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Noninvasive Blood Cell Count of Flowing Blood Cells Using Surface Charge of Blood Cells Current Practice and Future Prospects

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Abstract

Real-time noninvasive imaging of flowing blood cells is an emerging topic of interest in the field of research from the past many years. Non-invasive techniques offer unique opportunities to conduct tests, diagnose and analyze the characteristic dynamics and behavior of flowing blood cells. Measuring the composition of a patient's blood is often the first step in clinical diagnosis, and is most commonly performed by extracting a blood sample. Several approaches for noninvasive monitoring of blood components like ultrasound waves and optical imagining have been proposed already. This paper presents a mechanism for analysis based on electrical properties of blood cells. This approach utilizes more reliable parameters for the study of blood parameters and highlights the scope and future prospects of the proposed technique.

Keywords: Noninvasive techniques; Zeta potential; Electrophoretic mobilit

Introduction

The physical and the digital world are converging to make our lives smarter, efficient and comfortable. All industries including the healthcare industry are getting deeply influenced by this change. Innovations in electronic healthcare are revolutionizing the involvement of both doctors and patients in the modern healthcare system. With the convergence of the physical world with the digital world, individuals can actively participate in monitoring their heath on regular basis via mobile health applications and smart wearable sensors. This has introduced the concept of remotely monitoring patients [1].

This paper highlights the increasing advancement of healthcare industry by the introduction of noninvasive imaging techniques and proposes a mechanism for blood cell count based on more reliable parameters. In addition, when the blood count measurement hardware is integrated with a data aggregating software, it can serve as a real time health monitoring device. The health status would comprise of the pulse rate and blood content count (RBCs, WBCs, etc.) compared with their standard values. The mechanism would not require taking out blood or pricking needle to analyze the blood content. The parameters that are used to determine the blood cell count are more reliable since they deviate very little with the changes in human body and are characteristic features of particular kinds of cells [2] (Figure 1).

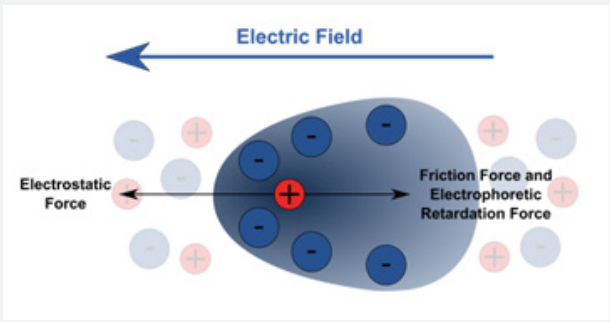

Figure 1: Electrophoresis mechanism.

Scope

Even in today's world, when the rate of digitalization is exponentially increasing, there are people who do not have access to affordable medical services. People living in remote areas are usually devoid of proper healthcare services, while many people avoid monitoring their health regularly because of the huge treatment costs. As per the doctors, very few of the patients actually go for the blood tests when recommended by the doctor. Undoubtedly, the blood test report would allow the

doctor to carry out better treatment but for the sake of continuing the treatment, the doctors recommend medicines based on their observations. As per the pathology labs, the number of children who come for the tests are much lower than the adults. They call it "THE PRICK ANXIETY". Even some adults do the same. Moreover, it is always preferable to avoid the use of needles since there are many risks and problems associated with the use of needles. Needle and equipment sharing transmits blood borne diseases like AIDS and HIV between users. Unsanitary conditions, blunt needles and dirty water contribute to various kinds of diseases and infection. Also, the use of blunt injecting equipment may give rise to scarring of the peripheral veins and cause track marks.

Basic Terminology

The concept on which this paper is based revolves around the phenomenon of electrophoresis and zeta potential [3].

Electrophoresis

The movement of a charged particle relative to the liquid it is suspended in under the influence of an applied electric field is termed as electrophoresis. Viscous forces acting on the particles tend to oppose this movement. When equilibrium is reached between these two opposing forces, the particles move with constant velocity.

B. Zeta potential

The development of a net charge at the surface of any particle affects the distribution of ions in the surrounding interfacial region, resulting in an increased concentration of counter ions, ions of opposite charge to that of the particle, close to the surface. Thus an electrical double layer exists round each particle. In a colloid, the liquid layer surrounding the particle exists as - inner region (where the ions are strongly bound) and an outer region where they are less firmly associated. The potential at this boundary is the zeta potential [4].

Proposed technology

Pulse rate measurement is the fundamental test performed to analyze health status of a person. It is necessary to have a normal pulse rate before proceeding to any other medical test. A normal pulse rate also ensures that the subject is ready to undergo any further medical test. The first component of the proposed technology is a pulse measurement device of the size of a wristband. The sensors start the counter as soon as ON button is pressed. The band will display the pulse rate after a minute. This test ensures that the person is ready to undergo further procedures [5].

The technology comprises of:

Prototype or analyzing hardware

A laser is used to provide a light source to illuminate the particles in the blood vessels. For electrophoretic mobility measurements, this light source is split to provide an incident and reference beam. The incident laser beam passes through the centre of the sample cell and the scattered light is detected at a certain angle of deviation. Light is passed through various combination of suitable lenses and focused on the blood vessels of lower lip at depths ranging from 70μm to 200μm under the tissue surface. When an electric field is applied to the system, any particles moving through the measurement volume will cause the intensity of light detected to fluctuate with a frequency proportional to the particle speed. The light after passing through the blood vessels is detected via a intensity detector. The intensity of the detected, scattered light must be within a specific range for the detector to successfully measure it. This is achieved using an attenuator, which adjusts the intensity of the light reaching the sample and hence the intensity of the scattering [6].

Data aggregating software

The data aggregating software produces a frequency spectrum bythe data acquired wirelessly from the detector. This is achieved by turning the detector into an IoT device. Correspondingly, electrophoretic mobility and hence zeta potential of each cell passing through that volume is calculated. The software acquires the data wirelessly, compiles the data and prepares a report of the different blood cell count based on the comparison with their standard zeta potentials. This non-invasive testing will save time and money. There will be no prick anxiety. The subject can perform the blood test anywhere and anytime [7-9].

Previous model

The previous model was based on optical microscopy of blood cells to visualize the morphology and dynamics of circulating cells. It presented a label-free approach for *in vivo* flow cytometry of blood using imaging probe that demonstrate sub cellular resolution imaging of red and white blood cells. The tests conducted using this method were successful but the results comprised of significant errors (Figure 2).

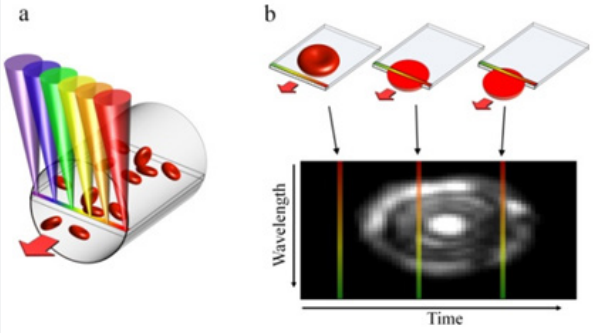

Figure 2: Existing concept.

Calculations

After acquiring data from the detector, the software prepares a frequency spectrum based on the data. Since the light fluctuates

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with a frequency proportional to particle speed, the different kinds of cells are identified. These velocities of particles in a unit electric field are referred to as its electrophoretic mobility. Zeta potential is a physical property which is exhibited by any particle in suspension. It can be used to optimize the formulations of suspensions and emulsions. From earlier research studies, zeta potentials of blood components have already been derived. Some of them are given below Table 1:

Cells	Zeta Potential
Erythrocytes	-31.8±1.1
Mononuclear cells	-21.9±0.2
MCF-7	-20.9±0.4
HeLa	-19.4±0.8
Lyposomes	-62.3±1.5
CELL	STANDARD COUNT(per µL)
Lymphocytes	1700-3500
Monocytes	200-600
Erythrocytes	Male: 4.7- 6.1 million
Female: 4.2 - 5.4 million	

Zeta potential is related to the electrophoretic mobility by the Henry equation:-

$$U_E = 2\,\varepsilon\, z\, f(\kappa a) / 3\eta$$

where U_E = electrophoretic mobility, z = zeta potential, ε = dielectric constant, η = viscosity and f(κa)= Henry's function. The units of κ, termed the Debye length, are reciprocal length. The parameter 'a' refers to the radius of the particle. Electrophoretic determinations of zeta potential are most commonly made in aqueous media. For particles in polar media the maximum value of F(ka) is 1.5 (Smoluchowski approximation). For particles in non-polar media the minimum value of F(ka) is 1 (Hückel approximation) . Thus, after calculating zeta potentials using Henry equation, it is easy to identify cells.

After identification, the next step is to calculate the concentration of such cells in whole body. This is achieved using the equation:

$$C = N / (\pi \times R^2 \times v \times T)$$

Where N denotes the total number of observed cells during a total imaging time T, and R denotes the estimated radius of the vessel.

The standard concentrations of blood components are given below Table 2:

Cell	Standard Count(Per µl)
Lymphocytes	1700-3500
Monocytes	200-600
Erythrocytes	Male: 4.7- 6.1 million
Female: 4.2 - 5.4 million	

Advantages

i. It will increase the estimated number of people undergoing blood tests.

ii. There will be no blood drawing and there will be no harmful effect of the light on the patient.

iii. The technology can be combined with the upcoming IoT techniques to develop a device which is user friendly and will help people living in remote areas to easily monitor their health without worrying about travelling to far off clinics and expensive medical tests.

iv. The efficiency of tests is expected to be more than that obtained from existing techniques.

v. Hardware used in the proposed technique is much simpler in design compared to existing techniques

Conclusion

Quantitative information on blood composition and blood cell morphology is frequently used for patient diagnosis using chemical analysis and optical microscopy. In recent years, several methods for obtaining useful clinical data from small drops of extracted blood have been developed, reducing pain and anxiety to patients. These technologies are attractive for many applications that require real-time diagnosis, involve difficult extraction of blood, or where proper sample handling cannot be maintained. Utilizing the electrical properties of blood components to determine their presence is entirely a new concept. This paper presents a technique for measuring zeta potential of the various blood components in real-time and at high spatial accuracy. The design of the model is quite simplified eliminating all the extra components which are required for accurate imaging of blood vessels.

The ability of this technique to directly and continuously visualize blood cells flowing inside human patients' vessels has the potential of providing noninvasive measurement of important blood parameters. In addition to domestic check-up, continuous tracking could be useful for monitoring of patients for detecting sudden changes in the circulation caused by internal bleeding, for example, online monitoring of WBC concentration could be highly useful in critical care to detect a rapidly developing inflammatory process including cellular deformation, aggregation and adhesion.

Future Aspects

This paper discussed only blood component count analysis to detect any discrepancies. The future developments may also include the use of this research and product for the early detection of diseases such as sickle cell anemia and beta thalassemia, which are manifested by unique cell morphologies. Other possible fields include end organ effects of diabetes which is characterized by abnormal blood cell dynamics. Finally,

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screening for hematological disorder could also be performed in developing countries.

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