CHAPTER 1
INTRODUCTION

With the advent of technology, there emerged multifarious changes in different fields of human life. This brought about rapid transformations not only in the domain of science but also in bio-medical science. For instance, it triggered advancements in the main areas like chemical analysis and computer-aided diagnosis in health care industries. The current trend is to develop certain diagnostic tools that are user friendly and can achieve measurements up to greater degree of accuracy. This work presents a unique method to find the blood parameters with highest possible accuracy that compare well with parameters obtained using standard and advanced equipment. The present study concentrates mainly on the separation of RBC and WBC components from whole blood to evaluate the counts. The literature survey reveals many methods for separation and determination of count values [1-7]. These methods invariably use centrifuge, magnetic, electromagnetic separation and gravitational methods [8-10]. The present-day machines used in hospitals employ these methods and they are very costly and range up to several lakhs. The centrifuge method employs taking the blood sample and adding some reagents to get the separation of RBC and WBC. In this method there is every chance of the cells in the blood being damaged due to reaction of the reagents used. Hence, this method is not only inaccurate but also very expensive and cannot be used in rural and small hospitals. Moreover this method requires more time for the analysis of blood. In order to overcome these limitations an attempt has been made to design a low-cost instrument which is handy, fast and yields precise results when compared to the commercially available equipment in the market.

1.1 COMPOSITION OF BLOOD AND SIGNIFICANCE OF RBC AND WBC

Needless to say that blood is crucial to life. Its purpose is homeostasis i.e., to keep up the steadiness of the inner environment of the human body. Blood controls the body's pH levels (about 7.4) and encourages all vital chemical reactions in the
body. Blood carries oxygen and expels carbon dioxide, allowing respiration to cells without which cells start dying and also it controls body temperature.

Sugar, one of the important components of blood acts as the key fuel for the cerebrum, nerves, spinal cord and is the single source of food for RBC from mitochondria. Blood discards waste material from the human body through the process of excretion.

The blood safeguards the body by opposing or obliterating and expelling foreign bodies, dead cells, and other unnecessary agents. The multifarious interface of blood cells and plasma fixes and repairs wounds with the help of its protective mechanism by developing the immunity from infectious agents. Hence blood is regarded as a noteworthy tissue, the main fluid tissue in the body and a mélange of a several types of unique cells or shaped elements. There are four primary types of blood components namely RBC or erythrocytes, WBC or leukocytes, platelets or thrombocytes and Plasma. Plasma is the fluid part of the blood and its major constituent is 90% of water. Plasma constitutes most part of the blood. The basic need of every cell is water to carry out the fundamental activities. RBC gets its red colour due to the presence the protein called haemoglobin which is the most important constituent of the blood.

Red Blood Corpuscles or erythrocytes are the most common cells formed in blood. They represent 95% of blood cells by number. A human RBC has the shape of a biconcave disc (like a doughnut which has incomplete opening), that gives an expansive surface and does not have nucleus. Owing to the smaller size of many capillaries, blood cells squeeze into a bullet shape while flowing through the capillaries. RBC may flocculate one on top of another cell, not like stacked coins, shaping a Rouleau structure. The key capacity of RBC is gas transport in terms of receiving O₂ and evacuating CO₂. The transfer of both O₂ and CO₂ is due to the presence of haemoglobin which eagerly connects with either CO₂ or O₂. The normal life span of an RBC is 120 days. The normal range of RBC for healthy men is 4.7 to 6.1 million cells/µl and for women 4.2 to 5.4 million cells/µl. The RBC plays very vital role to cause major diseases. If the number of RBC is lower than normal, it
indicates presence of anaemia or bone marrow failure or kidney disease. A person with low haemoglobin may have the following symptoms:

- Tiredness.
- Shortness of breath.
- Headache.
- Fast heart rate.
- Pale skin and/or pale gums.
- Dizziness etc.,

RBC and WBC are approximately in proportion of 1000 : 1. The WBC come in many varieties with different characteristics. They represent 0.13% of blood cells by percentage. It is a type of immune cells that have tiny granules (small particles) with enzymes released during infections. The white blood cells are combination of granulocytes, lymphocytes and monocytes. Granulocytes are about 60% of circulating WBC and it is a combination of neutrophils, eosinophils and basophils. Monocytes are spherical cells that make up 2 to 8 % of circulating WBC. The lymphocytes are slightly larger than monocytes and make up 20 to 30% of circulating WBC. White blood cells are made in the bone marrow and are found in the blood and lymph tissue. White blood cells help the body fight infections and other diseases [5]. The normal range of WBC for healthy persons is 4500 to 11000 cells/µl. The abnormal variation of WBC causes several diseases like.

- Fever and chills.
- Swelling and redness.
- Mouth sores, red or white patches in the mouth.
- Sore throat.
- Severe cough or shortness of breath.
- Pain or burning when urinating or foul-smelling urine.
- Diarrhoea.
- Pain, redness or swelling of the rectal area etc.,
The shapes of RBC and WBC are shown below in Fig.1.1

Platelets or thrombocytes are the tiniest cells of the blood. Platelets outnumber WBC approximately in a proportion 40 : 1. They occupy a small part of the volume. Similar to RBC, platelets also do not have a nucleus and are thus unequipped for cell division. They differ from RBC by righteousness of its internal structure and complex metabolism. They control and prevent bleeding which is called Haemostasis. This property helps platelets to adhere with each other and not with WBC or RBC.

Clot promoting substances in the shape of tiny granules are present within the platelets. Platelets are produced by the largest bone marrow cells called megakaryocytes. They have an average life span of 10 days [11].

1.1 SIGNIFICANCE OF DIAGNOSING BLOOD COMPONENTS

In modern medical laboratory system, simple and rapid processing of blood specimens is very essential, as blood plays a vital part for every organ and adjunct of the human body. A blood test often helps to trace any disease or problem in the human body. Complete blood count test is the most important of all types of blood tests and it is a technique that helps to numerate blood cells of different types in a specified sample of blood. The cells are examined for any abnormalities which can give clues for the presence of diseases [11]. Since many ailments have a known effect on the chemical composition of the blood, the blood count test renders to be a powerful tool to indicate illness and disease.
The significance of the blood count test and the latest literature review on the existing instrumentation for blood count prompted to design and develop a stand-alone, handy, cost effective apparatus for separation and detection of whole blood components for accurately calculating the count values of RBC and WBC by using ARM and FPGA processors. The apparatus aims at high accuracy, precision, and fast measurement. One of the significant properties is also that it should be a portable one, and uses low DC supply voltage instead of AC supply voltage, thereby the apparatus is not disrupted by power failures. So, such an instrumentation system is affordable to large rural sector of the country.

The diagnosis of the blood and its components reveals many ailments and their treatments can be predicted. The diagnosis also helps to understand blood’s properties [12].

1.1 MOTIVATION FOR THE RESEARCH WORK

The centrifugation process of existing methods involves the addition of reagents, gels and other diluting agents as per the research articles by Mary Amasia, Marc Madou [13] and Kunshan Sun, Hyuntaek Oh et.al [14]. The adding of these reagents causes distortion of physical parameters of a blood sample and gives inaccurate count values of RBC and WBC. Inaccurate count values result in fault diagnosis of diseases.

As none of the existing methods addresses to overcome the problems which arise due to diluting the blood by reagents, an instrumentation system is proposed with a method that involves no addition of reagents. The design features will make it suitable for rural areas. Mainly, the goal is to provide economic and efficient instrument to meet essential health needs of rural people.

1.2 PROBLEM DEFINITION AND RESEARCH SCOPE

The instrumentation systems in market now, use either continuous separation or non-continuous separation techniques to separate the components of the whole blood and find RBC and WBC. The following are the general drawbacks and technical gaps in those instruments.
1. Use of more blood sample  
2. Addition of reagents, gels etc.  
3. Processing time is more.  
4. Instruments work on AC supply.  
5. The instruments are expensive.  
6. They are not portable  
7. They are not easy to operate.  
8. Cost of service is more.  

Two instrumentation systems (ARM based instrumentation system and FPGA based instrumentation System) addressing the above issues are developed. Finally FPGA based instrumentation is selected as it gives results with minimum average error.

1.1 AIM AND OBJECTIVES

Aim

The aim of this research work is to design and develop ARM based and FPGA based instrumentation systems to find RBC and WBC of blood sample. The two systems employ centrifugation technique to separate blood components of a sample. The two systems are designed and developed separately using ARM processor and FPGA processor to sense and count RBC and WBC. They overcome the drawbacks of the existing instruments which work on different separation techniques. The most important features of the developed instruments are low cost and utility in rural areas. Out of ARM based and FPGA based instrumentation systems, FPGA system is selected for field use as it proves to be more accurate.

Objectives

- To design a capillary tube that holds very less blood sample (less than 1 ml) to find RBC and WBC  
- To develop an apparatus and a procedure that avoid reagents, gels and diluting agents in the process.
- To develop a composite apparatus that separates blood components and detects RBC and WBC counts simultaneously
- To design Morgan chopper to regulate the DC motor in ARM model.
- To find out suitable empirical relations between voltage emitted by segregated blood components and counts of RBC and WBC
- To write ALPs for ARM and FPGA to calculate RBC and WBC
- To design assembly of components of cost-effective apparatus.

1.6 PROPOSED SOLUTION AND METHODOLOGY

The methodology to design two instrumentation systems is described below. The main work is about the separation and detection of RBC and WBC components in whole blood by using centrifugation technique.

The experimental procedure is explained below. Totally 19 blood samples of different people are tested using this procedure.

- Whole blood sample of less than 1 ml, is poured into the capillary tube and the tube is placed on the holder over the motor shaft.
- The motor rotates with a speed of 10000 RPM for 5 minutes and stops because of Morgan chopper in ARM based instrumentation system.
- The centrifuge process separates particles of RBC at bottom, particles of WBC at middle and plasma at the top of capillary tube.
- The LEDs placed on the left side of capillary tube emit light into capillary tube and the photo detector placed on the right side of the capillary tube senses the voltage from the tube.
- ADC of ARM module reads the analog voltages from the photo detectors.
- The ARM processor calculates the count values of RBC and WBC from the calibrating equations based on inputs from ADC.
- The FPGA processor also calculates the count values of RBC and WBC from the calibrating equations based on inputs from ADC.
- The counts of RBC and WBC are displayed in the LCD panels in both ARM based and FPGA based systems.
1.7 ORGANIZATION OF THE THESIS

The organization of thesis is presented as noted below.

Chapter 1 of the thesis explains the vitality of blood and its components for the functioning of human body and significance of RBC and WBC in diagnosing diseases in the human body. Analysis of blood is the primary means to diagnose any ailment of the human body. This chapter further states motivation for the research, aims and objectives, problem definition of the research work and proposed solution with methodology.

The detailed report on literature survey and state of the art assessment of various separation techniques, qualitative comparison of cost and trade-off issues of different separation techniques are present in Chapter 2. This chapter also presents research work carried out by the various researchers and the shortcoming of their findings and limitations of the existing techniques identified as the research gaps.

The theoretical analysis involves discussion of different types of centrifuges, and their importance, nomogram and their significance, need and types of DC choppers, principle with power circuit for Morgan chopper. These are narrated in Chapter 3.

In the Chapter 4 the experimentation to optimize design parameters of capillary tube and design of Morgan chopper to meet the requirement of ARM based instrumentation are presented. The methodology for running DC motor at designed speed, spinning time for designed speed and optical disc for measuring design speed are discussed in this Chapter.

The development of ARM based instrumentation system to count RBC and WBC in human blood, minimum resources of proposed system, physical setup of ARM module, experimental procedure, performance analysis and work flow chart are explained with their results in Chapter 5.
In the Chapter 6 the development of FPGA based instrumentation is presented. The physical setup of instrumentation, experimental procedure, performance analysis and work flow chart are explained with their results in this chapter.

Chapter 7 deals with the summary, conclusion and the future scope of the present study.

1.8 SUMMARY

Blood is the vital part of existence of human life. The human body vis-a-vis blood is prone to various ailments and appropriate counts of its components will balance and keep proper functioning of the entire human body. Therefore analysis of blood and its constituents plays a significant role in the field of medical sciences. The whole blood is composition of RBC, WBC, platelets and plasma. There are various methods to separate them and one among them is centrifugation method. The drawbacks of existing methods are highlighted. The problem of research work is identified to develop new instrumentation systems which will overcome the limitations of existing systems. The aim, objectives and methodology are also described in this chapter.