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TITLE PAGE

UNIVERSITI TEKNOLOGI PETRONAS

Capacitive Air-Bubbles Detector for Extracorporeal Blood Circulation

By

Mawahib Gafare Abdalrahman Ahmed

A THESIS

SUBMITTED TO THE POSTGRADUATE STUDIES PROGRAMME

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DEGREE OF MASTER OF SCIENCE IN ELECTRICAL AND ELECTRONICS ENGINEERING

ELECTRICAL AND ELECTRONICS ENGINEERING

BANDAR SERI ISKANDAR,

PERAK

APRIL, 2009

DECLARATION

I hereby declare that the thesis is based on my original work except for quotations and citations which have been duly acknowledged. I also declare that it has not been previously or concurrently submitted for any other degree at UTP or other institutions.

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DEDICATION

To my mother's soul

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ABSTRACT

Extracorporeal blood circuits, or ECBC, have been used in hemodialysis, hemofiltration, plasmaphersis, and for assisted blood circulation during open-heart surgery for many years. ECBC devices consist of numerous individual parts which, dependent upon their operating characteristics, are potential generators of embolism or air bubbles in the blood. The purpose of this study is to construct a capacitive device capable of detecting these embolisms in an ECBC, and to investigate the relation between the size of air bubbles and change in capacitance and output voltage at various applied frequencies. Theoretical analysis of the system and simulation using Multisim2001 software were obtained and compared with experimental results. Results showed that the device was capable of detecting air bubbles with diameters 620 µm and over using Dextran70 and 730 µm using human blood. The capacitance of the capacitor was found to decrease as air bubble diameter increased whereas output voltage increased as air bubble diameter increased. The output voltage was found to increase when the frequency decreased, as theoretically predicted. The main finding was that air bubble, with diameters from 620 μm to 4.21 mm in Dextran70 solution and human blood, produced significant changes in the capacitance of the test cell device. In addition, experimental results were in good agreement with simulation and theoretical analysis. The sensitivity of the device for the Dextran70 was found to be 16.8 mV/nF obtained at 40 Hz and for human blood it was 16.4 mV/nF at 30 Hz.

ABSTRAK

Sejak beberapa tahun yang lalu, Extracorpal blood circuit atau dikenali sebagai ECBC telah digunakan dalam proses perubatan seperti hemodialisis, hemofiltration, dan plasmaphersis. ECBC turut membantu proses peredaran darah ketika pembedahan jantung terbuka yang sedang dijalankan. Alat ECBC ini terdiri daripada komponen - komponen yang berbeza bergantung kepada operasi yang dijalankan, di mana komponen tersebut berpotensi menghasilkan emboli atau gelembung udara dalam darah. Maka, tujuan utama kajian ini adalah untuk menghasilkan satu unit pengesan kewujudan emboli di dalam ECBC, pada masa yang sama untuk mengkaji hubungkait di antara saiz gelembung udara dengan perubahan kapasitan dan jumlah tenaga elektrik yang terhasil (voltan) pada beberapa frekuensi yang berbeza.. Bagi menunjukkan perbezaan untuk setiap keputusan dalam sistem dan analisis ini, satu perisian komputer dikenali sebagai Multisim2001 telah digunakan. Keputusan ke atas Dextran70 menunjukkan alat ini berupaya mengesan gelembung udara pada 620µm dan ke atas. Manakala dengan penggunaan sampel sebenar darah manusia ia mampu mengesan sehingga 730µm. Kapasitan bagi sesebuah kapasitor menurun apabila saiz gelembung udara meningkat manakala hasil jumlah tenaga elektrik (voltan) meningkat apabila saiz gelembung udara turut meningkat. Oleh itu jumlah tenaga elektrik yang terhasil akan meningkat sekiranya kadar frekuensi menurun seperti yang dinyatakan di dalam teori. Hasil kajian ini membuktikan emboli dengan saiz diameter dari 620µm sehingga 4.21mm di dalam larutan Dextran70 dan sampel darah manusia, telah menghasilkan perubahan dalam kapasitan bagi setiap sel alat yang diuji. Secara

keseluruhannya, keputusan eksperimen ini sejajar dengan simulasi yang telah dijalankan dan juga analisis teori. Kepekaan alat bagi Dextron70 dapat dilihat pada 40Hz dengan bacaan 16.8mV/nF manakala bagi sel darah manusia pada paras 30Hz dengan bacaan menunjukkan16.4mV/nF.

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ABBREVIATIONS AND SYMBOLS

ECBC	Extracorporeal Blood Circuit
HD	Hemodialysis
HF	Hemofiltration
ECMO	Extracorporeal Membrane Oxygenation
CPB	Cardiopulmonary Bypass
DCS	Decompression Sickness
HFAK	Hollow-Fiber Artificial Kidney
AVF	Arteriovenous Fistula
ARF	Acute Renal Failure
MES	Micro Embolic Signals
IR	Infrared
KVL	Kirchhoff's Voltage Law
C	Capacitance of the capacitor
$\varepsilon_{\circ}$	Permittivity of free space (8.85×10^{-12}F/m)
A	Area of the capacitor's plates
d	Distance between the two plates
ε_r	Relative dielectric constant of a material
R	Resistance of the resistor
NaCl	Sodium Chloride
AC	Alternating Current

X_C	Reactance of the capacitor
ω	Angular Frequency
f	Frequency
π	Mathematical constant (3.14)
V_C	The voltage across the capacitor
I	The current across the circuit
Z_{total}	Total resistance of RC circuit
V_{source}	The independent AC voltage from the source
V_{in}	Input voltage
V_R	The Potential Difference Across The Resistor
$-i$	The imaginary number
V_{Cpeak}	The magnitude of the peak potential difference across the capacitor
V_{rms}	Root Mean Squared Voltage
ρ	Density
σ	Conductance

Chapter 1

1. INTRODUCTION

1.1 Background

The rapid growth of biomedical engineering in the past few decades has led to the introduction of many medical electronic devices and procedures to meet patients' needs. They are used in diagnostic and therapeutic medicine (Webster, 1998: 4). One of the most important therapeutic procedures is the Extracorporeal Blood Circuit (ECBC), which is carried outside the body. It is a diversion of blood flow through a circuit located outside the body but continuous with the bodily circulation. Extracorporeal therapies are designed to remove various substances from the blood or add various substances to the blood circulation.

The ECBC is usually a procedure in which blood is taken from a patient's circulation to have a process applied to it before it is returned to the circulation (Venkataraman *et al*., 2003: 139). All the apparatus carrying the blood outside the body is termed the ECBC. Extracorporeal circuits have many types:

- Hemodialysis (HD)
- Hemofiltration (HF)
- Plasmaphersis

- Aphaeresis
- Extracorporeal Membrane Oxygenation (ECMO)
- Assisted blood circulation or heart-lung machine used during cardiopulmonary bypass (CPB) or open heart surgery

All of these machines generate air bubbles during blood purification outside the body. Almost every invasive procedure may cause the introduction of air bubbles into the blood stream. The more invasive the procedure, the greater is the risk of air bubble generation. There have been an increasing number of reports about air emboli in some procedures, such as cerebral angiography, left-heart catheterization, hemodialysis, and cardiopulmonary bypass (Guntupalli *et al*., 1990; karr *et al*., 1991; Markus, 1993; Woltmann *et al*., 2000; Bendszus *et al*., 2004).

Air bubbles usually originate in extracorporeal tubing, infusing with the fluids into the blood stream. The bubbles may be present while priming and preparing the lines for use; formed by the blood pump (Woltmann *et al*., 2000: 527); or newly formed as a result of turbulent flow in the tubing and at the vascular access. Differences in temperature are another possible reason for bubble generation in lines (Hartmannsgruber and Gravenstein, 1997). The movement of the bubble in an extracorporeal infusion set is affected by two principally opposing forces: firstly, the buoyant force of a bubble, which takes it upward in a standard drip chamber; and secondly, the driving force of the fluid flow, by which the bubble is carried into the patient's body.

The clinical outcome of air embolism depends on the size of the bubble; location of organ/tissue, general status and co-morbidity of the patient; plus many known and unknown factors (Muth and Shank, 2000). Large air embolism is fatal, both in the venous and arterial circulation. The natural course of a large venous embolism is migration into the pulmonary circulation and obstruction of the right ventricular outflow, acute increased resistance to the right ventricle and diminished left ventricular preload, followed by cardiovascular collapse (Petts and Presson, 1992; Muth and Shank, 2000). Air emboli in arterial vessels cause symptoms of end-artery obstruction and tissue ischemia and necrosis. Although arterial air emboli can reach any organ, occlusion of cerebral and cardiac circulation is particularly life-threatening because these systems are highly vulnerable to hypoxia and undergo irreversible cellular damage. The result of such an event may be a massive brain ischemia, clot, myocardial ischemia, infarction, and stroke. All could be dangerous and led to death. The detection of such catastrophic events and resuscitative measurements are well known (Orebaugh, 1992; Petts and Presson, 1992). Less is known about the effects of small air emboli in the venous or arterial circulation (Muth and Shank, 2000). A small quantity of micro bubbles may be clinically inert, while recurrent exposure to micro bubbles causes a slow, smoldering chronic effect that is difficult to detect but has important consequences. Attempts to prevent the threat of air embolism during extracorporeal blood machine usage have led to the design of numerous devices:

1. An Infrared light source with a photocell receptor was used as a tool capable of detecting the presence of macro air emboli i.e. 1 mL or larger (Vivian *et al*., 1980). However, false alarms might occur due to defibrillation of the patient, and from stray light which could reach the detector cell. These false alarms made the detector difficult to operate.

2. The use of ultrasound technology for detecting air bubbles was studied first on an animal model. Daniels *et al*. (1980) and Ringelstein *et al*. (1998) found that the continuous progress of technology improved equipment and facilitated better detection capabilities. Markus (1993) used a Transcranial Doppler Ultrasound making it possible to detect air bubbles in the cerebral circulation of patients during surgery. At the present time, extracorporeal blood machines are equipped with ultrasonic detectors of air larger than 850 µm (Barak and Katz, 2005:2923). However, it was reported that 850 µm could harm the patients and lead to death.

The main disadvantage of Doppler Ultrasound is the fact that bubbles are seen in the circulation without generating the alarm of the safety system (Jonsson *et al.*, 2007).

3. Another recent technique to detect air bubbles uses Tetra-polar Electrical Impedance Measurements (Nebuya *et al.*, 2004). Tested *in vitro*, this noninvasive device detected 0.5 mm diameter bubbles at a depth of 5.3 mm. However, this device is not sensitive enough to deal with air bubbles. Therefore, in medical procedures to detect air bubbles in extracorporeal blood circuit, the only current aid is still Doppler Ultrasound.

All these methods have serious drawbacks: some can only detect larger emboli i.e. 850 µm or 1 mL; others only exist theoretically or have only been used on animals; and some devices have difficulty operating because of the false alarms.

This study proposes a capacitor device with two parallel plates to investigate the effects of a single air bubble when it enters the capacitor stream. This device has good sensitivity, repeatability and low linearity error. According to Baxter (1997) the capacitance between two plates is determined by:

- Size of the plates because capacitance increases as the plate size increases.
- Distance between the plates because capacitance decreases as the distance between the plates increases.
- Material between the plates i.e. dielectric material, because this material will cause the capacitance to increase or decrease depending on the material itself.

In this study the size of the plates and the distance between them is fixed. However, the dialectic material is changed when the air bubbles are introduced between the capacitor plates.

1.2 Problem Statement

1.2.1 Problem Identification

In all cases involving extracorporeal circulation, negative pressure is generated in the venous line while blood is being siphoned from the patient. This negative pressure has the potential to extract dissolved gases from the blood, or pull atmospheric air into the circuit, creating air bubbles. Air bubbles are potentially fatal if they are to enter the patient's circulatory system.

Severe problems may appear if there are air bubbles existing in the returned patient's blood during any kind of extracorporeal blood circulation procedure. For example, the patient could suffer a bad cough, chest pains and nausea within the air embolism, or even worse, death when air bubbles enter the blood circulation.

The air bubbles could enter the blood line from various causes such as:

- Blood pump
- Fistula connection.
- Tube leakage.
- During the wash-out tube on the starting procedure.

At present, the extracorporeal machines use an ultrasonic detector to sense air bubbles. This system depends on the ultrasound energy trans-missive characteristic of fluids. The technology used is capable of determining only air bubbles of sizes greater than 850 µm in hemodialysis devices (Barak and Katz cited by The FDA Enforcement Report 2005).

During a cardiopulmonary bypass (CPB) a Transcranial Doppler Ultrasound is used to prevent the threat of air embolism but the main disadvantage of this detector is the fact that bubbles are seen in the circulation, but the consequences of this cannot be prevented (Ringelstein *et al*., 1998). However, it is reported that air bubbles less than 850 μm size can be dangerous to the patient. Thus the aim of the research is to improve air bubble detection and overcome this defect using capacitor technology.

1.2.2 Significance of the Study

The problem of air bubbles awaits a breakthrough technological solution that will provide their detection and elimination, facilitating better care for the patient. Consequently, a more accurate and discriminating method of detecting air bubbles is needed. Air bubbles with small diameters are hardly seen by the ultrasonic detector. However, their existence in the patient's blood could threaten the patient's life. This research is intended to find a reliable and cost-effective method to detect the presence of air bubbles. A highly sensitive detector for monitoring air bubbles with diameter less than 850 μm is required. Thus, the capacitive device is proposed in this study.

1.3 Objectives of the Study

The objectives of this study are:

1. To construct a capacitive device capable of detecting air bubbles in an extracorporeal blood circuit.
2. To investigate the relation between the size of air bubbles and the change in capacitance and the output voltage.
3. To investigate the effect of using different frequencies in the circuit on the output voltage from the device and compare it with the theoretical prediction and simulation.
4. To compare and benchmark this device with the device that is used in the extra-corporeal blood circuits.

1.4 Scope of Work

The aim of this research is to study an alternative method to detect air bubbles in the extracorporeal blood machines. To attain this, different issues must be investigated. To achieve the desired objectives of the proposed research study, the following scope of work was set:

As an essential part of this work, a capacitive device was constructed of two parallel plates of platinum encased within an acrylic material, to form a capacitor test cell into which Dextran70 fluid, selected to closely mimic blood rheology, and real human blood were separately introduced. The distance between the two platinum plates was nominally fixed and electric wires made of copper were attached to the plates. This was to measure the capacitance changes in the capacitor and the output voltage when Dextran70 solution and blood, both with or without air bubbles were introduced between the plates of the device.

The capacitor was placed with a resistor to form a series RC circuit. The prepared Dextran70 solution was introduced between the capacitor plates through inlet and outlet valves attached to both ends. The output voltage was then measured via the lead wires connected to the capacitor plates. Then an air bubble of an unknown diameter was introduced to the Dextran70 solution contained within the capacitor plates. Air bubbles with different diameters were used in order to investigate the changes in capacitance and the output voltage as a function of the bubble diameter. Then different frequencies were applied to the circuit.

Five different samples of real human blood were used separately as dielectric material in the capacitor. Then the capacitance and the output voltage were measured via the lead wires connected to the capacitor plates as an air bubble of an unknown diameter was introduced into the blood samples.

The second section of this work is a theoretical analysis of the circuit, to compare with the experimental measurements. In the third part of this work, Multisim2001 software is used to examine the output voltage change when there is a change in the capacitance of the capacitor device at different frequencies.

1.5 Research Contributions

The main contributions of this research are illustrated in the following points:

- The proposed device is really represents a reliable method to detect single air bubble diameter.

- The proposed device can detect air bubble with diameter 620 µm and greater, this indicate good sensitivity for this device compared with the ultrasonic device which could detect air bubble with diameter greater than 850 µm.

- The proposed device obtained better sensitivity at low frequency. For the dielectric material Dextran70, high sensitivity was obtained at 40 Hz i.e. 16.8 mV/nF. The frequency for all blood samples was 30 Hz, with one sample revealing similarly high sensitivity i.e. 16.4 mV/nF.

- The proposed device was able to detect foam and continue to operate, while others devices used to detect air bubbles failed to detect foam.

1.6 Organization of Thesis

This thesis is organized into five main chapters.

Chapter1

An introductory background which gives brief information about this research appeared in the first section of this chapter. The second section provides a discussion about the problem statement, objectives, and scope of the research.

Chapter 2

A literature review presenting the clinical effects of air bubbles in the blood stream. It mainly focuses on other detection methods and how the present method differs from what others have done.

Chapter 3

A research methodology is declaring the principle of operation, analysis of actual design, and proposing solutions for better results. It covers all the important materials and instruments that are used in this work.

Chapter 4

A results and discussion presenting the experimental measurements, theoretical analysis, and simulation results of the system.

Chapter 5

A conclusion and recommendation summarizing important findings and contributions and discussing possible future research trends.

Chapter 2

2. LITERATURE REVIEW

2.1 Introduction

The rapid advances in technology over the past few decades have brought new specialized devices to medical practice. One recent development is the detection of air bubbles in many medical procedures. Using different types of detectors, clinicians and researchers have found that the phenomenon of air bubbles is widespread. Air bubbles originate mainly in extracorporeal lines and devices such as cardiopulmonary bypass i.e. open heart surgery and hemodialysis machines i.e. artificial kidney. Air bubbles circulating in the blood stream, lodge in the capillary bed of various organs, causing local reactions. Barak and Katz (2005: 2918) note the use of artificial organs in clinical practice pose many problems, of which an important one is the presence of air bubbles in the Extracorporeal Blood Circulation (ECBC).

The purpose of this literature review is to study the effects of air bubbles in the blood stream and study the past and current detectors used in different extracorporeal blood circuits. Additionally it presents published data concerning the micro bubbles phenomenon and their detrimental consequences in different types of Extracorporeal Blood Circulation (ECBC).

2.2 Method of Extracorporeal Blood Circuit

Figure 2-1 illustrates an extracorporeal blood circuit. Blood is pumped from the patient, via access through the machine, and back to the patient. The arterial segment portion of the circuit from the patient to the machine and venous segment is the part from the machine back to the patient. The sites at which pressures in the blood circuit are measured are between the patient's access and the blood pump; at an arterial trap between the blood pump and the place where the processes are undertaken; and at the venous air trap located downstream of the machine. The air detector is located on the venous air trap with a clamp that is activated by the air detector, positioned just below the air trap.

Heparin for anticoagulation, is typically infused downstream of the blood pump. Keshaviah and Shaldon (1989: 277) stated that patient isolation from alarm conditions in the blood circuit is usually effected by stopping the blood pump and clamping the venous blood tubing.

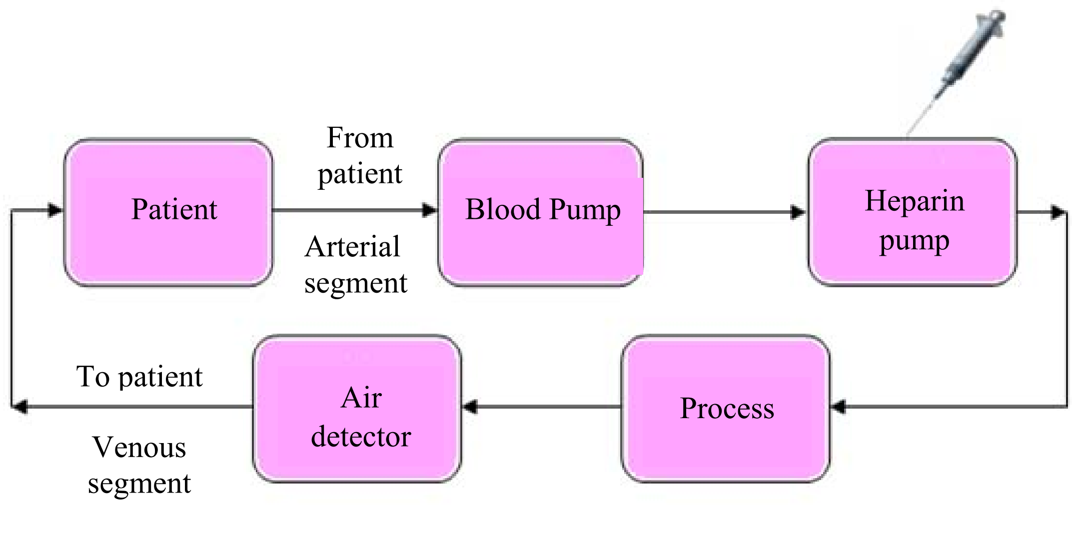


Figure 2-1 Block diagram of extracorporeal blood circuit

2.3 Air Embolism

Muth and Shank (2000: 476) defined an air embolism as an iatrogenic event in which air bubbles enter the circulation and can result in serious morbidity and even death. With the development of modern extracorporeal blood circuits, the incidence of life threatening air embolism has markedly diminished due to the use of air bubble detectors which can stop the blood pump when air is in the circuit. However, cases of air embolism are still reported (Yu and Levy, 1997: 453; Muth and Shank, 2000: 477).

According to Muth and Shank (2000: 477) air embolism can result from procedures performed in almost all clinical specialties as shown in Table 2-1, therefore it is important for all clinicians to be aware of this problem.

Table 2-1 Medical specialties with documented cases of air/ gas embolism

Specialty	**Mechanism of gas embolism**
All medical specialties	Inadvertent air through peripheral intravenous circuit
All surgical specialties	Intra-operative use of hydrogen peroxide, causing formation of arterial and venous oxygen emboli
Cardiac surgery	Entry of air into extracorporeal-bypass pump circuit, incomplete removal of air from heart after cardio-plegic arrest
Cardiology	Entry of air through intravascular catheter during angiographic study or procedure
Critical care	Entry of air through disconnected intravascular catheter.
Pulmonary	Pulmonary barotraumas, entry of air into extracorporeal membrane oxygenation circuit
Nephrology	Inadvertent entry of air through hemodialysis catheter and circuit on hemodialysis machine
Radiology	Injection of air or gas as a contrast agent; Inadvertent injection of air during angiography

Source: Muth and Shank (2000: 477)

Many studies have shown that rapid infusion of air bubbles may be fatal. Muth and Shank (2000: 481) concluded that the entry of air into the venous or arterial system is a risk in virtually all areas of clinical care. Venous emboli may lead to cardiovascular collapse or to paradoxical arterial emboli. Arterial emboli may occlude end arteries throughout the body and may cause serious diseases or death if they impede cardiac or cerebral vessels. Rapid aggressive treatment is essential to preserve life and bodily functions, irrespective of the mechanism responsible for the embolism.

Table 2-2 below shows the treatment of venous and arterial air embolism. For venous air embolism, the mainstays of treatment were the prevention of further air entry; volume expansion; and the administration of 100 percent oxygen, often with ventilator support. For arterial air embolism, hyperbaric oxygen is the preferential treatment immediately after cardiopulmonary stabilization has been achieved (Muth and Shank, 2000: 481).

Table 2-2 Treatment of air embolism

Type of treatment	Venous air embolism	Arterial air embolism
Prevention of entry of gas or air	Measures to increase venous pressure.	Identification and shutting down of entryway of gas
Primary therapy	Supportive	Hyperbaric oxygen therapy
Supportive therapy	Oxygen, intravascular volume expansion, catecholamine	Oxygen, intravascular volume expansion, catecholamine
Positioning of the patient	Supine, flat	Supine, flat
Evacuation of gas embolism	Aspiration with multi-luminal central venous catheter	Hyperbaric oxygen
Adjunctive therapy	Hyperbaric oxygen	Lidocaine, physical therapy

Source: Muth and Shank (2000: 481)

Gee and Gould (2003:1130) define an air embolism as the entry of air into the vasculature, and it can occur during the insertion or removal of central venous catheters. For air to enter the venous circulation there must be a direct communication between the atmosphere; a healthy vein and a pressure gradient favoring the passage of air into the circulation.

2.4 Air Bubbles during Extracorporeal Blood Circulations

Richardson (1985:55) maintains extracorporeal blood circuits are ‘a beneficial achievement in the field of artificial replacement therapy for patients who have failure in their organs’. However, this procedure also bears risks such as pulmonary disease when air bubbles enter the patient’s body.

Barak and Katz (2005: 2922) claim almost every invasive procedure may cause the introduction of air bubbles into the blood stream. The more invasive and interventional the procedure, the greater is the risk of air bubble generation. There have been an increasing number of reports about air emboli in certain procedures, e.g. cerebral angiography and left-heart catheterization. Although most air embolic events are inert, some are symptomatic and the phenomenon must be addressed. The authors concentrated on procedures in which the bubble load was high and affected critical organs, including the brain and the lungs. Air bubbles originate mainly in extracorporeal lines and devices, such as cardiopulmonary bypass, hemodialysis, and high- flow lines, but may be endogenous in cases of mechanical heart valves or decompression sickness (DCS).

As mentioned earlier, all apparatus carrying the blood outside the body is termed the extracorporeal circuit (Venkataraman *et al*., 2003:139). ECBC is used in many medical procedures such as:

- Hemodialysis (HD)
- Hemofiltration (HF)

- Plasmaphersis
- Aphaeresis
- Extracorporeal Membrane Oxygenation (ECMO)
- In heart lung machine (cardiopulmonary bypass (CPB)).

In all of these procedures air bubbles originated and lodged in the capillary bed of various organs after entering the blood stream, mainly in the lungs, thus causing tissue ischemia leading to death (Kaps *et al*., 1997; Taylor, 1998; Droste *et al*.,2002; Droste *et al*.,2003; Eaton and Dhillon, 2003).

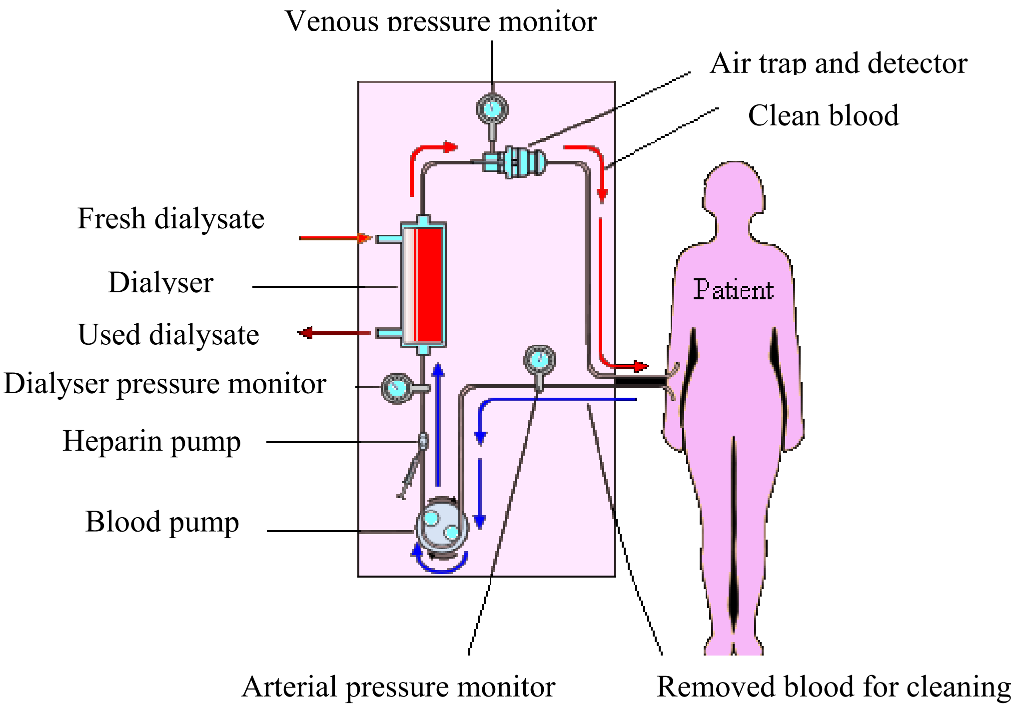
2.4.1 Hemodialysis and Hemofiltration

2.4.1.1 Definition of Hemodialysis

Hemodialysis (HD) is defined as a method for removing waste products such as potassium and urea, as well as free water from the blood when the kidneys are in renal failure (Stephen, 1981:487; Keshaviah and Shaldon, 1989:276). The principle of HD is the same as other methods of dialysis e.g. peritoneal dialysis, Hemofiltration. It involves diffusion of solutes across a semi-permeable membrane. HD utilizes counter current flow, where the dialysate is flowing in the opposite direction to blood flow in the extracorporeal circuit as shown in Figure 2-2 on page 16. In hemodialysis circuits, pulling large volumes of water across the semi-permeable membrane creates a convective current that "drags" additional solutes. While diffusion is effective at removing most small molecules, convection enhances the removal of small and mid-sized molecules. Thus, convection can be added to hemodialysis therapy to enhance solute removal.

Rolle *et al*. (2000: 1420) state that many procedures produce air bubbles during HD such as:

- Leaking in the tubes
- The blood pump
- Fistula connection
- Heparin infusion system
- During the wash-out tube on the starting procedure.



Source: Keshaviah and Shaldon 1989: 278

Figure 2-2 Adapted schematic diagram of hemodialysis circuit

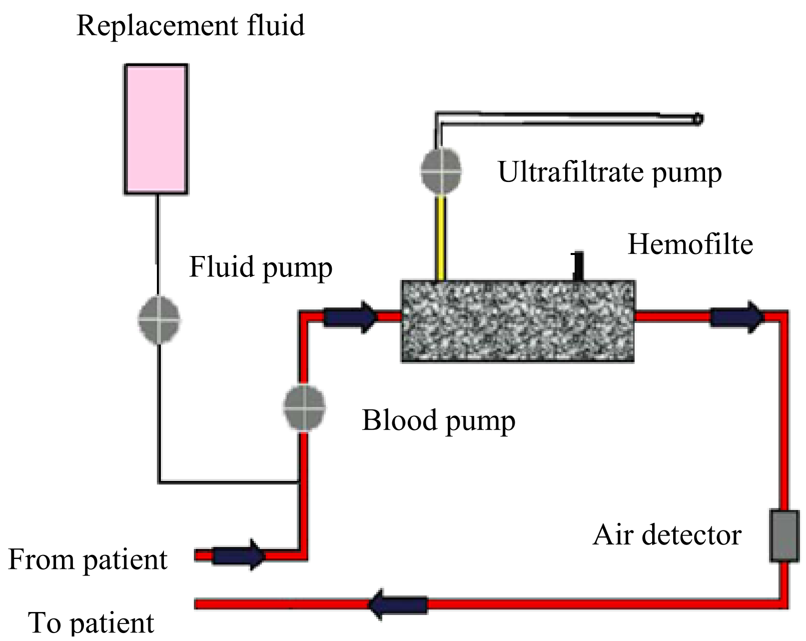
An end-stage renal failure patient will undergo about three sessions of hemodialysis weekly i.e. 150 sessions annually. A session takes a few hours, exposing a patient to a micro bubble shower. Barak and Katz (2005:2923) maintain micro bubbles are trapped in the pulmonary circulation from the dialysis tubes or filter flow in a venous vasculature. As a result, a micro bubble shower may cause both acute and chronic injury in a HD patient. With respect to the acute effect, hypoxemia, a well-known symptom during hemodialysis, is the principle clinical indication for respiratory insult.

2.4.1.2 Definition of Hemofiltration

Rabindranath *et al.* (2006:2) defined Hemofiltration (HF) or haemofiltration as a renal replacement therapy similar to hemodialysis, which is used almost exclusively in the intensive care setting. Thus, it is almost always used for acute renal failure or ARF (Garcia *et al*., 2008: 116). It is a slow continuous therapy in which sessions usually last between 12 to 24 hours and are usually performed daily.

Figure 2-3 on page 18 illustrates the schematic diagram of a hemofiltration circuit. During hemofiltration, a patient’s blood is passed through a filtration circuit i.e. a set of tubing via a machine to a semi-permeable membrane or hemofilter, where waste products and water are removed. Replacement fluid is added and the blood is returned to the patient (Dirkes and Hodge, 2007: 63).

To prevent loss of water in the patient’s body, any water removed during hemofiltration must be returned to the blood before it reaches the patient. This is called "replacement" fluid. Hemofiltration rates of 1 L/hr mean that one liter of fluid is removed from the patient's blood and eliminated in the drainage fluid and 1 L of replacement fluid is returned to the circuit before it reaches the patient. Hemofiltration rates are set by adjusting replacement rates. Any fluid removed during hemofiltration is returned to maintain a net neutral fluid balance. Replacement fluid must be sterile intravenous fluids with concentrations of electrolytes similar to plasma (Reiter *et al*., 2002).



Source: Drikes and Hodge 2007: 63

Figure 2-3 Adapted schematic diagram of hemofiltration circuit

2.4.1.3 Air Embolism during Hemodialysis and Hemofiltration

There was evidence of pulmonary micro embolization during HD as far back as 1975 (Bischel *et al.*, 1975: 335). The subject of dialysis induced-air bubbles has been revisited, mainly as a consequence of better detection technology, raising major concerns as to whether their presence can be overlooked or if practical means of emboli elimination must be developed. In their study they postulated that a dialyzer of different design such as the hollow-fiber artificial kidney (HFAK) might also be a significant source of air embolism.

A prospective study of 25 patients by Rolle *et al*. (2000: 1423) showed micro emboli in the sub-clavian vein, downstream from the Arteriovenous fistula (AVF). The authors concluded that gas micro emboli were formed by the blood pump of the HD machine.

Several theories have attempted to explain this event, such as hypoventilation due to changes of pH; the direct effect of acetate on the central respiratory center, and increased alveolar-arterial oxygen gradient due to complement activation during HD (Yigla *et al*., 2003; Amin *et al*., 2003). It has been established that 30% of hemodialysis, but not peritoneal dialysis, patients had pulmonary hypertension that normalized when kidney transplantation was performed.

Droste *et al*. (2002:462) used pulsed-Doppler ultrasound to demonstrate a continuous shower of micro emboli introduced into the pulmonary vasculature during HD and hypothesized that this may explain the high pulmonary morbidity in long-term dialysis patients. Those micro emboli are most probably gaseous, as suggested by the ultrasound high relative intensity signal. The origin of these micro bubbles may be air bubbles already in the HD tubes and filter before the procedure; entering the blood stream during connection and disconnection of the lines, or formation of gas bubbles as the result of pressure gradients and turbulent flow in the tubes and access.

They performed a study on 21 patients undergoing hemodialysis and 5 patients were treated by hemofiltration using different devices by Gambro Medizin-technik (Munchen, Germany), Fresenius Medical Care (Bad Homburg, Germany), and B. Braun Melsungen AG (Melsungen,Germany). They demonstrated that both HD and HF are associated with a large number of micro emboli. Hemofiltration is associated with a large number of air emboli, which may be reached through the cerebral circulation.

A follow-up study by Droste *et al*. (2003: 2377), found significant reductions of micro embolization when pre-filled instead of dry dialyzers were used. This may prevent repeated damage to the pulmonary vasculature and, thus, cause less pulmonary damage. However, this study gave insufficient evidence to the use of pre-filled dialyzers, because these are considerably more expensive than dry dialyzers.

The use of dialysis equipment has not been without controversy. A US Food and Drug Administration report, cited in Barak and Katz (2005:2923) reported two cases of dialysis equipment recall. In the first one in 1992, approximately 4,000 devices were rejected due to failure of the ultrasonic bubble system in air observed in the venous line reaching the patients. In the second, approximately 3,000 hemodialysis devices were recalled as air bubbles were detected in the extracorporeal system. Both cases highlight problems with the current ultrasonic bubble detectors, which expect to find relatively large bubbles but permit the entry of small significant micro bubbles.

It would seem that the consequences of micro bubbles could be more serious in cases of cardiac or extra cardiac right to- left shunt. Yu and Levy (1997:493) reported an intra-cardiac shunt patient having air embolism enter her cerebral circulation during hemodialysis, causing various cellar damages. Barak and Katz (2005:2924) conclude “it is reasonable to believe that a patient with a right-to-left shunt is at higher risk or morbidity as a result of venous air embolism during hemodialysis.” They add, however, that this problem is dependent upon the duration of the dialysis treatment and note that cerebral damage due to micro bubbles has still not been investigated.

Barak and Katz (2005:2923) note that hemodialysis devices today have ultrasonic detectors of air larger than 850 μm and alarms trigger the occurrence of an extremely large air bubble event. However, the alarms are not activated by smaller emboli, even in large numbers.

A recent study performed with hemodialysis machines by Jonsson *et al.* (2007: 139) and Stegmayr *et al*. (2007:166) concluded that air bubbles transported through the air trap and clot filter into the venous tubing line failed to generate the alarm of the safety system. Their study, an in-vivo system, showed that air bubbles will pass to the lungs where they are probably trapped and act as micro emboli before they are adsorbed.

2.4.1.4 Mechanisms of Air Embolism Incidence during Hemodialysis and Hemofiltration

According to Ward *et al.* (1971:77) there are three possible areas of air entry:

1. Between the patient and the blood pump, where a high negative pressure up to 250 mmHg routinely develops, making it possible for air to get sucked into the circuit. Air embolism may result from leaks in connectors or a crack in the Silastic tubing of the blood pump.

2. From air in the dialysate fluid diffusing across the dialysis membrane into the blood and forming bubbles in the venous air trap. However, no major episodes of air embolism have yet resulted from this mechanism.

3. From central venous catheters, this is a more important source of air entry today. They are frequently used for hemodialysis vascular access. Air embolization has been reported during catheter insertion or removal and also when a catheter gets disconnected from the line (Yu and Levy, 1997; Vesely, 2001).

2.4.1.5 Monitoring of Air Bubble Leakage during Hemodialysis and Hemofiltration

The performance of HD/HF without a blood pump means that the entire blood circuit is under positive pressure and therefore, embolism during air entry into the blood circuit is highly unlikely. However, the risk of air embolism has increased enormously as negative pressure develops between the arterial fistula needle and the blood pump, with the predominant use of the A-V fistula pump circuit today (Keshaviah and Shaldon, 1989:282). Multi-organ dysfunction can occur as a consequence of air entering into the blood circulation.

Ward *et al*. (1971: 74) observed air entering the blood circuit through an infusion bottle; a heparin syringe or line, or the insertion of a blood pump. They report five annual deaths in Britain alone regarding air bubble infusion into the blood circuit during hemodialysis. They also report seven cases of air embolism occurring during hemodialysis, two fatal and five non-fatal, as shown in Table 2-3.

Ward *et al*. (1971: 78) conclude that when hemodialysis is performed with blood pressure as the only driving force the whole blood circuit is pressurized and opportunities for air embolism are few. However, arteriovenous shunts were sometimes incapable of providing an adequate flow through modern dialyzers unless assisted by a pump. Moreover, a blood pump is essential with the arteriovenous fistula which is gradually replacing the shunt as the standard route of access to the circulation. Consequently most patients today are using blood pumps and all the accidents they described occurred in pumped circuits.

The first known cases of ultrasound findings of micro embolic signals (MES) in a dialysis access graft during dialysis were reported by Woltmann *et al*. (2000). They studied two hemodialysis patients, one with a synthetic graft and one with Arteriovenous fistula; showing MES during a dialysis session which was detected by duplex ultrasound. They postulated that these MES resulted from turbulent blood flow around the venous dialysis circuit or micro emboli arising from thrombus.

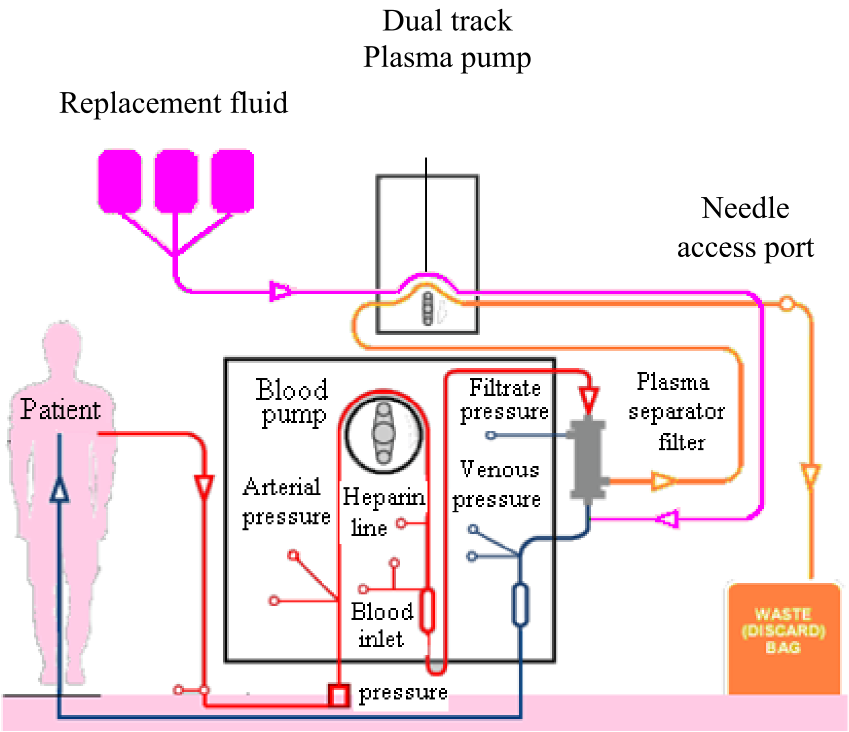
Table 2-3 Cases of air embolism occurring during Hemodialysis

No.	Patient	Treatment details	complications
1	Female, 48 years	Regular hemodialysis infusion of amino-acids into arterial line	Left unattended, patient’s venous line of blood circuit filled with air, leading to cardiac arrest. Nurse failed to reapply the clamp to the drip tubing, or applied it to the wrong tube.
2	Female, 40 years	18 months’ regular home treatment	Saline inserted into arterial line. Left unattended, patient found dead with dialyzer and venous line full of air. The clamp was accidentally applied to the arterial line and air pumped in place of blood.
3	Male, 44 years	2 weeks’ hemodialysis for renal failure	Developed headache, chest pain and respiratory problem. Fragmented air column in the venous line suggested air embolism. Movement of head resulted in expressive dysphasia, loss of vision. Recovered after 36 hours, but has amnesia for post-embolism event.
4	Male, 39 years	8 months’ regular hemodialysis for renal failure	Collapsed 15 minutes after the start of a dialysis, due to insertion of air from heparin infusion syringe. death 4 weeks later due to cardiac failure.
5	Male, 45 years	10 months’ regular hemodialysis	Air discovered in venous and arterial lines due to air leak from loose connection to heparin syringe. Administered 100% oxygen by face mask; semi-conscious for 2 hours. Hemodialysis performed 2 hours later without incidence; remained well on regular hemodialysis
6	Male, 55 years	30 months’ regular home dialysis	Patient saw air bubbles moving down his venous line 9 hours after overnight dialysis. Lost 500 mL of blood. Air bubbles due to crack in plastic tubing of blood pump.
7	Male, 41 years	3 years regular dialysis	Chest pain and respiratory difficulty due to air in arterial circuit which had entered through a ruptured connection line between heparin syringe and arterial line. Small volume of air therefore rapid recovery.

Source: Adapted from Ward *et al.* 1971: 74- 77

2.4.2 Plasmapheresis and Aphaeresis

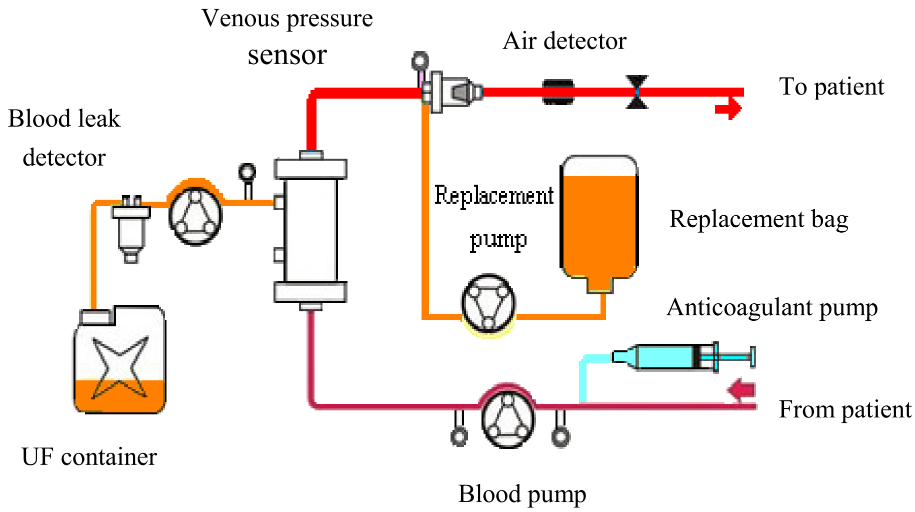
The term Plasmapheresis “from the Greek *plasma* meaning something molded and *aphaeresis* meaning taking away”, is used to describe the removal, treatment, and return of components of blood plasma from the blood circulation. Plasmapheresis is an extracorporeal therapy which can be used to collect plasma for further manufacture into a variety of medications (Kumar *et al*., 1995). During plasmapheresis, blood is removed from the body using a needle or previously implanted catheter. A cell separator removes plasma from the blood (Garica *et al*., 2008: 127). Figure 2-4 illustrates a schematic diagram of plasmapheresis circuit.



Source: www.smilegroup.com

Figure 2-4 Adapted schematic diagram of plasmapheresis circuit

As mentioned previously the term Aphaeresis from the Greek means "to take away". It is medical technology in which a donor or patient's blood passes through an apparatus to separate one particular constituent and return the remainder to the circulation. Like plasmapheresis it is also an extracorporeal therapy (Giuliano, 2000: 753). Figure 2-5 illustrates a schematic diagram of the aphaeresis circuit.



Source: www.csmc.edu

Figure 2-5 Adapted schematic diagram of aphaeresis circuit

Boer and Hene (1999:1851) reported a case of a 36-year-old man on plasmapheresis. During this procedure the patient suffered a fatal air embolism after removal of a double lumen jugular vein catheter. In their study they discussed the measures and ways to prevent air embolism during plasmapheresis after removal of central venous catheters. Their preventive measures include:

- Avoidance of heparin administration on day of removal.
- Patient placed in head-down position and instructed to hold breath during the removal.

- Gauze covering applied to exit site with inert ointment while catheter removed, providing instantaneous air seal.
- Air occlusive dressing applied whilst patient in head-down position.
- Patient observed for 30 minutes to check for bleeding.
- Air-occlusive dressing left in place for 24 hours.

2.4.3 Cardiopulmonary Bypass and Extracorporeal Membrane Oxygenation

Gravlee *et al*. (2007) write that cardiopulmonary bypass or CPB is an extracorporeal circulation technique that temporarily takes over the function of the heart and lungs during surgery, maintaining the blood circulation and the oxygen content of the body. The CPB pump itself is often referred to as a heart-lung machine or pump. Cardiopulmonary bypass pumps are operated by allied health professionals known as perfusionists in association with surgeons who connect the pump to the patient's body. Cerebral or coronary air embolism is one of the serious postoperative complications of open-heart surgery (Mendes, 2008:7).

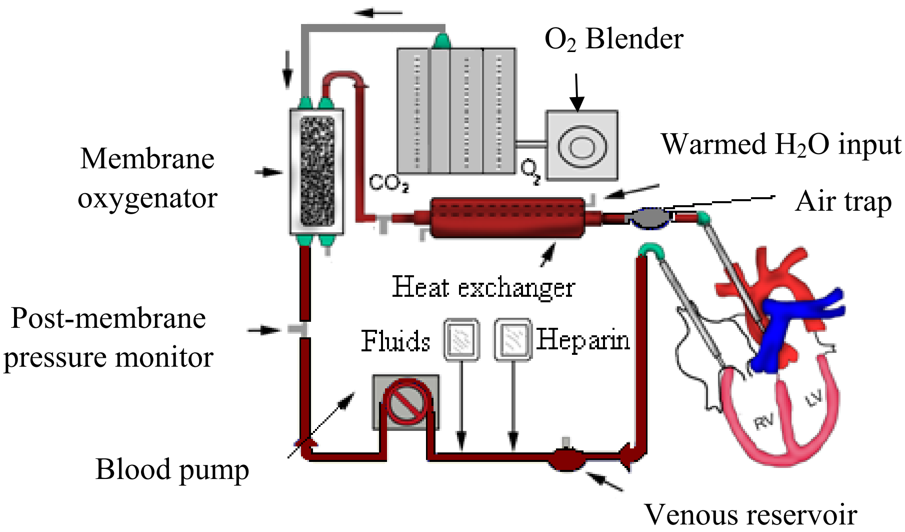
Extracorporeal Membrane Oxygenation or ECMO is another extracorporeal technique of providing both cardiac and respiratory support oxygen when patients' heart**s** and lungs are so severely diseased or damaged that they are unable to serve their function (Lewandowski, 2000: 156; Barnacle *et al*., 2006; Sachweh *et al.* 2007: 404).

ECMO apparatus consists of:

- A blood pump with raceway tubing, either a simple roller pump or constrained vortexes centrifugal pump
- A venous reservoir, used with the roller pump for neonatal ECMO

- A membrane oxygenator to transfer both oxygen and carbon dioxide, which is central to successful performance of prolonged ECMO
- A countercurrent heat exchanger to warm the blood. Blood is exposed to warm water that circulates within metal tubing (Rodriguez-Cruz *et al.*, 2006).

Figure 2-6 shows a schematic diagram of Extracorporeal Membrane Oxygenation.



Source: Rodriguez-Cruz *et al.* 2006

Figure 2-6 Adapted schematic diagram of ECMO circuit

Shang and Rosen (1968: 194) state that there is a danger of embolism from air trapped in the heart during any open-heart operation and extracorporeal membrane oxygenation. One way of reducing this is to displace the air in the wound by carbon dioxide. Replacing this air with an equal quantity of carbon dioxide diminishes the serious effects that follow air trapped in the arterial system. The authors conclude that the carbon dioxide probably needs to flow immediately before the risk of air embolization is present i.e. at closure of the incision.

Embolism from air retained within the open heart has been recognized as a potential hazard in direct vision intra-cardiac surgery (Zhou *et al*., 1984:56). M-mode echocardiography is defined as a device to detect air embolism and remove intra-cardiac air. Zhou *et al*. (1984:60) conducted experiments on 8 dogs and performed echocardiography on 19 patients undergoing open heart surgery. The standard M-mode echocardiogram was obtained in the experiment on an isolated dog's heart and Intra-cardiac air was recognized by the presence of linear echoes and a loss of echo free area. When 1.0 ml of air was injected intra-cardially, sensitivity and specificity were 93.2% and 95.0% respectively, and decreased to 85.7% and 80.6% when 0.25 ml was injected.

Jones *et al.* (2002) performed an experiment using an *in vitro* model of adult cardiopulmonary bypass to evaluate how effective CPB circuits are at removing gaseous micro emboli. They found that the introduction of 60 mL of air into the venous line always resulted in the detection of air bubbles in the arterial line. In 2003 a study of heart bypass operations, Schoenburg *et al*. reported that macro and micro emboli have both been implicated as a cause of cerebral damage. They added air emboli can be removed with a dynamic bubble trap.

Barak and Katz (2005:2922) state that cardiopulmonary bypass machines are used in most open-heart surgeries to oxygenate and pump the blood while the heart is arrested. The incidence of cerebral complications after cardiac surgery is dependent on age, sex, type of procedure, atherosclerotic disease of the aorta, among other factors (Hogue *et al*., 1999: 647; Hogue *et al*., 2001: 2137).

Massive arterial air embolism accompanying cardiopulmonary bypass is a very rare complication but it can result in serious brain damage or even death. Avishai *et al*. (1999) write that the key to controlling air embolism lies in prevention. They add that guidelines for managing gross air embolism should be established and each open heart team should be prepared if suddenly faced with this problem.

Arterial air embolism during cardiopulmonary bypass can result in serious brain damage or fatality, although the incidence is estimated to be 0.1% (Shahar *et al*., 1993; Huber *et al.,* 2000: 932). The authors mention that 3,500 operations with cardiopulmonary bypass are performed annually, so 3 patients with air embolism may be expected. Despite improvements in equipment and technology, these accidents still occur.

Cerebral emboli occur in children undergoing open heart surgery and cardiopulmonary bypass. These emboli are assumed to be composed of air, thrombi, or platelet aggregates. There are diverse sources of the embolic load during CPB, but they mainly relate to specific surgical maneuvers and to the components of the extracorporeal circuit. Cerebral embolization has been postulated as a potential cause of neurologic injury in adults, however the clinical significance of this phenomenon in children is currently unknown (Stump, 2005).

Rodriguez and Belway (2006: 247) performed a study to compare two different extracorporeal circuits on cerebral embolization during cardiopulmonary bypass in children. They concluded that cerebral emboli during CPB in children can be increased by variations in the design characteristics of extracorporeal circuits. The capacity of extracorporeal circuits to handle air emboli during CPB is assumed to depend on several factors e.g. the internal characteristics of both the oxygenator and venous reservoir, but others factors relate to the amount of emboli delivered into the circuit.

2.5 Infusion of Air in Extracorporeal Blood Circulation

Extracorporeal treatment of blood, such as hemodialysis, involves the risk of air or gas infusion. Injection of air bubbles into human blood vessels may be harmful, dangerous and even fatal (Ozeri *et al*., 2006). For this reason the extracorporeal system has to have tight connections. All pieces in the extracorporeal system are connected using standardized couplings to a closed system and the priming procedure is carefully clarified by the manufacturers to avoid air contamination of the blood. To reduce this risk, it is common to have a de-airing chamber in the blood line on the venous side or venous chamber prior to the infusion site of processed blood. Larger air bubbles are supposed to rise out of the blood in that chamber, therefore enabling evacuation of air. Similarly air detectors are used on the return line to prevent air infusion to the patient (Jonsson, 2006).

Teichgraber and Benter (2004) report a case of a 17-year-old girl female victim accident. In the ambulance, a central venous catheter was inserted and she was admitted to the emergency department with multiple injuries. The initial computed chest tomography scan showed both a lung contusion and air in the right ventricle and the patient died from her severe injuries three days after the accident. This example highlights how air embolism is a rare but potentially fatal complication of procedures involving central venous catheters. Air can enter the central venous system during puncture or through an opening in the intravenous infusion tubing during disconnection. It is possible for approximately 100 ml of air per second to pass through a 14-gauge needle.

2.6 The Clinical Consequences of Micro Bubbles Circulating during Extracorporeal Blood Circuits

The clinical outcome of air embolism depends on the size of the bubble, location i.e. organ or tissue, general status, co-morbidity of the patient, plus many known and unknown factors (Sanfeld *et al*. cited by Barak and Katz, 2005: 2921).

Large air embolism usually has serious consequences, for both venous and arterial circulation. A large venous embolism passes into the pulmonary circulation, obstructs the right ventricular outflow, increases resistance to the right ventricle, diminishes left ventricular preload, and is followed by cardiovascular collapse. In arterial vessels air emboli cause symptoms of end- artery obstruction, tissue ischemia and necrosis.

Although arterial air emboli can reach any organ, the result can cause a massive brain ischemia and stroke or myocardial ischemia, memory loss, infarction and other undesirable effects. The detection of such disastrous events and resuscitative measurements are well known, although the results of small air emboli in the venous or arterial circulation are less well known. A small quantity of micro bubbles may be clinically silent, but cause a slowly chronic effect that is difficult to detect but has equally serious consequences. The patient's co-morbidity may also influence the outcome of circulating air emboli. When there is a right-to-left shunt, venous air emboli may pass to the arterial circulation and cause organ ischemia (Barak and Katz, 2005: 2921).

The passage of air emboli from the venous to the arterial circulation can also occur when the volume of air is vast. The pulmonary circulation filtration capability has been studied by Butler and Hills (1985) in animal models. They found that when the volume of venous air emboli was smaller than 0.35 mL kg^{-1}, the filtration threshold was exceeded leading to an arterial spillover of bubbles in 50% of the animals. This increased to 71% for an air dose 0.40 mL kg^{-1}. Although this study was not conducted on humans, it drew attention to the possibility of each venous air embolism turning into an arterial one, depending on air volume and injection time. Air bubbles in the blood stream cause stroke, memory loss and other undesirable effects in the patient. Scientific evidence from humans is limited; nevertheless, it supports most of the laboratory findings (Kapoor and Gutierrez, 2003).

2.7 Air Bubble Detectors in Extracorporeal Blood Circulations

Several different physical principles have been employed in air bubble detection:

2.7.1 Infrared Light Source and Photocell Receptor

Infrared (IR) detectors are used to convert infrared energy into electrical signals (Khandpur, 2005). The earliest IR based air detectors consisted of a light source triggering a photocell situated on the opposite side of the bubble trap. The photo cell did not react if blood obstructed the light path (Keshaviah and Shaldon, 1989: 282). Figure 2-7 (a) illustrates infrared air bubble detector in a cardiopulmonary bypass (CPB).

Figure 2-7 (b) illustrates the air bubble detector mechanism using infrared light and photocell receptor. The blood pass in the tube without air bubbles in its stream, then the transmitted infrared light from the source will be reduced and no signal could reach the receiver. When an air bubble passed through the sensor unit the transmitted infrared light could reach the detector cell and trigger the alarm. The Infrared based air bubble detector can detect the presence of macroscopic air emboli i.e. 1 mL or larger (Vivian *et al*., 1980: 426).

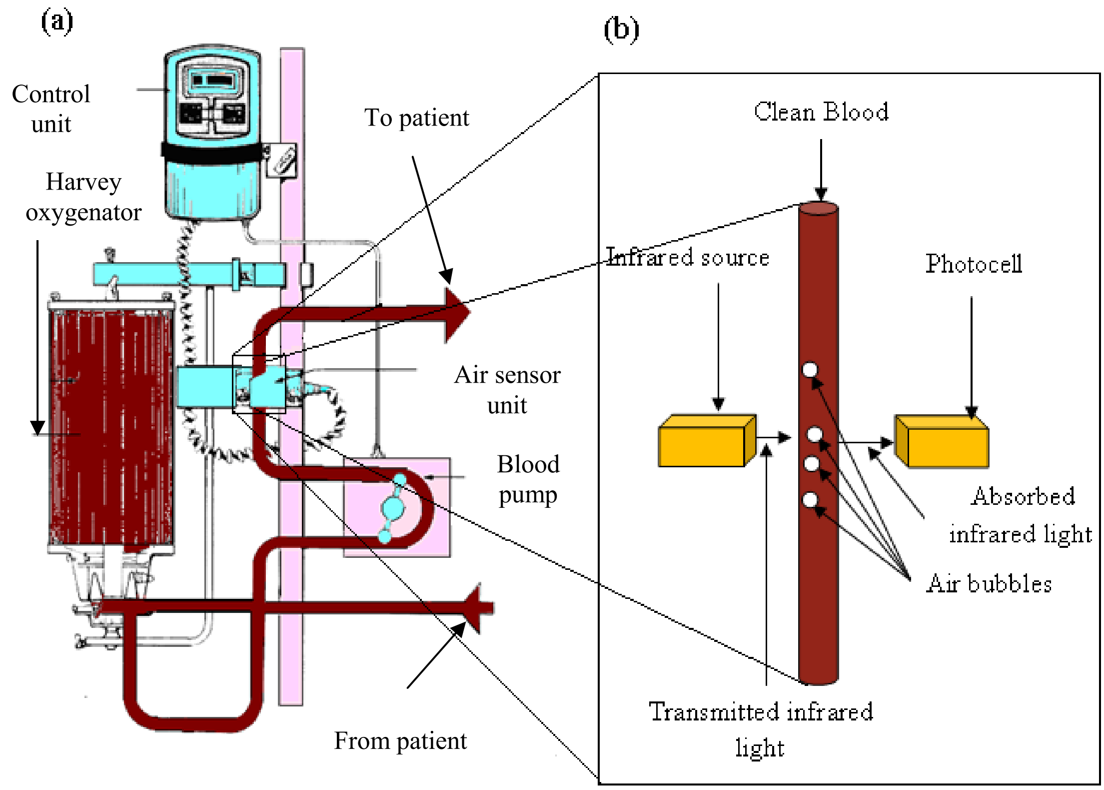


Figure 2-7 (a) Infrared photocell air-bubble detector system adapted in a cardiopulmonary bypass **(b)** Enlarged image of the system showing the Infrared light source and the photocell receptor system

2.7.1.1 Disadvantages of Infrared Light Source and Photocell Receptor

- False alarms triggered the pump shutoff e.g. ambient light reaching the photocell. Although infrared light and photocell device have increased sensitivity to air, they still cannot prevent obstruction to the passage of infrared waves. Additionally they are not sensitive enough to detect foam i.e. multiple, extremely small emboli, without causing multiple false alarms.

- Device would not react if the light path was obstructed by fibrin deposits on the inner wall of the bubble trap (Keshaviah and Shaldon, 1989: 282)

- Defibrillation of the patient which made the detector problematic to operate

- The absence of an alarm and/or the non-operating of an electrical failure light (Vivian *et al*., 1980: 428)

2.7.2 Ultrasonic Devices

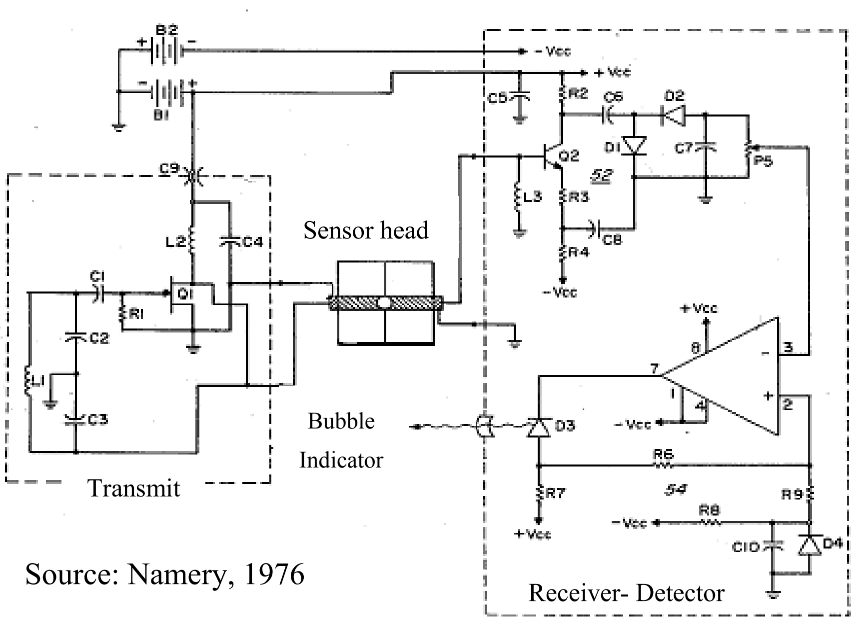
A number of attempts have been made to detect air bubbles during ECBC based on ultrasound and Doppler ultrasound. This section is a chronological review of various ultrasound devices.

Manley (1969) performed an experiment to detect small and large air bubbles in blood using the ultrasound method. A special chamber was designed in the extracorporeal circulation, so that good acoustic coupling was maintained with blood, and there was little interference to the general purpose of the extracorporeal system. The ultrasonic transducers were set outside the chamber, with links to the inside of the chamber. Manley concluded that bubbles were most noticeable when the ultrasonic signal was at 1st or 3rd harmonic of receiver crystal i.e. at 43 and 130 kHz.

Massie and Cosentino (1974) used a device for detecting the presence of air bubbles within a fluid-carrying tube. The tube was placed between a light source and an optical sensor which produced signals when bubbles passed through the tube. These signals were integrated and a switch changed state when the integration reached a predetermined value. The detector thus responded to a predetermined quantity of air, either a large air bubble or an accumulation of small air bubbles. In a later modification, the switch released a spring-loaded clamp which squeezed the tube when an excessive amount of air was detected.

Namery (1976) designed a new ultrasonic detector as shown in Figure 2-8 below. The transmission of sound from the transmitter, via the sensor head, to the detector's receiver was dependent upon the existence of a fluid within the tubing. Optimization of acoustic losses, operating frequency, and the distance between transmitter and receiver permitted constructive interference of energy transmitted to and reflected from the receiver. This resulted in a partial standing wave as in a resonant cavity. When an air bubble passed through the sensor head, a large acoustic discontinuity occurred, causing ultrasound to scatter and reflect from its normal path. These losses allowed a little ultrasonic energy to couple to the receiver. There were at least 30 to 1 reductions in signal when a small bubble i.e. 1 mm in diameter was present in the fluid-filled tube.

Daniels *et al*. (1980) provided an example of the use of ultrasound technology for detecting air bubbles on an animal model. They concluded that the pulse-echo ultrasonic imaging technique, after decompression, provides a powerful means of analyzing the distributions of bubble formation, both qualitatively and quantitatively. Their model had the important attribute of being able to monitor both moving and stationary bubbles simultaneously in a variety of tissue types.



Source: Namery, 1976

Figure 2-8 Ultrasonic bubble detector

Richardson (1985) mentioned several different methods to investigate bubbles in extracorporeal blood circuits, which are used in artificial kidney and open heart surgery.

- An optical method required small samples to be obtained for slipstream through a chamber with a gap narrow enough to allow optical detection. However, this method was unreliable for determining the bubble diameter.
- The diversion of blood stream into a collection chamber. The blood was allowed to sit in this chamber, and air bubbles rose to the top. This method was useful to estimate the air phase flow rate in the blood but was unreliable for determining the sizes of bubble.
- The diversion of a narrow stream of blood through a chamber in which changes in the effective electrical conductivity can be detected in the transient mode as bubbles pass electrodes. This method had limitations similar to those of the optical methods mentioned earlier.

- Ultrasound transmitted from a transducer mounted on the side wall of a tube. Echoes from acoustic reflectors passing in the blood flow could be detected. A significant problem with this method was determining the specific type of reflector that had produced the echo. Reflectors producing echoes could be a bubble, a platelet aggregate, or a piece of plastic that might have washed out of a manufactured component.

In a theoretical study, Luiz *et al*. (1992) showed the limitation of existing ultrasonic air bubble detectors for extracorporeal circuits in artificial kidney and open heart surgery. Their study was based on the wave attenuation caused by the presence of air bubbles in the blood circuit. They found that the minimum air bubble diameter that could be detected theoretically was 110, 74, 44 and 38 µm for ultrasonic frequencies of 50 kHz, 100 kHz, 1 MHz and 5 MHz, respectively. The researchers added that although a bubble trap and bubble barrier were used in the extracorporeal circuit to remove gaseous air emboli they can only eliminate air bubbles with a diameter larger than 200 µm. In this case it can be concluded that detection would fail in the above mentioned ultrasonic frequencies.

Markus (1993) used a trans-cranial Doppler ultrasound to detect air bubbles in the cerebral circulation of patients. The main disadvantage of trans-cranial Doppler ultrasound was the fact that bubbles were seen in the circulation without the capability of preventing the event. The same method was also used by Ringelstein *et al*. (1998) to detect micro embolic material, both gaseous and solid, within the intracranial cerebral arteries. The detection of micro emboli was based on the measurement of backscatter from emboli. From their study they found that the backscatter of the ultrasound from normal flowing blood is usually lower than the backscatter from solid emboli. The latter, however, is usually much lower than the back scatter from gaseous emboli of similar size.

Grosset *et al*. (1996) looked for micro emboli signals in 150 patients (95 women and 55 men), and found 1 or more signals during a 30 minutes recording in 89% of patients using 2 MHz trans-cranial Doppler ultrasound.

Rolle *et al*. (2000) performed *in vivo* studies for the detection of micro emboli during hemodialysis sessions and *in vitro* studies for determination of their origin. For the *in vivo* study they used a 2 MHz ultrasound probe to assess the number of micro embolic signals or MES in the sub-clavian vein downstream from the Arteriovenous fistula before the dialysis session and for 15 minutes at the beginning and end of hemodialysis sessions in 25 patients. No MES were detected during *in vivo* studies before hemodialysis sessions. MES were registered in all patients at the beginning and end of the hemodialysis procedure at an average of 12.7±9 and 16.7±11.5 signals/min respectively. They also detected MES after the blood pump and before the air trap. They concluded that in all patients, MES were recorded during hemodialysis sessions. For the *in vitro* study a similar probe was used to detect MES at different sites in the Dialysis machine. The results of *in vitro* studies indicated that MES were formed by the blood pump of the hemodialysis machine.

Droste *et al.* (2002) used pulsed-Doppler ultrasound to analyze a continuous shower of micro emboli into the pulmonary vasculature during dialysis. They hypothesized that this may explain the high pulmonary morbidity in long-term dialysis patients. These micro emboli are most probably gaseous, as suggested by the ultrasound high relative intensity signal. However, the origin of these micro bubbles may be in air bubbles already in the hemodialysis tubes and filter before the procedure; or entering the blood stream during connection and disconnection of the lines, or formation of gas bubbles as the result of pressure gradients and turbulent flow in the tubes and access.

Sassaroli and Hynynen (2004) suggested mathematical modeling using the ultrasonic method as micro bubbles have the ability to concentrate acoustic energy around them. In order to increase this property, one possible strategy is to operate the bubbles at their natural frequency of oscillation. However, resonance frequency is strongly affected by the vessel radius when bubbles are confined in blood vessels, and it is lower than their unbounded one. The free space resonance frequency is recovered asymptotically in large enough blood vessels, depending on the bubble size and blood vessel length.

Barak and Katz (2005) reported that advanced ultrasound and Doppler technology are used to detect micro bubbles in the human circulation of end-stage renal disease patients treated by hemodialysis. These micro bubbles originated in the extracorporeal lines and tubing of the hemodialysis machine. These emboli circulate in the blood stream until they lodge in the capillary bed of various organs, mainly the lungs. This causes various problems e.g. tissue ischemia, inflammatory response. Aggregation of platelets and clot formation occurs, leading to further obstruction of the microcirculation and subsequent tissue damage.

Jonsson *et al.* (2007) performed various *in vitro* dialysis settings using regular dialysis devices. The aim of their study was to evaluate if air bubbles could pass the venous chamber and pass the safety system detector for air infusion without triggering an alarm. A Dextran70 fluid was used to avoid the risk of development of emboli. Optical visualization, recirculation and the collection of eventual air into an intermediate bag were investigated. In addition, a specially designed ultrasound monitor was placed after the venous air trap to measure the presence of micro bubbles. From the optical vision they found that micro bubbles of air were seen at the bottom of the air trap and could pass the air trap towards the venous line without triggering the alarm of the safety system. In *in vivo* conditions, the micro bubbles will pass from the air trap to the lungs where they are probably trapped and act as micro emboli before they are absorbed.

A recent study performed by Palanchon *et al*. (2008) was to remove air bubbles from the venous line of the extracorporeal circuit before they reached the circulation of the patient's body. They designed an air bubble trapper contained in a main channel connected to the tubing of the hemodialysis machine. They found that when the bubble trapper was deactivated the number of micro emboli signal was higher than when the bubble trapper was activated.

2.7.2.1 Disadvantages of Ultrasonic Detectors

The problems with these detectors are:

- Ultrasound is expensive and it is neither able to accurately evaluate the size of individual bubbles, nor detect them as individual bubbles when they are in cluster.

- Ultrasound measures discontinuities in the bloodstream and therefore cannot distinguish between micro air and tiny blood clots.

- The accuracy of ultrasound measurements is poor for small diameter bubbles.

- In pulsing ultrasound applications, the propagation velocity of sound requires ultrasound pulses to be at least 10-20 μsec apart for a fast-moving 1.25 cm diameter bloodstream, so that tracking is not continuous.

- The attachment of an ultrasound transducer and maintenance of its direction towards a particular vessel for continuous measurement are extremely difficult.

Consequently, a more accurate discriminating method to detect micro air is needed (Nebuya *et al*., 2004: 142; Driel *et al*., 2003).

2.7.3 Electrical Impedance Measurement Devices

A few attempts have been made to detect small bubbles in blood by impedance measurement. One of the earliest uses of electrical impedance for air emboli detection was reported by Richardson (1985: 55), but no details were given.

Nebuya *et al*. (2004: 143-144) investigated the detection of air emboli in blood *in vitro* using a tetra polar electrical impedance measurement. They used a tank with a linear array of four electrodes, spaced approximately 1 cm apart down one side. The tank was filled with 0.2 Sm^{-1} saline and bubbles were generated using carbon dioxide gas. Electrical transfer impedance was measured every 8.2 ms at 1.25 MHz. The movement of bubbles was recorded by a video camera, and their size and depth from the middle of the array were measured using captured video images. Using the lead filed theory and experimental results; the fundamental limit on the detectable size of bubbles was estimated at the carotid artery. The experimental *in vitro* results showed that a bubble of 17.6 mm^3 in volume at a depth 5.3 mm could be detected. However, a bubble of 0.5 mm diameter at the same depth could not give a signal which agreed with the theoretical analysis.

2.7.3.1 Disadvantages of Electrical Impedance Measurement Devices

An electrical impedance measurement has many disadvantages:

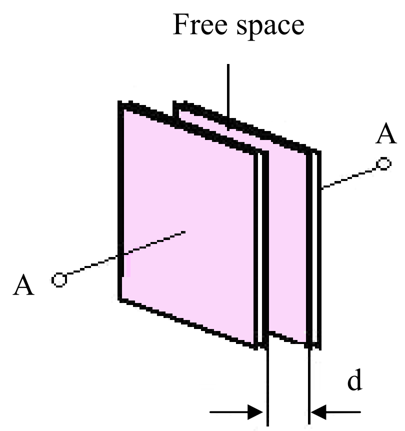
- It uses only for the detection of large emboli.
- The change in impedance caused by a bubble was expected to be very small and of short duration, so that *in vivo* detection will be difficult.
- The smallest detectable size of an air embolus was estimated only.

2.7.4 M-mode Echocardiography

This technique was used by Zhou *et al.* (1984: 56-60) to detect air bubbles on 8 dogs and 12 patients undergoing open heart surgery. They found that when 1.0 mL of air was injected, sensitivity and specificity were 93.2% and 95.0% respectively, and decreased to 85.7% and 80.6% when 0.25 mL was injected. They concluded that M-mode echocardiography may serve as a sensitive and specific tool for the detection and removal of air bubbles during open heart surgery.

2.7.5 Capacitive Devices with Two Parallel Plates

The simplest configuration of a capacitive sensor is two close-spaced parallel plates (Baxter, 1997). Figure 2-9 shows a simple structure of the capacitor with two parallel plates.



Source: Baxter, 1997

Figure 2-9 Capacitor structure with two parallel plates

Capacitance between two plates is determined by:

- Size of the plates.
- Distance between the plates.
- Material between the plates i.e. dielectric material (Webster, 1998: 56; Baxter, 1997).

The value of the capacitor is proportional to the area of the two metal plates (*A*) and is inversely proportional to the distance between them (*d*). In other words, a large value of a capacitor will have large plates separated by a very thin dielectric layer. The effective capacitance is given by:

$$C = \frac{\varepsilon_o A}{d} \qquad (2.1)$$

Where ε_o : is the permittivity of free space, is a constant equal to 8.85×10^{-12}F/m

Placing a dielectric material between the plates in a parallel plate capacitor causes an increase in the capacitance in proportion to the relative permittivity of the material, ε_r. So the effective capacitance becomes:

$$C = \frac{\varepsilon_o \varepsilon_r A}{d} \qquad (2.2)$$

Where ε_r : is the relative dielectric constant of the material.

In principle it is possible to monitor displacement by changing any of the three parameters: *A, d or* ε_r. However, the method used to change the structure of the material between the plates is commonly used by other researchers (Webster, 1998: 55).

The capacitor sensors can sense several features e.g. motion, distance position, and dielectric material etc. Capacitive sensors have a very high sensitivity (Baxter, 1997). The capacitor sensor for air detection is rarely used. In this review only two studies of capacitor device for detecting air bubbles were performed.

In 1971, Beullens *et al*. used the capacitance device to detect air bubbles. Their device was based upon the principle of change in the frequency of oscillator circuit, which will vary with the presence of air and with the thickness of air bubble trap wall. By using more than two capacitor's plates sensitive to different frequencies, which surround the bubble trap, change in oscillation can predict the presence of air. Theoretically, this device could fulfill all the requirements of the ideal detector. However, because of volume change within the bubble trap associated with alterations in the venous pressure, and variations in wall thickness of the bubble trap, this device has proven too difficult to use. It must be calibrated for each patient and the sensitivity adjusted accordingly. In addition, it is unreliable for foam detection (Keshaviah and Shaldon, 1989).

In 1986 Hufton *et al.* provided a device to detect the presence of air within a fluid system containing a dielectric fluid, i.e. oil. Their methodology depended on cylindrical capacitor plates surrounding the fluid tube. They performed the same principle of change in the frequency of oscillator circuit as Beullens *et al*. However their study failed to mention the smallest size of the air bubble that can be detected in the oil.

This review has only mentioned two studies of capacitor device for detecting air embolism, both having shortcomings. The purpose of this study is to investigate the affects of the presence of a single air bubble in the capacitor stream, and if there is any change in the voltage across the capacitor device regarding this event.

2.7.6 Comparison and summary of the devices used to detect air bubbles

The devices and methods used in the ECBC for air detection are not perfect detectors. Table 2-4 below illustrates the pro and con of the air bubbles detectors. All detectors of air bubbles have serious drawbacks: some can only detect larger emboli; others only exist theoretically; some have false alarms; and all these devices were insensitive to foam of air.

Table 2-4 Devices used to detect air bubbles in the ECBC with their pro and con

No.	Device	pro	con
1.	Infrared light with photocell receptor	• It could detect 1mL or larger air bubble • Low power device with DC source ranging between 8-9 volts (Vivian *et al*., 1980: 427).	• False alarm due to: Defibrillation of patient, intense lighting around the sensor unit(Vivian *et al*., 1980: 427). • The unit was not designed to detect micro air bubbles smaller than 1 mm (Vivian *et al*., 1980: 428). • No air bubbles trap in the arterial line (Vivian *et al*., 1980: 428). • Not sensitive to foam (Keshaviah and Shaldon, 1989: 282).
2.	Ultrasonic device	• 2 MHz is the transmitted frequency uses in this device (Dietrich *et al.*, 2006:282). • It can detect air bubble with diameter greater than 850 µm (Barak and Katz, 2005:2923).	• Smaller emboli, however, even in large numbers do not activate the alarm. • Not sensitive to foam. • Ultrasound measures discontinuities in the bloodstream and therefore cannot distinguish between micro air and tiny blood clots. • The attachment of an ultrasound transducer and

			maintenance of its direction towards a particular vessel for continuous measurement are extremely difficult (Nebuya *et al*., 2004: 142; Driel *et al*., 2003).
3.	M-Mode Echocardiography	• It could detect 1 mL air bubble (Zhou *et al.,* 1984: 56-60). • The device sensitivity was 93.2% at the mentioned air bubble diameter.	• Not sensitive to foam of air. • Not sensitive enough to detect micro air bubbles.
4.	Electrical Impedance	• It could detect 0.5 mm diameter of air bubbles at a depth of 5.3 mm (theoretically) (Nebuya *et al*. (2004: 144).	• Not sensitive enough to deal with micro air bubbles (Barak and Katz, 2005: 2926). • The smallest detectable size of an air embolus was estimated only. • Not sensitive to foam of air. • The change in impedance caused by a bubble was expected to be very small and of short duration, so that *in vivo* detection will be difficult.
5.	Capacitive detector	• Theoretically, it is ideal device to detect air bubbles. • No false alarm • Supplied with low power, 9 volt AC. • Sensitive to foam of air. • Has good reliability (Beullens *et al.,* 1971)	• It had proven too difficult to use due to: volume changes within the bubble trap associated with alternations in the venous pressure, variation in wall thickness of the bubble trap, and alterations in the blood viscosity according to individual hematocrit levels (Keshaviah and Shaldon, 1989). • It was not absolutely reliable for foam detection (Keshaviah and Shaldon, 1989: 282).

2.8 Summary of the Literature Review

The objective of this chapter was to determine the possible gaps in the existing research studies dedicated to air bubbles detectors for extracorporeal blood circuits. Based on the detailed review of literature as presented, the following summary helps to formulate the objectives of the current study:

- Embolism by large or microscopic bubbles remains a concern and a known risk of ECBC.

- No clear understanding exists of the amount of air that can be infused without causing a risk to the patient.

- Indeed, the micro bubble event and its significance have been proven in open-heart surgery and DCS. However, it awaits clinical confirmation in other conditions such as hemodialysis and rapid fluid infusion. To date, there is limited knowledge about the management of the micro bubble events. Nevertheless, acknowledgment of the problem is the first step on the path toward finding a solution. Contemporary technology offers us tools to cope with various difficulties. The problem of micro bubbles awaits a breakthrough technological solution that will provide their detection and elimination, facilitating better care for the patient.

- The contamination of air into the blood circuit may cause various clinical adverse effects. It is therefore important that this is more extensively explored.

Chapter 3

3. EXPERIMENTAL PROCEDURES

3.1 Introduction

The current section concerns the design of RC circuit to detect air bubbles in the ECBC. This circuit contains a capacitive device and a resistor. It may be differentiated from other methods and circuits used to detect air bubbles by virtue of its smaller size, design, and cost effectiveness. Also its composition is different i.e. it has two plates and the blood is in contact with the plates.

The two dielectric materials used in this capacitor are Dextran70 solution which mimics blood rheology, and real human blood. This methodology section aims to detect the presence of air bubbles in these two dielectric materials.

The project's methodology mainly consists of three parts:

- Experimental work
- Theoretical analysis of the system
- Simulation using Multisim2001

3.2 Experimental Work

Two samples were used to conduct the experiment. The first sample consisted of a mixture of Dextran70 with NaCl and Albumin, whereas the second was human blood. The mixture of Dextran70 was selected for the experiment because it has similar properties to human blood. The RC circuit was used to investigate the change in the output voltage of the capacitor when there was a single air bubble in the capacitor stream. When Dextran70 was used, it was possible to apply different frequencies in the circuit. However, when human blood was used, only a frequency of 30 Hz was applied in the circuit due to the risk of premature clotting.

The experimental methodology has four main parts:

- Fabrication of the detector cell
- Preparation of the solutions
- Design of the circuit
- Measurements of device parameters

3.2.1 Fabrication of the Detector Cell

To fabricate the detector cell, two plates of platinum, supplied by Benua Saina SDN BHD company, of area 0.75 cm^2 i.e. 1.5 cm x 0.5 cm, were encased within an acrylic material to form a capacitor into which the Dextran70 fluid and blood were introduced.

Platinum was used because it is highly malleable, soft, and extremely resistant to oxidation and corrosion by high temperatures or chemical elements. More importantly, it is a very good conductor of electricity. This precious metal has a silvery-white color and does not tarnish (Lagowski, 2004).

Diagrammatic representation of the capacitor detector cell is shown in Figure 3-1, on page 47. The distance between the two platinum plates is nominally fixed at 1.0 cm. because the tube's diameter used in the extracorporeal circuits has the same diameter i.e.

1 cm. Electric lead wires made of copper are attached to the plates to measure the changes in the capacitor's parameters when the Dextran70 solution and human blood are introduced between the plates.

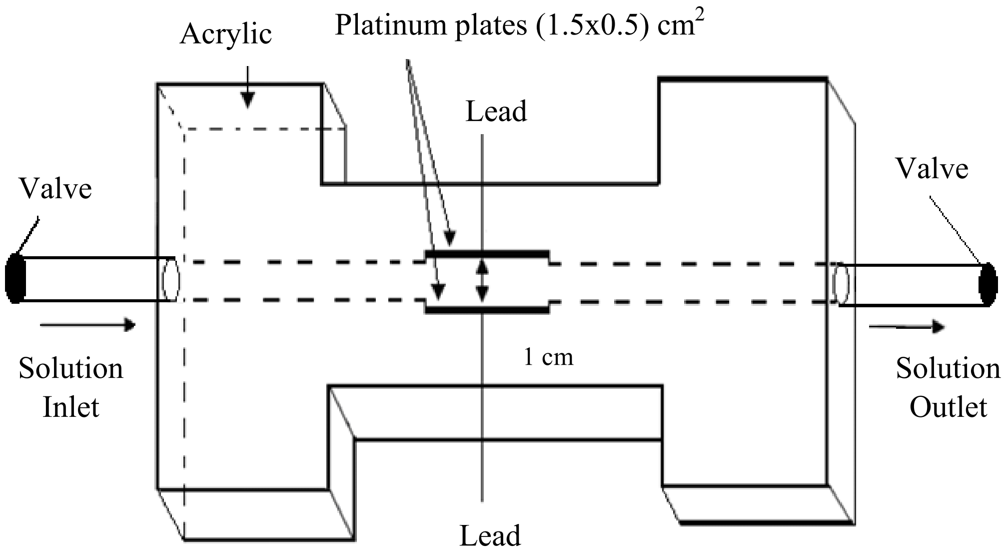


Figure 3-1 Schematic diagram of the capacitor device

Figure 3-2 shows the vertical perspective; Figure 3-3 shows the horizontal perspective, and Figure 3-4 shows the composition of the device and its image.

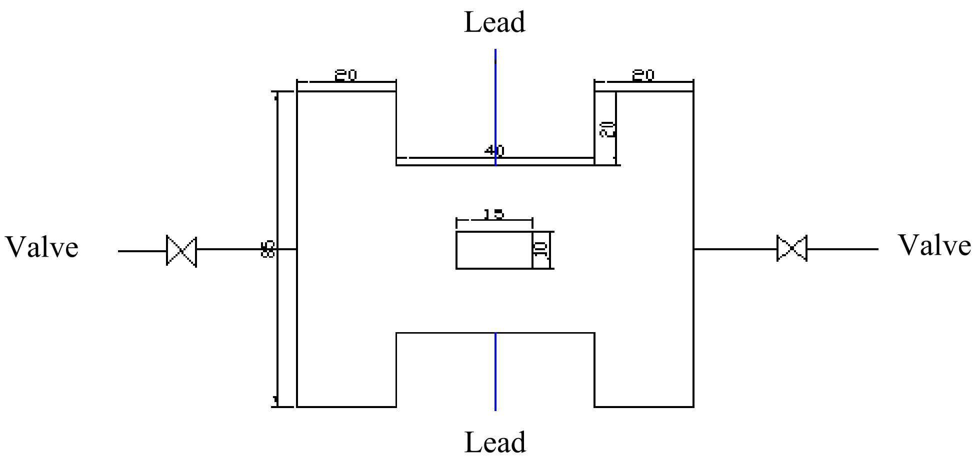


Figure 3-2 Vertical perspective of the device

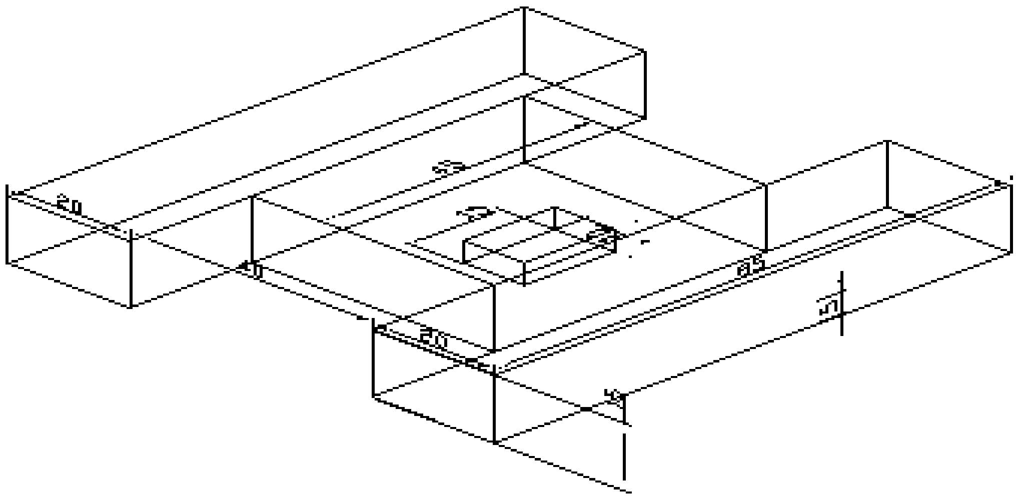


Figure 3-3 Horizontal perspective of the device

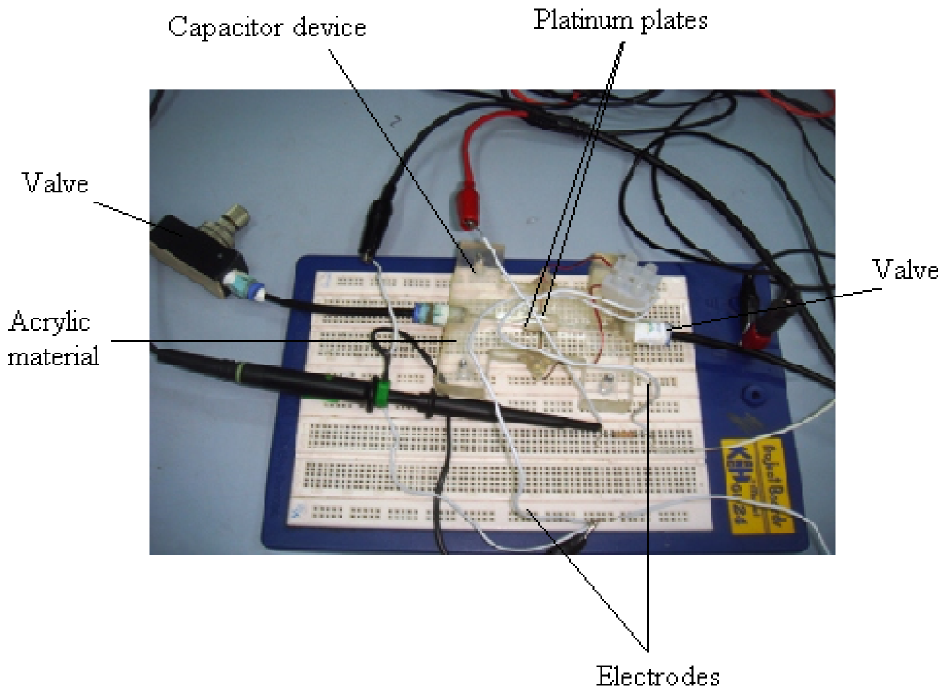


Figure 3-4 Composition of the device

3.2.2 Preparation of the Solutions

In this study two solutions were used as dielectric material of the capacitor:

- Dextran70 solution
- Human blood.

3.2.2.1 Dextran70 Mixture Preparations

To achieve approximate characteristics of blood, a fluid solution was used containing:

- 1L isotonic water
- 9 g NaCl (Sodium Chloride)
- 40 g/L Dextran70, manufactured by Sigma Aldrich
- 50 mL of a 20% concentrated Albumin solution (Stegmayr *et al.*, 2007:484).

The solution was stirred for one hour at $37^{\circ}C$ using a hot plate magnetic stirrer made by Bibby Sternilin Ltd. UK. The stirrer speed was set to 60 rpm or revolutions per minute. An AB204-S balance by Mettler Toledo, Switzerland, was used to measure the weight of NaCl. A portable Density Meter, Densito30p made by Mettler Toledo, Japan was used to measure the density (ρ) of the solution with accuracy ± 0.0005 at temperature $36.8\ ^{\circ}C$. A conductance/ TDS/ $^{\circ}C$/ $^{\circ}F$ meter, made by Eutech, Singapore was used to measure the conductance (σ) of the solution. Measurements of the viscosity of the solution were performed using a viscometer No.2F145 made by Cannon Instrumentation Company, USA. The viscometer constant was 0.0979 mm^2/s^2. To obtain the viscosity of the solution in mPa.s the efflux time in seconds was multiplied by the viscometer constant, multiplied by the density in g/mL. The viscosity was measured at $37^{\circ}C$ although the viscometer constant is the same at all temperatures. These instruments and the conversion of the viscosity are shown in Appendix A.

3.2.2.2 Blood Preparation

The second measurements were performed on five samples of blood, taken from healthy blood donors. 0.05 mL of heparin was added to each approximate 5 cm^3 blood sample to avoid clotting. According to Chelize (2002: 286) increasing heparin content to 0.35 mL per 10 cm^3 blood does not change the blood characteristics. The blood was kept at a constant temperature of 37°C.Then measurements for density, viscosity, and conductance were taken using the same pieces of equipment in Appendix A.

3.2.3 Design of the Circuit

The change in the values of the capacitance and the output voltage is measured using a series RC circuit. Figure 3.5 shows the circuit diagram for RC series circuit.

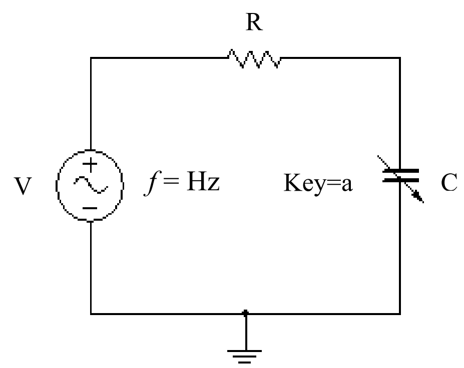


Figure 3-5 Circuit diagram for series RC circuit

Using a capacitor device in an AC circuit will introduce some reactance. Like resistance, reactance is expressed in ohms, and it behaves in the same way as resistance, in the sense that it tends to restrict the flow of current through a circuit (Rizzoni, 2000; Reese, 2000).A capacitor in an AC circuit exhibits a kind of resistance called capacitive reactance, measured in ohms. This depends on the frequency of the AC voltage, and is given by:

$$X_C = \frac{1}{\omega C} = \frac{1}{2\pi f C} \tag{3.1}$$

The voltage across the capacitor is given by:

$$V_C = I X_C \tag{3.2}$$

V and I are generally the root mean square i.e. rms values of the voltage and current. In a series RC circuit as shown in Figure 3.5, the total resistance of the system is given as

$$Z_{total} = R + X_C \tag{3.3}$$

Where R: is resistance of the resistor, X_C: is reactance of the capacitor.

The resistance of the resistor that was used in the circuit was R= 130 kΩ. It was chosen to be this value because the serial impedance must be sufficiently high in order to obtain high sensitivity. The root mean squared voltage for input voltage was 1.77 V i.e. value V.

Table 3-1 shows different frequencies were used when Dextran70 was the dielectric material of the capacitor device. However, a frequency of 30 Hz was applied when blood was the dielectric material of the capacitor as blood clotting occurs 24 hours after sampling from donor. The ambient humidity and temperature were measured during the experiment using Thermo-Hygrometer (Appendix A).

Table 3-1 Parameter values of the RC circuit for Blood and Dextran70 materials

Material	Resistance of the resistor (kΩ)	Input voltage (V)	Frequency
Blood	130	2.5	30 Hz
Dextran70	130	2.5	30 Hz- 30 kHz

3.2.4 Measurements of Device Parameters

3.2.4.1 Using Dextran70 Solution

To conduct the experiment, the prepared Dextran70 solution was introduced between the capacitor plates through an inlet valve. The inlet and outlet valves were closed to keep the fluid inside while the measurements were conducted. Then, the capacitance and the output voltage were measured via the lead wires connected to the capacitor plates. The capacitance was measured using digital LRC meter, CROTECH/4910 and the output voltage was measured using digital meter, FLUKE.

First the measurements were taken without air bubbles in the solution after every effort had been made to prevent air from entry to the device stream. For the second measurements, an air bubble of unknown diameter was introduced into the Dextran70 solution contained between the capacitor plates. Then, the measurement was taken of the capacitance, air bubble diameter, and the output voltage.

In order to investigate the change in capacitance and the output voltage, air bubbles with different diameters were used. Bubbles were produced ranging in size from 620 μm up to 4.21 mm using two different needles:

- One made of glass with diameter of 10 μm (Appendix A).
- The second made of plastic with diameter 980 μm.

Air bubble diameter was measured using an Absolute Coolant Proof Caliper and magnification lamp for accuracy (see Appendix A). Different frequencies were applied to study the effects and to select the optimum frequency. Figure 3-6 presents the measurement technique using Dextran70 solution.

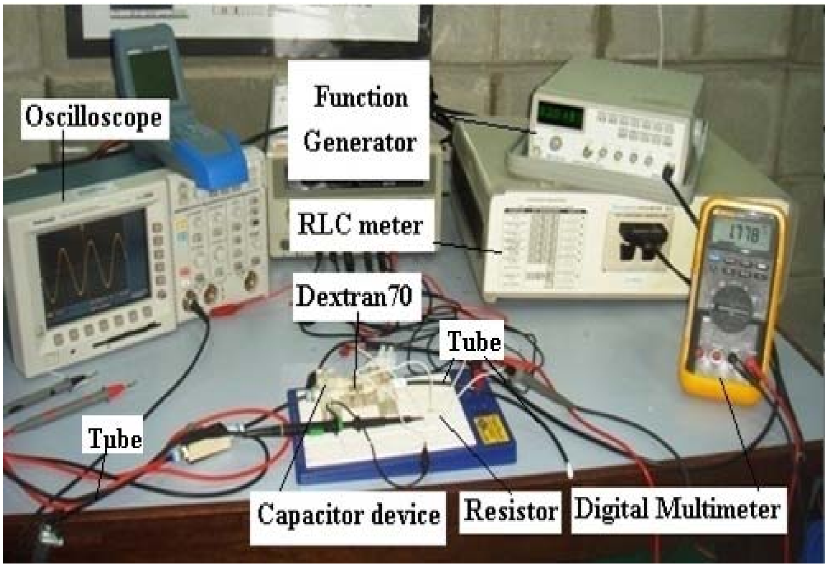


Figure 3-6 Test circuit with Dextran70 solution as dielectric material for the device

3.2.4.2 Using Human Blood

This part of the experiment was performed using five samples of blood from different healthy donors. Table 3-2 shows the data for each blood sample collected from Hospital Raja Permaisuri Bainon, in Ipoh; Perak, Malaysia. Each sample contained approximately 5 mL blood with 0.05 mL of heparin.

Table 3-2 Data for donors and their blood samples

Class	Age	Gender	Contain (Blood+ Heparin)
A	25	male	(4.5 + 0.05)mL
A	28	male	(5.0 + 0.05) mL
B	21	male	(5.5 + 0.05) mL
O	25	female	(5.0 + 0.05) mL
O	37	male	(5.0 +0.05) mL

Blood was introduced between the capacitor plates through the inlet valve. The inlet and outlet valves of the tube were closed to keep the blood inside while measurements were taken. The capacitance and the output voltage were then measured via the lead wires connected to the capacitor plates. Firstly, measurement without air bubbles in the solution. Then an air bubble of an unknown diameter was introduced into the blood. Air bubbles with different diameters were used in order to investigate the change in capacitance. The diameters of air bubbles used were ranged from 730 µm up to 4.31 mm. Figure 3-7 illustrates the measurement technique for conducting the experiment with human blood. The specifications of the apparatuses that were used in both studies are shown in Appendix A.

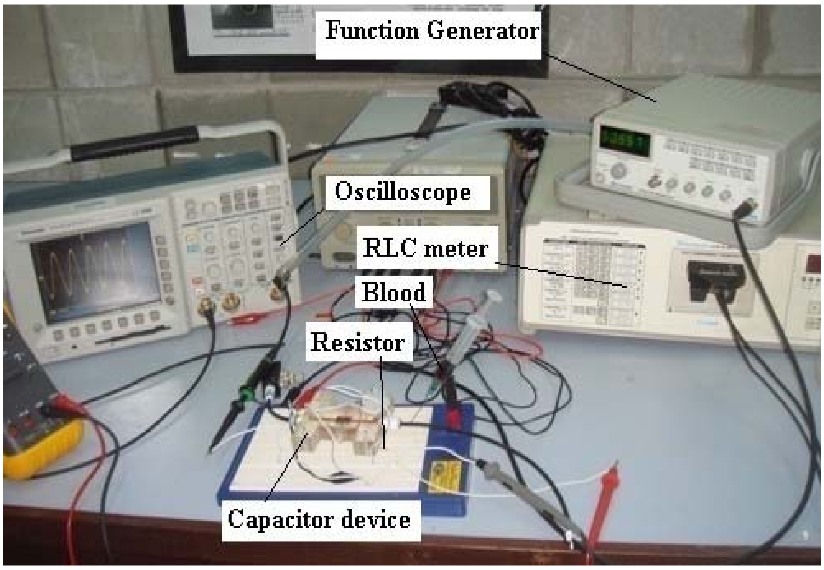


Figure 3-7 Test circuit with blood as the dielectric material for the device

Evaluations of analytical data are required to evaluate this device i.e. accuracy, linearity error, sensitivity, and reliability (Webster, 1998; Skoog *et al*., 1998).

- Accuracy is the degree of closeness of a measured or calculated quantity to its actual (true) value . It describes the correctness of an experimental result. The accuracy of a single measured quantity is the difference between the true value and the measured value divided by the true value. This ratio is usually expressed as a percent. Appendix A shows the calculation of the accuracy. The accuracy has a positive or a negative sign. A positive sign indicating that the measured value or result is smaller than its true value and a negative sign the reverse.

- Linearity error of a curve determines by comparing it with a calibration curve that is a straight line. This method is called least squares (Appendix A).
- The sensitivity of an instrument or a device is the ratio of the incremental output quantity to the incremental input quantity. The sensitivity can be obtained from the slope of the curve or it can be calculated (Appendix A).
- Precision describes the reproducibility of results; that is, the agreement between numerical values for two or more replicate measurements, or measurements that have been made in exactly the same way. Generally, the precision of an analytical method is readily obtained by simply repeating the measurement (Appendix A).

3.3 Theoretical Analysis of the System

In this section only some basics of RC circuit and capacitive device physics are used for the analysis of the proposed system. The objective of this analysis is to find:

- The AC current in the RC circuit
- The AC potential difference across the capacitor.

3.3.1 Finding AC Current

To analyze the circuit in Figure 3.5 on page 51, an approach from Reese, 2000:1022; Holler, 1998:35 was used.

To convert the circuit to the complex domain, the independent AC voltage source is changed to a complex voltage source phase. For a real source voltage $V_{in}\cos(\omega t)$ the complex source voltage is:

$$V_{source} = V_{in}\angle(\omega t) \tag{3.4}$$

Where V_{source}: is the independent AC voltage from the source

Figure 3.8 shows the impedance of the resistor and capacitor indicated next to their circuit symbols. The impedance of the resistor is just R, whereas the impedance of the capacitor is $-iX_c$

Where X_c is capacitance reactance and is given as:

$$X_C = \frac{1}{\omega C} \tag{3.5}$$

Where ω: is the angular frequency measured in radians per second, and C: is the capacitance of the capacitor.

The direction for the current phase (I) is indicated. Figure 3.8 shows the current phase enters the $(+)$ polarity terminal of the each impedance and exits at the $(-)$ polarity terminal.

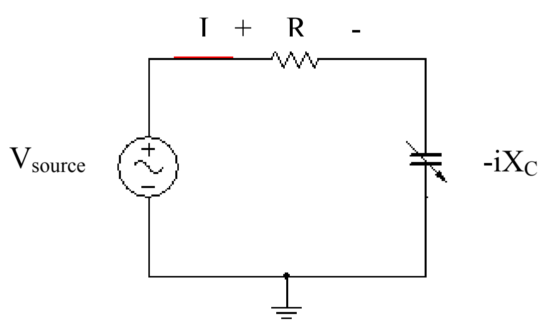


Figure 3-8 The current direction is indicated and the polarities of the impedances are marked accordingly.

The potential difference across impedance is found from AC version of Ohm's law

$$V = IZ \tag{3.6}$$

Where I: is the current in amperes, Z: is the complex impedance.

Hence the potential difference across the resistor is:

$$V_R = IR \tag{3.7}$$

Across the capacitor, the potential difference is:

$$V_C = I(-iX_C) \tag{3.8}$$

Where $-i$: is the imaginary number.

Kirchhoff's Voltage Law (KVL) is used to make a clockwise loop around Figure 3.8 beginning in the lower left hand corner of the loop. Then the KVL becomes:

$$-V_{source} + IR + I(-iX_C) = 0 \tag{3.9}$$

$$\Longrightarrow \quad I(R - iX_C) = V_{source} \tag{3.10}$$

The current is thus:

$$I = \frac{V_{source}}{R - iX_C} \tag{3.11}$$

The polar form of $(R + iX_C)$ is:

$$R - iX_C = \left[R^2 + (-X_C)^2\right]^{1/2} \angle \tan^{-1}\left[\frac{-X_C}{R}\right] \tag{3.12}$$

Since $\tan(-\alpha) = -\tan\alpha$

Then $\tan^{-1}\frac{-X_C}{R} = -\tan^{-1}\left[\frac{X_C}{R}\right]$

ϕ is defined as:

$$\phi = \tan^{-1}\left[\frac{X_C}{R}\right] \tag{3.13}$$

Thus Equation (3.12) becomes:

$$R - iX_C = \left(R^2 + X_C^2\right)^{1/2} \angle(-\phi)$$

Substituting this into the expression for the current (Equation 3.11), obtains:

$$I = \frac{V_{source}}{\left(R^2 + X_C{}^2\right)^{1/2} \angle -\phi} \tag{3.14}$$

Division by complex numbers in polar form means that $\angle(-\phi)$ can be moved from the denominator of Equation (3.14) into the numerator by changing the sign of the angle, becoming:

$$I = \frac{V_{source}\angle\phi}{\left(R^2 + X_C{}^2\right)^{1/2}} \tag{3.15}$$

Substituting the source voltage in polar from Equation (3.4) yields:

$$I = \frac{V_{in}}{\left(R^2 + X_C{}^2\right)^{1/2}} \angle(\omega t)\angle\phi$$

When multiplying complex numbers in polar form, the angles add, which means the current phase becomes:

$$I = \frac{V_{in}}{\left(R^2 + X_C{}^2\right)^{1/2}} \angle(\omega t + \phi) \tag{3.16}$$

To find the real current *I(t)* as a function of time, the real part of the current phase is taken:

$$I = \mathrm{Re}\, I$$

$$I(t) = \frac{V_{in}}{\left(R^2 + X_C{}^2\right)^{1/2}} \cos(\omega t + \phi) \tag{3.17}$$

The angle ϕ is given by Equation (3.13)

3.3.2 The AC Potential Difference across the Capacitor

According to Ronald (2000) the potential difference across the capacitor V_C is found by Equation (3.18).

$$V_C = IZ_C \tag{3.18}$$

Using $Z_C = -iX_C$ and Equation (3.16) for the current, Equation (3.18) becomes:

$$V_C = \frac{V_{in}\angle(\omega t + \phi)}{\left(R^2 + X_C{}^2\right)^{1/2}}(-iX_C) \tag{3.19}$$

Since the complex number $-i$ in polar form is:

$$1\angle\left[-\frac{\pi}{2} rad\right]$$

Equation (3.19) becomes:

$$V_C = \frac{V_{in}\angle(\omega t + \phi)}{\left(R^2 + X_C^2\right)^{1/2}}\left[1\angle\frac{-\pi}{2}rad\right]X_C$$

Once again, the product rule for the complex number in polar form means the angles in the numerator are added together, yielding:

$$V_C = X_C\frac{V_{in}\angle(\omega t + \phi - \pi/2rad)}{\left(R^2 + {X_C}^2\right)^{1/2}} \tag{3.20}$$

The phase difference between the potential difference phase and the current phase is $-\pi/2rad$. This is a constant for a capacitor.

The real potential difference across the capacitor $V_C(t)$ is the real part of its potential difference phase V_C

$$V_C(t) = \mathrm{Re}V_C$$

$$V_C = X_C\frac{V_{in}}{\left(R^2 + {X_C}^2\right)^{1/2}}\cos(\omega t + \phi - \pi/2rad) \tag{3.21}$$

The actual potential difference across the capacitor i.e. Equation (3.21) and actual current Equation (3.17) also has a phase difference of $-\pi/2rad$.

The magnitude of the peak potential difference across the capacitor as a function of angular frequency (V_{Cpeak}) is:

$$V_{Cpeak} = \frac{X_C V_{in}}{\left(R^2 + {X_C}^2\right)^{1/2}}$$

$$V_{Cpeak} = \frac{V_{in}}{\frac{1}{X_C}\left(R^2 + X_C{}^2\right)^{1/2}}$$

Introducing X_C into the square root, the equation then becomes:

$$V_{Cpeak} = \frac{V_{in}}{\left[\frac{R^2}{X_C{}^2} + 1\right]^{1/2}}$$

Since $X_C = \frac{1}{\omega C}$

The peak potential difference across the capacitor is:

$$V_{Cpeak} = \frac{V_{in}}{\left[1 + (\omega RC)^2\right]^{1/2}}$$

Since $\omega = 2\pi f$

The peak potential difference across the capacitor is:

$$V_{Cpeak} = \frac{V_{in}}{\sqrt{1 + (2\pi fRC)^2}} \tag{3.22}$$

During the experiment V_{rms}, Root Mean Squared Voltage was measured. Theoretical calculation was also required.

Since $V_{rms} = \frac{V_{peak}}{\sqrt{2}}$

Therefore Equation (3.22) becomes:

$$V_{rms} = \frac{V_{in}}{\sqrt{2\left(1 + (2\pi fRC)^2\right)}} \tag{3.23}$$

3.4 Simulation using Multisim2001

3.4.1 Overview of Multisim2001

There are numbers of software that can be used to simulate this RC circuit. For example:

- Numerical method (Mat lab)
- P-spice
- Multisim2001

In this research, Multisim2001 software is used because it is a complete system design tool offering a very large component database, schematic entry and full analog/digital simulation. It has post processing features and seamless transfer to PCB, printed circuit board layout packages e.g. Ultiboard from Electronics Workbench. It offers a single, easy-to-use graphic interface for all design needs. Multisim2001 provides all the advanced functionality needed to take designs from specification to production. Multisim2001 provides with many different types of analyses. Each one includes step-by-step instructions, provided on-line, to guide through its use. When an analysis is performed, the results are displayed on a plot in the Multisim2001 grapher and saved.

3.4.2 RC Circuit Simulation

Multisim2001 software examines the changes in output voltage of the capacitor device during changes in the capacitance of the capacitor at different frequencies range from 30 Hz to 30 kHz due to the appearance of a single air bubble in the stream. The capacitor is placed with a resistor its value is 130 kΩ to form a series RC circuit and the output voltage is measured across the capacitor device using a digital meter. Figure 3.5 shows the simulated circuit.

3.5 Summary of the Experimental Procedures

A capacitive device was constructed of two parallel plates of platinum encased within an acrylic material, to form a capacitor test cell into which Dextran70 fluid, selected to closely mimic blood rheology, and real human blood were separately introduced. The distance between the two platinum plates was nominally fixed and electric wires made of copper were attached to the plates. This was to measure the capacitance changes in the capacitor and the output voltage when Dextran70 solution and blood, both with or without air bubbles were introduced between the plates of the device.

The capacitor was placed with a resistor to form a series RC circuit. The prepared Dextran70 solution was introduced between the capacitor plates through inlet and outlet valves attached to both ends. The output voltage was then measured via the lead wires connected to the capacitor plates. Then an air bubble of an unknown diameter was introduced to the Dextran70 solution contained within the capacitor plates. Air bubbles with different diameters were used in order to investigate the changes in capacitance and the output voltage as a function of the bubble diameter. Then different frequencies were applied to the circuit.

Five different samples of real human blood were used separately as dielectric material in the capacitor. Then the capacitance and the output voltage were measured via the lead wires connected to the capacitor plates as an air bubble of an unknown diameter was introduced into the blood samples.
The second section of this work is a theoretical analysis of the circuit, to compare with the experimental measurements.

In the third part of this work, Multisim2001 software is used to examine the output voltage change when there is a change in the capacitance of the capacitor device at different frequencies.

Chapter 4

4. RESULTS AND DISCUSSION

4.1 Dextran70 as a Dielectric Material for the Capacitor Device

4.1.1 Experimental Dextran70 Solution Conditions

For this study the presence of air bubbles was detected by measuring the change in the output voltage across the capacitor in the circuit. The experiment was repeated for different frequencies when Dextan70 was used. The condition of the Dextran70 solution when the experiment was conducted is shown in Table 4-1. The solution shows close similarities to blood i.e. the average density of whole blood for a human being is about 1.06 g/cm^3 (Cutnell and Johnson, 1998: 308) and the average viscosity is 3.3 mPa.s (Stegmayr *et al.,* 2007). For the frequencies between 40 Hz to 30 kHz the temperature of the Dextran70 solution was 37.1°C to mimic blood's temperature, except 30 Hz the temperature was 25°C.

Table 4-1 Experimental Dextran70 solution conditions compared with Human Blood characteristics

Material	Density (g/cm^3)	Conductance (ms)	Viscosity (mPa.s)	Temperature ($^{\circ}$C)
Dextran70	1.057	15.48	3.41	37.1
Blood	1.060	-	3.30	36-37

4.1.2 Results of the Circuit using a Frequency of 30 Hz

The capacitance of the capacitor of Dextran70 solution was found to be in the range from 43.5 nF up to 39.1 nF when a frequency of 30 Hz was applied. Various diameters of air bubble ranging from 0 up to 4.1 mm were injected randomly in the stream of the solution. Thus the output voltage across the capacitor increased as a result of the appearance of the air bubbles as shown in Table 4-2. From simulation and theoretical analysis (Equation 3.23), the output voltage from the capacitor was found to increase from 1.209 V up to 1.276 V and from 1.21 V up to 1.277 V respectively. It was observed that 620 μm diameter of air bubble made a significant change in the capacitance of the capacitor. Comparison of the experimental measurements to theoretical predictions, taking the theoretical value as the true value (Webster, 1998: 19), displayed percentages differences of the measured data as shown in Table 4-2 for each air bubble diameter.

Table 4-2 Percentage difference for the measured data compared to theoretical prediction at 30 Hz

Air bubble diameters (mm)	0	0.62	1.66	1.86	2.29	2.8	3.7	4.1
Percentage difference (%)	0.16	- 0.08	0	0.16	0.4	0.16	1.1	1.4

From Table 4-3, the initial value of the output voltage when Dextran70 solution was introduced between the plates of the capacitor device was 1.208 V. By injecting an air bubble with diameter 620 μm the output voltage increased to 1.217 V. This shows a difference of 9 mV between the two cases. The capacitor was then returned to the initial value, without an air bubble, then an air bubble with a diameter of 1.66 mm was injected into the Dextran70 stream and the output voltage increased to 1.225 V. Again the capacitor was returned to the initial value and different diameters of air bubbles were injected. At 2.29 mm diameter of air bubble the output voltage across the capacitor was 1.238 V, while an air bubble diameter of 2.8 mm generated 1.242 V across the capacitor.

This gives a difference of 4 mV between the readings. It is therefore a reasonable hypothesis that the capacitor has a good response for detecting less than 620 µm.

Table 4-3 Measured capacitance and voltage values of Dextran70 for several air bubble diameters at frequency of 30 Hz

No.	Capacitance of the capacitor (nF)	Air bubble diameter (mm)	Experimental output voltage (V)	Simulated output voltage (V)	Theoretical output voltage (V)
1	43.50	0	1.208	1.209	1.210
2	43.10	0.62±0.02	1.217	1.215	1.216
3	42.47	1.66±0.02	1.225	1.225	1.225
4	41.88	1.86±0.02	1.232	1.234	1.234
5	41.32	2.29±0.02	1.238	1.242	1.243
6	41.19	2.8±0.02	1.242	1.244	1.244
7	40.03	3.7±0.02	1.248	1.262	1.262
8	39.10	4.1±0.02	1.259	1.276	1.277

Figure 4-1 shows the output voltage from the capacitor as a function of the capacitance from experimental work, simulation, and theoretical analysis at a frequency of 30 Hz. To calculate the linearity error, calibration data was compared to the straight line that would best fit the points. This straight reference line was calculated from the calibration data using a technique called “least squares fitting” (Webster, 1998: 22). Thus, the linearity error from the experiment, simulated results, and theory was determined to be 2.78%, 0.01%, and 0.04% respectively.

Sensitivity indicates how much the output voltage changes as a result of a change in the capacitance of the capacitive sensor when air bubbles entered. The experimental sensitivity of the device at a frequency of 30 Hz was found to be 11 mV/nF. This means that for every 1 nF of change in the capacitance of the capacitor, the output voltage will change 11 mV. The experimental sensitivity has shown a close agreement with the simulation and theoretical sensitivity, which is found to be 15.2 mV/nF for both.

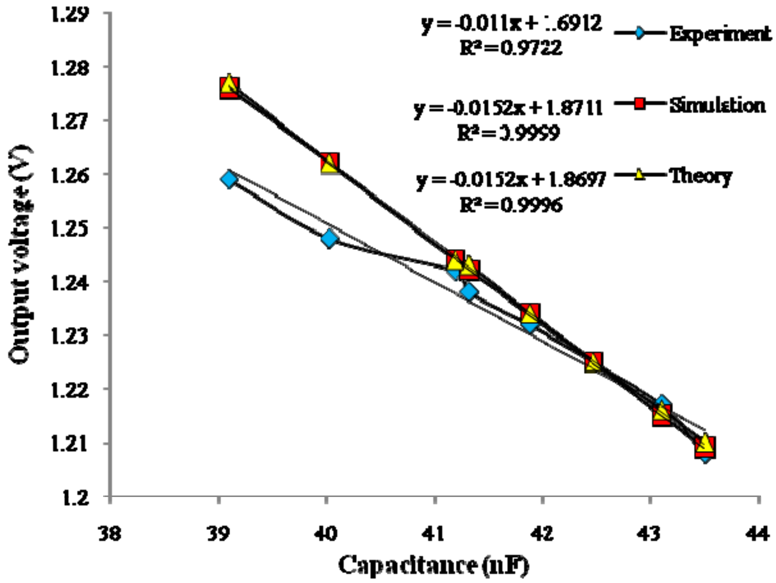


Figure 4-1 Output voltage versus capacitance at 30 Hz

Figure 4-2 illustrates the output voltage as a function of the air bubble size. It is observed that the relation between the output voltage and the air bubble diameter is directly proportional. The output voltage increased when the size of air bubble inside the capacitor device increased. The sensitivity was found to be 11.7 mV/mm. The linearity error was found to be 2.13 %.

It was also observed that the data point for higher diameter of air bubbles is higher than the ideal data. This may be due to the experimentations error e.g. the effects of instability of the 1 function generator's signal; or air bubble with higher diameter may make turbulent flow in the solution. This was noted for each frequency applied in the circuit except at a frequency of 50 Hz.

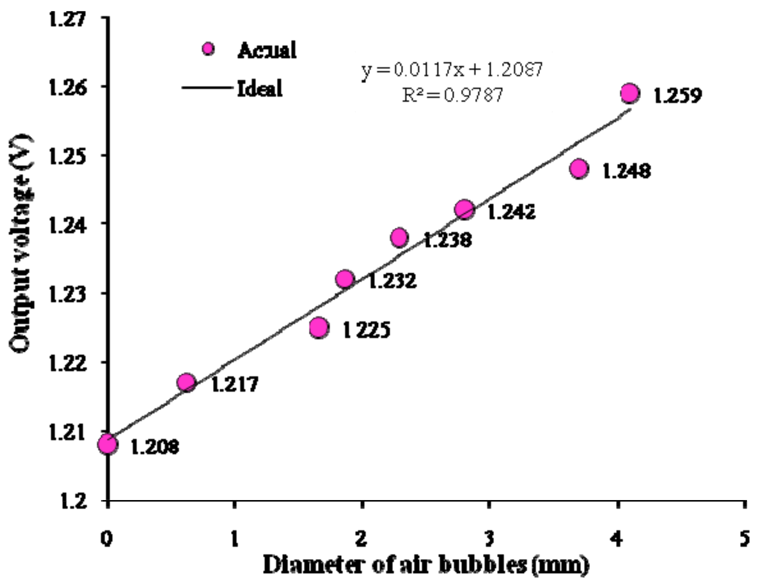


Figure 4-2 Output voltage as a function of air bubbles diameter at a frequency of 30 Hz

4.1.3 Results of the Circuit using a Frequency of 40 Hz

The Dexran70 solution was used in the RC circuit, as shown in Figure 3-5 and a frequency of 40 Hz was applied. The output voltage of the capacitor was increased from 1.009 V up to 1.088 V with decreasing capacitance of the capacitor from 43.5 nF up to 38.88 nF when air bubbles were randomly injected from 0 up to 4.19 mm as shown in Table 4-5. The smallest diameter of the air bubble made a significant change in the capacitance of the capacitor i.e. 640 µm. The percentage difference of the measured data is computed at this frequency and it was shown in Table 4-4.

Table 4-4 Percentage difference for the measured data compared to theoretical prediction at 40 Hz

Air bubble diameters (mm)	0	0.64	1.66	1.87	2.29	2.82	3.71	4.19
Percentage difference (%)	0.88	0.58	0.09	0.28	0.54	0.19	0.28	0.55

Table 4-5 Measured capacitance and voltage values of Dextran70 for several air bubble diameters at frequency of 40 Hz

No.	Capacitance o the capacitor (nF)	Air bubble diameter (mm)	Experimental output voltage (V)	Simulated output voltage (V)	Theoretical output voltage (V)
1	43.5	0	1.009	1.017	1.018
2	42.90	0.64±0.02	1.021	1.027	1.027
3	42.47	1.66±0.02	1.033	1.033	1.034
4	41.86	1.87±0.02	1.041	1.043	1.044
5	41.32	2.29±0.02	1.047	1.052	1.053
6	41.18	2.82±0.02	1.053	1.054	1.055
7	40.01	3.71±0.02	1.071	1.074	1.074
8	38.88	4.19±0.02	1.088	1.093	1.094

Figure 4-3 shows the output voltage from the capacitor as a function of the capacitance for experimental work, simulation, and theoretical analysis at a frequency of 40 Hz. The linearity error from the simulation and theory was found to be the same, i.e. 0.04%. The linearity error from the experimental results was found to be 0.77% showing a close correlation with the simulated results and theoretical prediction. The experimental sensitivity of the capacitor device at a frequency of 40 Hz was found to be 16.8 mV/nF. This means that for every 1nF of change in the capacitance of the capacitor, the output voltage will change 16.8 mV. Both simulation and theoretical sensitivity were found to be 16.4 mV/nF. The experimental sensitivity showed a close correlation with the simulation and theoretical sensitivity.

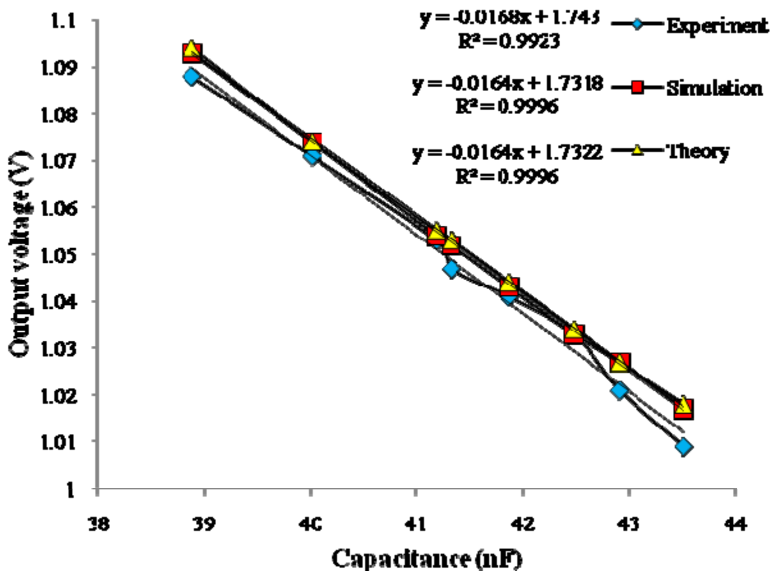


Figure 4-3 Output voltage versus capacitance of the capacitor at a frequency of 40 Hz

Figure 4.4 shows the relation between the output voltage from the capacitor and the air bubble diameter. It was observed that the data point for higher air diameter of air bubble i.e. 4.19 mm is higher than the ideal data. As mentioned previously, this may be due to the experimentation error. The output voltage changed from 1.009 V, without air bubbles in the stream, to 1.021 V in a measuring range of 640 µm air bubble diameter. The output voltage changed from 1.041 V to 1.047 V for a small change in the measuring range of 420 µm. Therefore, the capacitive device has a high sensitivity. The linearity error between the output voltage and the air bubble diameter at a frequency of 40 Hz was found to be 1.89 % and the sensitivity was found to be 17.8 mV/mm.

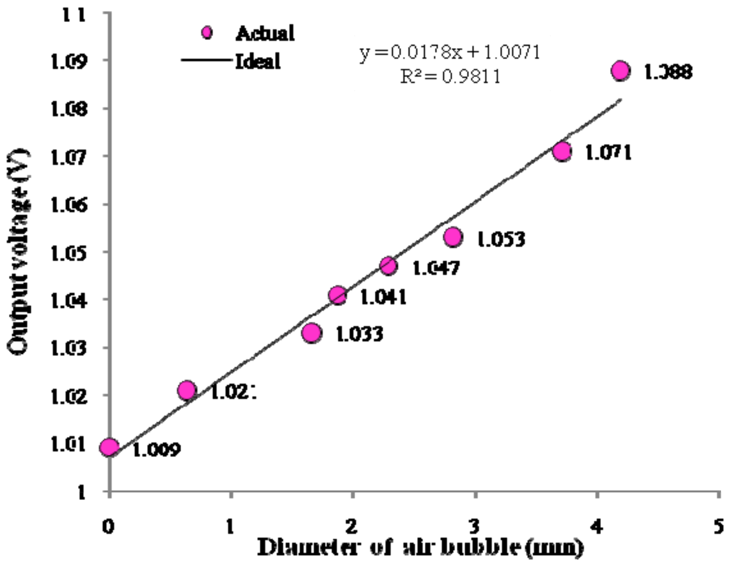


Figure 4-4 Output voltage as a function of air bubble diameter at a frequency of 40 Hz

4.1.4 Results of the Circuit using a Frequency of 50 Hz

As shown in Table 4-7 the output voltage across the capacitor increased from 859.8 mV, for no air bubbles, up to 922.2 mV for 4.19 diameter air bubble at a frequency of 50 Hz. Comparing the experimental result of the output voltage with the theoretical prediction, as a true value, the accuracy was found to be 0.88% when there was no air bubble in the stream of the device. The simulated results and theoretical predictions are in a close agreement. An air bubble with a diameter of 640 µm made a significant change in the capacitance of the device. The capacitance was 43.5 nF before the mentioned diameter was injected, then it became 42.9 nF afterwards. The percentage difference of the measured data was computed at this frequency as shown in Table 4-6.

Table 4-6 Percentage difference for the measured data compared to theoretical prediction at 50 Hz

Air bubble diameters (mm)	0	0.64	1.66	1.87	2.29	2.82	3.71	4.19
Percentage difference (%)	0.88	1.45	0.61	0.87	1.02	0.46	1.07	2.14

Table 4-7 Measured capacitance and voltage values of Dextran70 for several air bubble diameters at frequency of 50 Hz

No.	Capacitance of the capacitor (nF)	Air bubble diameter (mm)	Experimental output voltage (mV)	Simulated output voltage (mV)	Theoretical output voltage (mV)
1	43.50	0	859.8	867.087	867.449
2	42.90	0.64±0.02	863.9	876.429	876.661
3	42.47	1.66±0.02	877.9	882.916	883.281
4	41.86	1.87±0.02	885.1	892.519	892.887
5	41.32	2.29±0.02	892.3	901.166	901.535
6	41.18	2.82±0.02	899.6	903.430	903.800
7	40.01	3.71±0.02	913.2	922.724	923.098
8	38.88	4.19±0.02	922.2	942.002	942.380

As shown in Figure 4-5 the experimental sensitivity of the device at a frequency of 50 Hz was found to be 14.326 mV/nF. This means that for every 1 nF of change in the capacitance of the capacitor, the output voltage will change 14.326 mV. The experimental sensitivity shows less of an agreement with the simulation and theoretical sensitivity, i.e. 16.194 mV/nF, 16.209 mV/nF and it was less than that found at 40 Hz. The linearity error from the experiment was 2.83%, while it was 0.05% for the simulation and theoretical results.

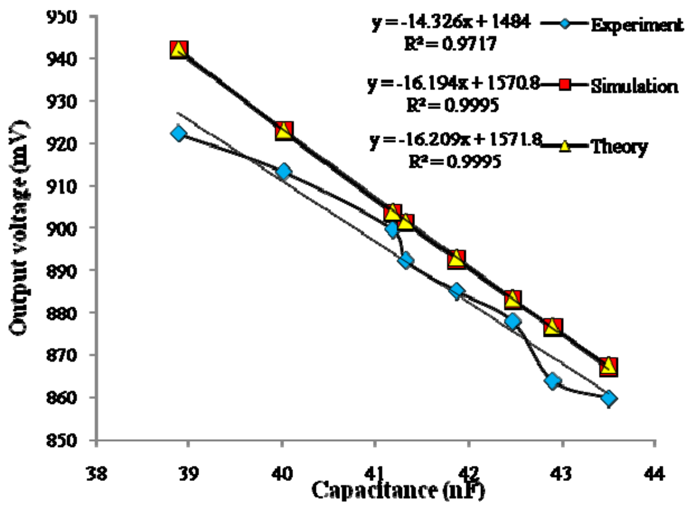


Figure 4-5 Output voltage as a function of capacitance at a frequency of 50 Hz

Figure 4-6 shows the relation between the output voltage from the capacitor device and the air bubble diameters at a frequency of 50 Hz. The experimental output voltage changed from 859.8 mV, when there were no air bubbles in the stream, to 863.9 mV in a measuring range of 640 µm, showing a small diameter that can be detected. The linearity error between the output voltage and the air bubble diameter at a frequency of 50 Hz was found to be 1.03% and the sensitivity, 15.419 mV/mm. It clear that the data for the higher air bubble diameter is in range with ideal data.

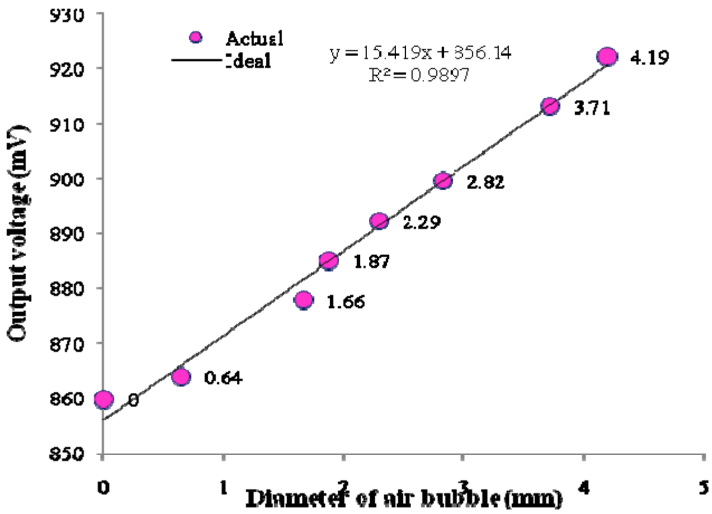


Figure 4-6 Output voltage versus air bubble diameter at 50 Hz

4.1.5 Results from the Circuit at a Frequency of 100 Hz

Table 4-9 below shows the output voltage from the experimental results at 100 Hz changed from 479.4 mV for zero diameter of air bubble up to 529.212 mV for 4.19 mm diameter of air bubble. From simulation the output voltage of the capacitor was found to increase from 478.91 mV up to 530.934 mV. The theoretical analysis, using Equation3.23, showed the output voltage increased from 479.142 mV up to 531.186 mV. It was found that 640 µm of air bubble diameter could make a significant decrease in the capacitance value, and a significant increase in the output voltage. The percentage difference of the measured data was computed at this frequency as shown in Table 4-8.

Table 4-8 Percentage difference for the measured data compared to theoretical prediction at 100 Hz

Air bubble diameters (mm)	0	0.64	1.66	1.87	2.29	2.82	3.71	4.19
Percentage difference (%)	0.05	0.27	0.11	0.11	0.46	0.07	0.29	0.37

Table 4-9 Measured capacitance and voltage values of Dextran70 for several air bubble diameters at frequency of 100 Hz

No.	Capacitance of the capacitor (nF)	Air bubble diameter (mm)	Experimental output voltage (mV)	Simulated output voltage (mV)	Theoretical output voltage (mV)
1	43.5	0	479.400	478.910	479.142
2	42.9	0.64±0.02	484.029	485.107	485.341
3	42.47	1.66±0.02	490.464	489.644	489.879
4	41.86	1.87±0.02	497.008	496.220	496.458
5	41.32	2.29±0.02	500.130	502.185	502.425
6	41.18	2.82±0.02	503.624	503.759	503.995
7	40.01	3.71±0.02	519.010	517.240	517.487
8	38.88	4.19±0.02	529.212	530.934	531.186

Figure 4-7 shows output voltage as a function of the capacitance of the device at 100 Hz from the experimental, simulated, and theoretical results. The sensitivity of the experimental work was found to be 11.07 mV/nF from simulation, 11.25 mV/nF and from theorerical analysis 11.25 mV/nF. The linearity error for experiment, simulation, and theory was found to be 0.7%, 0.1%, and 0.1% respectivly.

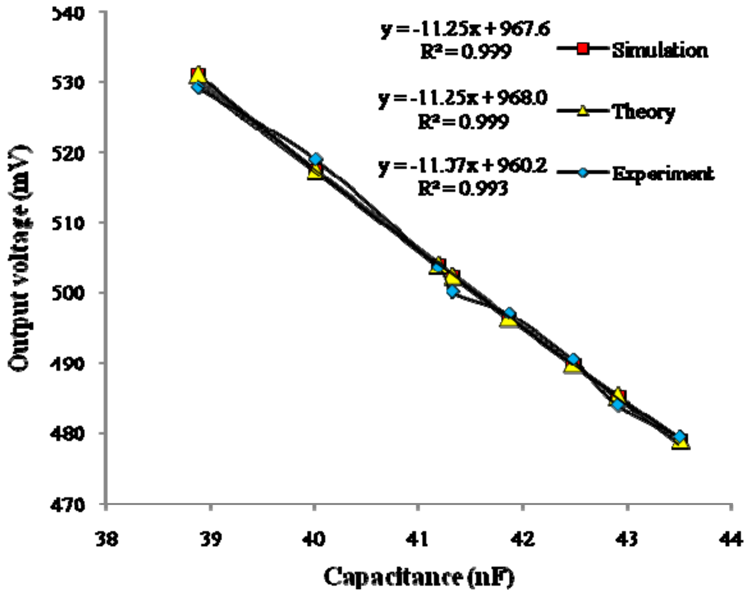


Figure 4-7 Output voltage versus capacitance for Dextran70 at 100 Hz

Figure 4-8 shows the output voltage from the capacitor device as a function of air bubble diameters at 100 Hz. The output voltage increased across the capacitor when the air bubble diameter increased in the stream of the Dextran70 solution. It was observed that the data point for higher air bubble diameter i.e. 4.19 mm is higher than the ideal data. As mentioned previously, this may be due to the experimentations error. The sensitivity of the capacitor device at this frequency was found to be 11.594 mV/ mm, which is less than that at 50 Hz. This means for 1 mm change in air bubble diameter the change in the output voltage is 11.594 mV. The linearity error was found to be 4.29%

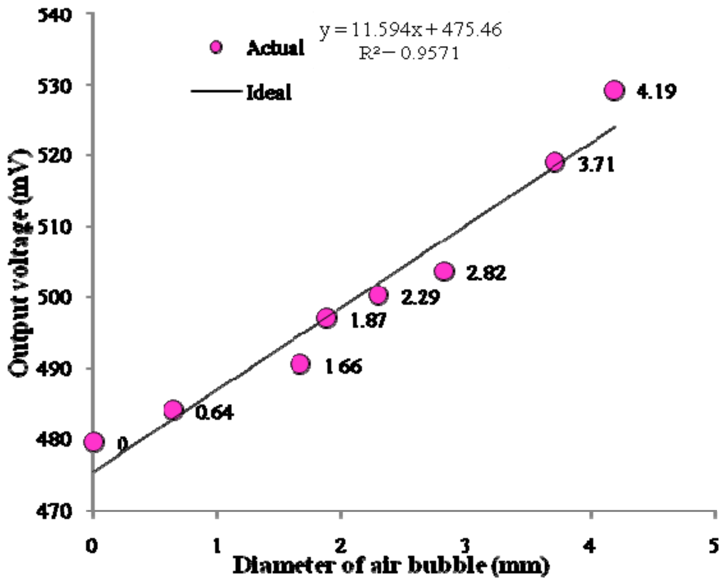


Figure 4-8 Output voltage versus air bubble diameter at a frequency of 100 Hz

4.1.6 Results of the Circuit at a Frequency of 250 Hz

In Table 4-11 the output voltage was increased from 196.2 mV for no air bubble up to 219.71 mV for 4.19 mm diameter air bubble. The accuracy of the capacitor device is found to be 0.84% at this frequency. Table 4-10 shows the percentage difference of the measured data at this frequency.

Table 4-10 Percentage difference for the measured data compared to theoretical prediction at 250 Hz

Air bubble diameters (mm)	0	0.64	1.66	1.87	2.29	2.82	3.71	4.19
Percentage difference (%)	0.84	0.77	0.15	0.67	0.99	0.06	0.93	0.59

Figure 4-9 shows the output voltage as a function of the capacitance of the capacitor. The sensitivity of the experiment, simulation, and theory is determined to be 4.969 mV/nF, 5.006 mV/nF, and 5.008 mV/nF respectively. The linearity error was found to be 1.1% for experiment; 0.02 % for both simulation and theory.

Table 4-11 Measured capacitance and voltage values of Dextran70 for several air bubble diameters at frequency of 250 Hz

No.	Capacitance of the capacitor (nF)	Air bubble diameter (mm)	Experimental output voltage (mV)	Simulated output voltage (mV)	Theoretical output voltage (mV)
1	43.50	0	196.20	197.755	197.859
2	42.90	0.64±0.02	199.05	200.486	200.590
3	42.47	1.66±0.02	202.30	202.489	202.595
4	41.86	1.87±0.02	204.14	205.400	205.508
5	41.32	2.29±0.02	206.10	208.048	208.156
6	41.18	2.82±0.02	208.98	208.745	208.854
7	40.01	3.71±0.02	212.87	214.761	214.873
8	38.88	4.19±0.02	219.71	220.906	221.021

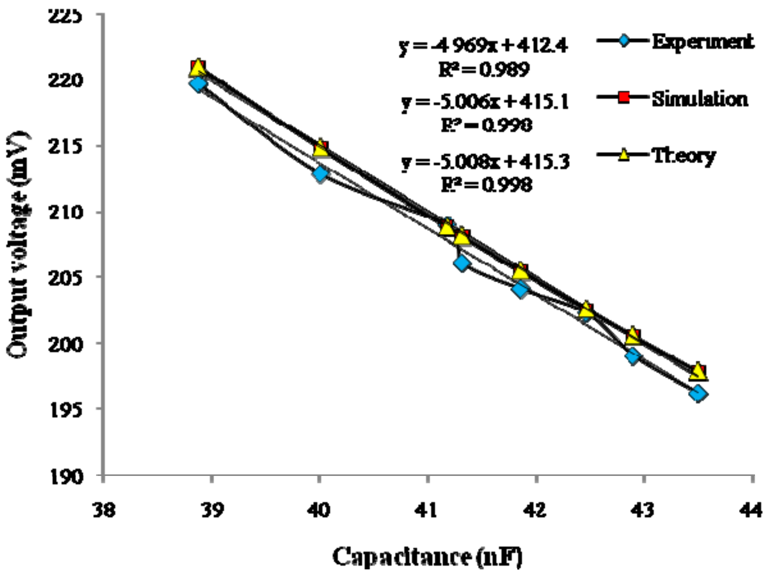


Figure 4-9 Output voltage versus capacitance at 250 Hz

As shown in Figure 4-10 the relation between the output voltage from the capacitor device and the diameter of air bubble is directly proportional. The linearity error was found to be 3.9% and the sensitivity was found to be 5.222 mV/mm. It was observed that the data point for higher air bubble diameter i.e. 4.19 mm is higher than the ideal data. As mentioned previously this may be due to the experimentations error.

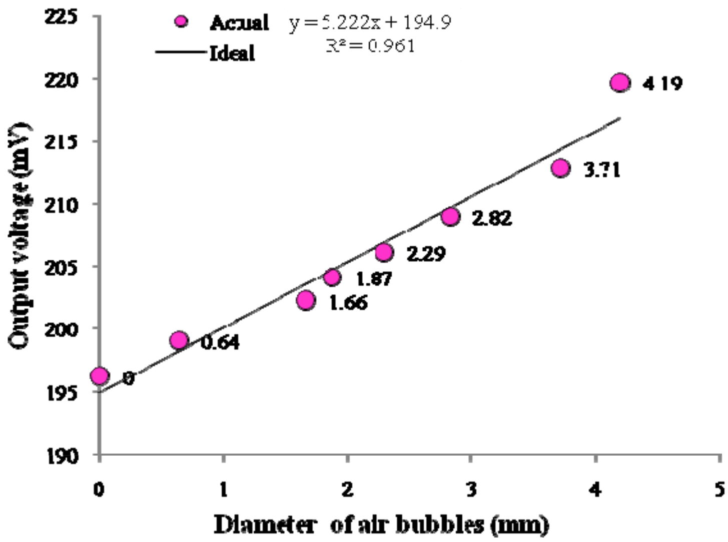


Figure 4-10 Output voltage versus air bubble diameter at 250 Hz

4.1.7 Results of the Circuit at a Frequency of 500 Hz

At 500 Hz the experiment was conducted and the data recorded in Table 4-13. The output voltage increased from 97.44 mV without air bubbles up to 109.87 mV for 4.19 mm diameter air bubble. The experimental graph was compared to the theoretical solution computed from Equation (3.23), as the true value, and the accuracy was calculated and found to be 1.97%. The smallest diameter of air bubble made a significant difference in the output voltage, i.e. 1.59 mV. Table 4-12 shows the percentage difference for the measured data compared to the theoretical results at 500 Hz.

Table 4-12 Percentage difference for the measured data compared to theoretical prediction at 500 Hz

Air bubble diameters (mm)	0	0.64	1.66	1.87	2.29	2.82	3.71	4.19
Percentage difference (%)	1.97	1.74	0.13	0.2	0.98	0.34	1	1.16

Table 4-13 Measured capacitance and voltage values of Dextran70 for several air bubble diameters at frequency of 500 Hz

No.	Capacitance of the capacitor (nF)	Air bubble diameter (mm)	Experimental output voltage (mV)	Simulated output voltage (mV)	Theoretical output voltage (mV)
1	43.50	0	97.44	99.339	99.397
2	42.90	0.64±0.02	99.03	100.724	100.783
3	42.47	1.66±0.02	101.93	101.740	101.800
4	41.86	1.87±0.02	103.07	103.218	103.279
5	41.32	2.29±0.02	103.96	104.562	104.624
6	41.18	2.82±0.02	104.62	104.916	104.978
7	40.01	3.71±0.02	106.95	107.973	108.037
8	38.88	4.19±0.02	109.87	111.099	111.164

In Figure 4-11 the simulated results are in good agreement with theoretical results, the linearity error was found to be 0.2% for both. The sensitivity of the device for simulation was found to be 2.543 mV/nF, and for theoretical analysis was found to be 2.544 mV/nF. The measured and simulated results are in good agreement during third, fourth, and sixth measurements. The linearity error for experimental result was found to be 2.62%, and the sensitivity of the device was found to be 2.604 mV/nF.

Figure 4-12 presents the output voltage as a function of air bubble diameter. Air bubbles with an initial diameter of 640 µm, 1.66 mm, 1.87 mm, 2.29 mm, 2.82 mm, 3.71 mm, and 4.19 mm, were explored by changing the values of the output voltage from the device. The linearity error was found to be 1.8%, and the sensitivity was computed to be 2.79 mV/nF. It was observed that the data point for higher air bubble diameter i.e. 4.19 mm is higher than the ideal data. As mentioned previously, this may be due to the experimentations error.

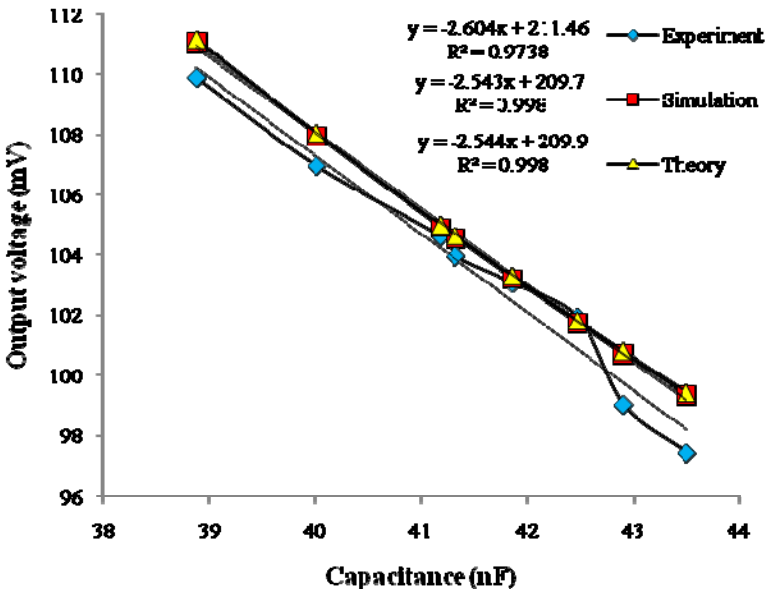


Figure 4-11 Output voltage versus capacitance for Dextran at 500 Hz

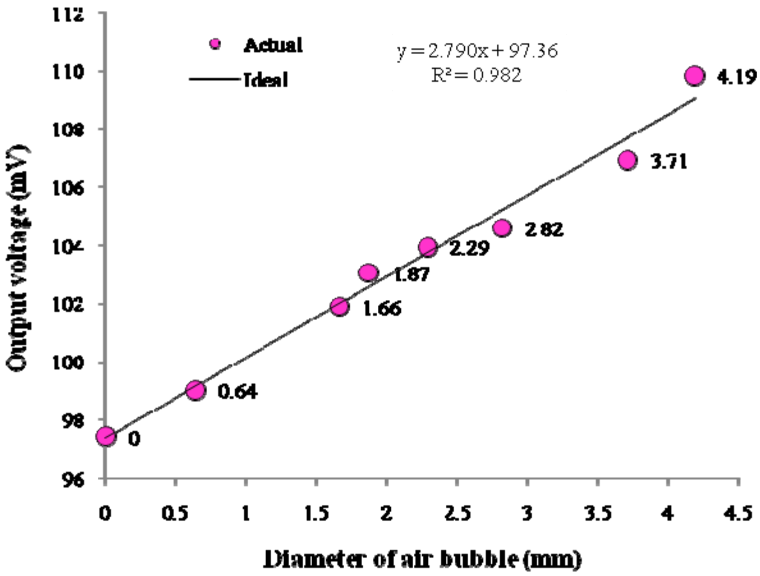


Figure 4-12 Output voltage versus air bubble diameter at 500 Hz

4.1.8 Results of the Circuit at a Frequency of 700 Hz

From Table 4-15, the difference between the experimental output voltages when there was no air bubble is 0.185 mV i.e. 70.82 when compared to the simulated result i.e. 71.005. Furthermore, the simulated output voltages when different diameters were in the Dextran70 stream are in near agreement with the theoretical predictions (Equation 3.23). The percentage difference of the measured data is computed at this frequency as it is clear from Table 4-14.

Table 4-14 Percentage difference for the measured data compared to theoretical prediction at700 Hz

Air bubble diameters (mm)	0	0.64	1.66	1.87	2.29	2.82	3.71	4.19
Percentage difference (%)	0.33	1.41	0.75	0.73	0.62	0.07	0.36	1.25

Table 4-15 Measured capacitance and voltage values of Dextran70 for several air bubble diameters at frequency of 700 Hz

No.	Capacitance of the capacitor (nF)	Air bubble diameter (mm)	Experimental output voltage (mV)	Simulated output voltage (mV)	Theoretical output voltage (mV)
1	43.50	0	70.82	71.005	71.053
2	42.90	0.64±0.02	71.03	71.996	72.045
3	42.47	1.66±0.02	72.23	72.724	72.774
4	41.86	1.87±0.02	73.29	73.782	73.832
5	41.32	2.29±0.02	74.33	74.744	74.795
6	41.18	2.82±0.02	75.00	74.998	75.049
7	40.01	3.71±0.02	76.96	77.187	77.240
8	38.88	4.19±0.02	78.49	79.426	79.480

In Figure 4-13, the output voltage increased when the capacitance of the capacitor decreased, thereby agreeing with theoretical prediction. The linearity error was found to be 1.28% for experimental measurements, and 0.2% for simulated results and theoretical prediction. The sensitivity of the device at this frequency for experimental measurements was found to be 1.7877 mV/nF; for simulated results 1.821 mV/nF; and for theoretical prediction 1.822 mV/nF.

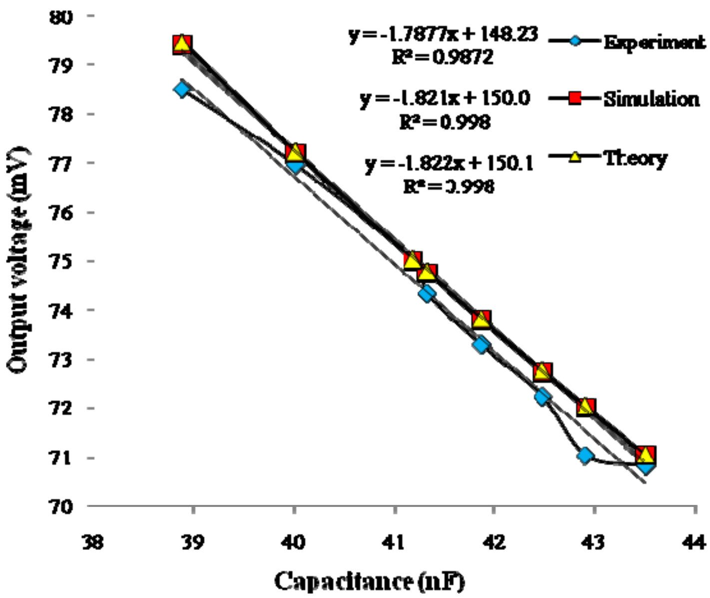


Figure 4-13 Output voltage versus capacitance at 700 Hz

Considering Figure 4-14, the output voltage increased from 70.82 mV for no air bubble up to 78.49 mV for the maximum air bubble diameter used. If an air bubble with diameter 640 µm was presented in the Dextran70 stream, the output voltage increased 210 µV. It can be deduced that the larger the air bubble diameter, the higher the output voltage. The linearity error was computed to be 3.9%, and the sensitivity was found to be 1.881 mV/mm. It was observed that the data point for higher air bubble diameter i.e. 4.19 mm is higher than the ideal data. As mentioned before, this may be due to the experimentations error.

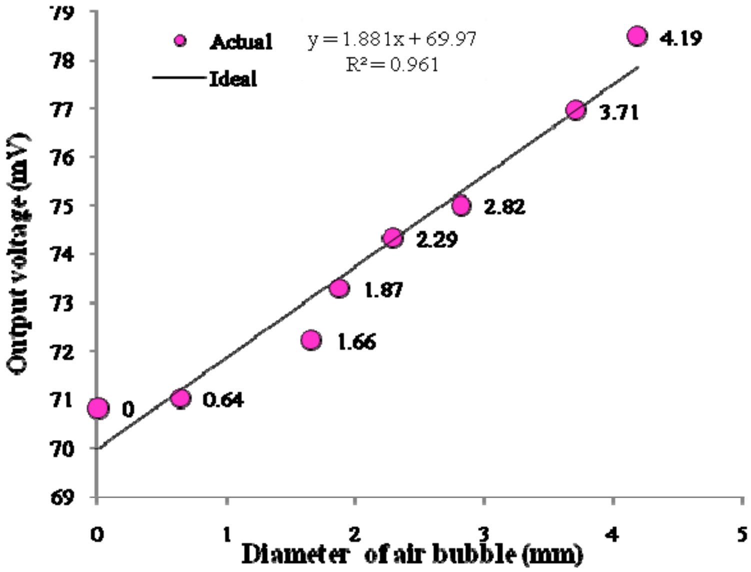


Figure 4-14 Output voltage versus air bubble diameter at 700 Hz

4.1.9 Results of the Circuit at a Frequency of 30 kHz

From Table 4-17, a frequency of 30 kHz was applied to the circuit Figure 3-5. It was observed that the initial value of the capacitance of the capacitor decreased when the air bubbles diameter increased. It is clear that the experimental measurements are in close agreement with the simulated results. The percentage difference for the measured data was compared to theoretical prediction at this frequency and it shown in Table 4-16.

Table 4-16 Percentage difference for the measured data compared to theoretical prediction at 30 kHz

Air bubble diameters (mm)	0	0.66	1.66	1.88	2.29	2.82	3.71	4.21
Percentage difference (%)	2.35	3	3.4	1.45	1.6	1.66	2.11	1.78

Table 4-17 Measured capacitance and voltage values of Dextran70 for several air bubble diameters at a frequency of 30 kHz

No.	Capacitance of the capacitor (nF)	Air bubble diameter (mm)	Experimental output voltage (mV)	Simulated output voltage (mV)	Theoretical Output voltage (mV)
1	43.50	0	1.620	1.637	1.659
2	42.87	0.66±0.02	1.653	1.661	1.683
3	42.47	1.66±0.02	1.665	1.677	1.699
4	41.84	1.88±0.02	1.700	1.702	1.725
5	41.32	2.29±0.02	1.718	1.723	1.746
6	41.18	2.82±0.02	1.723	1.729	1.752
7	40.01	3.71±0.02	1.765	1.780	1.803
8	38.86	4.21±0.02	1.824	1.833	1.857

As shown in Figure 4-15, the capacitance of the device is inversely proportional to the output voltage, as expected from the theory. The linearity error at 30 kHz was computed to be 0.41% for the experimental measurements, 0.2% for simulated results, and 0.2% for theoretical results. The sensitivity of the measured results was found to be 42.7 µV/nF, 42 µV/nF for the simulated results, and 42 µV/nF for theoretical results.

Using Dextran70 the experiments were conducted when different frequencies were applied. These results were shown in Appendix C.

Figure 4-16 shows the output voltage from the capacitor as a function of air bubble diameters. The sensitivity was 44 µV/mm and the linearity error was computed to be 5.5%. It was observed that the data point for higher air bubble diameter i.e. 4.19 mm is higher than the ideal data. As mentioned previously, this may be due to the experimentations error.

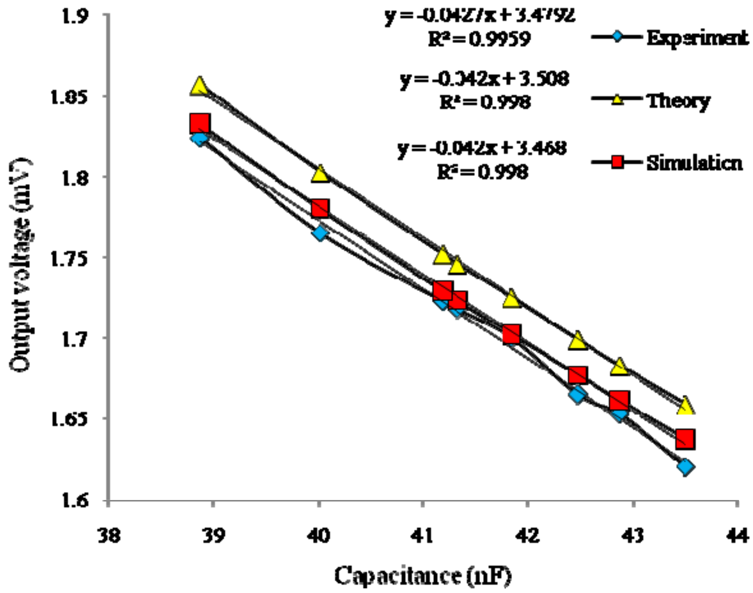


Figure 4-15 Output voltage versus capacitance at a frequency of 30 kHz

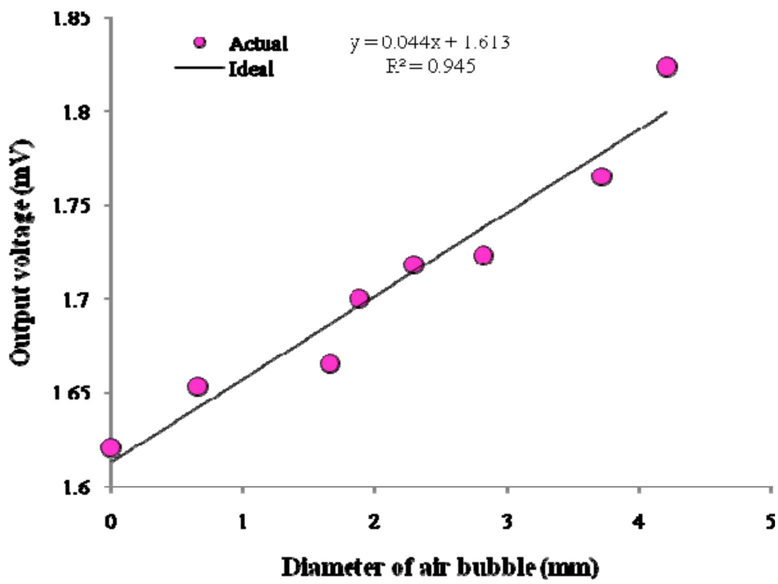


Figure 4-16 Output voltage versus air bubble diameter at a frequency of 30 kHz

All experiments using Dextran70 were replicated in the same conditions to study the precision of the device. For instance Table 4-18 shows the repeatability and the precision of the capacitor device. The standard deviation and the coefficient of variation at 30 kHz were found to be 7.071×10^{-4}, and 0.041% respectively. The experiments were conducted in different conditions of temperature and relative humidity. The effects of these conditions are shown in Appendix B.

Table 4-18 Precision of the device for dextran70 at a frequency of 30 kHz

$Capacitance_1$ (nF)	Air bubbles diameter (mm)	Output $voltage_1$ (mV)	$Capacitance_2$ (nF)	Air bubbles diameter (mm)	Output $voltage_2$ (mV)
43.5	0	1.62	43.5	0	1.62
42.87	0.66±0.02	1.653	42.87	0.66±0.02	1.653
42.47	1.66±0.02	1.665	42.47	1.66±0.02	1.665
41.84	1.88±0.02	1.7	41.84	1.88±0.02	1.7
41.32	2.29±0.02	1.718	41.31	2.29±0.02	1.719
41.18	2.82±0.02	1.723	41.18	2.82±0.02	1.723
40.01	3.71±0.02	1.765	40.01	3.71±0.02	1.765
38.86	4.21±0.02	1.824	38.86	4.21±0.02	1.824

4.2 Summary of Results for Dextran70 as Dielectric Material

Dextran70 solution was used as a dielectric material of the capacitor device, instead of blood, to avoid clotting, and because of the difficulty in obtaining blood. The device was placed in a circuit (Figure3-5) to investigate the effects and changes that appeared when air bubbles were introduced in the stream of the device.

The presence of air bubble in the stream of the dielectric material of the capacitor device decreased the capacitance of the device, and thus increased the output voltage from the capacitor device.

In this section the frequencies are divided to two ranges:

- The first from 30 Hz up to 700 Hz
- The second from 1 kHz up to 30 kHz (Appendix C)

It was observed that when the frequency increased the output voltage decreased (Figure 4-27, and Figure 4-28). This is clearly in agreement with the mathematical relation in Equation 3-23.

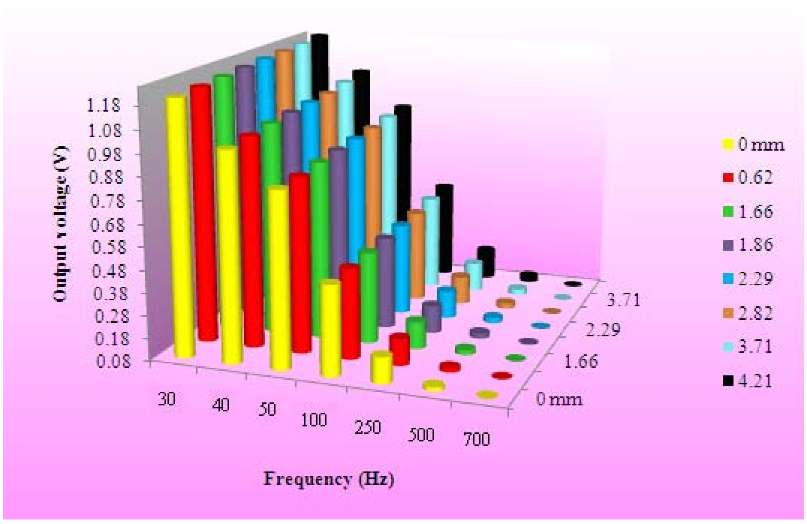


Figure 4-17 Output voltage versus frequency from 30 Hz- 700 Hz for several air bubble diameters

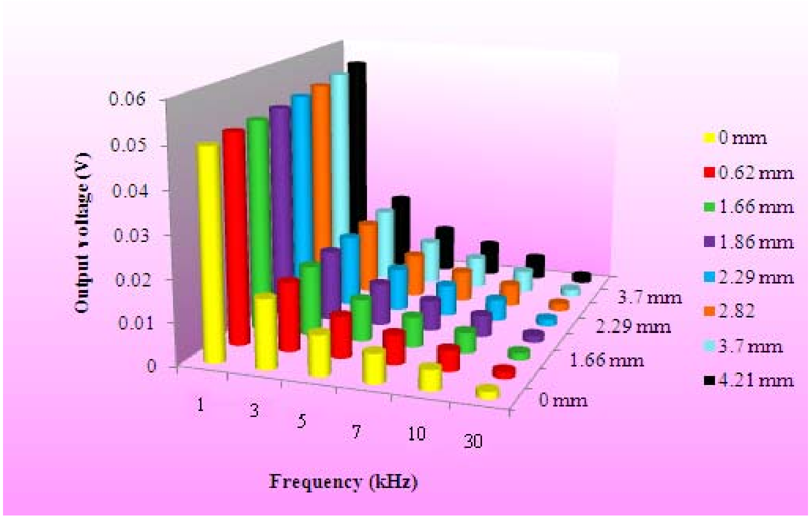


Figure 4-18 Output voltage versus frequency from 1 kHz- 30 kHz for several air bubble diameters

Analysis of experimental data from the above results of Dextran70 shows that the smallest diameter that could be produced was 620 µm. This diameter produced a significant change in the output voltage when it was introduced between the capacitor plates. For instance, at a frequency of 30 Hz the output voltage changed from 1.208 V to 1.217 V when a 620 µm air bubble was injected. A 9 mV change in the output voltage was noted when this size of air bubble was introduced. The same diameter made 5 mV change when introduced in the same device at a frequency of 3 kHz.

During the investigation, the device was sensitive to foam of air bubbles and the output voltage rose immediately. This contrasts with others systems for detecting air bubbles that do not respond when foam occurs (Keshaviah and Shaldon, 1989: 282).

In the present study different frequencies were used. It was observed that better sensitivity was obtained in the low frequencies. Figure 4-29 shows that the best sensitivity of the device was obtained at 40 Hz. The sensitivity at 30 Hz is lower than the sensitivity at 40 Hz, 50 Hz, and 100 Hz. This anomaly is explained by the temperature of the solution. At 30 Hz, the temperature was 25°C whereas the temperature of the solution for the other frequencies was 37.1°C. It is believed that at higher temperature, the ions have higher mobility (www.hyfoma.com). This leads to higher conductivity and thus, much higher sensitivity. The experimental sensitivity shows good agreement with simulation and theoretical sensitivity.

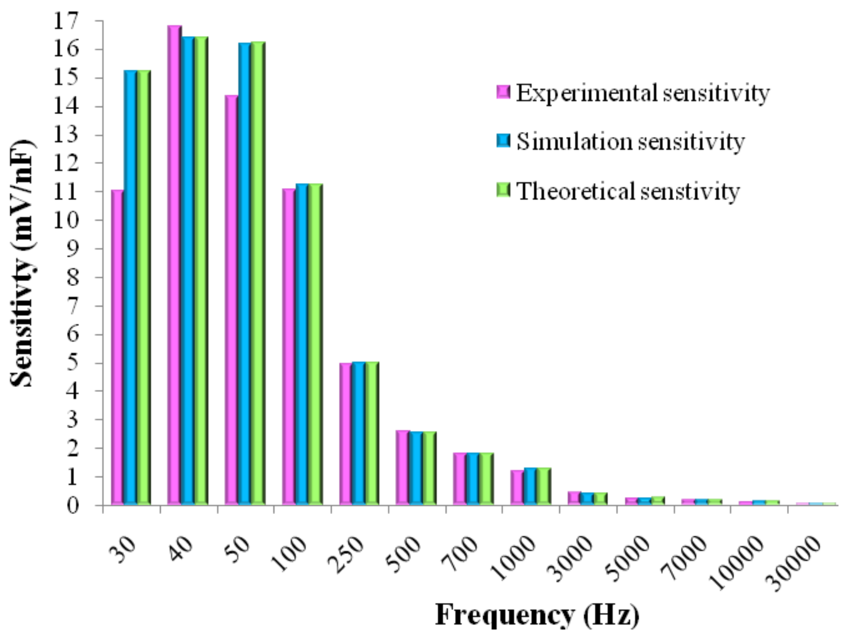


Figure 4-19 Sensitivity of the capacitor device for different frequencies

It was observed that when a larger air bubble entered the point of detection in the capacitor device followed immediately by another bubble, the system reacted to this situation by detecting the two as one air bubble.

Unfortunately, due to the limitations of the apparatus used in this study, it was not possible to produce air bubbles with diamter from 1μm to 619 μm. Therefore, the effect of air bubble within this range was not investigated.

This device eventually has an operating limit. The device output did not respond at a low frequency of 10 Hz, and at a high frequency of 250 kHz.

4.3 Blood as a Dielectric Material of the Capacitor Device

In the following section, results were measured for five different samples, when real human blood is used as the dielectric material in the capacitor device, are compared with the simulated and theoretical results.

4.3.1 Experimental Blood Conditions

It was initially important to determine the properties of the blood samples used in this study. In Table 4-15, different types of blood were collected from different donors of different ages and gender. The measurements of the density, viscosity, and conductance of the blood samples are approximately the same as the values mentioned in the literature (Cutnell *et al*. 1998; Christorfer *et al* 2007). During the experiment, 29.7 $^{\circ}$C was the ambient temperature and 74.3% RH was the relative humidity.

Table 4-19 Blood samples and characteristics

Donor	Type	Gender	Age	Density(g/cm3)	Conductance(ms)	Viscosity(mPa.s)
1	A	male	25	1.059	15.28	3.41
2	A	male	28	1.061	16.04	3.24
3	B	male	21	1.059	15.18	3.33
4	O	female	25	1.062	15.78	3.28
5	O	male	37	1.061	15.14	3.42

For the experiments, only blood was introduced between the plates of the capacitor and the output voltage measured. The output voltage across the capacitor was measured when a frequency of 30 Hz was applied for each individual sample. The resistance of the resistor that is used was 130 kΩ, and the input voltage was 2.5 V. An air bubble was randomly injected into the blood stream and the diameter of the air bubble was measured.

A small amount of heparin (0.05 mL) was added to each sample, to prevent clotting and maintain the characteristics of blood. Different values of the capacitance of the capacitor were obtained when the samples were introduced between the capacitor plates. This was due to the different volume of blood that was added to the same volume of heparin, resulting in differences in density, viscosity, and conductance.

4.3.2 Human Blood Sample Donor-1

The blood sample from this donor contained 4.5 mL blood and 0.05 mL heparin as mentioned in Table 3-1. Table 4-16 shows that a signal of 30 Hz was applied to the circuit Figure 3-5 and the detection of air bubbles was possible by measuring the output voltage across the capacitor. The initial value of the capacitance of the capacitor device was 41.6 nF and output voltage 1.219 V for blood without an air bubble. When a 730 µm diameter air bubble was injected, the capacitance decreased to 40.93 nF and the output voltage increased to 1.237 V. The output voltage for both simulation results and theoretical predictions showed good agreement when compared to the measured output voltage. The table shows that when the air bubble diameter increases, the capacity decreases and the output voltage rises.

Table 4-20 Measured capacitance and voltage values for blood from donor-1 for several air bubble diameters at a frequency of 30 Hz

No	Capacitance of the capacitor (nF)	Air bubble diameter (mm)	Measured output voltage (V)	Simulated output voltage (V)	Theoretical output voltage (V)
1	41.60	0	1.219	1.238	1.238
2	40.93	0.73	1.237	1.247	1.249
3	40.37	1.25	1.250	1.256	1.257
4	39.50	2.10	1.267	1.270	1.271
5	37.44	4.30	1.289	1.303	1.303

Figure 4-30 shows that the relation between the output voltage and the capacitance of the capacitor is inversely proportional. The simulated results and theoretical predictions are in good agreement, the linearity error for the theoretical predictions was computed to be 0.01%, and for the simulated results was computed to be 0.1%. Conversely, for experimental measurements, the linearity error was computed to be 5.6%.

The sensitivity of the capacitor device for experimental measurements was found to be 16.4mV/nF; for the simulated result was found to be 15.8 mV/nF; and for the theoretical predictions was 15.6 mV/nF. It was noted that the same results were obtained using Dexran70 at a frequency of 40 Hz.

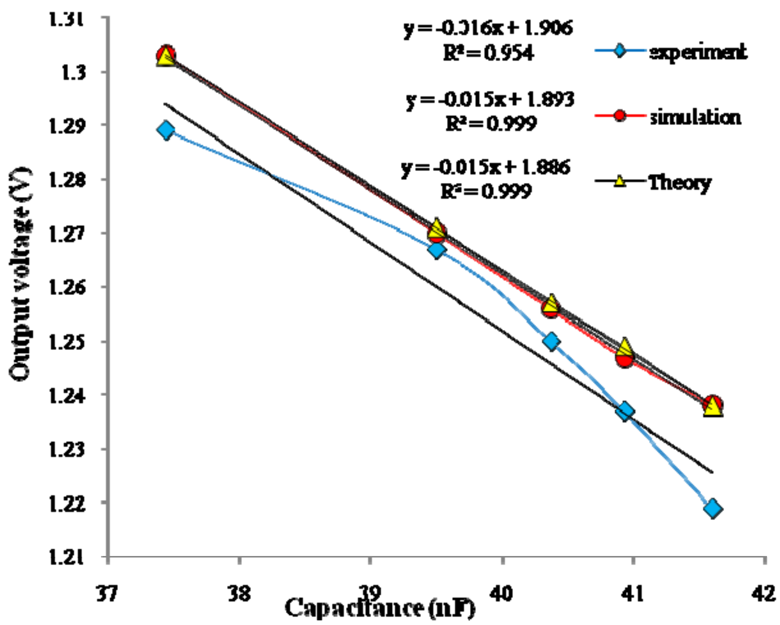


Figure 4-20 Output voltage versus capacitance of blood from donor-1

4.3.3 Human Blood Sample Donor-2

This sample of blood was also type A, containing 5 mL blood and 0.05 mL heparin. Table 4-17 verifies the relation between the output voltage of the capacitor device and the diameter of the detected air bubble in the blood. The table shows that the simulated and theoretical results are in very close agreement, and only two readings have 0.001 mV difference. The smallest diameter bubble of 820 μm made a significant change in the capacitance of the capacitor, and thus a significant change in the output voltage from the device. It was observed that the initial value of the capacitance i.e. 44 nF, was in close agreement with the initial value when the dielectric material was Dextran70 i.e. 43.5 nF.

Table 4-21 Measured capacitance and voltage values for blood from donor-2 for several air bubble diameters at a frequency of 30 Hz

No	Capacitance of the capacitor (nF)	Air bubble diameter (mm)	Measured output voltage (V)	Simulated output voltage (V)	Theoretical output voltage (V)
1	44.00	0	1.193	1.202	1.203
2	43.34	0.82	1.207	1.212	1.212
3	43.12	1.16	1.211	1.215	1.216
4	42.16	2.00	1.223	1.230	1.230
5	39.79	3.85	1.259	1.266	1.266

Figure 4-31 shows the linearity error was computed to be 0.6% for the experimental measurements, 0% for the simulated results, and 0.1% for theoretical predictions. The sensitivity was found to be 15.2 mV/nF for the experimental results; 15.2 mV/nF for simulated results; and 15 mV/nF for theoretical predictions.

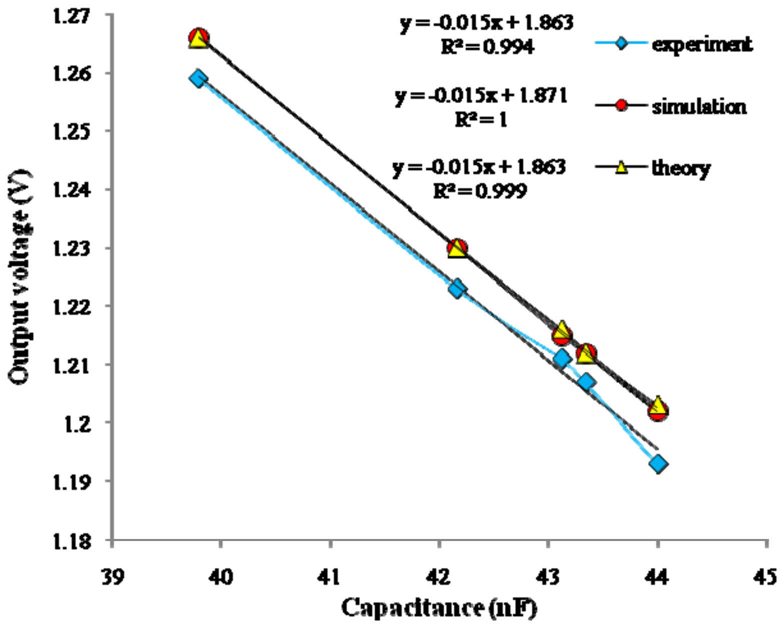


Figure 4-21 Output voltage versus capacitance of blood from donor-2

4.3.4 Human Blood Sample Donor-3

The blood sample contained 5.5 mL blood with 0.05 mL heparin. Results in Table 4-18 were obtained when a frequency 30 Hz was applied. It shows that the simulated results and theoretical prediction are in close agreement. The accuracy of the initial value of the output voltage for blood minus air bubble was 0.73% compared to 0.33% for blood with an 810 µm diameter air bubble. For instance, the output voltage changes from 1.213 V to 1.229 V in a measuring range of 810µm and the output voltage changes from 1.229 V to 1.232 V in a measuring change of 260 µm. Therefore, the capacitive device has a high sensitivity.

Table 4-22 Measured capacitance and voltage values for blood from donor-3 for several air bubble diameters at a frequency of 30 Hz

No	Capacitance of the capacitor (nF)	Air bubble diameter (mm)	Measured output voltage (V)	Simulated output voltage (V)	Theoretical output voltage (V)
1	42.70	0	1.213	1.222	1.222
2	41.93	0.81	1.229	1.233	1.233
3	41.68	1.07	1.232	1.237	1.238
4	40.76	2.06	1.247	1.251	1.251
5	37.91	4.31	1.288	1.295	1.296

In Figure 4-32 the linearity error was computed to be 0.5% for experimental measurements; 0.1% for simulated results, and 0.1% for theoretical results. The sensitivity of the capacitor device in this case was found to be 15.3 mV/nF for experimental measurements, 15.3 mV/nF for the simulated results, and 15.5 mV/nF for the theoretical predictions.

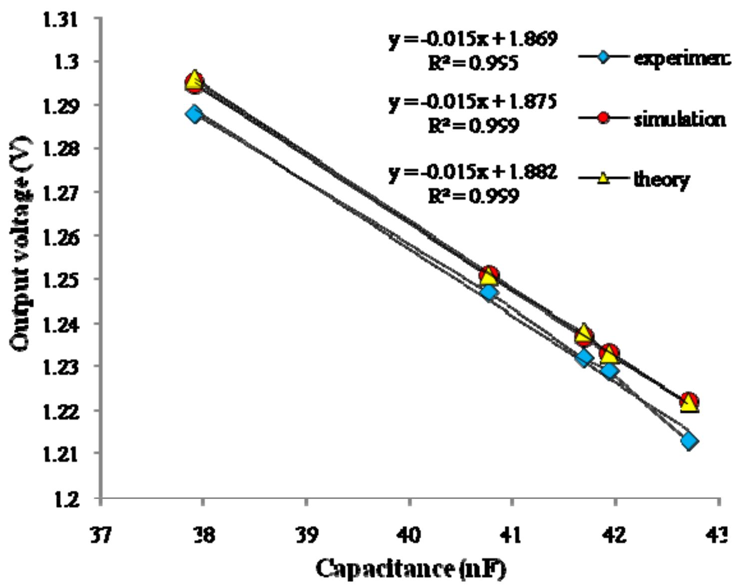


Figure 4-22 Output voltage versus capacitance of blood from donor-3

4.3.5 Human Blood Sample Donor-4

The blood sample from this donor contained 5 mL blood and 0.05 mL heparin. Table 4-19 shows the initial value of the capacitance of the device is 42.3 nF when the fourth sample of blood was introduced between the capacitor plates. The output voltage changes from 1.221 V to 1.238 V when a 1mm bubble is introduced; from 1.238 V to 1.248 V with a measurement change of 910 µm and from 1.248 V to 1.25 V with a measurement range of 120 µm. Therefore, the capacitive device has a high sensitivity.

Table 4-23 Measured capacitance and voltage values for blood from donor-4 for several air bubble diameters at a frequency of 30 Hz

No	Capacitance of the capacitor (nF)	Air bubble diameter (mm)	Measured output voltage (V)	Simulated output voltage (V)	Theoretical output voltage (V)
1	42.30	0	1.221	1.227	1.228
2	41.38	1.00	1.238	1.241	1.242
3	40.70	1.91	1.248	1.252	1.252
4	40.57	2.03	1.250	1.254	1.254
5	38.50	3.16	1.280	1.286	1.286

As shown in Figure 4-33 the simulated results are in close agreement with theoretical results, while the measured results are in good agreement with simulated results. The linearity error was computed to be 0.35% for measured results, and 0.01% for both theoretical and simulated results. The sensitivity of the device was found to be 15.3 mV/nF for the experimental measurements; 15.6 mV/nF for simulation; and 15.3 mV/nF for theoretical predictions.

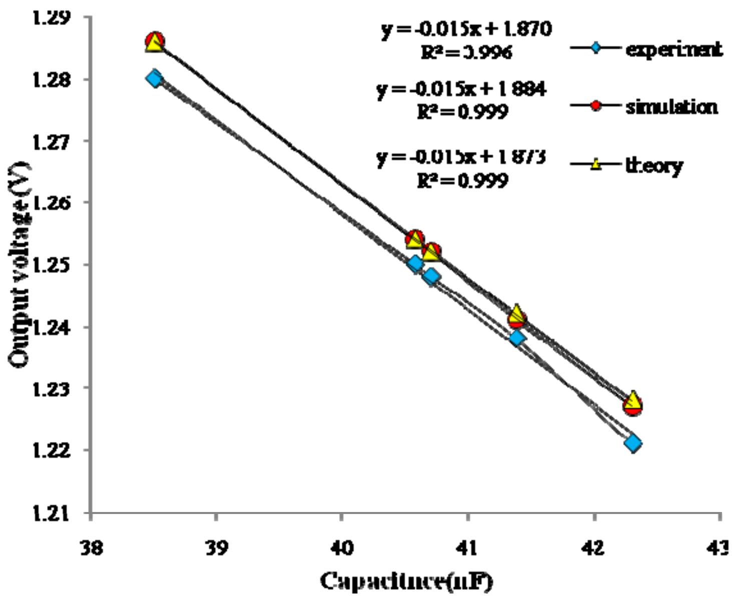


Figure 4-23 Output voltage versus capacitance of blood from donor-4

4.3.6 Human Blood Sample Donor-5

The fifth sample contained 5 mL of blood and 0.05 mL heparin. From Table 4-20, when the capacitance of the capacitor was measured without air bubbles i.e. 43.1 nF it was in close agreement to the capacitance when Dextran70 solution was used i.e. 43.5nF. The experimental results were compared to the theoretical solution, computed from Equation (3.23), as the true values. Thus the accuracy was found to be 0.41% for the initial value.

Figure 4-34 shows the linearity error was calculated and computed to be 0.52% for the measured; 0.02% for simulated; and 0.04% for the theoretical results. For this sample the sensitivity was found to be 15.6 mV/nF for the experimental measurements; 15.26 mV/nF for simulated results and 15.36 mV/nF for theoretical predictions. Using this sample repeatability and precision of the device has been calculated and it is less than 0.13% of output voltage error (Appendix A).

Table 4-24 Measured capacitance and voltage values for blood from donor-5 for several air bubble diameters at a frequency of 30 Hz

No	Capacitance of the capacitor (nF)	Air bubble diameter (mm)	Measured output voltage (V)	Simulated output voltage (V)	Theoretical output voltage (V)
1	43.10	0	1.211	1.216	1.216
2	42.44	0.78	1.218	1.225	1.226
3	41.54	1.83	1.231	1.239	1.239
4	41.27	2.13	1.239	1.243	1.243
5	38.79	3.77	1.277	1.281	1.282

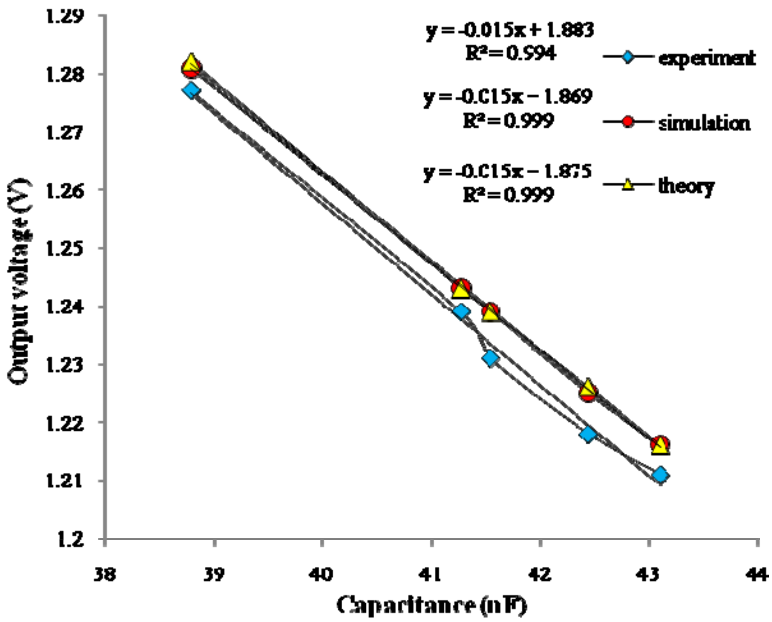


Figure 4-24 Output voltage versus capacitance of blood from donor-5

4.4 Summary of Blood as the Dielectric Material of the Device

Initially, only blood existed in between the capacitor plates and then output voltage was measured. Air bubbles were injected and the change in the ouput voltage was measured. The initial values of the capacitor when different samples were introduced between the capacitor plates were 41.6 nF,44 nF,42.7 nF, 42.3 nF, and 43.1nF. The capacitance of each sample is different from the others may be due to the differences in the time sampling. It was not possible to conduct further tests, using different frequencies or more diameters of air bubbles, as blood clotting occurs 24 hours after sampling from donors.

Figure 4-35 shows the output voltage from each donor samples, plotted as a function of change in capacitance of the device. All the results seem to be in the same range. A few points were not in the range, due to the different values for the capacitance of the capacitor.

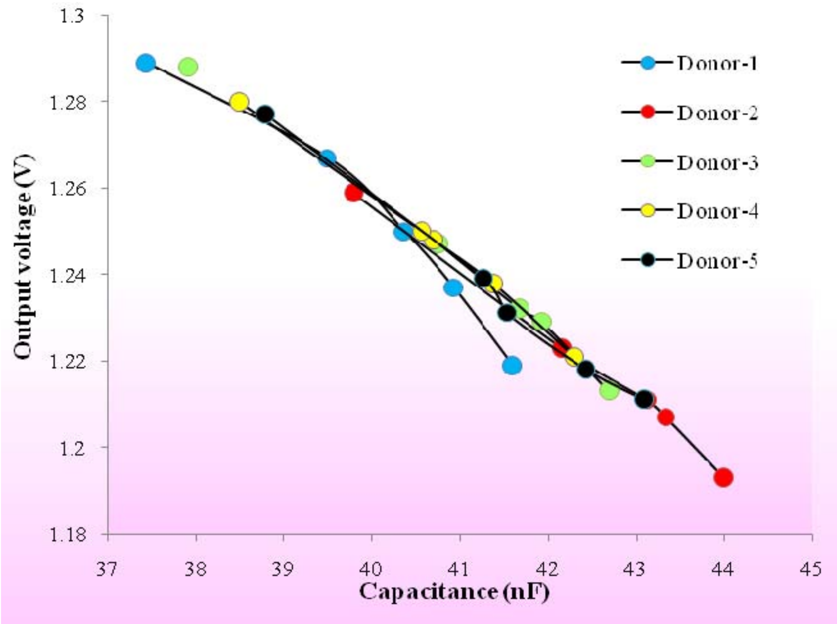


Figure 4-25 Output voltage versus capacitance for all blood samples

Figure 4-36 verifies the relation between the output voltage and the diameter of air bubbles for the different blood samples. Results show that the difference in the output voltage for all samples in the presence of blood, minus air bubble, was only slight.

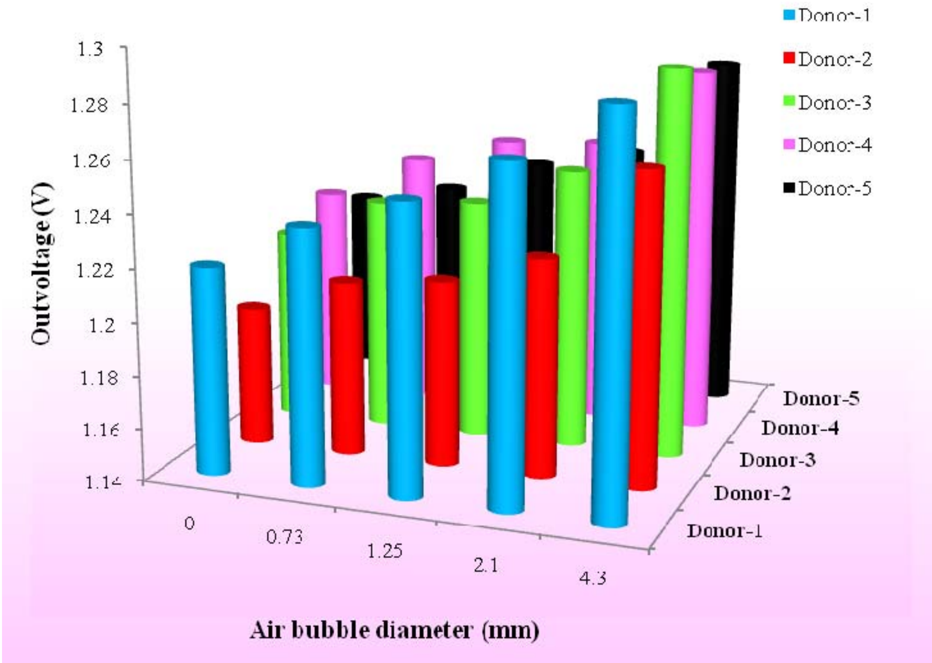


Figure 4-26 Output voltage versus air bubble diameters for all blood samples

During the experiment, it was noted that the most accurate reading was obtained when the air bubble was in the middle of the capacitor device.

Figure 4-37 shows that the sensitivity of the capacitor device using different samples of blood seems to be almost the same. The experimental sensitivity shows close agreement with simulation and theoretical one.

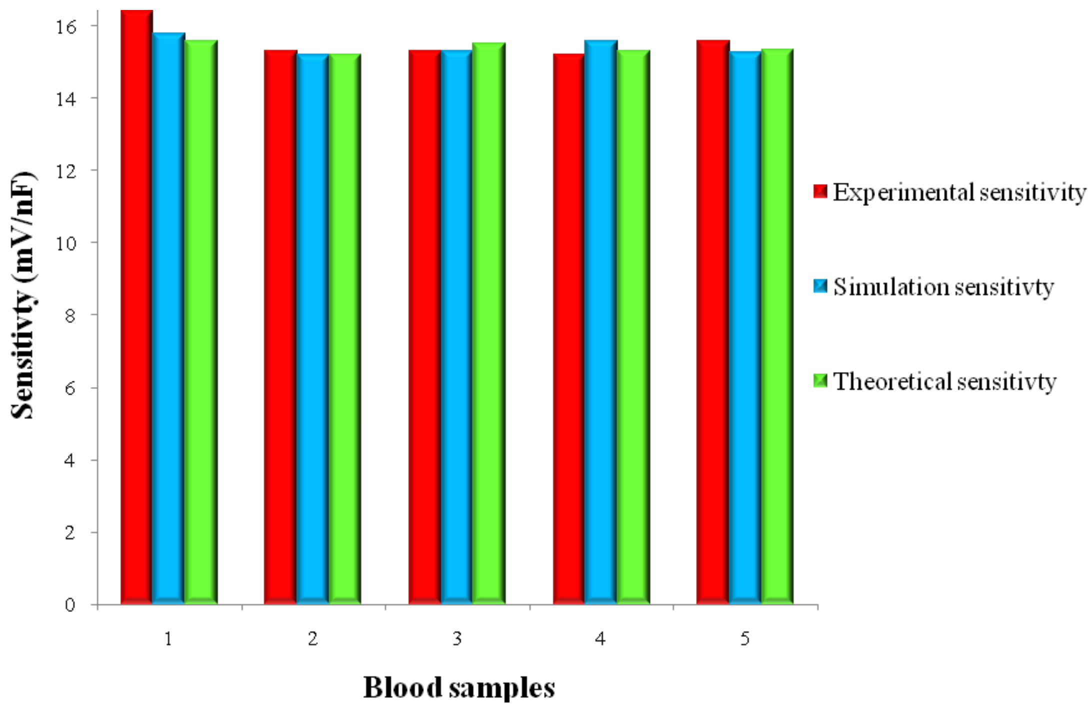


Figure 4-27 Experimental Sensitivity compared to the simulation and theoretical predictions of the blood samples

4.5 Comparison between Dextran70 Solution and Blood Results

Comparing the experimental results obtained from both dielectric materials i.e. Dextran70 and human blood, it was observed that for both cases the introduction of air bubbles in the stream made a significant change to the measured data.

A large change in the capacitance was obtained when the air bubbles were introduced, which made the detection process easier for both Dextran70 and blood. For instance, for 30 Hz with Dextran70 as a dielectric material and 620 μm diameter of air bubble, the change in the capacitance was 0.4 nF. For the blood (first sample as an example) 730 μm produced a 0.67 nF change in capacitance. These results show that the capacitor device has the ability to detect a size of air bubble of less than this diameter.

Comparing Dextran70 solution and blood results, it may be said that the capacitor device was ideally stable with the ambient temperature and the relative humidity in both cases. Theoretical predictions and simulation presented in this study are in good agreement with experimental findings.

Sensitivity of the capacitor device for both dielectric materials shows a good agreement. However, better sensitivity was obtained at 40 Hz for dextran70 solution. It was 16.8 mV/nF compared to 16.4 mV/nF for the first sample of blood. The difference in the sensitivity occurred due to the difference in characteristics of the Dextran70 and Human blood i.e. density, viscosity, and conductance.

Chapter 5

5. CONCLUSION AND RECOMMENDATIONS

5.1 Conclusion

This chapter presents the major purpose and progress that this research intends to achieve. This is followed by the limitation of this study and finally some recommendations are given for future research.

The purpose of this study was to construct a capacitor device capable of detecting potentially fatal air bubbles occurring in extracorporeal blood circuits e.g. hemodialysis machine. It was necessary to produce a device with sufficient sensitivity to detect air bubbles of differing diameter size, although research to date has not identified which size of air emboli may be fatal. The intention of this research was to concentrate on the device and the relationship between capacitance and air bubble size and the output voltage from the device when air bubbles appeared. To explore the sensitivity of the capacitor, two dielectric materials were used: Dextran70 and human blood.

The research revealed several findings, most notably that the device appears to represent a reliable method to detect a single air bubble in a circuit. Experimentation also indicates that the relation between the capacitance of the device and air bubble diameter, is inversely proportional. In other words, as the air bubble diameter increases, capacitance decreases resulting in increases of the output voltage. It was also observed that better sensitivity was obtained at low frequency. For the dielectric material Dextran70, high sensitivity was obtained at 40 Hz i.e. 16.8 mV/nF. The frequency for all blood samples was 30 Hz, with one sample revealing similarly high sensitivity i.e. 16.4 mV/nF. The standard deviation of this device using Dextran70 was found to be 7.071×10^{-4} for blood it was found to be from 1.414×10^{-3} to 7.071×10^{-4}. The coefficient of variation using Dextran70 was found to be 0.041% for this device at 30 kHz and for blood it was found to be 0.0585 up to 0.12%. The smallest air bubble diameter that has been detected using this capacitor device is 620 µm, and this is the one of the main contributions of this study.

Previous experiments for detecting air emboli failed to operate during exposure to air bubble foam. However, this device was able to detect foam and continue to operate. Furthermore, measurements did not appear to be affected by humidity and ambient temperature. In conclusion, the objectives of this study are achieved and the device has demonstrated good reliability and cost-effectiveness, compared to ultrasound detection methods.

5.2 Recommendations and Limitations of Research

This study hopefully represents the beginning of further, more detailed experimentation using a capacitor to monitor air bubbles. For example it is not yet known how the device reacts to a quantity of air bubbles of varying diameters. To test this particular device, only a single air bubble was used, therefore all results are based on one bubble.

The device itself requires modification. For biomedical application, it requires greater accuracy and the ability to monitor even smaller diameter air bubbles. Further modification may reveal a sensitive, cheaper alternative to platinum for fabrication of the parallel plates of the device.

Previous studies have highlighted the unreliability of ECBC machines to warn of the presence of emboli in the lines. It is therefore suggested that this model should be equipped with an alarm system.

It has only been in the last 30 years that the life- threatening presence of bubbles has been recognized, and this study has at least shown that it is possible to detect air emboli. However, the problem of air bubbles awaits a breakthrough technological solution to detect and eliminate them before they become life-threatening. Co-operation between medical specialists, scientists and engineers is recommended to provide the technology which facilitates better care for patients and thereby reduces fatalities.

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APPENDICES

Appendix A

Instrumentations and Calculation of Viscosity, Accuracy, Linearity Error, and Sensitivity

Hot-plate magentic stirring
Made in UK (By Bibby Sterrilin LTD)
230 volt, 50 Hz

AB204-S Balance
Made in Swizerland (METTLER TOLEDO)
8-14.5 volt, 50-60 Hz

Portable Density Meter (type:Densti30P)
Made in Japan (METTLER TOLEDO)
Accuracy +/- 0.0005
Temprature range (10-40)^{0}C

Conductance Meter / TDS/^{0}C/^{0}F Meter
Made in Singapore (EUTECH)

Tamson Viscometer Unit
Model: ARMFIELD

Absolute Coolant Proof Caliper (No. 99MAD011B)
Resolution= 0.01mm
Repeatability= 0.01mm
Accuracy= +/- 0.02mm
Operating Temprature=0 to 40 ^{0} C
Made in Japan

Thermo-Hygrometer
Temperature Range= 0^{0} C - 50^{0} C , 32^{0} F - 122^{0} F
Resolution= 0.1^{0} C
Accuracy= +/- 1^{0} C
Humidity Range (2%-98%) RH
Resolution= 1%RH
Accuracy= +/- 5%RH

Syringe with diameter 0.01 mm
Made in Korea

Oscilloscope

- TDS3012B
- With two channel color Digital phosphor
- 2 MHz
- Made in USA

Function Generator

- INSTEK
- Model GFG-825OA
- Made in Malaysia

Digital Multimeter

- FLUKE.
- Accuracy: ±0.001 mV.
- Made in USA

Digital LRC meter

- CROTECH
- Auto compute 4910

Thermo-Hygrometer

- Temperature range: 0°C- 5°C
- Accuracy for temperature:±1
- Humidity range: 2%- 98% RH
- Accuracy:±5% RH
- Made in China

Calculations of the viscosity

For Dextran70 solution. (Dextran70 solution from Benua Sains SDN BHD Company, Selangor Darul Ehsan, Malaysia. With density 1.06kg/m^3The price is 2,400RM.)

sample	Efflux time (sec)	Viscometer constant (mm^2/s^2)	Density (g/cm^3)	Viscosity (mPa.s)
Dextran70	32.95	0.0979	1.057	3.41±0.1

For blood samples

Class	Efflux time (sec)	Viscometer constant (mm^2/s^2)	Density ($g/cm^{3)}$	Viscosity (mPa.s)
A	32.93	0.0979	1.059	3.41±0.1
A	31.14	0.0979	1.61	3.24±0.1
B	32.18	0.0979	1.059	3.33±0.1
O	31.59	0.0979	1.062	3.28±0.1
O	33.02	0.0979	1.061	3.42±0.1

Calculations of the accuracy

$$Accuracy = \frac{the\ ture\ value - measured\ value}{the\ true\ value}$$

Calculations of the linearity error and sensitivity

In applying the method of least squares, it assumes that a straight line is good model for the relationship between (y) and (x) axis as given by the equation:

$$y = mx + b$$

From this equation m is the slope of the straight line which is represents the sensitivity. The vertical deviation of each point from the straight line is called residual. The line generated by the least squares method is the one that minimizes the sum of the squares of the residuals for all of the points. The least-squares value on the chart represents the linearity error.

Precision

Two terms are widely used to describe the precision of a set of replicate data including standard deviation and coefficient of variation.

The mean ($\bar{x}$) of a set of data defined by the equation:

$$\bar{x} = \frac{\sum_{i=0}^{N} x_i}{N}$$

Where x_i represents the value of the *ith* measurements. N is number of measurements.

The standard deviation provides statically significant measures of the precision of a data. The standard deviation (s) is given by the equation:

$$s = \sqrt{\frac{\sum_{i=0}^{N} \left(x_i - \bar{x}\right)^2}{N-1}}$$

The coefficient of variation (CV) for the data is given by:

$$CV = \frac{s}{\bar{x}} \times 100\%$$

For example:

For the blood sample from donor-5 the precision was found from the table below

$Capacitance_1$ (nF)	Air bubbles diameter (mm)	Output $voltage_1$ (mV)	$Capacitance_2$ (nF)	Air bubbles diameter (mm)	Output $voltage_2$ (mV)
43.10	0	1.211	43.10	0	1.213
42.44	0.78	1.218	42.44	0.78	1.217
41.54	1.83	1.231	41.54	1.83	1.231
41.27	2.13	1.239	41.27	2.13	1.239
38.79	3.77	1.277	38.79	3.77	1.277

From the first row:

$\bar{x}$=1.212

s=1.414x10^{-3}

CV=0.12%

From the second row:

$\bar{x}$=1.2175

s=7.071x10^{-4}

CV=0.058%

Appendix B

EFFECTS OF AMBIENT TEMPARTURE AND RELATIVE HUMIDITY

Effects of ambient temperature and relative humidity in the capacitor device measurements

The table below shows the effects of measuring the capacitance and output voltage for several values of the air bubbles diameters at 30 Hz

Temperature (˚C)	Humidity (RH %)	Air bubbles diameter (mm)	Capacitance (nF)	Output voltage (mV)
27.9	53	0	43.50	1.208
25.0	56	0	43.50	1.208
28.1	61	0.62±0.02	43.10	1.217
26.2	55	0.62±0.02	43.10	1.217
28.0	63	1.66±0.02	42.47	1.225
25.0	55	1.66±0.02	42.47	1.225
27.8	60	1.86±0.02	41.88	1.232
28.0	52	1.86±0.02	41.88	1.232
25.1	57	2.29±0.02	41.32	1.238
26.0	53	2.29±0.02	41.32	1.238
25.3	53	2.8±0.02	41.19	1.242
25.5	55	2.8±0.02	41.19	1.242
27.6	51	3.7±0.02	40.03	1.248
25.0	53	3.7±0.02	40.03	1.247
27.1	60	4.1±0.02	39.10	1.259
25.2	55	4.1±0.02	39.10	1.259

The table below shows the effects of measuring the capacitance and output voltage for several values of the air bubbles diameters at 30 kHz.

Temperature (˚C)	Humidity (RH %)	Air bubbles diameter (mm)	Capacitance (nF)	Output voltage(mV)
27.6	63	0	43.5.0	1.620
27.0	55	0	43.5.0	1.620
27.5	52	0.66±0.02	42.87	1.653
28.1	61	0.66±0.02	42.87	1.652
25.1	66	1.66±0.02	42.47	1.665
25.0	55	1.66±0.02	42.47	1.665
28.0	52	1.88±0.02	41.84	1.700
27.7	53	1.88±0.02	41.84	1.700
25.0	55	2.29±0.02	41.32	1.718
27.3	52	2.29±0.02	41.32	1.718
25.1	56	2.82±0.02	41.18	1.723
27.0	61	2.82±0.02	41.18	1.723
26.3	52	3.71±0.02	40.01	1.765
28.0	52	3.71±0.02	40.01	1.765
28.0	63	4.21±0.02	38.86	1.824
25.6	55	4.21±0.02	38.86	1.824

Appendix C

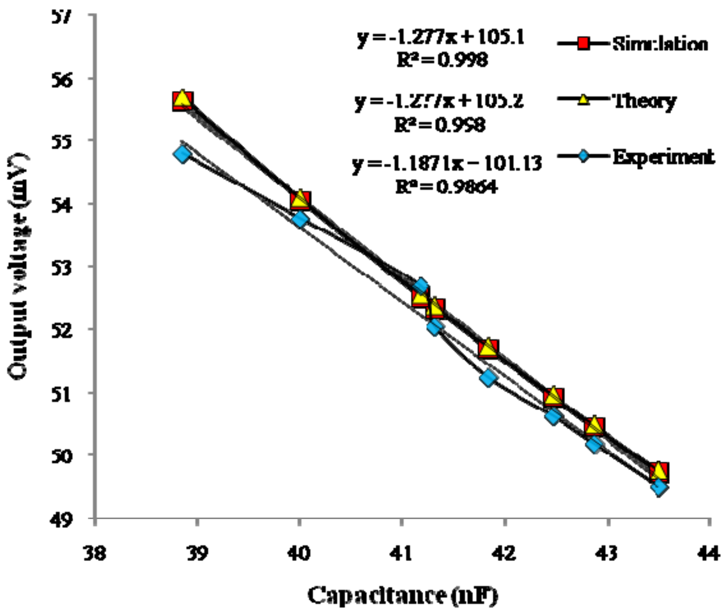
Results of the Circuit at a Frequency of 1 kHz

Percentage difference for the measured data compared to theoretical prediction at 1 Hz

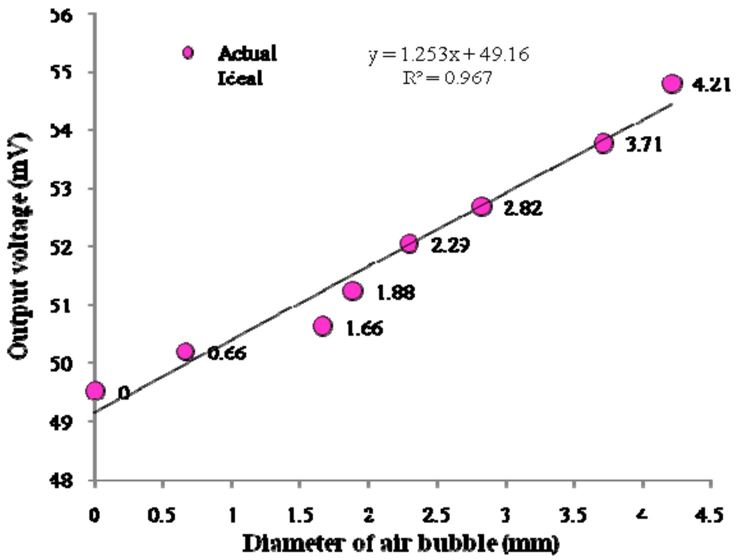
Air bubble diameters (mm)	0	0.64	1.66	1.88	2.29	2.82	3.71	4.21
Percentage difference (%)	0.5	0.59	0.65	0.95	0.63	0.25	0.59	1.6

Measured capacitance and voltage values of Dextran70 for several air bubble diameters at frequency of 1 kHz

No.	Capacitance of the capacitor (nF)	Air bubble diameter (mm)	Experimental output voltage (mV)	Simulated Output voltage (mV)	theoretical output voltage (mV)
1	43.50	0	49.51	49.716	49.758
2	42.87	0.66±0.02	50.19	50.446	50.488
3	42.47	1.66±0.02	50.63	50.921	50.963
4	41.84	1.88±0.02	51.24	51.687	51.730
5	41.32	2.29±0.02	52.05	52.337	52.380
6	41.18	2.82±0.02	52.69	52.515	52.558
7	40.01	3.71±0.02	53.77	54.049	54.090
8	38.86	4.21±0.02	54.80	55.647	55.693



Output voltage versus capacitance at a frequency of 1 kHz



Output voltage versus air bubble diameter at a frequency of 1 kHz

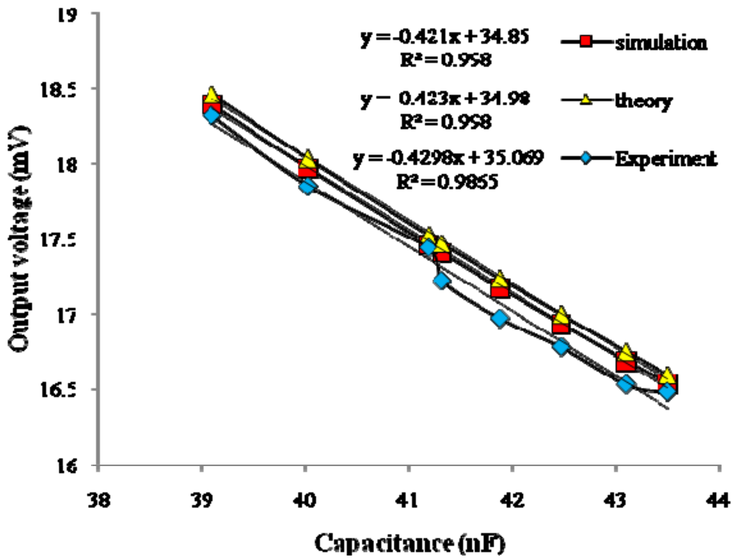
Results of the Circuit at a Frequency of 3 kHz

Percentage difference for the measured data compared to theoretical prediction at 3 Hz

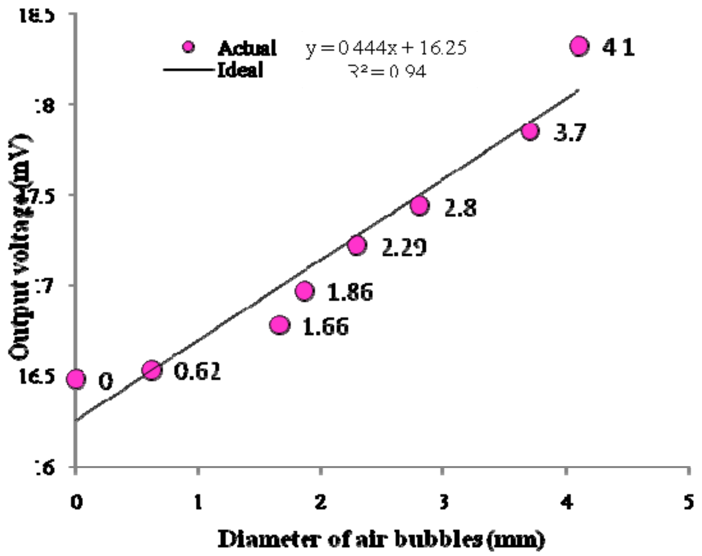
Air bubble diameters (mm)	0	0.62	1.66	1.85	2.29	2.80	3.70	4.10
Percentage difference (%)	0.66	1.29	1.26	1.52	1.41	0.47	0.99	0.75

Measured capacitance and voltage values of Dextran70 for several air bubble diameters at frequency of 3 kHz

No.	Capacitance of the capacitor (nF)	Air bubble diameter (mm)	Experimental output voltage (mV)	Simulated output voltage (mV)	Theoretical output voltage (mV)
1	43.5	0	16.48	16.535	16.591
2	43.1	0.62±0.02	16.53	16.687	16.746
3	42.47	1.66±0.02	16.78	16.935	16.994
4	41.88	1.86±0.02	16.97	17.173	17.233
5	41.32	2.29±0.02	17.22	17.407	17.467
6	41.19	2.8±0.02	17.44	17.462	17.522
7	40.03	3.7±0.02	17.85	17.967	18.03
8	39.1	4.1±0.02	18.32	18.394	18.459



Output voltage versus capacitance at a frequency of 3 kHz



Output voltage versus air bubbles diameter at a frequency of 3 kHz

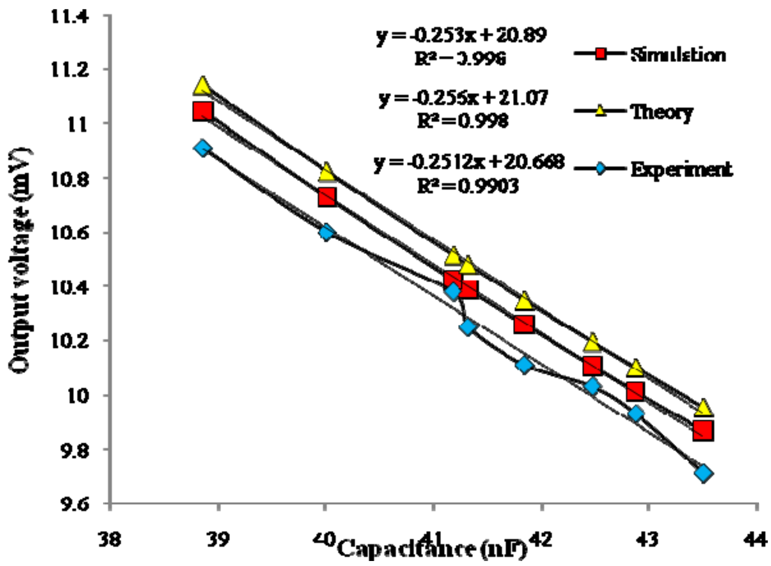
Results of the Circuit at a Frequency of 5 kHz

Percentage difference for the measured data compared to theoretical prediction at 5 Hz

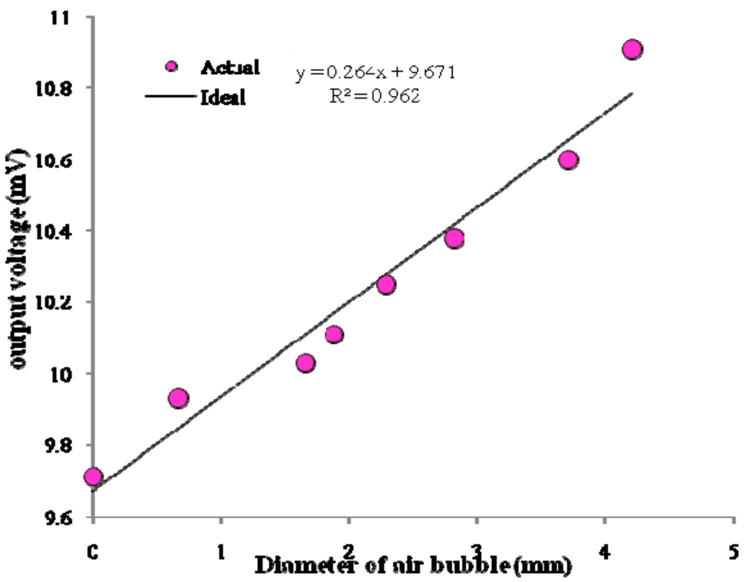
Air bubble diameters (mm)	0	0.66	1.66	1.88	2.29	2.82	3.71	4.21
Percentage difference (%)	2.46	1.7	1.63	2.32	2.2	1.29	2.07	2.09

Measured capacitance and voltage values of Dextran70 for several air bubble diameters at a frequency of 5 kHz

No.	Capacitance of the capacitor (nF)	Air bubble diameter (mm)	Experimental output voltage (mV)	Simulated output voltage (mV)	Theoretical output voltage (mV)
1	43.50	0	9.71	9.868	9.955
2	42.87	0.66±0.02	9.93	10.013	10.102
3	42.47	1.66±0.02	10.03	10.108	10.196
4	41.84	1.88±0.02	10.11	10.260	10.350
5	41.32	2.29±0.02	10.25	10.389	10.481
6	41.18	2.82±0.02	10.38	10.424	10.516
7	40.01	3.71±0.02	10.60	10.729	10.824
8	38.86	4.21±0.02	10.91	11.047	11.144



Output voltage versus capacitance at a frequency of 5 kHz



Output voltage versus air bubbles diameter at a frequency of 5 kHz

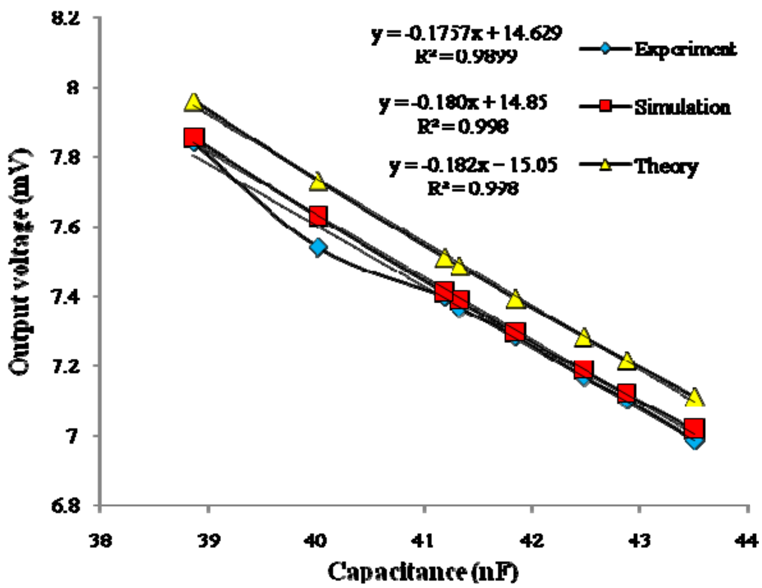
Results of the Circuit at a Frequency of 7 kHz

Percentage difference for the measured data compared to theoretical prediction at 7 Hz

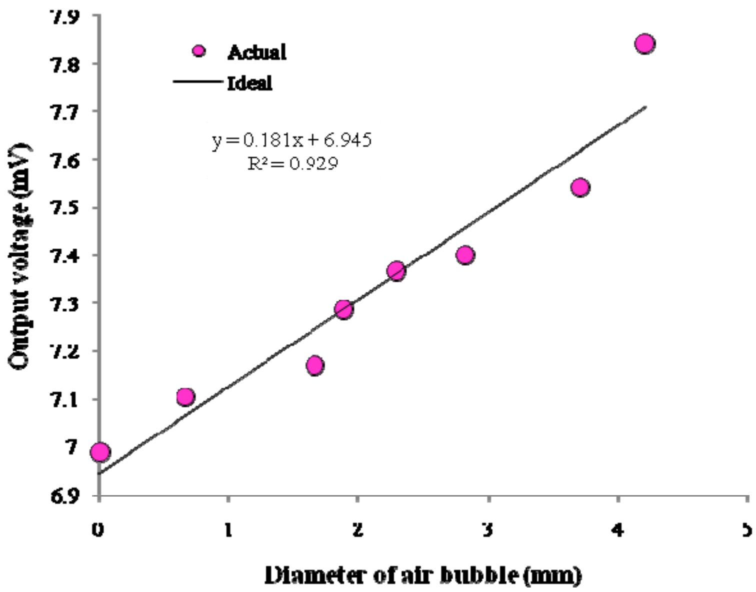
Air bubble diameters (mm)	0	0.66	1.66	1.88	2.29	2.82	3.71	4.21
Percentage difference (%)	1.74	1.55	1.56	1.46	1.6	1.49	2.47	1.5

Measured capacitance and voltage values of Dextran70 for several air bubble diameters at a frequency of 7 kHz

No.	Capacitance of the capacitor (nF)	Air bubble diameter (mm)	Experimental output voltage (mV)	Simulated output voltage (mV)	Theoretical output voltage (mV)
1	43.50	0	6.987	7.016	7.111
2	42.87	0.66±0.02	7.103	7.119	7.215
3	42.47	1.66±0.02	7.169	7.186	7.283
4	41.84	1.88±0.02	7.285	7.294	7.393
5	41.32	2.29±0.02	7.366	7.386	7.486
6	41.18	2.82±0.02	7.399	7.411	7.511
7	40.01	3.71±0.02	7.540	7.628	7.731
8	38.86	4.21±0.02	7.840	7.854	7.960



Output voltage versus capacitance at a frequency of 7 kHz



Output voltage versus air bubble diameter at a frequency of 7 kHz

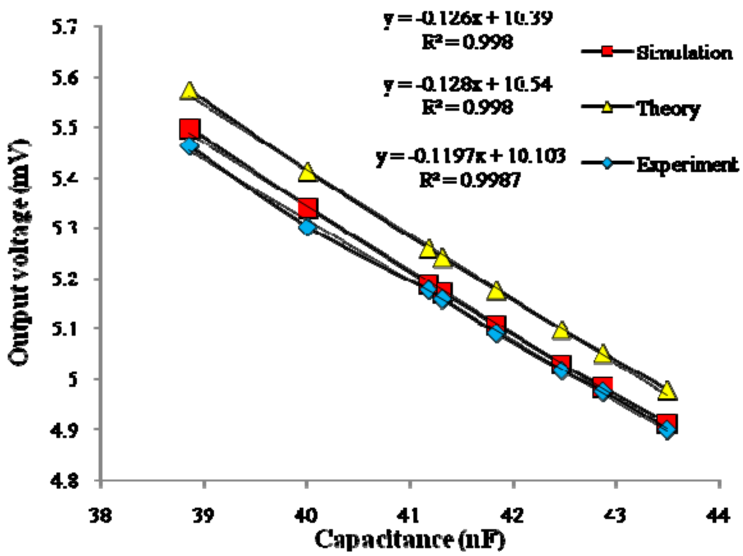
Results of the Circuit at a Frequency of 10 kHz

Percentage difference for the measured data compared to theoretical prediction at 10 Hz

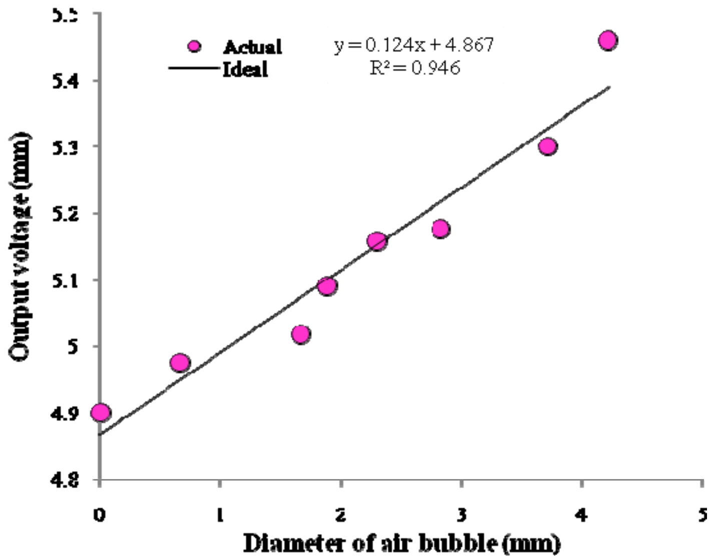
Air bubble diameters (mm)	0	0.66	1.66	1.88	2.29	2.82	3.71	4.21
Percentage difference (%)	1.57	1.49	1.57	1.64	1.57	1.56	2.03	1.99

Measured capacitance and voltage values of Dextran70 for several air bubble diameters at a frequency of 10 kHz

No.	Capacitance of the capacitor (nF)	Air bubble diameter (mm)	Experimental output voltage (mV)	Simulated output voltage (mV)	Theoretical output voltage (mV)
1	43.50	0	4.899	4.911	4.977
2	42.87	0.66±0.02	4.975	4.983	5.050
3	42.47	1.66±0.02	5.017	5.029	5.097
4	41.84	1.88±0.02	5.09	5.106	5.175
5	41.32	2.29±0.02	5.158	5.170	5.240
6	41.18	2.82±0.02	5.176	5.188	5.258
7	40.01	3.71±0.02	5.301	5.339	5.411
8	38.86	4.21±0.02	5.461	5.497	5.572



Output voltage versus capacitance at a frequency of 10 kHz



Output voltage versus air bubble diameter at a frequency of 10 kHz

LIST OF PUBLICATIONS

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Mawahib Gafare Abdalrahman Ahmed, Abdallah Belal Adam, John Ojur Dennis and GailSylvia Steele. A low-cost capacitive device for detection of potentially fatal air bubbles in extracorporeal blood circuits. Journal of Sensors and actuators. SNA-S-09-00421.

Mawahib Gafare Abdalrahman Ahmed, Abdallah Belal Adam, John Ojur Dennis and GailSylvia Steele. Detection of Air Embolism in Extracorporeal Blood Circuits Using a Capacitive Device and Human Blood as the Dielectric Material. Journal of Sensors and actuators. SNA-S-09-00423.

CONFERENCE PAPERS

Mawahib Gafare Abdalrahman Ahmed, Abdallah Bellal Adam, John Ojur Dennis. "Detection of Air Bubbles in Artificial Kidney using Capacitive Detector at a Frequency of 2MHz". National Postgraduate Conference on Engineering Science and Technology (NPC) 31 March 2008, Universiti Teknologi PETRONAS, Malaysia

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Mawahib Gafare Abdalrahman Ahmed, Abdallah Bellal Adam, John Ojur Dennis, and Gail Sylvia Steele. Capacitor Device for Air Bubbles Monitoring. The International Conference on Control, Instrumentation and Mechatronics Engineering (CIM 2009). 2-3 June 2009. Malacca, Malaysia

AWARDS

Mawahib Gafare Abdalrahman Ahmed, Abdallah Bellal Adam, John Ojur Dennis. "Capacitive Micro Air Bubbles Detector in Moving Blood (Artificial Kidney Application)". Engineering Design Exhibition 21 Universiti Teknologi PETRONAS. 16th – 17th April 2008. Bronze Medal.

Mawahib Gafare Abdalrahman Ahmed, Abdallah Bellal Adam, John Ojur Dennis. "Capacitive Air Bubble Detector Operated at 30 kHz for Application in Hemodialysis" Engineering Design Exhibition 22 Universiti Teknologi PETRONAS. 15th – 16th October 2008. Silver Medal.