oxide and aluminum electrodes), type III (sensor design using PANI, gold nanoparticles and aluminum electrodes), type IV (sensor design using PANI, gold nanoparticles, hanging glass slide and silver paste as electrodes) and Type V (free-standing or free-lan sensor design using PANI, gold nanoparticles and silver paste as electrodes) are presented in chapter 5.

Synthesized sensors are tested for laboratory glucose; glucose and leukocyte counts of real time blood sample. Various enzymes such as glucose oxidase, hydrogen peroxide and horse radish peroxidase are used for experimental work. Hanging glass slide sensors are tested for the laboratory glucose using potassium phosphate buffer. Also the free-lan sensors are tested for both I-V and I-T characteristics.

The designed nano and pico amperes signal conditioning circuits are simulated using MULTISIM and NI LabVIEW software; and these results are successfully compared with the hardware set-up results developed in the laboratory. A detailed report of results and discussion is included in chapter 5.

Conclusions and scope for future work are presented in Chapter 6.