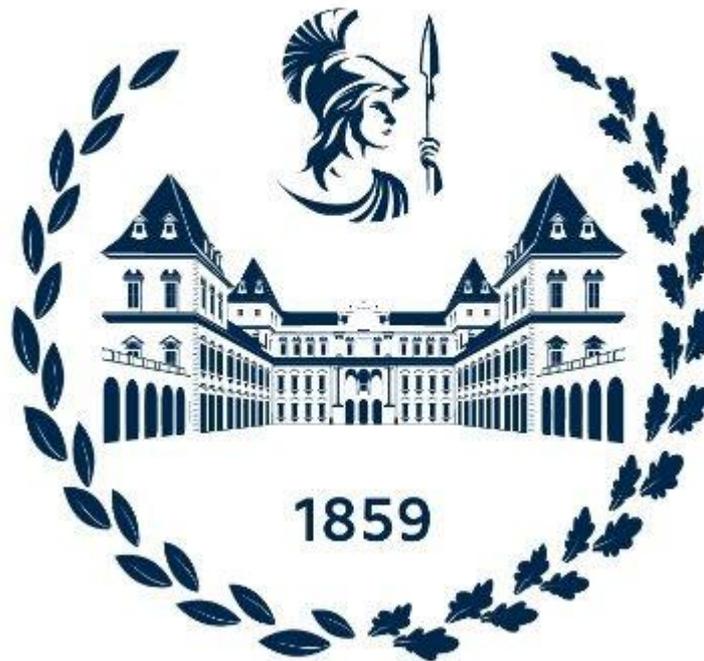


POLITECNICO DI TORINO

**MASTER OF SCIENCE IN COMMUNICATIONS AND COMPUTER NETWORKS
ENGINEERING**

MASTER'S THESIS TITLE

**Study of Circuit Modelling of Sensors for Smart Biomedical
Implants**



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Abstract

World is moving towards smartness and automation in every field including medicine. Conventional health care system with evasive decision along with modern technology can produce brilliant results. Health care systems as well as remote surgeries operations are undergoing in the experimental phases. Different type of IOT based system are being studied and considered. These biomedical implants are in testing phase with direct contact of skin to study anomalies of any kind. Biomedical implants field is revolutionizing the medical science. Experiments are being carried from a decade to adapt this technology as soon as possible. To be able to transplant such technology safety parameters are considered at its highest.

The primary goal of this thesis is to study a real time patient monitoring system. Our focus is to study biomedical sensors that can measure our vital signs, give cautions in case of emergency and delivers drugs when it is necessary. I started with the study of important parameters are that required to be monitored in the patients such as blood Oxygen level(spO₂), glucose level and temperature. Then I studied different sensors which can be used and a simulation of such a system that is designed on Proteus. The main purpose of this simulation is to understand how these sensors are working and how we can integrate different type of sensors with each other. Moreover, research carried in different institutes and the developing model of such type are being studied. In pursue of this quest, we also reach out to institutes and different companies for in depth view and arrange some test bed as basic building block towards a suitable design.

The recent event of COVID-19 supports the concept of telemedicine and telemonitoring of patient at home to reduce the physical interaction as much as possible. Furthermore, the application of biosensors is not limited only to the medical field but it has also enhanced its ways to our daily routine life. Hence, A study of profound IOT based system is the focus of this research.

Chapter one: Introduction:

1.1 Background:

The quest of biosensors starts early in the twentieth centuries. This field grows by the time passes. Today, we are in the experimental phase where biosensors are very much close to be implantable inside the body. Sensors are the electronic devices that yields results [1]. Biosensors are design on the same principle. A heartbeat sensor is a simple example. When it is being exposed to finger, the light in these sensor responds to the capillaries fluctuation that is response of the blood flow. This transduce the effect of voltage and as result heartbeat of the person is obtained. Medical profession is being influenced by these sensors and it is heading towards smartness. Telemedicine is a hot topic related to this technology. Telemedicine is basically a concept where remote diagnosis and monitoring of patient's health is done through information and communication technologies to act quickly and reduce the physical interaction where it is necessary [2]. Some medical conditions are of such type where exposure to the physicians and other person can be harmful. So, to avoid contagious diseases and act quickly as soon as possible, the modern way of treating and checking the vitals of patients are introduced with the time.

Not only the literature about biosensors is never ending but they are also appealing not only in terms of academics, but also from the industry point of view. The key point in biosensors is that they exploit the distinctive properties of the biological recognition along with the electronics properties to enable the gateway towards the smartness and easiness. It has also opened a new frontier, along with the technology for daily use, in the scientific research in the healthcare system. Researcher along with professionals thinking out of the can be a great contribution towards something sustainable.

With the passage of time, biosensors have impacted every important aspect of our life. They have a very wide range of applications starting from medical applications, food safety, water quality management to the soil quality testing and environmental monitoring. One of the main purposes of the biosensor is to identify the molecules related to the disease. This will lead to the discovery of drugs that are helpful in curing the disease[3]. Biosensor can also be used to make sure the food safety, traceability, quality and nutrition values [4]. Such type of

activity is considered as “single shot”. Most of the time biosensor are used for long term activity. For example, pollution monitoring requires monitoring for a longer time period varying from some hours to many days.

1.2 Inadequacy of current system:

The issue with the conventional health care system is that it is slow, requires more manpower. The mechanical instruments in the health system can generally make mistakes. Moreover, it is very hard to keep the track of a patient time to time. For example, in a young person the normal heartbeat is 140 to 170 beats/min and in old person it is around 115 to 140 beats/min. So, in this scenario it is very hard to find any irregularities in the heart rate of patient. So, we need such type of system that can keep track of vital signs of a patient that can be helpful in diagnosis. Biosensors are playing a very important role to revolutionize the medical field now a days. But all of this requires some limitations in terms of manufacturing cost, system design, communication system and the sensor size which is most important one. Common design problem may be like they must be resilient to dust and humidity otherwise the system can be compromised. The communication system must be reliable and proficient that can send the information correctly. It must not be affected by the surroundings and do not be harmful to the body. Man handling operation of patients is delayed even to give the emergency medic. So, during the design of such system it is kept in mind that some initial medic should be released into the patient system that will be helpful in stabilize the patient’s condition.

1.3 Approach to Circuit Modelling:

In first step, I studied the working of biosensors and understand how they work. Mainly biosensors are based on the principle of signal transducing. Transducers have the tendency to convert the energy from one form to another. The intensity of signals is being converted and then displayed on the screen at the remote end. A simulation based on different sensors is made to understand the behaviour and working principle. Proteus is a one of the commercially available software which allows the user to exhibit and design the required circuit. I used this software to design a telemonitoring system with a heartbeat sensor and a temperature sensing IC LM35. The feasible microcontroller used is Arduino uno which

allows to program and calibrate these sensors. After completing the designing, simulation results are monitored that are generated by self-induced change in the voltage using a potentiometer. Simulation results are promising and helped us to understand that how these sensors are working. The next task is to customize a specific chip with required sensors so that this chip can be implanted on 3D modelled printed bone for the test purposes. For this purpose, we are trying to reach the industries that are related to nano technology and working on this type of technology. One of them is Zimmerandpeacock. We are trying to design and build a compact system which can be implanted on the bone model and be ready for experimental phase. We are intending to dip this model along with the sensor embedded chip in some fluid that will be a mixture of different salts, measures the reading and compare it with the actual reading to check how much reliable is the system.

Chapter 2: Overview and Mainline:

2.1 Brief Overview:

Conventional diagnosis of the infectious diseases is time consuming, require a centralized system of laboratories and need more manpower. We must develop this typical system into something that is rapid, fast in the initial medication and more less about using the bulky lab equipment to build a greater health public system. The emerging field of biosensors with recent advancement have potential to provide the instant diagnosis service, care to the point service that will be more accurate, less time consuming and less expensive. Biosensors are widely classified labelled or non-labelled, exploiting the transducing effect based on the optical, electrical and mechanical sensing[5]. Biosensors require the nanofabrication technical assistant in the design. Despite of all this advancement, most of biosensors are still limited to the experimental laboratories due to their limitations. Standard process follows the collection of samples and bring it to the lab where it is being tested and after a time, the results become available for the further diagnosis. In the contrast, a biosensor converts the molecular recognition of the target into measurable signal through a transducer. A simple example is glucose sensor which generate optimal result when the sensor electrodes are subjected to the patient's blood within a time period of seconds.

As it has been already mentioned, biosensors are prohibited to implant inside the bodies because of the complications, so currently they are being tested on the body. Sweat is a mixture of different salts and somehow it also provides the reading of temperature that is near to the optimal. So, in this fist phase such we intended to use such type customized embedded system for the experimental phase. Our aim to study and try to develop a circuit of specified sensors which can be implemented on a bone and then further it can release initial medication when needed or when it is operated remotely by the doctor. For this purpose, we have been looking and contacting with industrial experts who has been already doing this kind of work and can help us on developing the prototype of our own basic idea.

2.2 Characteristics of Biosensors:

Characteristics behaviour defines the optimization of the products. In the same way, biosensors have static and dynamic attributes that reflects their performance, defines their optimization and how much they are reliable. A few of them are listed below [6].

2.2.1 Reproducibility:

Multiple tests are carried out in case to check the credibility of the sensors. We see that how much value is varying in each repetition. Biosensor went through a setup of duplicate experiment to check whether it is generating identical result or not. Precision and accuracy are two main things that define the reproducibility of a biosensor. Precision is defined as alike result that s sensor get whenever a duplicate experiment is performed and accuracy is defined as how much mean result are closer to the true value. The lesser the difference, greater the accuracy and vice versa. This thing defines the reliability of the biosensor how much we can rely on the result. Reliability is the main building block of the robustness.

2.2.2 Linearity:

the idea of linearity is basically the same as in mathematics. We check the result how much they are varying from a straight line of true values. This thing depicts the accuracy of the biosensor. The equation for the straight line in the mathematics is given by

$$Y=mc$$

This equation defines some parameters that are listed below

- Y represent the output signal
- c corresponds to the intensity of the analyte in the sample.
- m represents the sensitivity of the biosensor. (Discussed later)

Linearity is linked with the resolution. Resolution is defined as the smallest change in the intensity of analyte required to bring a change in the biosensor's response. Most of the time the goal is not only to measure the specific analyte but also the amount of that analyte. So, in this regard resolution is an important factor. Biosensor with good resolution factor means it can detect smallest changes. Another term that is associated with linearity is "Linear

Range.” It basically tells us that up to what amount of change, a biosensor can sustain with its linear behaviour.

2.2.3 Sensitivity:

Sensitivity is also known as limit of detection. As the name depicts, this is the minimum amount of the sample that a biosensor can measure present in a mixture of the fluid. It is one of most important features of the biosensor. In different kind of medical sample, a sensor is required to detect a substrate as low as ng/ml and even less. In simple words, sometimes there are just the traces of the analyte in the sample and sensor have to detect those traces. In most of the sensors, we have a conflict between accuracy and the sensitivity. So, there is trade-off between these parameters where we can get some optimized results.

2.2.4 Stability:

When a biosensor is exposed to a sample, the sample contains the additional component along with the target one. So, these additional items can produce anomalies in the result. Stability of biosensor is the ability to sustain such type of environmental disturbances. This is most critical parameter because when the biosensor has to make a live speculation. Stability can be traced to the electronics component of the sensor and their tuning. Well-tuned electronics components is key to make the sensor stable. Another factor that can comprise is that bioreceptor over the time can lose the credibility. So, after a time, the stability can be compromised.

2.2.5 Selectivity:

It is the ability of a biosensor to correctly detect the analyte that we are intending to be measured. It is one of the key characteristics. Biosensor should be intelligent enough to select the specific analyte from a mixture.

2.4 Basic Idea:

There are different approaches for circuit modelling of such system. One might use different type of sensor and communication channel according to the requirements. So, according to our requirements, the circuit modelling proposed is as following in figure 2.1



Microcontroller based motherboard

Figure 1 : 2.4.1 Transmitter Side

Different kind of sensors are aligned towards the signal processing unit. This unit is analysing the electrical signals from sensors and these signal responses are being fed to the microcontroller where necessary calculations are performed. Afterwards, this information is being transmitted to the receiver end where it being monitored and logged for the future purpose. The receiver side works is shown in figure 2

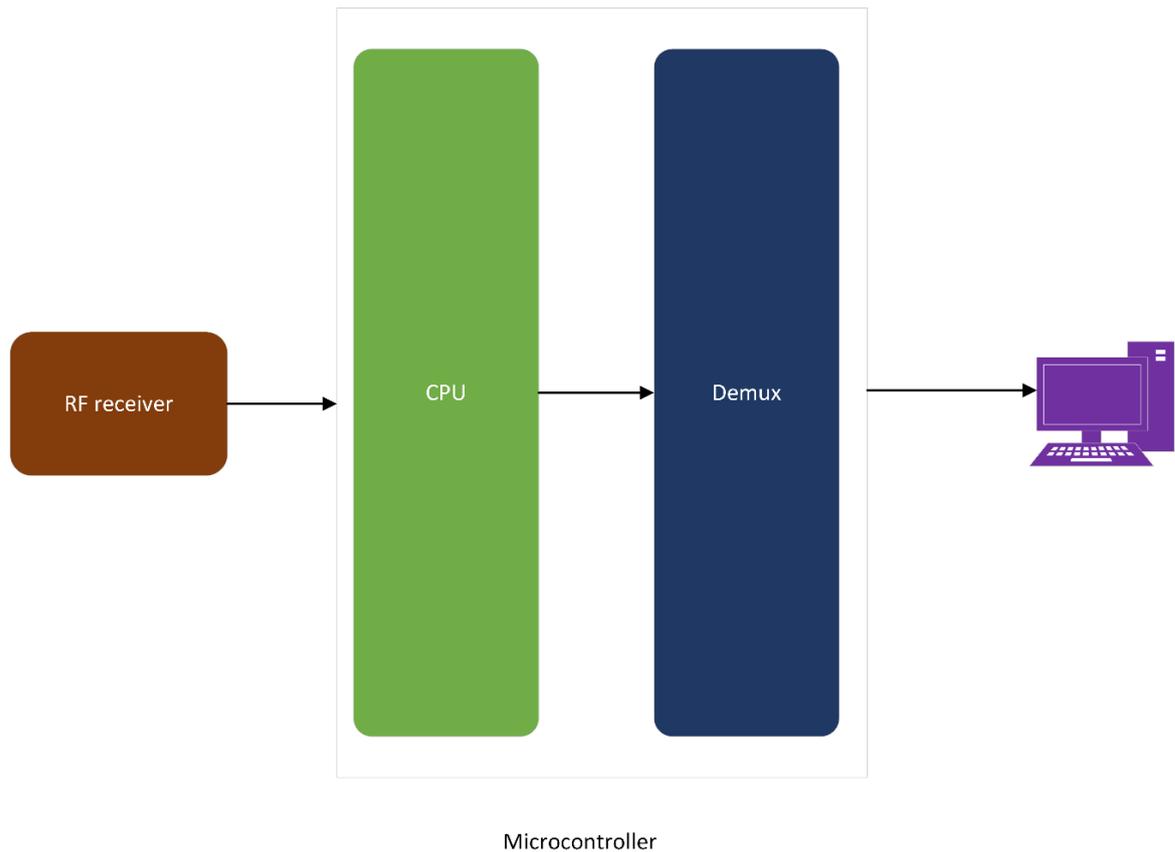


Figure 2 2.4.2 Receiver side

The received information is being fed to the microcontroller and then after necessary decoding it is being downloaded in the PC where this information can be monitored and stored as patient history. In simple words we can say that:

- 1) The sensors attached to the transmitter electronics.
- 2) The receiver attached to a PC
- 3) Basic SW to collect this data on a pc.

2.5 Sensors and their types:

Sensors are devices which detects the changes in their surrounding and convert those changes in to corresponding analogue electrical signal. Changes depends on the environment to which sensors are being exposed. They can be mechanical like stress, heating, vibrations etc. as well as dynamic like change in frequency, light etc. The corresponding analogue electrical signal is then transmitted in the form of bits. The

necessary operation of analogue to digital conversion is being carried out before the transmission took place. Depending on the type of transducing and activity, biosensors are of following type [7].

- Thermal Biosensors
- Optical Biosensors
- Electrochemical Biosensors
- Ion sensitive Biosensors.
- Piezoelectric Biosensors

These are a few types of the biosensors. As already described the criteria for the types, the biosensors can be purpose related like tissue based and enzymes-based sensors. Following are few sensors that are studied and some of them are used in simulation.

2.5.1 Ph sensor:

Ph is basically a scale to measure acidity and basicity level of the solution. It is glass rode shaped with glass electrode and a sensor. The movement of hydrogen ion between the electrodes gave a tendency to the relative Ph units [8].

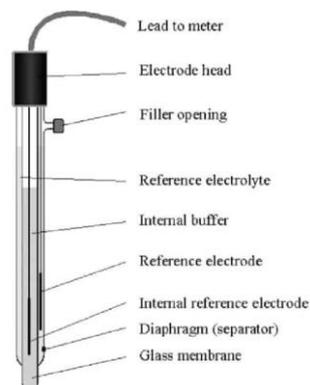


Figure 3 2.5.1.1 PH sensor

2.5.2 SpO₂ and pulse oximetry:

SpO₂ is measurement of concentration of oxygen in the blood. There are 2 forms of haemoglobin in the blood i.e oxygenated and deoxygenated. The results are found according to the following formula:

$$SpO_2 = 100 * \frac{C[HbO_2]}{C[HbO_2] + C[RbO_2]}$$

HbO₂= Oxygenated Haemoglobin

RhO₂= Deoxygenated Haemoglobin

Pulse rate is measured as a result of the change of transmitted modulation and absorption of light sensor in the arterial blood [9].



Figure 4 2.5.1.2 MAX32664D

2.5.4 Temperature Sensor:

Temperature is one of the vital signs that depicts various abnormalities in the area where it is raised or drops. Usually, a rise in temperature shows us the damaged area. There is different type temperature sensing device like some used infrared light and some use a diode in which when the temperature rises, the voltage across the diode also increases. I used LM35 in the simulation which works on the principle of rise in volage across the diode [10].

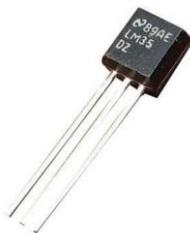


Figure 5 2.5.4.1 LM35

2.6 Limitations and issues of Biosensors:

There are issue and limitations of every technology that has been developed over the time. Here there are few important that are discussed related to the biosensors [11].

2.6.1 Accuracy:

This is one of the main aspects that is considered related to technology. Accuracy of biosensors should be great because the difference of a few percentages in the concentration of salt or other thing which us meant to be measured can lead to drastic results. Accuracy can also be compromised as result of poor calibration because of the field.

2.6.2 Detection time:

Sensor should be proficient enough that it takes minimal time to detect and measure the intensity of things that is being exposed to it. It can be protein, enzymes or tissues. Sensitivity should not compromise while reducing the detection time.

2.6.3 Detection Limit:

Detection limit is the least detectable amount of the concentration of analytes that can be distinguishable from zero. Sensor's ability should be enough to distinguish the target present in the mixture during a biochemical reaction.

2.6.4 Specificity:

It is defined as sensor should be intelligent to differentiate between target and non-target of biological units in the model. It also has great impact on the sensitivity. It is considered the most essential quality for the sensor.

2.7 Nanotechnology and Biosensors:

Discussion about biosensor is incomplete without the follow up of nanotechnology. Nanotechnology has played an extensive role in bringing out the revolution to the practical application of biosensor at larger scale. The reduction in the size of biosensor while

maintaining the quality and communication factors like signal to noise ratio are not compromised, all the credits go to nanotechnology. It helps us to move towards micro as well as nano scale with effect of reduction in cost and improvement in the performance.

Nanomaterials are the building block of nano biosensors. Mechanical and electrical properties of these materials are exploited to make better transducing affect as well as biological signalling of the sensors. The electron movements in these materials are very convenient which results in improvement of better detection and better sensitivity. On one side, we can say that biosensors based on the nanotechnology signify the combination of biochemistry, material science along with molecule engineering and on the side, it shows a betterment in the sensitivity and specificity in recognition of the analyte in the various fields like food and environmental monitoring, disease detection and clinical investigation [12].

2.8 Nanomaterials- A building block for biosensors:

Conventional materials used for the fabrication of the common electronics component. Such materials can not be used in the nanotech fabrication. Because materials have properties like sensitivity that changes along the size of materials. For example, the surface area of a certain material is not effective in smaller size as much as of a nanomaterial. Nanomaterials allow us to enhance the immobility of the bioreceptor at low level more precisely at reduced volume. Gold nanoparticles, carbon monotubes, quantum dots and nano diamonds have great properties and due to key materials, they are hot topic for research. A few of them are described below [13].

2.8.1 Gold Nanoparticles:

Gold nanoparticles have great biocompatibility which means that they are compatible with the living tissue. They don't have any harmful effect when they are exposed to the body. Along with biocompatibility, their electronic and optical properties. Mostly the principle used while having gold particle is redox enzymes biosensing. Redox is termed as a mixture of two words oxidation and reduction. The former one indicates the addition of the oxygen and the later one tells the removal of oxygen during the sensing reactions take place. The drawback of this technique is that most of the ions are absorbed in the electrodes and a few

reaches to the solution. The size mostly happens in between 1nm to 100nm depending on the type of the application.

2.8.2 Quantum Dots:

Quantum dots belong to a compulsive class of materials named as luminescent semiconducting nano crystals. Cadmium based quantum dots have the ability of large absorption of spectrum with narrow emission spectrum. As these are nanocrystals, so sometimes the structure of the crystal lattice can be compromised which can result in trap of excited electrons. While going to the relaxed state, these electrons do not radiate any energy. This might compromise with optical properties.

2.8.3 Carbon Nanostructures:

Carbon occurs naturally mostly by forming a covalent bond. The properties of being covalent are exploited while defining a method for immobilization technique. These structures possess good electronic properties as well as they are biocompatible. Field effect transistor-based biosensor have the building block carbon nanotube.

Among many challenges, one of the major key steps in designing the biosensor is how to immobilize enzymes on the transducer's surface. There are different kind of immobilization techniques such as conventional adsorption, cross linking, covalent bonds and entrapment. Adsorption is basically mixing of the analyte with chemical to form a mixture that will be applied to the surface of the sensor and left for a certain time period to settle down. The simple example that we can understand is the finding of the right blood group. The most popular method of immobilization is covalent because it prevents the leakage of enzymes by providing a strong bond between support matrix and enzyme.

2.9 Biosensor and Cybersecurity:

Biosensors system on chip fall into the concept of the internet of things so does it is also exposed to the security issue due to complex architecture. There are many risk assessment frameworks that have been developed over the time for securing the domain of IOT. A few of those frame works are NIST, OCTAVE, TARA and the list keeps on going. The development in this field also increases the risk of misconfigured databases, malware attacks, phishing

attacks. The real time monitoring of the medical devices associated to the task give a potential rise to the security risk that can affect electronics of the device and can manipulate electronic health records. Furthermore, the telemedicine and remote surgeries must be secured enough that they do not compromise the patient privacy and safety.

Therefore, a risk handling system has been proposed based on the doctor's assessment of the device that can yield the worst-case scenario for a patient. A stride model has been developed by Microsoft that can assess threats[14]. The most used risk management framework is provided by the NIST that works in following steps:

- Identify
- Protect
- Detect
- Respond
- Recover

The core of this framework is not providing any checklist of action to be performed but it tells us the possible outcomes of the cybersecurity that help the stakeholder to manage the situation. There are four elements of core that works as follows[15]:

2.9.1 Functions:

They usually work in the order that has been described above keeping the highest priority level. They help the organization in addressing the problem by collecting and classify the data, enable the risk management decisions and learning from the previous outcomes.

2.9.2 Categories:

The functions are sub-divided into categories that is mainly associated with the programmatic need and particular activities. It mostly includes the asset management, detection process and access control.

2.9.3 Subcategories:

These are the further subdivision of the categories. They bring forth a set of results to help the support for the outcomes of each category. Mainly it can be described as cataloguing of

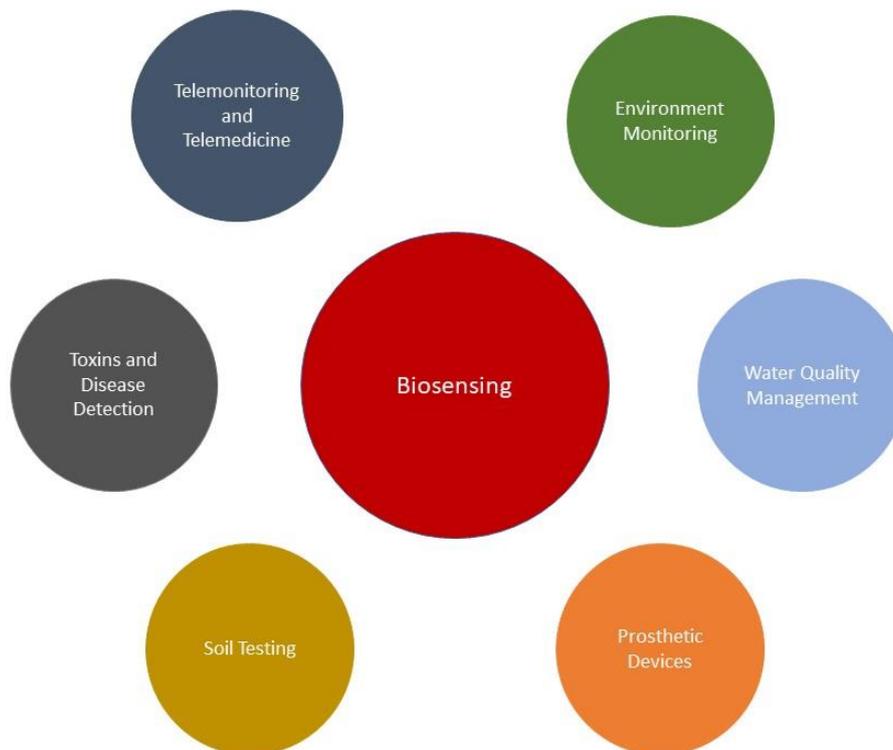
the external information, assessment of the notification from the system and protect the data at rest.

2.9.4 Information reference:

These includes the guidelines and defined standards that defines a sophisticated method to yield the outcomes related to each category.

2.10 Impact of Biosensor:

The amount of literature conjugated with biosensors makes them undoubtedly an attraction not only in the research field but also form industry point of view. The impact of biosensing is not limited to the medical application but also, they have gained an importance in safety standards in terms of food nutrition control, water quality and environmental monitoring.



Biosensors have given control and allowed to individual human being to analyse and take care of situation depending on the condition. Glucometer is the best example. Furthermore,

the 3D printed prosthetic devices have enabled all the person to perform diligently in various aspects of life.

Chapter 3 Modelling and Simulation:

3.1 Testbed Setup:

To understand the working of biosensors, a simple schematic is designed in Proteus. Proteus design suite is developed by Labcenter Electronics Ltd which allow to design and simulate the electronics circuits. It is basically a whole package of electronics entities used in the real world. From a set of resistors to several microcontrollers. Along with this, it also enables to make a Printed Circuit Board (PCB) layout which can easily be implemented to bring the following design into physical form. It also allows us to flash the microcontrollers. In this schematic, I have used a heartbeat sensor, a temperature sensor and some data logging device to store the results.

3.1.1 Heartbeat Sensor:

in order to use the heartbeat sensor in the proteus, we have to import the related libraries. In reality, the heartbeat sensor works on the principle of reflection of the IR. The sensor senses the difference between the reflected and transmitted IR that might in form of frequency or change in modulation and generate a corresponding signal. Microcontroller usually convert this analogue sensor into digital output. For this operation to work, finger should be on the sensor but in the simulation a potentiometer is used to get an imaginary electrocardiogram [16].

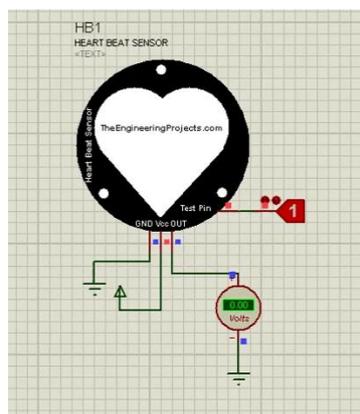


Figure 8 3.1.3.1 Display Segment

3.1.4 Microcontroller:

I have used Arduino Mega in this simulation. It is a development kit based on Atmega 2560 microcontroller. This board is good for the projects that require more wiring and pins. This unit works with the DC supply, and it also has a usb interface with which it can be connected to the computer. Arduino has also developed a software to support the programming of the microcontroller which is “Arduino Nightly”. This software platform helps the user to interact with microcontroller. It has 54 digital input/output, 6 of which are analogue, 4 UARTS, reset button, power and usb connection [18]. UART is communication protocol that enables a serial communication asynchronously. UART stands for Universal Asynchronous Receiver Transmitter.

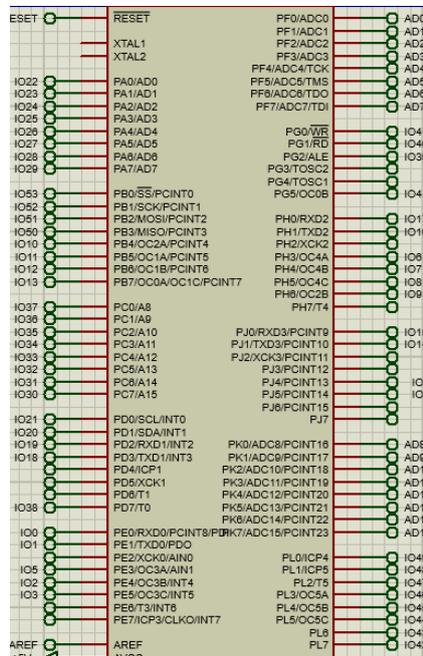
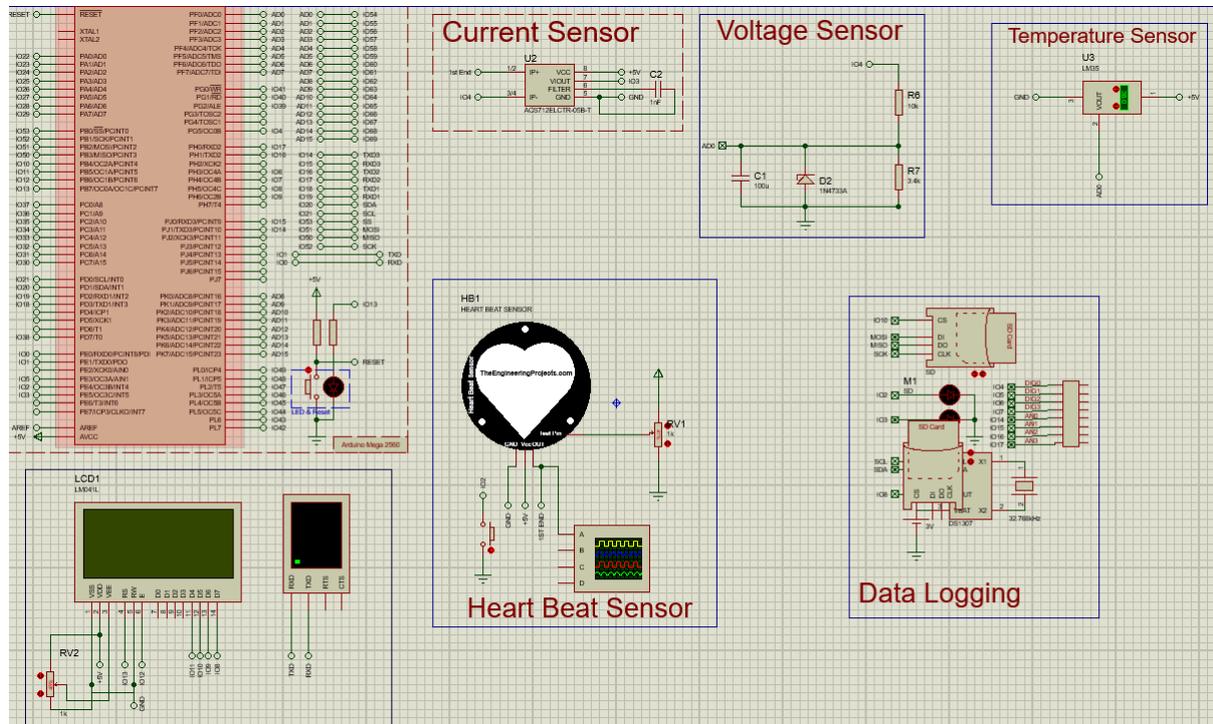


Figure 9 3.1.4.1 Arduino ATmega

3.2 Simulation and Results:

The testbed is setup by making the connection between the components and microcontroller. As soon as the simulation started, serial monitor starts to update itself with the current information after each delay. The complete setup can be seen in the following



figure

The update in the serial monitor and lcd unit is also captured as following:

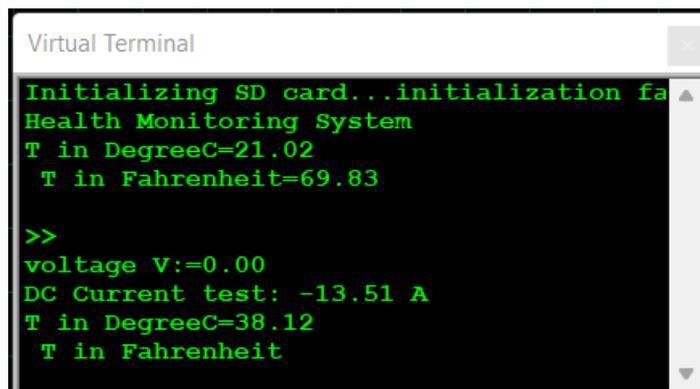


Figure 11 3.2.2 Serial Monitor Update

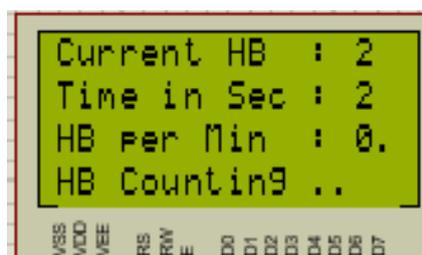
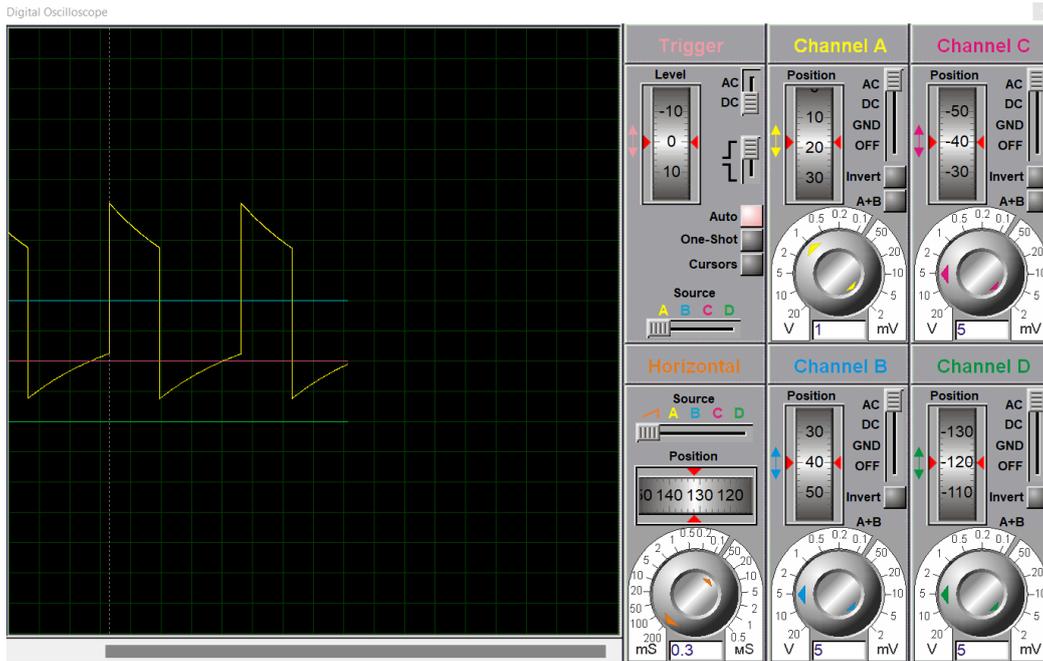


Figure 12 3.2.3 LCD unit

For the virtual electrocardiogram we have set up an oscilloscope across the heartbeat sensor, which is showing an imaginary reading as there is not physical source that we can put in the simulation to get the pulse rate. Here is the oscilloscope result.



The purpose of this simulation is to understand how the things are works. How the sensor integrated with each other together. What percentage of voltage is implemented in the divider circuit.

Chapter 4

Conclusion:

Biosensor's development is a topic of keen interest and over past few years a lot of development has been made in the academic area. Besides all this development, a very few biosensors have been globalized at retail level. There are few reasons behind this. One of them is the difficulty to translate the academic research into feasible prototype at industrial level. Biosensor's fabrication is not just a single hand job. There are various departments like material engineering, biomedical engineering, biochemistry, embedded system, communication engineering etc that contribute their roles in moulding a research model into commercially practical prototype. The amount of effort and research funding has been displayed in the academic research, should also be the same in the fabrication process. As a biosensor require the recognition of the analyte molecule and then immobilization of the molecule to the sensor surface. Device design, integration of different aspects from different fields that satisfy the biological facts and figures. An ultimate product is a result of testing thousand prototypes. Along with this there are a lot of factors stability, cost factor and ease of manufacturing process.

So far in vitro biosensors have a huge capacity of digitization the medical treatment. They have a great impact in every aspect of our life from telemedicine, health monitoring to food and water quality control. The rapid development in this field is due to many things but important of them are listed as following

- Discovery of suitable bio-recognition entities.
- Development in the field of nanofabrication technologies
- Nanomaterials and the fabrication of nanostructured products.
- Better understanding between medical science and engineering.

Although the work that has been done till now enables us to perform in vitro biological diagnosis but it is more likely that we will get a system on chip that can draw and deals with the raw samples directly in this decade. Now the quest to get the maximum benefits can be

unfolded by increasing the range of number samples being handled by a single chip system. In a nutshell, we can say that the dream of 100-dollar personal genome can be addresses in this decade by overcoming the nanopore technology.

The recent outbreak of the COVID-19 emphasizes us to understand the crucial role of biosensing and mould our approach to handling the medical situation in more effective and safe way. The study of data about the mortality rate due to this pandemic reveals that the countries using biosensing approach have handled the situation much better.

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