

## Review

# Novel idea to monitor and measure blood hemoglobin noninvasively

A. H. Ar-Rawi\*, M. Moghavvimi and W. Ibrahim

Faculty of Engineering, University of Malaya, Malaysia.

Accepted 10 December, 2010

**Measuring blood hematocrit noninvasively is reviewed in this paper. Although there is an inclination to measure the hematocrit by determining the bioelectrical impedance of the blood, *in vitro* experimental methods still remain practically inapplicable. The blood sample size is determined when blood samples are examined. Determining the impedance and volume of blood is the biggest challenge in measuring the hematocrit noninvasively without drawing a blood sample. Calculating the blood impedance *in vivo* requires developing an impedance measurement using a multi-frequency method and also calculating the change in pressure simultaneously during the heart's pulsatile cycle.**

**Key words:** Blood, hematocrit, measurement.

## INTRODUCTION

Currently, a standard method is used for checking the blood components in order to diagnose patients infected with any blood viruses, such as human immunodeficiency virus (HIV) and dengue hemorrhagic fever (DHF), among others. This method analyzes the blood sample to detect the blood's chemical components, obtaining a comprehensive blood picture of the patient. This technique has many disadvantages, particularly when patients are suspected to be infected with specific viral diseases, such as DHF, HIV and Hepatitis B virus (HBV), or even the bird flu virus and other blood transmitted diseases. These disadvantages require precious personal time for drawing blood samples and may cause a substantial delay before data are available, depending on the proximity of the testing laboratory. Moreover, frequent blood sampling from the patient may cause further injuries to the subcutaneous tissue, subsequently contributing to delusional anemia (Abdulrahman, 2003). Frequent blood sampling can cause inflammation and fever associated with blood

flow increase, activation of phagocytes, increase in capillary permeability, complement activation, clotting reaction walls of the region, regional temperature increase and activation of specific defenses in the blood (Ibrahim et al., 2004).

The bioelectrical impedance analysis (BIA) is used to overcome all these disadvantages. In recent years, BIA has become an increasingly popular modality in the assessment of human body composition, that is, bioelectrical tissue conductivity, mass distribution and water compartments.

This research is conducted to study the possibility of designing and developing a bioelectrical impedance apparatus for checking and monitoring blood hematocrit. Generally, this method has many advantages:

1. Fast results.
2. No blood drawing.
3. Low-cost instrumentation.
4. Ease of applicability in practice.
5. Online monitoring.

\*Corresponding author. E-mail: [owner@aoday.com](mailto:owner@aoday.com).

**Abbreviations:** HB, Hemoglobin; BIA, bioelectrical impedance analysis; RBC, red blood cell; ESR, erythrocyte sedimentation rate; TBW, total body water; SF-BIA, single frequency BIA; MF-BIA, multi-frequency BIA.

## THEORY OF BIOELECTRICAL IMPEDANCE

All living things are comprised of cells. Cells are membrane-bound compartments filled with a concentrated solution of chemicals and salts. Groups of cells

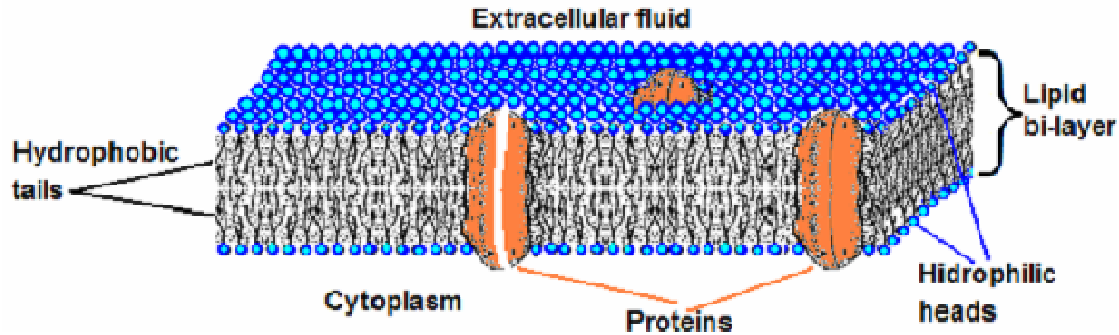


Figure 1. Lipid bi-layer structure of the plasma membrane (Fernando, 2007).

perform specialized functions and are linked by an intricate communication system. The cell membrane maintains an ion concentration gradient between the intracellular and extracellular spaces. This gradient creates an electrical potential difference across the membrane, which is essential to cell survival. Electrical gradients are necessary to support the movement of oxygen, carbon dioxide and nutrients. Therefore, the cell membrane has electrically insulating qualities to maintain an electrical gradient. Damage to the cell membrane and its functions is as lethal to the cell as direct damage is to the nucleus itself (Figure 1).

In a healthy living body, the cell membrane consists of a layer of non-conductive lipid material sandwiched between two layers of conductive protein molecules. Biologically, the cell membrane functions as a permeable barrier separating the intracellular (cytoplasm) and extracellular components. The lipid membrane is transversed by proteins, which are soluble in water, creating pores through which water, ions and other chemicals can enter and exit the cell. Controlling the flow of these materials is essential to life. The cell membrane protects the interior of the cell, while allowing passage of some materials to which it is permeable. The cell membrane is composed mostly of a double layer of phospholipids arranged tail to tail along the width of the cell membrane. This structure is called the lipid bilayer and it acts as an electrical insulator (dielectric) in a similar manner as in fats and oils. The heads of the phospholipids are polar (carry a charge), whereas the tails are non-polar. The heads interact with water, whereas the tails are repulsed by water aligning them tail to tail with the heads facing the outside and inside of the cell.

Impedance is a complex quantity that has both a resistive and reactive component. It has a magnitude and a phase angle. Specifically, it is the vector sum of resistance and reactance, where reactance is the Y coordinate and resistance is the X coordinate. The square root of the squared sums of X and Y is the impedance. The phase angle is the angle (degrees) between the resistance coordinate and impedance magnitude (line). For example, if there was zero resistance and any value of reactance, then the phase angle would be 90 degrees. In contrast, if

the reactance was zero and the resistance had any finite value, then the phase angle would be zero degrees. Phase angle is a simple method of expressing the effective ratio of resistance and reactance from 0 to 90° and describing electrically, how voltage and current lead or lag each other in any circuit of resistors and capacitors. Impedance and phase angle only exist with alternating current (Aroom et al., 2009) (Figures 2 and 3).

Hence:

$$X_m = 1/(\omega C_m) \quad (1)$$

where  $X_m$  is the capacitive reactance Ohm,  $C_m$  is the capacitance value in Farad, and  $\omega$  is the radian frequency

$$\omega = 2\pi f \quad (2)$$

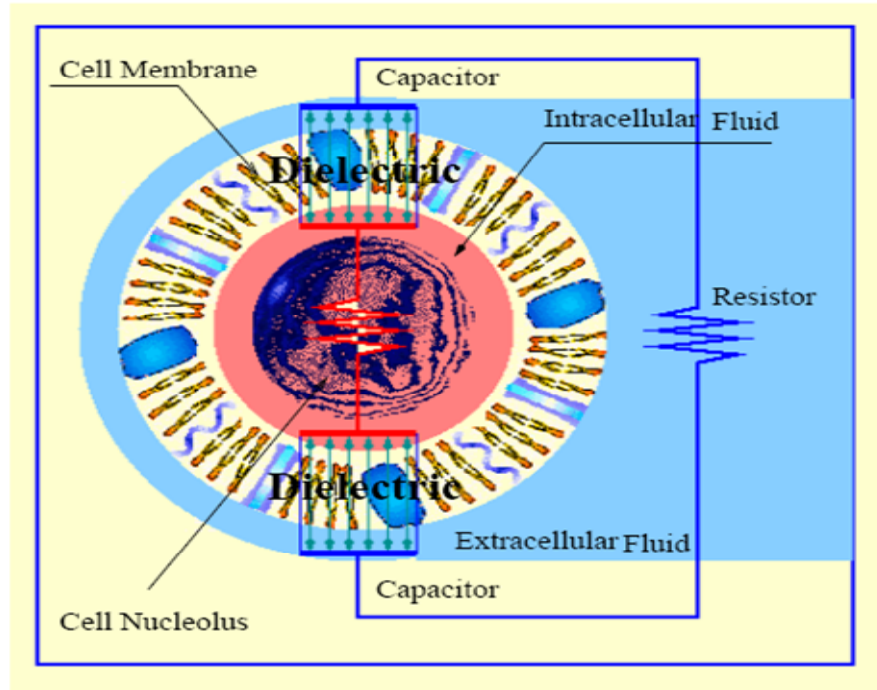
where f is the frequency and  $\pi = 3.142$

Referring to Equations 1 and 2, the reactance is inversely proportional to frequency. Based on the aforementioned studies, the cell with currents below 50 KHz works as a resistor only. In very high frequencies, the capacitor acts as a short circuit that allows the equivalent circuit of the cell to become similar to the two resistors in parallel (Mager et al., 2008; Aroom et al., 2009) (Figure 4).

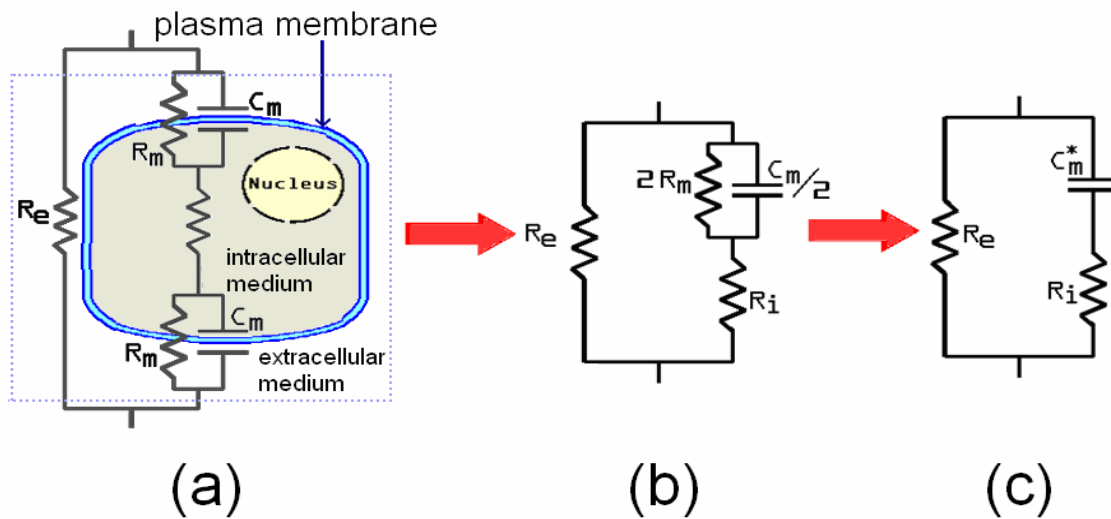
The bioelectrical properties of an organism depend on its geometry and specific resistivity. The latter varies as a function of the composition of the tissue and the frequency of the test signal. Hoffer et al. (1969) proposed that the complex geometries of the human body could be treated as a single conductor of uniform cylindrical geometry. Assuming that the test signal frequency is constant, then the impedance (Z) is a function of the cross sectional area (A) and length (L) of the conductor (Figure 5a)

$$Z = \rho L/A \quad (3)$$

where  $\rho$  is the specific resistivity.



**Figure 2.** How an electrical capacitor is formed from the outer boundary of a cell and its dielectric nature. The outer boundary of the cell is a plasma membrane of phospholipids molecules that become a dielectric to form an electrical capacitor when a radio frequency is introduced to the cells environment.



**Figure 3.** Equivalent electrical circuit of a cell. The circuit in (b) is the equivalent of the model in (a) after performing some circuit simplifications and considering the large value of  $R_m$ . The circuit in (c) is the equivalent circuit of the cell, neglecting the effect of  $R_m$ . Note the  $C_m$  (Fernando, 2007).

Multiplying the right side of Equation 3 by  $L/L$  and setting  $AL$  equal to the volume ( $V$ ) of the conductor, yields the following:

$$Z = \rho L^2/V \tag{4}$$

Rearranging Equation 4 gives:

$$V = \rho L^2/Z \tag{5}$$

Thus, the volume of the conductor can be related to two

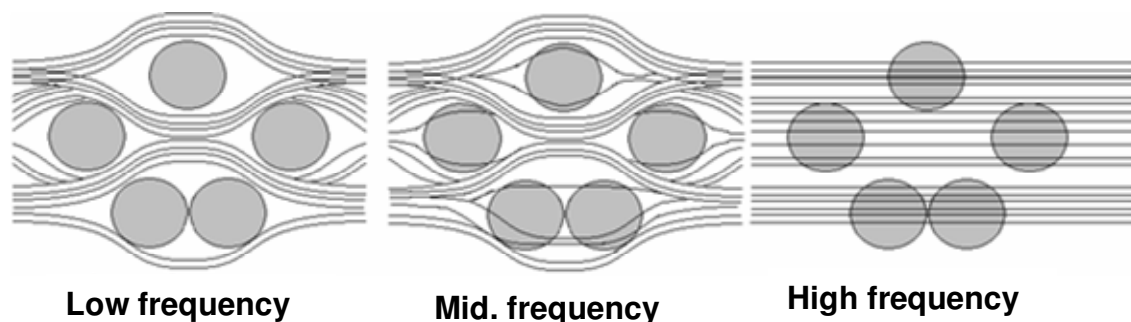


Figure 4. Current paths in a suspension of cells at various frequencies (Fernando, 2007).

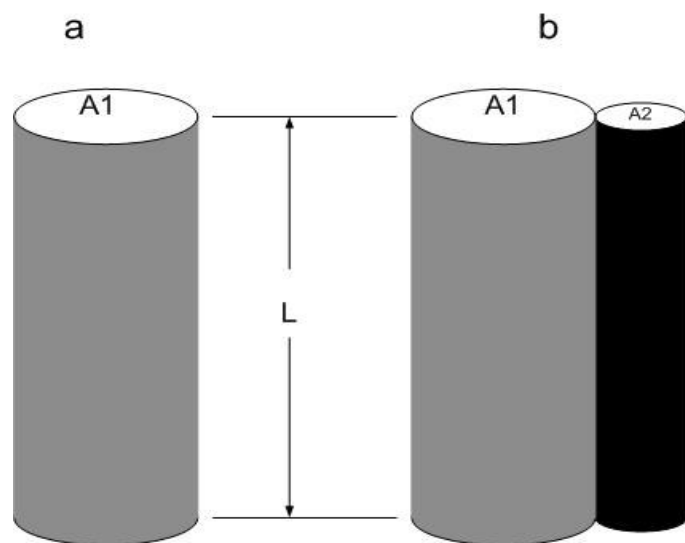


Figure 1. Conductor showing (a) its cross sectional area and length, (b) different resistivities arranged in parallel (Schoeller et al., 1989).

readily measured parameters of length and impedance. This volume can be interpreted with respect to body composition if the body is viewed as several components with differing resistivities arranged in parallel (Figure 5b). Using this model, the volume estimated from length and impedance is approximated by that of the component with the lowest resistivity. The resistivity of the adipose tissue is considerably greater than that of the muscle and the difference is proportional to the water content of these tissues (that is, about 75% of weight for muscle and 5 to 20% for adipose). Based on this difference, fat, which is anhydrous, has a very high resistivity and the volume derived from Equation 5 is related to fat-free mass or, more specifically, some compartment of water in a fat-free mass. This fat-free compartment depends on the frequency of the test signal. At frequencies between 100 and 100 MHz, cell membranes have low electrical permittivity; thus, the impedance reflects the extra cellular fluid. At higher frequencies, the resistance of the cell membrane begins to short out because of the capacitance of

the cell. At 300 MHz, there is virtually no difference between the resistivity of normal saline and lean tissue. Thus, at higher frequencies, the volume derived from Equation 5 is related to the total body water. However, the impedance depends on electrolyte concentration; hence, the comparison should be against normal saline rather than water. The dependence on electrolyte concentration could be a problem, except that the concentrations of electrolytes in body fluids are relatively constant in healthy subjects. Moreover, the choice of frequency is less critical than is usually required (Jaffrin et al., 2008; Schoeller et al., 1989).

As discussed, body impedance can be represented as various resistors and capacitors connected in series and parallel as shown in Figure 6 (Schoeller et al., 1989). The International Society for Electrical Bio-Impedance registers the resistivity of various body tissues as follows (Sutton et al., 1999):

1. Blood: 150  $\Omega$ .cm
2. Urine: 30  $\Omega$ .cm
3. Muscle: 300 to 1600  $\Omega$ .cm
4. Lung: 1275  $\Omega$ .cm
5. Fat: 2500  $\Omega$ .cm

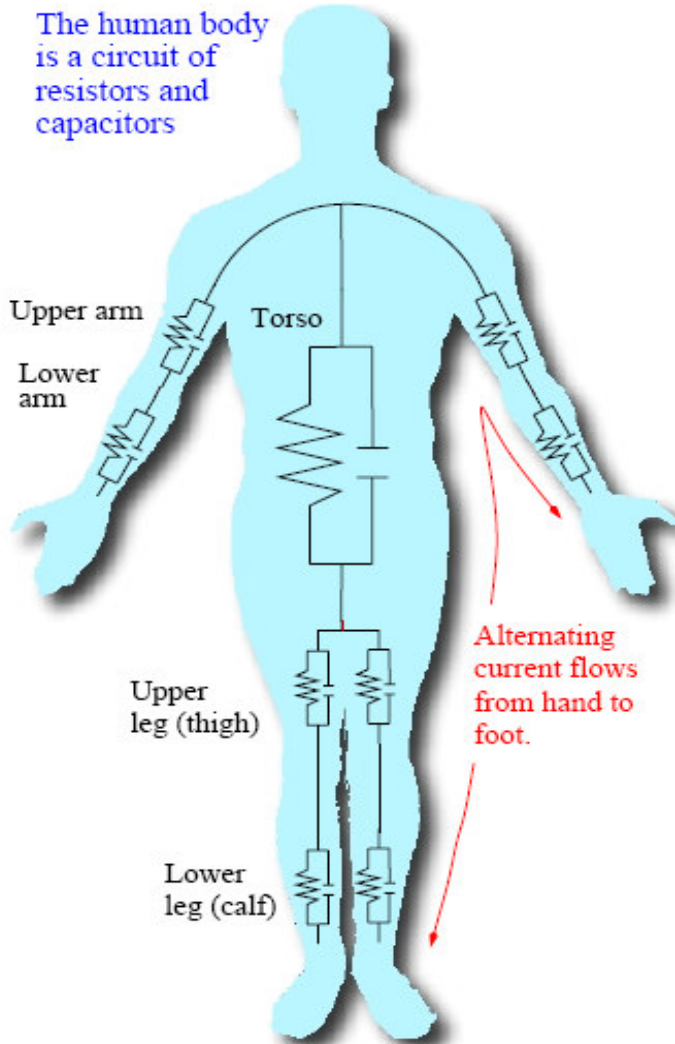
Based on the aforementioned resistivities, fat tissues have high impedance, whereas urine tissues have the lowest.

The frequency also affects impedance as shown in the aforementioned equations. Thus, each tissue type conducts in the frequency range depending on the tissue geometry itself (Hills et al., 1998).

## BIOELECTRICAL IMPEDANCE TECHNIQUES

The bioelectrical impedance technique is defined as the measurement of biocell electrical impedance by applying a fixed current and measuring the voltage and phase shifts, allowing the bioimpedance to be calculated.

There are two main methods for measuring bioimpedance: The two-electrode method and the four-electrode method. Each method has its own advantages and disadvantages. However, the second method is more widely used as thus explained.



**Figure 6.** The human body as a circuit of resistors and capacitors, connected in series and parallel.

### Two-electrode technique

This technique is simple. It applies the current source through the cells and measures the voltage and phase angles, allowing the impedance to be calculated as follows (Figure 7):

$$Z = R + jX_c$$

$$\frac{V}{I} = \sqrt{(R^2 + X_c^2)}$$

$$Q = \tan^{-1}\left(\frac{X_c}{R}\right)$$

Both resistance and reactance can be calculated based on the aforementioned equations. The two-electrode technique has several limitations (that is, bioimpedance and bioelectricity basics). The results from this technique are often irreproducible due to the excessive interference by electrochemical reactions at the subcutaneous needle electrode surface, causing additional electrode polarization anomalies. In addition, the small diameter of the electrode needles results in a much greater current density near the electrodes than in the rest of the body. Therefore, the integrity of the tissue near the electrodes and the electrode size can affect the measurement of impedance between electrodes and confuse the desired data (Grimnes et al., 2000). To surmount these limitations, the four-electrode method is used.

### Four-electrode technique

The four-electrode system is preferred when the distal volume segment of the current part is the zone of interest and when the effect of the zones proximal to the current-carrying electrodes has to be eliminated. Four-electrode systems correspond to a '2-port four-terminal network' equivalent. Transfer functions may be set up to describe the signal path from the current-carrying to the signal-recording electrodes. This is the case in impedance plethysmography or impedance imaging. They are also the best systems for measuring excised tissue samples *in vitro*. An *in vitro* version is shown in Figure 8.

The measured segment is determined by the position of the two recording electrodes,  $R$  and  $R'$ , or more exactly by the position of their electrolyte/salt bridge connections to the measuring cell. The two stippled equipotential lines indicate that this current is recorded with a current-reading operational amplifier. The recording electrodes are connected each to one buffer amplifier. No current flows in the electrode leads; thus, the electrodes cannot be polarized externally (but internal currents may polarize them). Electrolyte/salt bridge connections are used to increase the electrode metal area, increase electrode admittance and reduce noise. Large electrodes inserted directly into the measuring cell disturb the ionic current flow pattern, causing polarization to occur on the metal surface. The electrode metal should not be in direct contact with the electrolyte, but must be recessed instead (Figure 9) (Grimnes et al., 2000).

The electrolyte is contained in a tube with isolating walls. When part of this wall is substituted by electrode metal, the current prefers the high conductivity path of the metal. The current lines deviate from the path parallel to the tube walls, causing the current to enter one part of the area and leave the other. Thus, the electrodes are polarized, but not by a current in the external leads. The polarization may not be uniform over the electrode surface area, and polarization occurs according to the local current direction and polarization admittance. When

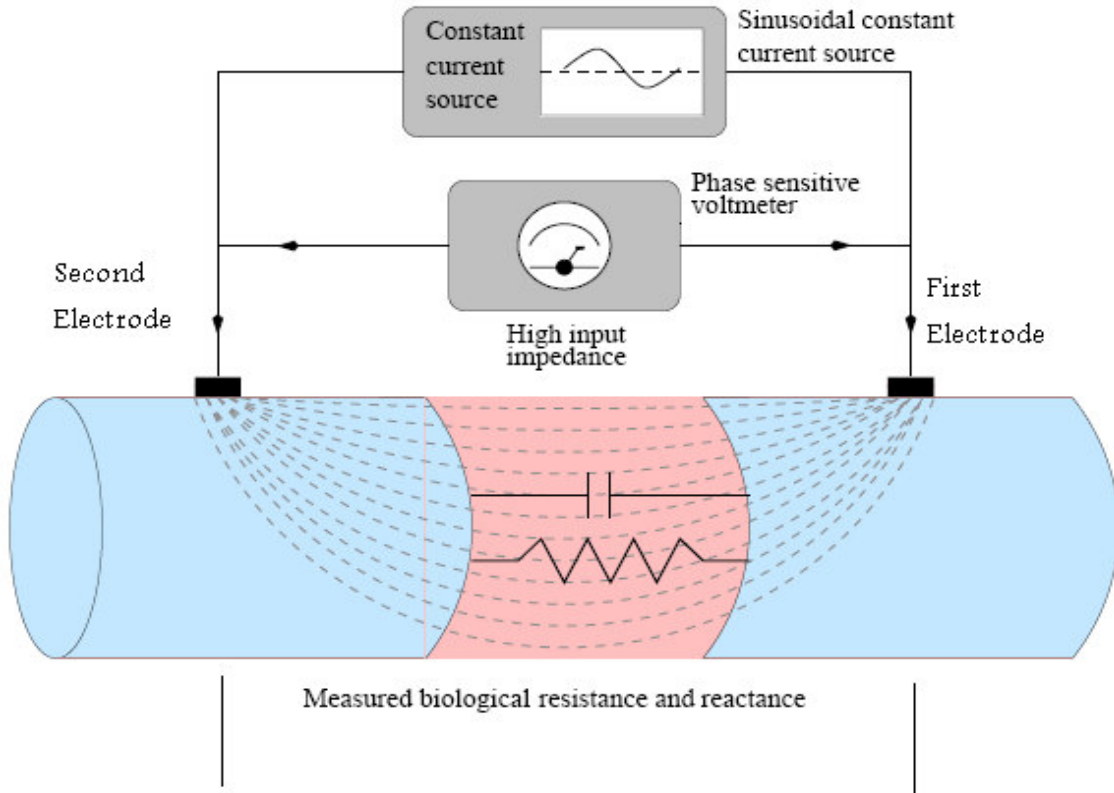


Figure 7. Two-electrode system.

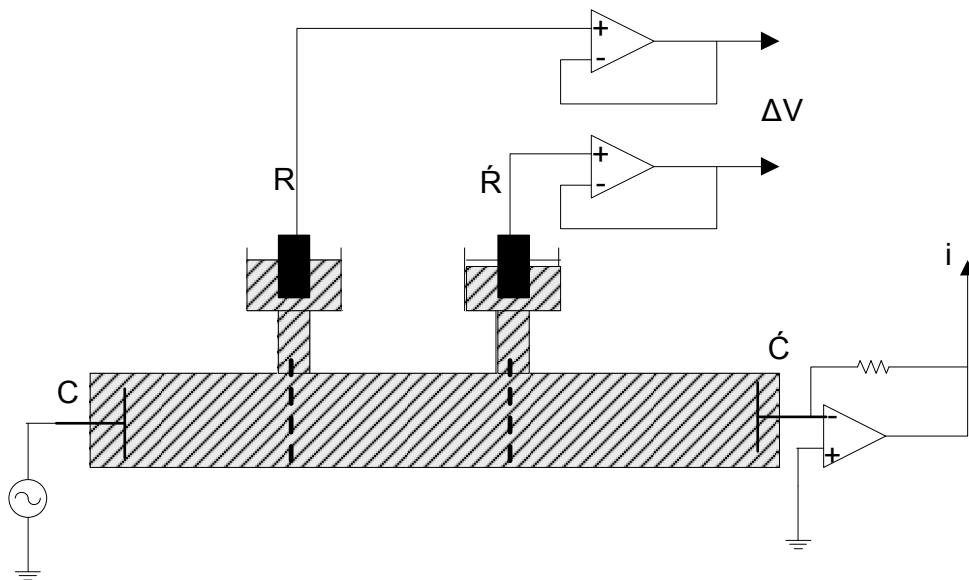
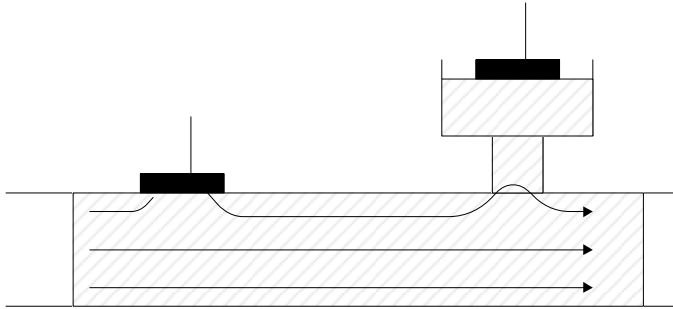


Figure 8. Four-electrode system. Tubular *in vitro* version (Grimnes, 2000).

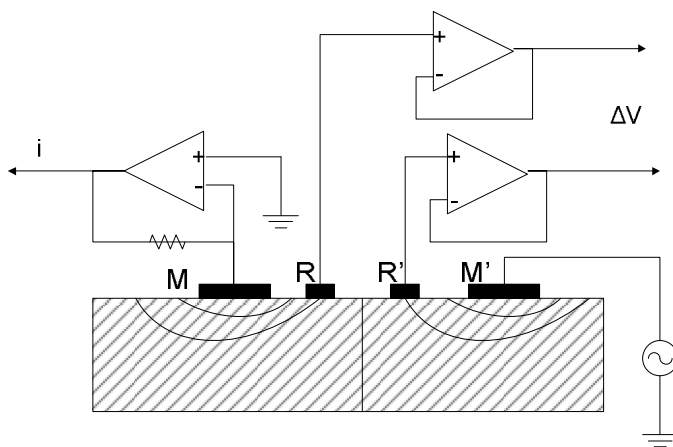
the metal is recessed, the current also deviates into the electrolyte of the bridge path, but does not pass through any metal surface. Thus, polarization does not occur.

Figure 10 shows a four-electrode *in vivo* skin surface version. The two recording electrodes ensure that only

the current path segment between these electrodes contributes to the result. The stippled equipotential lines indicate the segment being measured. However, not all tissue volumes contribute equally. Sensitivity is proportional to the local current density in the measured volume



**Figure 9.** The non-recessed electrode on the left implies polarization from the current entering and leaving the metal (Grimnes et al., 2000).



**Figure 10.** Four-electrode system, in vivo version. Equipotential lines are shown in the tissue. The position of R -R' determines the tissue segment measured and the size of the proximal zones measured by M and M'.(Grimnes et al., 2000).

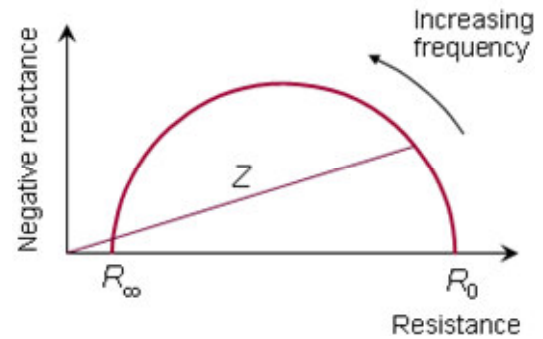
segment. Sensitivity is zero in the two segments proximal to the current-carrying electrodes as long as the potential difference is taken from the R -R' electrodes. Measuring all three voltages, M-R, R-R', and R'-M', simultaneously, as well as the admittance/impedance of the two constrictional zones and one distal volume is also possible (Grimnes et al., 2000).

**BIOELECTRICAL IMPEDANCE METHODS**

When alternating current (AC) is used, various methods can be applied to measure the BIA depending on the frequency. The variance in tissue membrane makes the capacitance of the membrane differ in each tissue type. Referring to the tissue equivalent circuit in Figure 3,

$$Z = R_0 \parallel (R_i + X_c) \tag{6}$$

and



**Figure 11.** Cole-Cole plot.

$$X_c = \frac{1}{2\pi FC} \tag{7}$$

Based on the aforementioned equations, if the frequency has a very large value, then X<sub>c</sub> will be near zero:

$$Z = Z_\infty = R_0 \parallel R_i \tag{8}$$

and will be called Z infinity (Z<sub>∞</sub>). If the frequency F is zero, X<sub>c</sub> will then act as an open circuit:

$$Z = Z_0 = R_0 \tag{9}$$

Between zero and infinity, the impedance, Z varies depending on the X<sub>c</sub> variation with frequency, Z and both the imaginary and real parts are frequency dependent as shown in the Cole-Cole plot in Figure 11. Figure 11 shows that the very high and very low frequencies of the impedance become pure resistance. It is due to this reason (that is, the impedance changing with frequency) that various methods are used.

**Single frequency measurements (SF-BIA)**

Single frequency BIA (SF-BIA) is used to simplify the calculations. This method is used particularly in measuring body composition applications. A single frequency from 10 KHz to less than 10 MHz is used depending on the tissue to be diagnosed. For example, blood tissue does not conduct at low frequencies and requires the use of high frequencies to check. Lean tissues can be verified at frequencies less than 100 KHz. Simplicity is the main advantage of this method, but it is not accurate and has many limitations. For accurate readings and diagnostics, the Multi-frequency BIA (MF-BIA) is preferred.

**Multi-frequency measurements**

As with SF-BIA, MF-BIA uses empirical linear regression

models, but includes impedances at multiple frequencies. MF-BIA uses different frequencies (that is, 0, 1, 5, 50, 100, 200 and 500 kHz) to evaluate FFM, TBW, ICW, and ECW. At frequencies below 5 kHz and above 200 kHz, poor reproducibility has been noted, especially for the reactance at low frequencies. MF-BIA is more accurate and less biased than SF-BIA for the prediction of ECW, whereas SF-BIA, compared with MF-BIA, is more accurate and less biased for TBW in critically ill subjects. Moreover, some researchers have noted that MF-BIA, compared with bioelectrical spectroscopy (BIS), results in better prediction of TBW and equal prediction for ECW in surgical patients. They determined that MF-BIA is unable to detect changes in the distribution or movement of fluid between the extracellular and intracellular spaces in elderly patients (Ursula and Ingvar, 2004)

### BIOELECTRICAL IMPEDANCE APPLICATIONS

In 1940, clinically induced changes in hydration status were first correlated with total body changes in resistance and capacitive reactance. In the same year, some researchers also pioneered studies on bioelectrical impedance changes to dynamic changes in pulsatile blood flow to organs, arterial pulse waveforms and respiration. The applications of impedance plethysmography or the measurement of electrical impedance changes in limbs, organs and other body sites to detect dynamic blood. Volume changes have been validated extensively by many investigators.

The relationship between TBW and electrical impedance was first reported by Thomasett (1962) and further delineated by Hoffer et al. (1969). For over a decade, there were no subsequent attempts to determine the usefulness of impedance in the analysis of human body composition. Nyboer et al. (1983) applied the electrical volume resistivity principles of impedance plethysmography to the study of body composition using static total body impedance measurements. From 1983 onwards, BIA has been used for many applications in medical diagnosis.

### Blood measurements

Various studies have used BIA methods to measure blood characteristics. These methods guide us in making non-invasive diagnostics through the body. Blood consists mainly of plasma and erythrocyte cells. Blood, as with any body tissue, has the same equivalent electric circuit as shown in Figure 3, where  $R_o$  denotes the plasma,  $R_i$  denotes the interior water of the erythrocyte and  $C_i$  is the membrane capacitance of the erythrocyte.

Fricke (1925) measured the impedance of several blood samples in the frequency range between 800 Hz and 4.5 MHz *in vitro*. Fricke found that blood below 100

KHz behaves as a resistor because the red cell does not conduct at low frequencies. The study by Fricke was followed by similar studies by Cole (1968), Frewer (1972), Jenin and Schwan (1980) and Ludt and Herrmann (1973). The properties of blood can be measured, but the measuring technique is complicated. Zhao (1996) found a novel approach to measure the blood properties (that is,  $R_o$ ,  $R_i$ ,  $C_i$ ) using only three frequencies (that is, 0.1, 0.8, and 1.2 MHz). All these studies have significant results, but they are still experimental (that is, *in vitro* only). As the blood volume is known, the plasma and red blood cell (RBC) resistivity can be calculated depending on the general equation  $\rho = \frac{ZV}{L^2}$ , where  $Z$  is the impedance,  $V$  is the blood volume,  $L$  is the length of the tested segment, and  $\rho$  is the resistivity.

Recently, Adler and Dai (2006) and Charles (2006) measured the blood non-invasively using the blood pulsatile. This method is used to measure the impedance of blood in the systole and diastole cycles. The difference between the two impedances is the blood impedance; however, some difficulties in the measurement of blood resistivity are still encountered. Only the impedance can be measured; thus, the problem is with the blood volume. Yamakoshi and Tanaka (1994) proposed a novel method to obtain blood volume. However, their results were still not accurate because the measured frequency was 50 KHz, and the resistivity was attributed to the plasma only.

### Blood impedance measurements using pulsatile state

Nyboer et al. (1950), Weltman and Ukkestad (1972), Yamakoshi and Tanaka (1994), Adler and Dai (2006) and Charles (2006) measured blood impedance using blood pulse non-invasively. The basis of this method depends on the difference between the tested segment impedance in the diastole and systole cycles. The impedance of a segment in body consists of three impedances in parallel as shown in Figure 12, and includes the following:

1. Body tissue impedance ( $Z_T$ ), which includes all the tissues inside the tested segment excluding blood tissue (that is, bone, lean, fat..., etc.)
2. Artery blood impedance ( $Z_{AB}$ ) during the systole cycle in the tested segment
3. Impedance of blood increment during the diastole cycle ( $Z_{IB}$ ) (Figure 12):

$$\frac{1}{Z_{total}} = \frac{1}{Z_T} + \frac{1}{Z_{AB}} + \frac{1}{Z_{IB}} \quad (10)$$

Taking  $Y=1/Z$ , where  $Y$  is the admittance of the material,



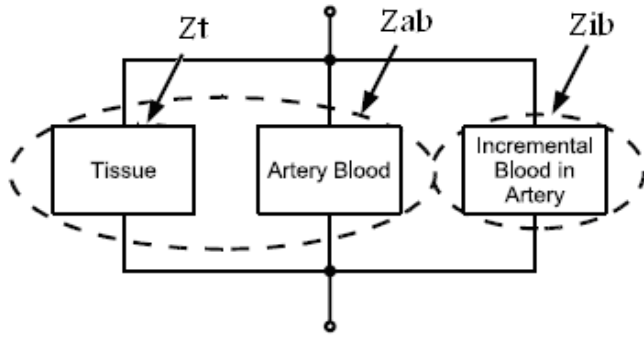


Figure 12. Segment impedances.

we obtain:

$$Y_{total} = Y_t + Y_{AB} + Y_{IB} \quad (11)$$

where  $Y_t, Y_{AB}, Y_{IB}$  and  $Y_{total}$  are the admittance of tissue, artery blood, incremental blood, and the total, respectively. From Equation 11, we obtain:

$$Y_{IB} = Y_b = Y_{total} - Y_t - Y_{AB} \quad (12)$$

where  $Y_b$  is the blood admittance, and  $Y_b = 1 / Z_b$ . We assume

$$Y_{fix} = Y_t + Y_{AB} \quad (13)$$

where  $Y_{fix}$  is the total admittances of the non-blood tissue and artery blood impedances. Rearranging Equation 12, we obtain

$$Y_b = Y_{total} - Y_{fix} \quad (14)$$

where  $Y_{total}$  is the admittance in the diastole cycle, and  $Y_{fix}$  is the admittance in the systole cycle (Papezova, 2003).

### Impedance and blood component

Hill et al. (1975), Zhao (1993) and Treo et al. (2005) conducted various tests and studies on the hematocrit in blood *in vitro* and related it to bioelectric impedance. They found that there is an exponential relation between the hematocrit and blood resistivity.

Zhao (1996), Kichul and Elaine (1994) and some other researchers investigated the relation between erythrocyte sedimentation rate (ESR) and blood resistivity and found a relation between ESR and blood resistivity. Fuller (1991) investigated the plasma in blood *in vitro* using the bioelectrical impedance method and found that the resistivity of plasma changes when the plasma component

changes, such as in NaCl, dextrose, urea and albumin, among others. All the aforementioned results are significant, but they are still experimental and *in vitro* (that is, invasive). Most of the aforementioned studies also used a single frequency to obtain the results. A more accurate result is expected using the multi-frequency test.

### Triple frequency approach

As discussed in the review, there are two methods in BIA, that is, single frequency and multi-frequency. The single frequency is easier to use, but is not accurate especially with blood investigations. In contrast, multi-frequency is more accurate, but has a more complicated process of measurement.

Zhao (1993) used only three frequencies to diagnose blood, making his method less complicated. He used 100 KHz, 800 KHz, and 1.2 MHz to compute the three electrical components of blood,  $R_i$ ,  $R_o$  and  $C_m$  (that is, plasma resistance, RBC intracellular water resistance and RBC membrane capacitance).

Hence, the relation between blood components and resistivity, not with impedance, and the relation between impedance and resistivity depend on the volume. However, the important question is how to determine a method to calculate the volume of blood pulse.

### Yamakoshi approach

Yamakoshi and Tanaka (1994) designed an apparatus to calculate hematocrit using a novel approach to measure the blood volume (Figure 13).

He used a comparative electrolyte solution with known resistivity that surrounds the limb (tested segment). He conducted impedance measurements, which appear as two systems working in parallel: One system to measure the impedance of electrolyte solution and the other to measure limb impedance. Increasing limb volume during the blood pulse travel decreases the solution volume and the impedance of the solution changes (Figure 14).

The Yamakoshi and Tanaka (1994) approach is used as the basis of our apparatus, whereas the triple frequency method is used for collecting various information needed for our study.

### CONCLUSION

Many previous studies on the electrical impedance of blood were carried out at only one frequency below 100 KHz. However, because blood cells do not conduct at low frequencies, the measured resistivity relates only to the properties of the plasma and the volume concentration of blood cells. The method was used to measure hematocrit, cardiac output and ESR, among others. It was extended to monitor fluid volume and measure other body tissues.

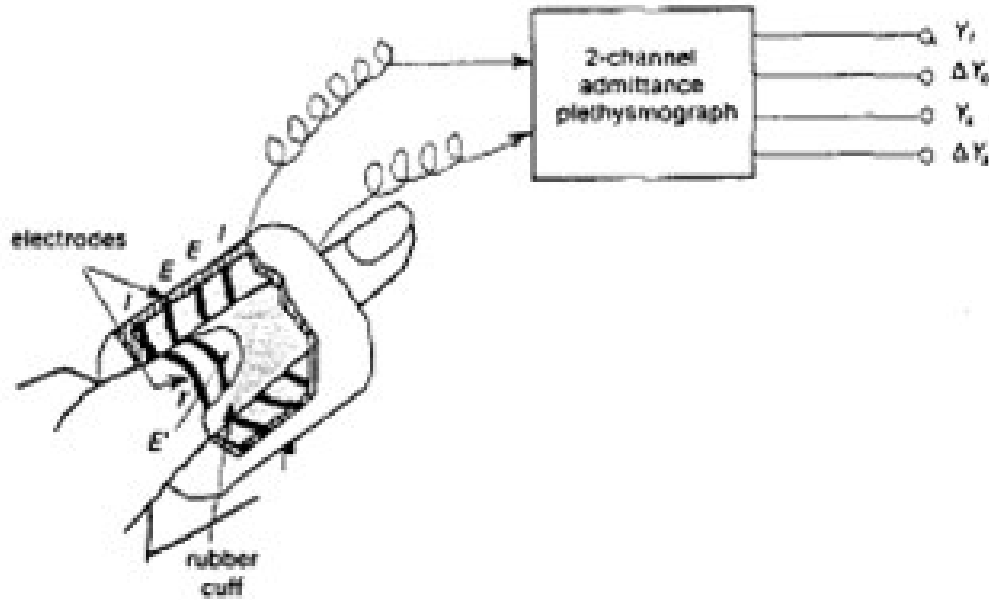


Figure 13. Yamakoshi approach in the measurement of blood volume.

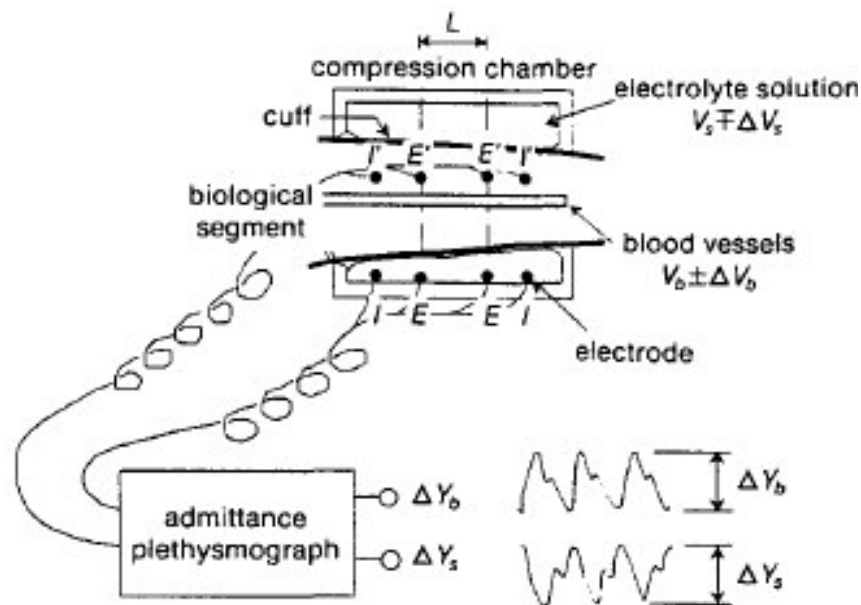


Figure 14. Changes in the impedance of the electrolyte solution.

However, such a single-frequency method could not fully utilize the possibilities of the impedance technique for clinical applications. In particular, the determination of the capacitive component of the impedance may yield information on the membranes of RBC, which is difficult to measure with other techniques (Zhao, 1996).

Some investigators measured blood impedance over a large frequency range, from several hundred Hz to several MHz (that is, Cole-Cole plot). The properties of blood

cells and plasma could be obtained, but the measuring procedure was complicated (Zhao, 1996).

Blood, as a vital body fluid, has been extensively studied using the electrical impedance technique. As determined late in the last century, the conductance of blood decreases as the erythrocyte concentration increases. Successive studies reveal that the RBC membrane is a very poor conductor, whereas the interior fluid is an electrolyte with a resistivity of  $200 \Omega\text{cm}$ . Later, Philipson measured the

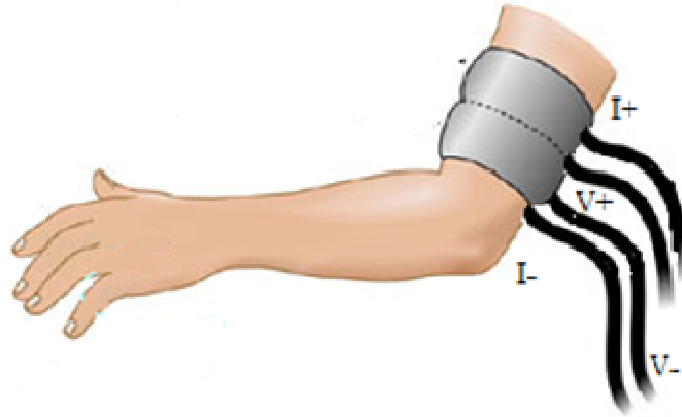


Figure 15. Sending of data from a PC through a serial port.

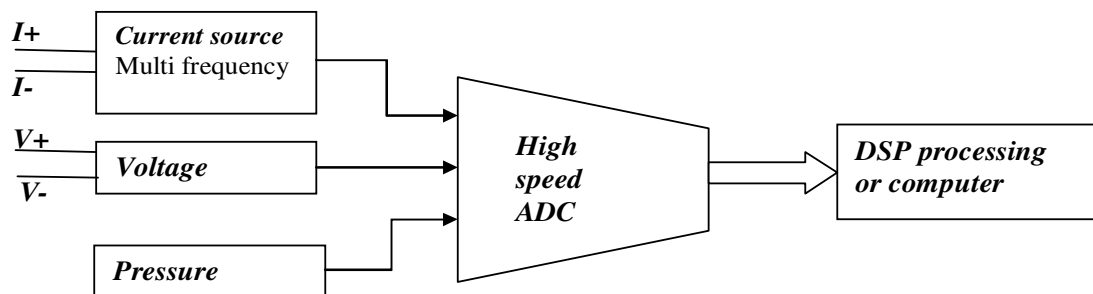


Figure 16. Complete block diagram of the proposed device.

impedance amplitude of packed blood cells over a frequency range of 500 Hz to 3 MHz and found that the internal resistivity of RBCs was about 3.5 times that of plasma (Ibrahim et al., 2004).

Extensive studies on blood impedance, both theoretically and experimentally, were carried out by Fricke and Morse (1925). They determined the capacity of the RBC membrane to be  $0.81 \mu\text{F}/\text{cm}^2$  and measured the impedance of RBC suspensions over the frequency range of 800 Hz-4.5 MHz. They represented these results by an equivalent circuit as shown in Figure 1.

Although these studies provide us with significant results, the results are still not applicable. They are only experimental and require laboratory devices to measure.

For further research, the work aims at developing and designing a non-invasive bio-impedance multi-frequency instrument for checking and monitoring blood hematocrit. This system is expected to be non-invasive, compactable, low cost, locally made and applicable to real applications.

The instrument will be designed using three components:

1. For a non-invasive method using BIA measurements, we will use bio-impedance sensors (probes) and reshape the sensors to fit the upper arm portion. The brachial artery

makes the impedance change in this part noticeably.

2. Using a sphygmomanometer cuff to measure the change in the blood pressure will allow us to know when the blood volume changes.

3. High speed analog to digital technique (ADC) will be used to convert the measured data from analog to digital form. The converted data will be sent to the microcontroller embedded unit for calculation and for evaluating the impedance and  $X_c$ . Finally, the data will be sent to the PC through a serial port (RS232) (third component) (Figure 15).

4. The PC software will read the data from the microcontroller unit through a serial port and saves it to a database for later analysis and creation of reports.

The complete suggested block diagram of the complete system is shown in Figure16.

## REFERENCES

- Abdulrahman FN (2003). "Physiological and chemical changes in blood picture of jaundice." J. Iraqi Med. 3: 346-355.
- Aroom KR, Harting MT, et al, (2009). "Bioimpedance Analysis: A Guide to Simple Design and Implementation." J. Surg. Res. 153(1): 23-30.
- Charles Davis L (2006). Noninvasive method of determining arterial wall tension and arterial segmentation by pulse transit time and pulse wave velocity. U. S. P. A. P. (10). USA. 2006/0247538 A1.

- Cole KS (1968). "Membranes, ions and impulses." (University of California Press.
- Adler A, Dai T (2006). "Blood Impedance Characterization from Pulsatile Measurements." IEEE CCECE/CCGEI.
- Fernando SM (2007). Electrical Bioimpedance Cerebral Monitoring: Fundamental Steps towards Clinical Application. Department of Signals and Systems. Göteborg, Chalmers University of Technology. PhD: p. 137.
- Frewer RA (1972). "The effect of frequency changes on the electrical conductance of moving-and stationary blood." Med. Bid. Eng. Comp. 10: 734-41.
- Fricke H (1925). "The electric capacity of suspensions with special reference to blood." J. Gen. Physiol. 9: 137-152.
- Fricke H, Morse S (1925). "The electric resistance and capacity of blood for frequencies between 800 and 4.5 million cycles." J. Gen. Physiol. 9: 153-167.
- Grimnes S, Martinsen OG (2000). Bioimpedance and bioelectricity basics, Academic Pres.; April 19.
- Fuller HD (1991). "The Electrical Impedance of Plasma: A Laboratory Simulation of the Effect of Changes in Chemistry." Ann. Biomed. Eng. 19: 123-129.
- Hill DW, Thompson FD (1975). "The effect of haematocrit on the resistivity of human blood at 37°C and 100 kHz." Medical and Biological Engineering.
- Hills P, Andrew et al., (1998). "Bioelectrical Impedance and Body Composition Assessment." Malaysian J. Nutr. 4: 107-112.
- Hoffer EC, Meador CK, et al., (1969). "Correlation of whole body impedance with total body water volume." J. Appl. Physiol. 27: 531.
- Ibrahim F, Abas WABW, et al., (2004). "Bioelectrical tissue conductivity in adult's dengue patients using bioelectrical impedance analysis." IFMBE, 7: 247-250.
- Jaffrin MY, Morel H (2008). "Body fluid volumes measurements by impedance: A review of bioimpedance spectroscopy (BIS) and bioimpedance analysis (BIA) methods." Med. Eng. Phys. 30(10): 1257-1269.
- Jenin PC, Schwan HP (1980). "Some observations on the dielectric properties of haemoglobin's suspending medium inside human erythrocytes." Biophys. J. 30: 285-94.
- Kichul CHA, Elaine Brown F, et al., (1994). "A new bioelectrical impedance method for measurement of the erythrocyte sedimentation rate." Physiol. Meas. 15: 499-508.
- Ludt H, Herrmann HD (1973). "In vim measurement of tissue impedance over a wide frequency range." Blophysik, 10: 337-45.
- Mager JR, Sibley SD, et al., (2008). "Multifrequency bioelectrical impedance analysis and bioimpedance spectroscopy for monitoring fluid and body cell mass changes after gastric bypass surgery." Clin. Nutr. 27(6): 832-841.
- Nyboer J, Kreider MM, et al., (1950). "Electrical Impedance Plethysmography: A Physical and Physiologic Approach to Peripheral Vascular Study." Am. Heart Assoc., Inc. 2: 8.821-11
- Nyboer J, Liedtke RJ, et al., (1983). Nontraumatic electrical detection of total body water and density in man. VIth ICEBI.
- Papezova S (2003). "Signal processing of bioimpedance equipment." Sensors and Actuators B: Chemical, 95(1-3): 328-33.5
- Schoeller DA, Kushner RF (1989). "Determination of Body Fluids by the Impedance Technique. March " IEEE Eng. Med. Biol. Mag. 8(1): 19-21.
- Sutton R, Ryden L, et al., (1999). The Foundation of Cardiac Pacing, PT, II: An Illustrating Practical Guide to Rate Variable Pacing. Armonk, New york, Futura Publishing company Ltd.
- Thomasett A (1962). "Bioelectrical properties of tissue impedance." Lyon Med. 207: 107-118.
- Treo EF, Carmelo J, Felice, et al., (2005). "Hematocrit Measurement by Dielectric Spectroscopy." IEEE Trans. Biomed. Eng.
- Ursula G Kylea, Ingvar Bosaeusb, et al., (2004). "Bioelectrical impedance analysis part I: review of principles and methods." Clin. Nutr. 23: 1226-1243.
- Weltman G, Ukkestad AFD (1972). "A Field-Theory Model of Blood-Pulse Measurement by Impedance Plethysmography." Ann. Biomed. Eng. 1: 69-86.
- Yamakoshi K, Tanaka S, et al., (1994). "Electrical admittance cuff for non-invasive and simultaneous measurement of haematocrit, arterial pressure and elasticity using volume-oscillometric method." Med. Biol. Eng. Comput. 32: 99-107.
- Zhao TX (1993). "Electrical impedance and haematocrit of human blood with various anticoagulants." Physiol. Meas. 14: 299-307.
- Zhao TX (1996). "New applications of electrical impedance of human blood." J. Med. Eng. Tech 20: 115-120.