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Blood Typing and Sensors: A Review

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ABSTRACT: *Knowledge of blood typing is necessary because receiving incompatible blood during a transfusion can result in severe and potentially lethal transfusion responses. The properties of blood are vital for clinical applications, and numerous blood tests are frequently conducted in medical settings to diagnose and monitor a wide range of medical disorders. The blood's electrical properties and constituents are measured over the frequency spectrum from less than 100 Hz to more than 100 GHz. The invasive process or traditional method often induces human error during the procedure or can misinterpret large samples. Automated machines use for blood type determination in a large hospital, but they are extensive and costly. The identification of a person's blood type can be accomplished through the use of several different methods, such as blood typing according to ABO utilizing serological techniques, ABO blood typing with the use of molecular techniques, blood type determination using serological techniques for Rh, molecular approaches to the testing of Rh blood types, typing of blood by the use of flow cytometry, mass spectrometry for blood typing laser speckle contrast imaging for blood typing, typing of blood by the use of fast diagnostic tests, the typing of blood by the use of microarray-based technologies and melting analyses performed at a high resolution are used to type blood. Understanding the electrical characteristics of blood is critical for designing and deploying non-invasive physiological sensors capable of determining blood type without the need for blood extraction could improve patient comfort and accessibility while retaining accuracy and dependability.*

Keywords: *blood typing; sensor; electrical properties; transfusion; ABO blood.*

I. INTRODUCTION

Clinical applications depend heavily on blood's properties, and it is a different form of corpuscle, such as erythrocytes, leukocytes, and thrombocytes (Schwan, 1983). Knowledge of an individual's blood type is necessary because receiving incompatible blood during a transfusion can result in severe and potentially lethal transfusion responses. Blood typing is also essential for organ and tissue transplantation, as the compatibility of the donor and recipient must be established beforehand (Pedro et al., 2020). The properties of blood are vital for clinical applications, and numerous blood tests are frequently conducted in medical settings to diagnose and monitor a wide range of medical disorders.

Blood comprises four main components; red blood cells (RBC), white blood cells (WBC), plasma cells, and platelets. 54.3 % of the blood content consists of plasma, 45 % of RBC, 0.7 % of WBC, and less than 1 % of platelets. With a pH of 7.4, blood is more viscous and slightly denser than water (Schwan, 1983). Required substances such as oxygen (O_2), carbon dioxide (CO_2), and nutrients are transported through the body through the RBC. RBC or erythrocytes occur in a disc-shaped diameter of 7-8 µm and consist of hemoglobin molecules

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that make blood red. Low hemoglobin levels make the blood look darker red, such as deoxygenated blood in the veins. Hemoglobin molecules cause RBC to be attached to O_2, called oxyhemoglobin (Lopez, 2011). The blood volume must be proportional to the blood pressure to ensure adequate blood distribution across the body's tissue in a tissue perfusion phase.

II. ELECTRICAL PROPERTIES OF BLOOD

The blood's electrical properties and constituents are measured over the frequency spectrum from less than 100 Hz to more than 100 GHz. The microfluidic system is a workable and easy solution for evaluating blood samples' electrical and rheological activity. Generally, human blood's electrical properties have gained much attention for various reasons a few decades back. First, the paths of current flow through the body are known. Thus, they are essential in studying various biomedical applications, such as functional electrical stimulation, diagnosis, and treatment of various physiological conditions with weak electrical currents, radiofrequency hyperthermia, body composition, and electrocardiography (Lopez, 2011). Various cell shapes, distribution inside the cytosol, and the blood components' various properties make the microscopic approach very difficult. Thus a macroscopic definition of the response is most commonly used to distinguish field distributions in blood and biological systems (Banu, 2018; Mankar, 2017; Pathan & Rathod, 2017).

The electrical properties of the blood can change due to the difference in the physiology of the blood. With this principle, different medical conditions track via various impedance diagnostic methods. Abdalla et al. (2010) and Jaspard et al. (2003) have explained that micro-and macro-effects can be accomplished, such as micro-level osmosis, which causes swollen cells and tissue damage, while metabolism continues throughout the macro phenomenon until the blood flow disrupt, which leads to narrower extracellular pathways and increases in low-frequency impedance (<10 kHz) (Perelman et al., 2021; Moslemi et al., 2023). The blood type determination is significant and is a basic test of all the tests conducted. The doctor can do the first thing during any emergency, or whether we admit to the hospital, to assess the blood type. Thus, a minute delay can lead to death in an emergency (Kondratov et al., 2017). Identification of the blood type during blood transfusion is essential for safe transfusion. Each person has a different blood type based on an antigen present in their blood (Bularzik et al., 2010). Severe injury can cause high blood loss due to bleeding. A healthy adult will lose about 20% of the blood volume before the first symptom and restlessness starts and about 40% of the volume before the shock begins. An unfair or uneven transfusion would make a blood clot, leading to significant and sudden death (DeSimone et al., 2021). Furthermore, a minute delay during transfusion or emergencies can risk the patient's life.

The invasive process or traditional method often induces human error during the procedure or can misinterpret large samples. Automated machines use for blood type determination in a large hospital, but they are extensive and costly. The traditional approach has many disadvantages, so a modern blood type detection system operates (Katti et al., 2015; Zhang et al., 2017). Burr-Brown (2015) suggested a method used to assess the amount of voltage present in the blood. The components used LED, OPT101 Detector, Arduino Board, and PC Display. LED (light-emitting diode) is a p-n junction diode that emits light when energized. The LED light passes through the finger and is reflected/deflected or passed. The scattered light is detected by the OPT101 detector (Burr-Brown, 2015). The first part is the sensor. The sensor has two IR and red LEDs, while the light detector is on the other side. For example, the pulse oximeter used the same probe type (Fidanboylu & Efendioğlu, 2009; Giallorenzi & Bucaro, 2017; Turgeon et al., 2019). The OPT101 combines a single-chip photodiode and an impedance amplifier. It uses to transform the light into a voltage. The photodiode absorbs a large amount of light, making it possible to calculate high sensitivity (Fidanboylu & Efendioğlu, 2009). The integrated combination of the photodiode and trans-impedance amplifier on a single chip eliminates the risk typically encountered in discreet designs, such as leakage current errors, noise, pick-up, and peak gain due to stray capacitance. The resulting voltage increases linearly with the light's strength - the amplifier is designed for single or dual-power operation. Electrical properties of blood play a crucial role in studying biomedical applications such as the diagnosis and treatment of various physiological disorders with low/low electrical currents, radiofrequency hyperthermia, and ECG. The elements of the electrical properties of the blood are

alternating current and spectroscopy. These properties are perceived in a range of less than 100 Hz (Bularzik et al., 2010; Haxha & Jhoja, 2016; Patel et al., 2019; Schwan, 1983; Sultan et al., 2019; Zhang et al., 2017).

III. TECHNIQUES IN BLOOD TYPING

The identification of a person's blood type can be accomplished through the use of several different methods, such as blood typing according to ABO utilizing serological techniques, ABO blood typing with the use of molecular techniques, blood type determination using serological techniques for Rh, molecular approaches to the testing of Rh blood types, typing of blood by the use of flow cytometry, mass spectrometry for blood typing laser speckle contrast imaging for blood typing, typing of blood by the use of fast diagnostic tests, the typing of blood by the use of microarray-based technologies and melting analyses performed at a high resolution are used to type blood as shown in Table 1. Blood typing by ABO utilizing serological methods is the way that is used the most frequently. This method combines a blood sample with antibodies specific to A, B, or both antigens found on red blood cells. It is possible to determine an individual's blood type based on the reaction of the blood when it is exposed to antibodies. This approach to ABO blood type uses molecular technologies, and it entails detecting the presence of specific genes that, when present on red blood cells, encode for the A, B, or O antigens.

Flow cytometry involves studying cells' physical and chemical features, including red blood cells, using a flow cytometer. Blood types can be determined using this method. Labeling the cells with specific antibodies or dyes and analyzing the cells' fluorescence or light scattering properties are viable methods for accomplishing this goal. This method involves evaluating the protein and glycan profiles of red blood cells through mass spectrometry, which can reveal information on the blood type of the individual based on the particular protein and glycan patterns. Laser speckle contrast imaging studies the speckle patterns produced when laser light is dispersed by red blood cells in the blood vessels. This technique is also known as "blood typing with lasers." The contrast between the speckles and the background can reveal information about the individual's blood flow and blood type. This method involves using paper-based or microfluidic devices that contain particular antibodies or antigens that can react with the blood sample and identify the individual's blood type. The microarray platform detects the presence of specific antibodies or antigens in the blood sample, allows the simultaneous analysis of many samples, and provides high-throughput blood typing. The high-resolution melting analysis is a method for blood typing that incorporates detecting the melting curves of PCR amplicons unique to the ABO and Rh blood typing genes. The specific melting temperature and pattern can provide information about an individual's blood type, and the melting curves can provide this information based on the pattern of the melting temperature.

A slide test is performed by mixing the individual's blood with the antigens A, B, and D separately on the slide. This test requires 10-15 minutes, could offer an instant result, involve a low cost, and require a small amount of blood. However, this slide test is the least sensitive compared to other techniques (Sultan et al., 2019). A drop of the patient's blood is combined with separate drops of anti-A and anti-B sera on a microscope slide for this test. The slide is then examined under a microscope. After that, the blood and the sera are combined carefully, and a lookout is kept for any signs of clumping, suggesting agglutination. The density of antigens affects the antibody-antigen response. Excessive antigens acquire fewer antibodies to maintain a low agglutination level. If the antibody has a small binding constant, the test's sensitivity can improve by adding the number of antibodies (Tovey, 1969). Tube Exam of the presence or absence of A and B antigens in RBCs, and the reverse grouping indicates the presence or absence of anti-A and anti-B in the serum. Blood was applied to two test tubes, and one droplet of each antigen (ANTI-A and ANTI-B) was added separately in these tests (Nakamura et al., 2019). These tubes were held for centrifugation for a few minutes and then shaken to see the blood clumping. Centrifugation aims to combine blood and antigens properly. Its advantage is that the test is more sensitive than the slide test, requires a low amount of reagent, and specific unintended antigens may also identify (Gayathri et al., 2018). The agglutination reactions reveal whether or not specific antigens are present in the patient's red blood cells; as a result, the individual's blood type can be deduced from this information.

Microplate technology uses an indirect antiglobulin test (IAT) by mixing the red blood cells of a patient

with reagents that are readily accessible on the market and contain antibodies to identify particular blood types. The mixture is then placed on a microplate and incubated at a specified temperature. After that, anti-human globulin (AHG) serum is added in order to identify any interactions that may have occurred between the patient's red blood cells and the antibodies. The microplate is then read with a spectrophotometer or another type of plate reader to identify whether or not agglutination took place. The microplate consists of several tiny tubes, each holding a few microliters of reagent, which is used to test blood samples (Malomgré & Neumeister, 2009; Plapp et al., 1989). This method offers several advantages, including a quick response time, a small reagent volume, and high throughput analysis (Zhang et al., 2017). Gel centrifugation applied anti-A, anti-B, and anti-D reagents to the blood in small microtubes containing controlled incubation and centrifugation gel. The gel medium traps the agglutinate, and the non-agglutinated blood cells can pass through the column. Its advantages are sensitive, straightforward, and reasonably easy to operate for less-skilled workers. This approach takes 45 minutes to be done and the most accurate result to be obtained (Katti et al., 2015).

Table 1: Blood typing techniques

Test	Detection	Test Principle	Technology	Time (min)
Slide	Blood Types	Agglutination	Manual Invasive	10-30
Tube	Blood Types	Agglutination	Manual Invasive	10-30
Microplate	Blood Types	Agglutination	Manual Automated Invasive	10-30
Enzyme	Rhesus for Blood Types	Agglutination can be performed as tube assay or gel centrifugation	Manual Automated Invasive	30
Molecular	Blood Types	Nucleic acid amplification techniques (PCR-RFLP, PCR-SSP, PCR-SSO)	Manual Invasive	Hours
Gel Centrifugation	Blood Types	Agglutination and separation from non-agglutinated erythrocytes by centrifugation	Manual Automated Invasive	10-45

IV. NON-INVASIVE PHYSIOLOGICAL SENSORS

Non-invasive physiological sensors are applied to the body to control or measure the patient's health. An international team of researchers has designed a portable device that can be used for blood type detection without a blood test. Vijay (2016) has upgraded this system by combining light-emitting diode (LED) and portable optical systems. The multi-wavelength light (MWL) scatter method has been used in this technique, identifying a blood type based on antigens' presence on the RBC surface. Light rays travel through the epitopes of antigens, allowing light with a specific wavelength to respond accordingly. Some of the compounds in the samples deflected towards the light as soon as the specific light energy hits the samples, depending on incoming ray energy. Susceptible camera photodetectors capture several images once the deflected light is detected. Thus, the blood type can be determined based on the deflected pattern of light captured.

This non-invasive technique detects a blood type without penetrating the skin. This device can capture cell-resolution surface capillary images when placed on the fingertips. The images obtained are analyzed using specific algorithms to determine the WBC and its concentration. Capillary images have been captured using a small portable optical device (camera) lens. At some frequency, the light was absorbed only by RBC hemoglobin. WBC appeared as tiny translucent particles in the capillary, allowing image processing algorithms to examine these effects and estimate the blood concentration (Bhatia & Singh, 2015; Mehare et al., 2018; Sultan et al., 2019; Zhang et al., 2017).

Besides, another team of researchers has proposed a non-invasive method to examine blood typing. Gayathri et al. (2018) proposed a blood type detection without skin puncture that consumes a shorter processing time and a more straightforward interpretation of the results. This method involves a low cost and is convenient even during an emergency. The main component is a light-emitting diode (LED), an optical detector, a controller unit, and a PC display. In addition to RBC agglutination, the interface between antibodies

and antigens is considered. It can be examined by observing the agglutination that occurs if there is an antigen-antibody response (Gayathri et al., 2018)

Zhang et al. (2017) used chemical reactions between blood serum protein and green bromocresol dye. The result appeared to be color changes when the antigen is present in the sample and, if not, appears brown. This method uses only the paper strip; no centrifugation process is involved (Zhang et al., 2017). Baranski (2011) proposed that optical fiber was used as a medium for transmitting pulsating light. This light is then transmitted through the blood sample, and the variation in the intensity of the light is measured based on which the blood types are determined.

Selvakumari (2011) researched blood type detection using fiber optics. The blood typing that has been done so far is an invasive process. As far as hospitals and blood banks are concerned, several blood samples must be identified quickly. The invasive process is laborious and time-consuming (Banu, 2018; Selvakumari, 2011). In improving the blood type system, which enables us to identify them more efficiently and safely, even a few have done so. An alternative solution is to seek the lab's assistance and develop methods to meet their needs. Malomgré & Neumeister (2009) suggested that blood typing should be done in laboratories or hospitals using either an invasive slide or semi-automatic gel technology method.

This project uses an optical fiber sensor that modulates the measured output and produces electrical output variations for different blood types. This variation is sufficient to identify blood types. Giallorenzi & Bucaro (2017) and Turgeon et al. (2019) have indicated the advantages of optical fibers when used as sensors. These sensors convert optical variations into electrical variations that can be calibrated to identify blood types (Kakarla et al., 2014). The transmitter generates 10 KHz pulses using a fiber optic sensor. These pulses are amplified and fed to the LED, which converts electrical and optical variations. The optical signals are sent to the fiber. They pass through the blood sample and are received by the receiver, which converts optical variations back to electrical variations. These electrical signals are amplified, filtered, rectified, and then fed to a condenser philter that changes the different voltages for different blood types (Kakarla et al., 2014; Selvakumari, 2011).

V. CONCLUSION

The existing procedures need blood extraction from the human body using huge and expensive biomedical machinery. These intrusive treatments, while effective, can be painful and pose hazards to those undergoing blood type testing. Understanding the electrical characteristics of blood is critical for designing and deploying non-invasive physiological sensors capable of determining blood type without the need for blood extraction. The development of non-invasive blood typing technologies that improve patient comfort and accessibility while retaining accuracy and dependability.

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