KWAME NKRUMAH UNIVERSITY OF SCIENCE AND

TECHNOLOGY

COLLEGE OF ENGINEERING
DEPARTMENT OF COMPUTER ENGINEERING
BIOMEDICAL ENGINEERING
FINAL YEAR PROJECT
AUTOMATED NEONATAL EXCHANGE TRANSFUSION SYSTEM

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DECLARATION

We hereby declare that, except for references and figures, the content of this report is exclusively based on our individual contributions through research, ingenuity and skill. This project was carried out as a requirement for the award of a BSc. Biomedical Engineering Degree under the supervision of Mr. Prince Odame in the 2021/2022 academic year.

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ABSTRACT

This project to design, fabricate and test a device for the automation of the exchange transfusion process which is a procedure performed on neonates with severe cases of jaundice or hyperbilirubinemia. This project has become necessary as a result of the unavailability of a device to perform this task in Ghana especially in rural areas and the complications associated with performing this procedure manually.

Exchange transfusion is a procedure which is more pronounced in some parts of Africa as well as rural areas around the world where early detection devices for hyperbilirubinemia and jaundice are rarely found. Treatment methods are also limited due to the unavailability of medical devices such phototherapy devices and incubators in these areas. Sunlight exposure which used to be a considered method for managing such cases is no longer recommended for treatment of jaundice due to risk of sunburn and overheating. These among other problems make the occurrence of very severe cases of hyperbilirubinemia and jaundice in infants more pronounced. Phototherapy becomes less effective for treating infants with severe hyperbilirubinemia and there is a need for different treatment methods the most common one being exchange transfusion and just like any technique in science, the application of this process can be improved through engineering to improve its efficiency and effectiveness.

The aim of the project will be to reduce human intervention in the exchange transfusion process. The proposed project would be beneficial for medical practitioners to do proper and better treatment devoid of human errors, a higher guarantee for consistency, accuracy and efficiency all at a reasonable cost.

DEDICATION

This project is dedicated to our parents, whose prayers and encouragements have kept us throughout these four years and to our lecturers for their consistent support throughout our stay in the university.

AKNOWLEDGEMENT

We thank the Almighty God for providing us with the wisdom, knowledge understanding and strength to complete this project.

We are also grateful to our lecturer ad supervisor, Mr. Prince Odame, for his support, invaluable advice and guidance throughout our stay in the school and during this project.

In addition we would like to extend our gratitude to Mr. Godwin, Mr. Gyan and all staff of the pharmacy department animal house for their help and guidance throughout this project.

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CHAPTER ONE

INTRODUCTION

1.1 BACKGROUND

It has become a common occurrence in Ghana for newborns to be readmitted in hospital usually within the first week of birth and this is often due to blood related complications such as jaundice and hemolytic disease of the newborns. These develop as the result of the newborns not being able to break down unconjugated bilirubin or due to other factors such as blood incompatibilities and although a lot of these cases are managed, in some cases due to the level of bilirubin in the blood further complications may arise if immediate and effective treatment is not given. Severe cases may lead to kernicterus which a form of brain damage which occurs due to bilirubin in the brain, deafness, cerebral palsy, mental retardation and even death.

Early detection and treatment of blood related diseases in infants such hemolytic disease of the newborn jaundice and hyperbilirubinemia may be difficult in newborns because it may not be visible in the neonate's skin until the bilirubin concentration levels have increased (exceeds 70 – 100 micromol/L) also prediction of the degree of jaundice in darkly pigmented newborns particularly may be inaccurate. Alternately, the eyelids through which jaundice can also be detected since it appears in the sclera of the eye with SBR of 35 – 40 micromol/L are usually closed or swollen. Advances such as the use of percutaneous bilirubinometers in the early

detection of jaundice and other blood related diseases made in some countries have made the occurrence of severe jaundice, hyperbilirubinemia and hemolytic disease of the newborn relatively uncommon.

This occurrence however is more pronounced in some parts of Africa where these early detection devices are rarely found. Treatment methods are also limited due to the unavailability of medical devices such phototherapy devices and incubators in these areas. Sunlight exposure which used to be a considered method for managing such cases is no longer recommended for treatment of jaundice due to risk of sunburn and overheating. These among other problems make the occurrence of very severe cases in infants. Phototherapy becomes less effective for treating infants with severe hyperbilirubinemia and there is a need for different treatment methods the most common one being exchange transfusion and just like any technique in science, the application of this process can be improved through engineering to improve it's efficiency and effectiveness.

The aim of the project will be to reduce human intervention in the exchange transfusion process. The proposed project would be beneficial for medical practitioners to do proper and better treatment devoid of human errors a higher guarantee for consistency, accuracy and efficiency all at a reasonable cost.

1.2 PROBLEM STATEMENT

Exchange Transfusion is a very tedious and time consuming process and this makes the procedure although a life-saving one seem unappealing

Exchange transfusion is performed by slowly withdrawing the blood of the patient usually through catheters inserted into blood vessel and replacing it with fresh blood from a donor. The procedure takes about two hours to perform, during which a physician together with a supporting nurse do the drawing and pumping of blood to and from the patient. In some cases, or medical conditions, the procedure is repeated a couple of times to exchange all or part of the patient's blood supply still at a slow rate in order to prevent damage to internal organs like the heart. The time-consuming nature of this procedure makes it very tedious to perform for health professionals which may lead to errors. This makes the procedure although a life-saving one seem unappealing.

The automation of the procedure will make it quick and less time consuming with the elimination of human errors.

Figure 1 Exchange transfusion being performed on a neonate

1.3 OBJECTIVES

The key objective of this project is to design and build a device that automates the neonatal exchange transfusion process and run tests on it to ensure its mechanical and clinical effectiveness.

The device incorporates all the details used in the manual process into its operation. The movement of the syringe to draw blood and deliver blood will be controlled by a motor at a steady rate using programming. The manual switching of valves by the physician during the exchange procedure will also be replaced by motors. This will almost eliminate any human intervention in the procedure.

1.4 SIGNIFICANCE OF THE PROJECT

The automation of the procedure provides a less human-dependent device with higher guarantee for consistency, accuracy, efficiency and less human errors. Human errors due to tiredness or fatigue and miscalculations will be reduced during the process and allow it to be performed at a

more stable and consistent rate. In addition, the automation of the neonatal exchange transfusion process will bring relief clinicians which will allow them attend to their other duties. Furthermore, its cost as compared to many other medical devices is relatively low, and can be purchased by the average hospital in Ghana. This will go a long way to save lives of neonates in both rural and urban areas.

1.5 SCOPE OF THE PROJECT

This project seeks to improve upon ANET 2.0 by solving ANET 2.0 challenges and performing animal tests on it which will aid in the further detection of more challenges with the device. ANET 2.0 succeeded in automating the entire exchange transfusion process but this was not without a few challenges. In order to be able to perform further tests and animal tests on the device, these challenges will be tackled.

2 CHAPTER TWO

LITERATURE REVIEW

2.1 HISTORY OF EXCHANGE TRANSFUSION.

Exchange transfusion is a therapy developed throughout the 1940s by Louis Diamond and a group of surgeons at the Children's Medical Centre in Boston, Massachusetts. Throughout the 1940s, a group of paediatricians at the Children's Medical Centre refined the technique of exchange transfusion to originally treat erythroblastosis fetalis, EF. EF arises during foetal development when the immune system of the pregnant woman attacks the red blood cells of the foetus. In 1951, Louis Diamond, Fred Allen, and William Thomas, physicians at the Children's Medical Centre, published an article in the New England Journal of Medicine describing improved techniques for exchange transfusion to treat elevated bilirubin levels due to EF in new-born infants. They suggested using the umbilical vein as the site of transfusion, and that a single polyethylene tube be used to withdraw the infant's blood and sequentially replace it with donor

blood. They stated that the umbilical vein is the best location for transfusion because there is less chance for scarring and it is easily identified through the umbilical cord on new-borns.

2.2 THE EXCHANGE TRANSFUSION PROCESS.

In the exchange transfusion procedure, aliquots of the patient's blood, which is designated as being 'bad blood', are removed and replaced with aliquots of the donor's blood, designated as 'good'. This is what calls for its name – exchange transfusion, blood is removed and replaced; an exchange. Because of this, exchange transfusion is also called substitution transfusion or replacement transfusion. In simple blood transfusions, blood is imply added, but not removed; there is no exchange of blood. It is called a blood transfusion process because, there is some mixing/fusion of the 'old' blood and the 'new' blood. Exchange transfusion is always allogenic, i.e. the new blood which is clean is always from a donor.

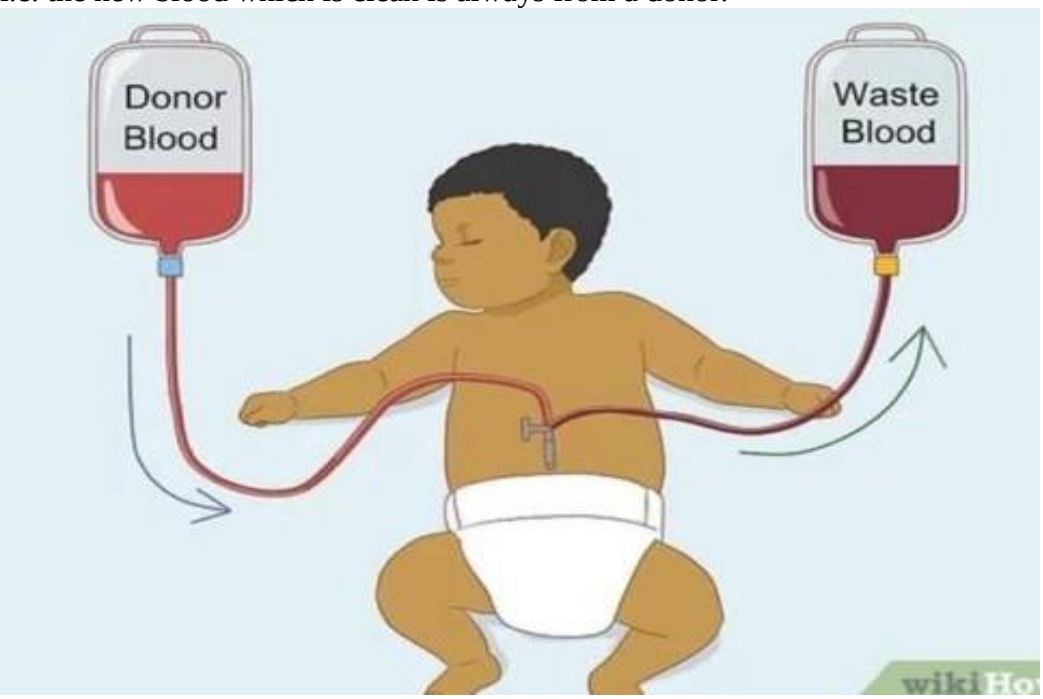


Figure 2 Exchange of blood in exchange transfusion

When performing neonatal exchange transfusion, the aim depends on the problem. So, for hyperbilirubinemia, it is to reduce the serum bilirubin (SBR) level and to lower the risk of brain damage. Hyperbilirubinemia refers to a medical condition in which there is a build-up of so much bilirubin in the blood, resulting in a yellow discoloration of the skin and eyes; a state called jaundice. Bilirubin is a natural bi-product from the breakdown of red blood cells. The liver plays the role of converting unconjugated bilirubin to conjugated bilirubin. Unconjugated bilirubin is simply bilirubin that is 'free', it is not bonded or bound. It is very dangerous when in high amounts; it becomes very toxic. For new-born babies, their liver is immature and does not play this role properly. Hence there is a little build-up of bilirubin in the blood. A few days after birth, the liver may now function well. But if it doesn't or due to other conditions, there will be a great build-up of bilirubin in the blood, which will result in jaundice.

For haemolytic disease of the new-born, it is to remove the infant's affected red blood cells and the circulating maternal antibodies to reduce destruction of the baby's red blood cells. Haemolytic disease of the new-born (HDN) refers to the medical condition where there is the premature breakdown of the new-born baby's red blood cells because of incompatibility of the blood types of the mother and the baby. The mother's antibodies attack the baby's red blood cells and they are broken down and destroyed (a process called haemolysis). HDN causes enlargement of organs and hyperbilirubinemia. The doctor may also aim for the correction of anaemia and the treatment of any potential for heart failure whilst maintaining a normal amount of blood.

2.3 CATHETERIZATION TECHNIQUES FOR THE EXCHANGE TRANSFUSION

Blood exchange transfusion (BET) may be performed in two ways. It is either performed with the single catheter exchange transfusion method which employs a single catheter in the umbilical vein or the double catheter exchange transfusion which uses a catheter each in umbilical vein and umbilical artery.

2.3.1 SINGLE-CATHETER PULL PUSH TECHNIQUE

This method is usually performed by one medical personnel. It is a traditional method, where only one single umbilical venous catheter is used. The umbilical vein catheter is connected to two three-way taps or stopcocks that are connected in series and the end of this series connection is connected to a syringe. Blood is drawn in aliquots of 5-20mL depending on baby's size and replaced with exact volume of blood. This is because per the weight of the baby, if greater than a certain amount of blood is withdrawn, the baby may pass out, or develop some organ failures. Blood is also withdrawn at a rate of 1.5-2mL/kg/min. During the procedure a nurse records the blood volume drawn and administered for each cycle. Vital signals of the baby must also be recorded.

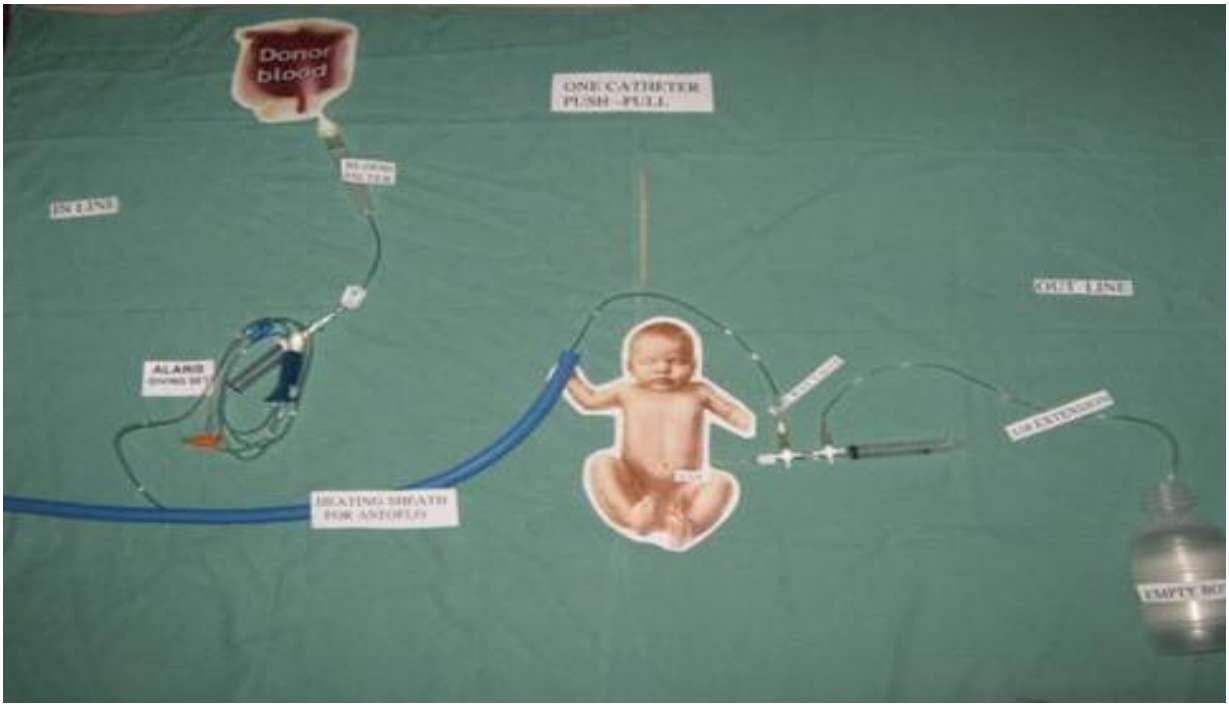


Figure 3 Single catheter exchange transfusion

2.3.2 DOUBLE-CATHETER PULL PUSH TECHNIQUE.

Another name for double-catheter pull-push technique is the Isovolumetric method. This process is performed by two personnel. Here equal quantities of blood are withdrawn and administered simultaneously through different catheters placed in different blood lines. The blood lines used are umbilical vein and umbilical artery. Blood is taken from the baby through the umbilical artery and equal volume of blood is simultaneously infused into the baby through the umbilical vein. This can also be done with different bloodlines but arterial lines are mostly for withdrawals and not for administering donor blood, this is because arterial blood pressure is much higher than venous blood pressure.

Figure 4 Double catheter exchange transfusion

2.4 BLOOD VOLUME CALCULATIONS

For any neonatal exchange transfusion, we calculate the blood volume to be exchanged using an estimate of the baby's circulating blood volume. For term babies, the estimate is between 70-90ml/kg, and for preterm babies, the estimate is between 85-110ml/kg. On the average, 80ml/kg is used for terms and 100ml/kg is used for preterm babies. Depending on the severity of the situation that calls for exchange transfusion, there are basically two main approaches that either is employed, although the latter is mostly preferred.

2.4.1 Single Volume Exchange Transfusion

Here, the estimated volume to be exchanged is equal to the circulating blood volume of the baby. For example, performing single volume transfusion on a term would require just 80ml/kg of blood volume. This approach replaces about 60-65% of the baby's blood volume or red blood cells.

2.4.2 Double Volume Exchange Transfusion

In simple terms, it is performing the single volume exchange transfusion twice. The estimated volume is equal to two times the circulating blood volume of the baby. For example, performing double volume exchange transfusion on a term would require 160ml/kg (80ml/kg ×2) of the blood volume. It replaces about 85-88% of the baby's blood volume or red blood cells.
The latter is the most commonly used and it is mainly used for the management of hyperbilirubinemia and haemolytic disease of the new-born. One might have expected the double volume exchange transfusion to be twice as efficient as the single volume exchange transfusion. But it is not actually so. The efficiency increases by an average of just 25% (i.e. from 80 to 85).

It is almost impossible to exchange 100% of the baby's blood circulating volume. This is because the baby's blood mixes with the incoming blood during circulation. Comparing the efficiency to the number of circulating blood volumes, the double volume exchange transfusion is ideal; minimizing waste by saving time, energy and resources while keeping a good efficiency.

The volume of blood that is exchanged as an aliquot, is dependent on the baby's weight. This is because, per the weight of the baby, if greater than a certain amount of blood is withdrawn, the baby may pass out, or develop some organ failures. Hence, the criterion below is used to choose the volume of blood to be exchanged in a cycle. The physician may not go by this to the letter due to the baby's situation; he/she may use smaller volumes than these or greater.

Table 1 Volumes per cycle for each weight of baby

BABY WEIGHT	**VOLUME PER CYCLE (ml)**
Less than 1500g (1.5kg)	5ml
1500g – 2500g (1.5kg – 2.5kg)	10ml
2500g – 3500g (2.5kg – 3.5kg),	15ml
Greater than 3500g (3.5kg)	20ml

Summing up all that has been said above, now consider the following noting that exchange transfusion is to be performed on the baby:
1. A baby that is preterm, whose weight is about a kilogram of mass.

Since the baby is preterm, the parameter for average amount of blood to be exchanged is about 200ml/kg of the baby's weight. To obtain the total volume that of blood to be exchanged, we multiply this parameter by the baby's weight. $i.e.\ 200mlkg \times 1.0kg = 200ml$
This implies that a total volume of about 200ml is to be exchanged. Also, since the baby's weight is less than 1.5kg, it implies that aliquots of blood with a volume of 5ml should be exchanged per cycle.
To find the number of cycles that will be carried out in order to exchange a total blood volume, we divide the total blood volume by the volume per cycle. $i.e.\ 200ml5ml = 40\ cycles$

As already stated, the procedure is carried out very slowly in about 4-5 minutes per cycle. So looking at this case, the total time for the exchange transfusion on the baby being considered will be the time used per cycle multiplied by the total number of cycles. $i.e.\ 40\ cycles \times 4minscycle = 160mins = 2\ hrs\ 40\ mins$

2. A baby that is term, whose weight is about two kilograms of mass.
Since the baby is term, the parameter for average amount of blood to be exchanged is about 160ml/kg of the baby's weight. To obtain the total volume that of blood to be exchanged, we multiply this parameter by the baby's weight. $i.e.\ 160mlkg \times 2.0kg = 320ml$
This implies that a total volume of about 320ml is to be exchanged. Also, since the baby's weight is above 1.5kg, it implies that aliquots of blood with a volume of 10ml should be exchanged per cycle. To find the number of cycles that will be carried out in order to exchange a total blood volume, we divide the total blood volume by the volume per cycle. $i.e.\ 320ml10ml = 32\ cycles$

Looking at this case, the total time for the exchange transfusion on the baby being considered will be the time used per cycle multiplied by the total number of cycles. $i.e.\ 32\ cycles \times 4minscycle\ 18$

$= 128mins = 2\ hrs\ 8\ mins$

2.5 COMPLICATIONS OF EXCHANGE TRANSFUSION

Exchange transfusion, even though effective and considered to be a very safe procedure, is not without a few complications. Its mortality rates range between 0.5% and 3.3%, hence, current recommendations for carrying out an exchange transfusion are based on the balance between he risks of encephalopathy and the complications related to the procedure. However, most of these complications can be avoided if the procedure is carried out very slowly, with the right hygiene and care. Often the best management of these complications is to slow down or pause the exchange.

The most commonly reported adverse events during or soon after exchange transfusion:

- Catheter related complications
- air emboli; thrombosis
- Haemorrhage

- Haemodynamic (related to excess removal of injection of blood): hypo or hypertension, intraventricular haemorrhage (preterm)
- Hypo or hyperglycaemia
- Hypocalcaemia, hyperkalaemia, acidaemia

Potential complications related to exchange transfusion:

- Arrhythmias
- Bradycardia
- Neutropenia, dilutional coagulopathy
- Feed intolerance, necrotizing enterocolitis
- Septicaemia, blood born infection
- Hypo or hyperthermia

2.6 PREVIOUS PROJECTS ON EXCHANGE TRANSFUSION

Ever since its inception in the twentieth century, quite a number of people have done some work on exchange transfusion. Several methods for its automation have been proposed; however, most of them have not been commonly used throughout the world because of technical difficulties.
An example of such automation attempts is;
Huseyin Altunhan, Ali Annagur, Nuriye Tarakci, Murat Konak, Sabahattin Ertugrul, and Rahmi Ors, "Fully automated simultaneous umbilical arteriovenous blood exchange transfusion in both term and late preterm infants with neonatal hyperbilirubinemia", June-2015.
In this study, the efficacy and safety of two different catheterization techniques of exchange transfusion used in the therapy of newborn jaundice were compared: fully automated two-way exchange transfusion technique and the classical one-way exchange transfusion. The study included babies at gestational age greater than thirty-four weeks. In total, one hundred and seven exchange transfusions were performed on eighty-six babies. Totally, the umbilical vein (UV) group included fifty-four babies having undergone sixty-nine exchange transfusions and the UV/UA group included thirty-two babies having undergone thirty-eight exchange transfusions. With respect to the results, the declines in bilirubin levels right after exchange transfusion and eight hours after exchange transfusion were higher in the fully automated UV/UA technique than in the classical UV technique. Furthermore, the duration of intensive phototherapy following exchange transfusion was shorter in the UV/UA method than in the UV method. There was no difference between the two methods in terms of exchange transfusion associated complications. They concluded by saying that, in neonatal hyperbilirubinemia, exchange transfusion with fully automated UV/UA technique is more efficient than the classical exchange transfusion technique, causing no additional side-effects. It is also more physiological than the classical technique, since it minimizes the fluctuations in the blood volume and intravascular pressure during exchange transfusion.

2.6.1 ANET 2.0

Automated Neonatal Exchange Transfusion (ANET) 2.0 aimed to combine mechanics, electronics and programming to control the entire exchange transfusion set-up with little or no human interference. This was achieved by;

1. A syringe pump for the withdrawal of blood from the patient and for the pumping of blood to the patient. In order to achieve this action, a push and pull segment was used which consists of a bipolar stepper motor, lead screw and guiding rods. The stepper motor rotates clockwise. Its rotation causes the threaded rod to rotate in the same direction because of its attachment to the shaft of the motor.
   A pusher block was designed which was responsible for transferring the rotation caused by the motor into the push and pull of the syringe plunger. The pusher block, which is coupled to the rod, propels forward in a linear motion. The linear motion is achieved with the help of the guide rods as it restricts the pusher block from moving sideways. As the pusher block moves forward, it pushes the plunger of the syringe, which causes a pumping action.
   To cause a sucking action, the motor rotates counter clockwise which causes the threaded rod to rotate in that regard. This setup replaced the manual drawing and delivering of blood by the clinicians.

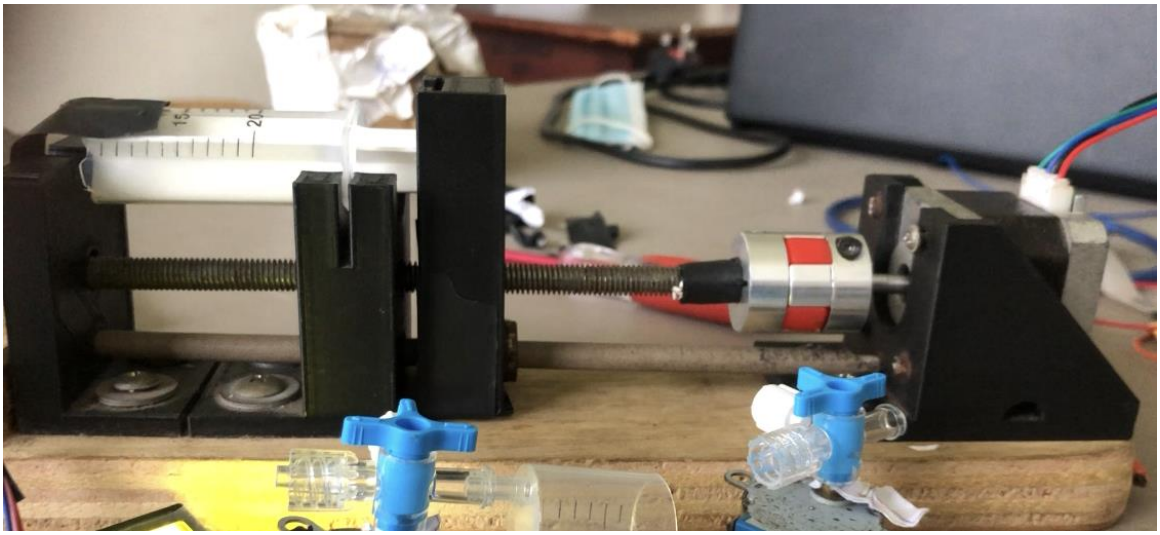


Figure 5 Setup of syringe for automated single catheter exchange transfusion

2. A valve switching system, which replaces the manual switching of valves with motors controlled by a program which will be written to the microcontroller. The program synchronizes the push-pull segment and the valve control segment to successfully complete the processes of drawing out blood and replacing it with fresh donor blood.
   The valve switching system used in ANET 2.0 used two unipolar stepper motors, two three-way valves in series and catheter ends connecting to the donor blood bag, waste container and to the baby. This system however had a problem with the coupling of the

motors with the three-way valves since the valves were designed in a way that requires them to be turned by human hands.

3 CHAPTER THREE

METHODOLOGY

This chapter discusses the entire process of data acquisition and analysis, tools and materials used to design the automated neonatal exchange transfusion device and the design process based on the analysis done from the data collected.

3.1 DATA COLLECTION

The data collection process involved the use of both primary and secondary data. A lot of data was collected form discussions held with the developers of ANET 2.0. A visit was made to the school of veterinary medicine where enquiries were made on the types of animal tests done there and how they were executed. The animal house of the pharmacy department was the next source of information on animal tests where we were advised on how to go about our animal tests.

Secondary data on the other hand was obtained from literature such as articles, journals among others and also watching YouTube videos on content related to the following topics:

i. Exchange transfusion and hyperbilirubinemia
ii. Medical device regulation
iii. Animal tests and clinical tests on medical devices
iv. Mechanics of motors, nuts and lead screws
v. Valving technology

3.2 DATA ANALYSIS

Data was primarily analysed using qualitative approach. Brainstorming sessions, coupled with reading of previous literature guided the analysis approach. Previous literature on animal tests performed on devices related to ANET such as dialysis machine as well as information collected from officials of the veterinary medicine school and lab technicians of the pharmacy department animal house guided our choice of animal subject for tests as well as the techniques to be used. Discussions with the developers of ANET 2.0 as well as bench tests performed on the device aided in identifying the drawbacks of ANET .2.0 that will prove to be challenges during animal tests.

3.3 DESIGN PROCESS

The goal of this project is to combine mechanics, electronics and programming to control the entire exchange transfusion set-up and perform tests on it to prove its efficiency and effectiveness.

To do this, the tests will be performed on an already existing prototype of the automation device, ANET 2.0 from which drawbacks and challenges of the device will be identified to aid further improvement of the device in ANET 3.0.

The current model is an upgrade of an already-existing model (ANET 1.0). The previous models had their positives and negatives, our task was to enhance the positive aspects of the model while working on all the problems inherited. The main issues with the device are discussed below, together with the techniques used in tackling them.

The unipolar stepper motors coordinated the valve switching as programmed by the microcontroller. However, due to the strong torque needed to turn the valves, the switching was not as accurate as we expected it to be. To solve this problem these options will have to be employed:

- Replacing the motors with higher torque motors
- Designing new coupling to transfer the rotational motion of the motor to turn the valves

The threaded rod is responsible for converting the rotatory motion of the bipolar stepper motor into a linear motion. To do this, the rod is coupled with the motor using a coupler. The nut moves along the rod when it rotates. From simulations, the threaded rod recorded very large stress values. This was quite understandable, considering the work it does in converting rotatory motion into linear motion. This is also due to the fact that threaded rods are made for fastening purposes and thus the high friction they create. As a solution, lead screws would be used in place of the threaded rods. Lead screws are designed specifically for the purpose of translating rotatory motion to linear motion.

3.3.1 DEVICE TESTING

The aim of testing the device will be to check working of mechanical parts, check clinical effectiveness, check for risks and adverse events that may arise in its application. Animal tests will be used for the assessment of these devices and typically provide initial evidence of device safety, their potential performance when used in a living system, and the biologic response that a living system may mount towards the device.

3.3.2 ANIMAL TESTING

Animal research or animal testing, also known as animal experimentation, and in vivo testing, is the use of non-human animals in experiments for medical purposes. Animal research has contributed to major advances in treating conditions such as breast cancer, brain injury, childhood leukemia, cystic fibrosis, multiple sclerosis, tuberculosis, and more, and was instrumental in the development of pacemakers, cardiac valve substitutes, and anesthetics.

3.3.3 SIGNIFICANCE OF ANIMAL TESTING

Checking the safety and effectiveness and efficiency of a medical product is very essential before being subjected into clinical phase. This assist us determine what changes should be made before being finally let on the market. Animal studies are utilized for the assessment of these devices and typically provide initial evidence of device safety, their potential performance when used in a living system, and the biologic response that a living system may mount towards the device. FDA recommends that animal studies for medical devices be designed with the objective of studying the risks that are predicted from the design of the device, any known risks of the device type, and any new risks that may have emerged in prior investigations.
For example, some cosmetics and health care skin products are tested on animals to ensure their safety and also several health professionals and biomedical researchers endorse the use of animal testing which helps in the ethical use and safety of various animals pertaining to medical device regulations.

3.3.4 MAIN OBJECTIVES OF ANIMAL TESTING

3.3.4.1 **Evaluate the efficacy of the device or to demonstrate proof of principle.**

Tis would involve verifying the accuracy and consistency of duration of cycles, accuracy and consistency of volume of blood (aliquots) per cycle and the whole procedure and also monitoring or any signs of ill health during or after procedure

3.3.4.2 Provide evidence of safety

Evidence of device safety, including performance and handling and compare with existing automation attempts and procedure. Recommendations for evaluating safety are performance and handling, device safety, physiological response, evaluate whether or not the device can have effects remote to the site of use(mechanical or biologic stresses), unexpected morbidity and mortality that is all observed instances of animal illness and death and whether such events are or are not device-related.

3.3.4.3 Risk assessment for risk management

A risk is combination of the probability of occurrence of harm and the severity of the harm. Risk assessment comprises two processes, risk analysis and evaluation. Risk analysis is the use of available information to identify hazards and to estimate the risk. Risk evaluation on the other hand is the process of comparing the estimated risk against given risk criteria to determine the acceptability of the risk.

Figure 6 Risk management process

3.3.5 SELECTING AN ANIMAL FOR THE TEST OF THE AUTOMATED NEONATAL EXCHANGE TRANSFUISON DEVICE

Several animals are being conducted on for animal research and animal experimentations. These animals include rats, mice, rabbits, guinea pigs, dogs, monkeys, chimpanzees, orangutans and even fishes and birds. All these animals have particular features and peculiar characteristics which enable researchers to bring out the best outcome of scientific findings. Rats and mice are most effectively used in the researching of cosmetic and skin care products. Rabbits would be the best pick because the share a majority of their and physiology to that of humans and also the weight of the rabbits is very close to that of neonates. Another important consideration is the size of the device and its parts relative to the test subject. For instance, the catheter which would need to fit into the blood vessels of the test subject.

3.3.6 ANIMAL TEST PROCEDURE

3.3.6.1 How data will be collected

One of the aims of the animal tests will be to collect data that will aid in evaluating the device and to demonstrate proof of principle and design verification. Data that will be collected include the volumes withdrawn or transfused per cycle, time taken per cycle and also cumulative volumes to be able to determine the total volume transfused.

3.3.6.2 Complications of exchange transfusion

Exchange transfusion is not without a few complications. Its mortality rates range between 0.5% and 3.3%, hence, current recommendations for carrying out an exchange transfusion are based on the balance between he risks of encephalopathy and the complications related to the procedure. However, most of these complications can be avoided if the procedure is carried out very slowly, with the right hygiene and care. Often the best management of these complications is to slow down or pause the exchange.

3.3.7 Risk analysis and evaluation

The hazards associated with the device are grouped into;

I. Hazards associated with blood related devices and exchange transfusion.

These are hazards that have been identified from literature to be associated to most blood contacting devices and the exchange transfusion process. These hazards include;

- Catheter related complications
- Air emboli
- Thrombosis
- Hypo and hyperthermia
- Hemodynamic (related to excess removal of injection of blood): hypo or hypertension
- Hypo or hyperglycemia

II. Hazards predicted from design and bench testing of device

These hazards where identified as possible complications that can arise from the device design and bench tests performed on the device.

- Coagulation of blood
- Air emboli
- Thrombosis
- Endurance of device
- Ergonomic hazards (repetitive movements, improper set up)

III. General device hazards

These are hazards that related to general device use in both normal and fault conditions. Some examples include;

- Electrical hazards
- Misuse
- Mechanical hazards
- And Unforeseen malfunctions

Risk Assessment Table

I. Hazards predicted from design and bench testing

Table 2 Risk assessment table

Hazard	**Reasonable foreseeable sequence or combination of events**	**Hazardous Situation**	**Harm**	**Probability of occurrence**	**Severity**
Coagulation of blood	Blood clots after leaving patient body or donor bag	Thrombosis	• Pain and swelling • Stroke /heart attack • Death		
Air emboli	Air bubble or foam trapped in blood line due to line – pump separation	Blood vessels blocked	• Heart attack • stroke • Respiratory failure • Death		
Thrombosis	Blood clots get into the blood vessels from the blood line	Blood clots accumulate or block blood vessels	• Pain and swelling • Stroke /heart attack • Death		
Endurance of device	Device ability to perform well for long periods	Device stops before procedure is completed	• Shock • Inconsistencies in operations • Death		
Ergonomic hazards (repetitive movements, improper set up)	Device not set-up correctly Blood line separation	Inaccurate measurements Air emboli Pressure altered			

II. Hazards associated with blood related devices and exchange transfusion

Hazard	Reasonable foreseeable sequence or combination of events	Hazardous Situation	Harm	Probability of occurrence	Severity
Catheter related complications	Allergy, Poor catheterization, Blood line breaks	The wrong type of catheter or catheterization used	• Thrombosis • Air emboli		
air emboli; thrombosis	Air bubble, foam or clots blocking blood vessel	Blood vessels blocked	• Heart attack • stroke • Respiratory failure • Death		
Hypo or hyperthermia	Reactions to blood being exchanged	Temperature rises above normal temperature			
Hemodynamic (related to excess removal of injection of blood): hypo or hypertension	Inaccurate timing of blood pumping, Inaccurate, inconsistent volume drawn and pumped	Too much or too little blood drawn or pumped Blood drawn or pumped too early or too late	• Shock • Heart rate complications • Heart attack • Death		
Hypo or hyperglycemia	Inaccurate, inconsistent volume drawn and pumped	Too much or too little blood drawn or pumped	• Shock • Death		

III. General device hazards

Hazards	Reasonable foreseeable sequence or combination of events	Hazardous Situation	Harm	Probability of occurrence	Severity
Electrical hazards	User comes into contact with live wire, Fluids come into contact with electrical components	User is exposed to electricity	• Injury • Death		
Mechanical hazards	Improper contact or entanglement to machine parts	Exposure to injurious machine parts	• Injury • Death		
Misuse	Use of device or its parts for wrong purpose				
Unforeseen malfunctions					

3.3.8 RESULTS FROM FIRST TRIALS

The animal testing was supervised and conducted with the help of Mr.Gyan and Mr.Godwin of the Faculty of Pharmacy.The Carlifonia rabbit breed was carefully selected and preffered for the animal testing because of various reasons which includes particularly the weight of the animal.It weighs 2.292 kilograms.

The animal was given a dosage of a pentobarbital drug(a form of anesthethic drug usually injected to animals before an surgery) was administered to the animal to control its aggresiveness and also made it easier for the cannularization and the catetherization. A small dose was used in other not to put the animal fully to sleep and reduce blood pressure in its blood vessels which will make work difficult.Xylene was applied to the animals ear to make the veins much more visible for cannularization. A tube connecting the cannular to the mouth of the valve and to the syringe was made shorter to help the flow of the blood into the syringes because a longer one would make the flow erract in a way which would not sync with the flow of the device. A syringe and three way valses were set up onto the device for the exchange transfusion process. . A 10ml syringe was used instead of the 20ml syringe as suggested earlier due to the scarsity of

the 20ml on the market. Although the exchange transfusion process involves the withdrawal of blood from the animal and replacing it with blood from a blood bag it was suggested by the lab technicians at the animal house that in order to avoid future complications, we take a turn from our initial plan to withdraw blood from the rabbit which will then be transfused back into the rabbit and test just the withdrawal and transfixing ability of just the strings pump and all challenges encountered from this test will be attended to before a full exchange transfusion test is performed.

Figure 7 Setup of device and animal for test

3.3.8.1 Complications during the test

The test on the syringe pump revealed a number of complications that need to be fixed.One particular problem encounted was the clotting of the blood which initially was identified in our previous bench test with the technicians. In a way of preparing in advance to tackle we acquired hepaarin (an anticoagulant used to decrease the clothing ability of blood) to be used during the proces to prevent the clothing of blood in the catheers which made it difficult for the blood to flow through tubes and into the syringes. During the test it was identified that the clothing persisted even with the use of heparin and this was discovered to be due the cannulalization used. In general the cannulization was an issue because it was difficult to find a cannula that fitted properly with the catheters used. Different cannulas where used which were not able to fit with our catheters and in other cases had to be modified or have some parts cut-off before they were able to fit with the catheters. The clotting that occurred was as a result of the sizes of the cannula needle which made it difficult for blood to flow through and thus due to duration of time blood stayed in the cannula it clotted. A blood sample of the rabbit was not made available because of the difficulty in the cannularization.

Figure 8 Cannulization of the blood vessel of the rabbit

3.4 ANET 3.0

ANET 3.0 based on the problems faced in ANET 2.0 and results from the animal trials would have some differeces from previous editions. These new additions aim at reducing or curbing the issues that were faced in previous editions. This edition seeks to elaborate on the various components that make up the mechanical and electronics as well as software of ANET 3.0.

3.4.1 Mechanical components

3.4.1.1 Push and pull segment

This segment aims at replacing the manual drawing and delivering of blood by clinicians with a customized automated syringe pump.This syringe pump consists of

- a bipolar stepper motor
- Flex coupler
- 3D printed parts
    - Chassis
    - Carriage (Pusher block)
    - Syringe holder (adapter)
- lead screw and nut
- 8mm guiding rods and linear bearings

The stepper motor rotates clockwise. Its rotation causes the lead screw to rotate in the same direction because of its attachment to the shaft of the motor. The pusher block which is attached to the lead screw propels forward in a linear motion. The linear motion is achieved with the help of the guide rods that restricts the pusher block from moving sideways. As the pusher block moves forward, it pushes the plunger of the syringe which causes a pumping action.

To cause a sucking action, the motor rotates counter clockwise which causes the threaded rod to rotate in that regard. Because the syringe holder of the pusher block holds the syringe tightly, it pulls the plunger of the syringe along which causes a sucking action as it moves backward. The continuous rotations of the stepper motor and its direction causes us to suck and pump blood in and out of the baby.

- Bipolar stepper motor
  A stepper motor is an electric motor whose main feature is that its shaft rotates by performing steps, that is, by moving a fixed amount of degrees. Stepper motors generate high torque with a compact body and are ideal for quick acceleration and response. It is made up of a stator and a rotor.

Figure 9 Bipolar stepper motor

- Flex coupler
  Couplers are designed to couple two rotating shafts together. In our application, the coupler couples the rotating shaft of the stepper motor and the lead screw which are inserted at its opposite ends to trasmit the rotatory motion of the motor to the lead screw to provide drive for the push pull segment.
  Shaft misalignment can limit a machine's performance, cause excessive vibration, high reaction loads, and accelerated wear, and often leads to premature equipment failure. Flexible Shaft Couplings (flex couplers)can help prevent these issues by transmitting torque while compensating for parallel, angular, and axial misalignment between drive components. When installed correctly, flexible shaft couplings can also reduce vibration, minimize noise, and protect driveshaft components.

Figure 10 Flex coupler

- 3D printed parts
  - Chassis : The chassis acts as the housing that holds all the other components of the push and pull segment.It was designed and customized to perform this

function specifically and was 3D printed. This chassis performs this housing function while eliminating the weight and cumbersome nature of the previous editions.

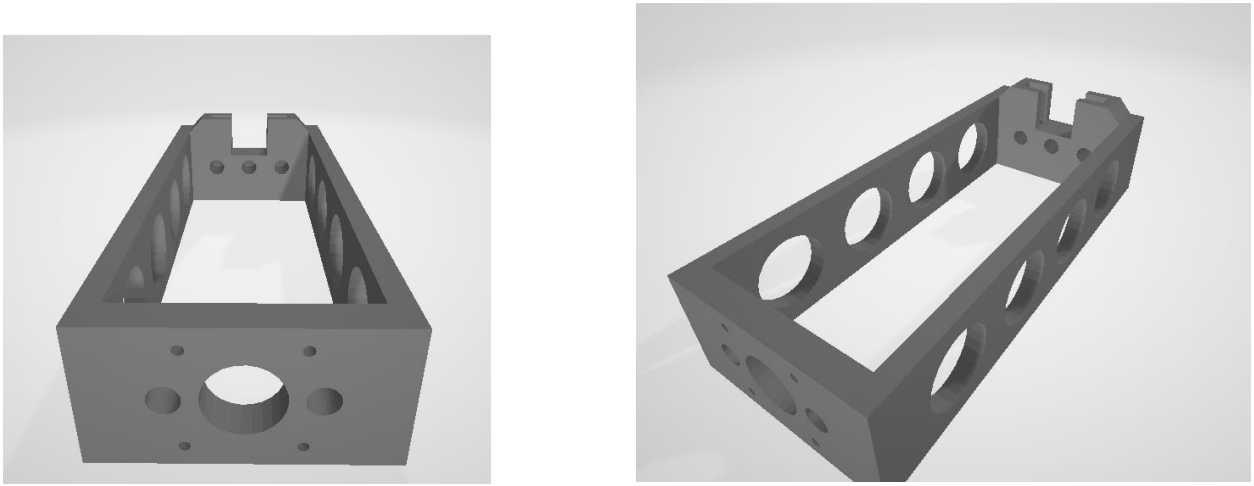


Figure 11 3D model of chassis of syringe pump

- Carriage (Pusher block)
  This part takes the motion of the nut as it is threaded on the lead screw and uses it to push and pull the plunger of the syringe for the pumping and drwing action. This also is a custom design and comes with two holes for two linear sharfts for more stability and steediness in the movement of the syringe plunger.

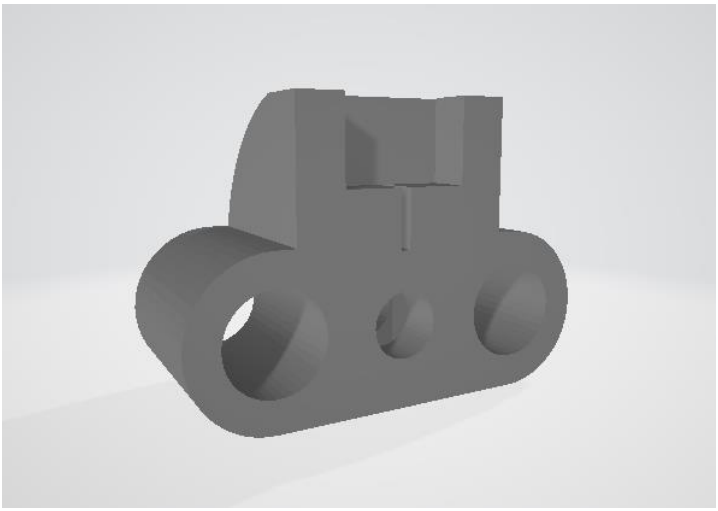


Figure 12 3D model of Carriage (Pusher block)

- Syringe holder (adapter) : This part holds the syringe handle to keep the syringe in place and allow the pushing and pulling action to be effectiive. This is customized for different sizes of syringes.

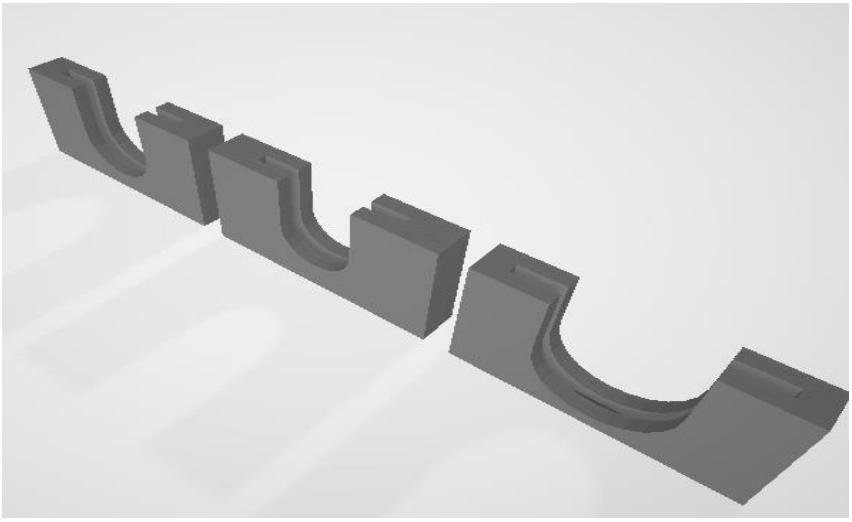


Figure 13 3D model of Syringe holder (adapter)

- lead screw and nut : A lead screw shaft is a cylindrical shaft that has a series of grooves running around its length. It is a mechanical linear actuator that converts rotational motion to linear motion .It's operation relies on the sliding of the screw and nut threads with no ball bearings between.

Figure 14 Lead screw and nut

- 8mm guiding rods and linear bearings : Linear rods same dimensions as the lead screw are passed through linear bearings placed in the pusher block and their purpose is to aid in keeping the push pull segment stable. The linear shafts used in this project are wooden and have been shaped and sized for this purpose.

3.4.1.2 Valve switching segment

The approach is to replace the manual switching of valves by the physician with motors which will be responsible for turning the valves. The motors will be controlled by a program written to a microcontroller. The program synchronizes the push-pull segment and the valve control segment to successfully complete the processes of drawing out blood and replacing it with fresh donor blood.The components involved in the valve control segment include

- two Nema 17 stepper motors
- Flex couplers
- 3d printed clutch
- two three-way valves in series and catheter ends connecting to the donor blood bag, waste container and to the baby.

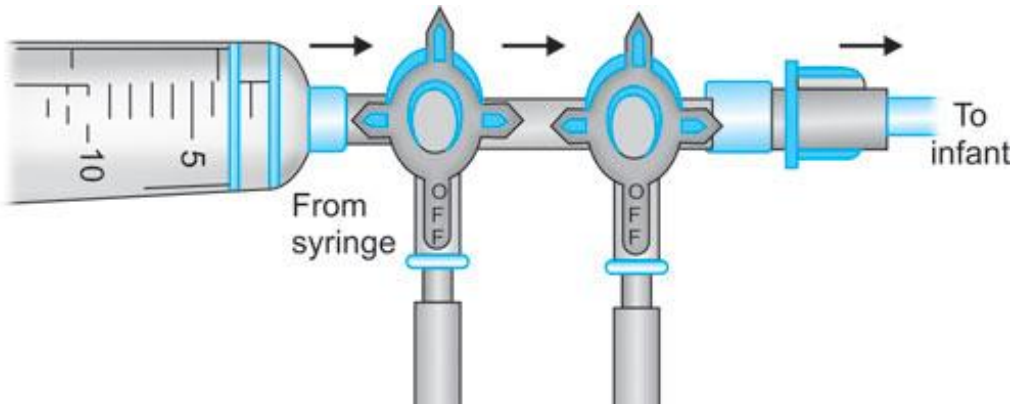


Figure 15 Figure representing the valving system used in exchange transfusion

- 3d printed clutch

This is a 3d printer part that is located on top of the motor where it is connected to the flex coupler and its top is placed on the buttom of the valves. The outer edges of the valve is held by the 3d printed clutch and with the drive provided by the stepper motor through the flex coupler is able to turn the valves.

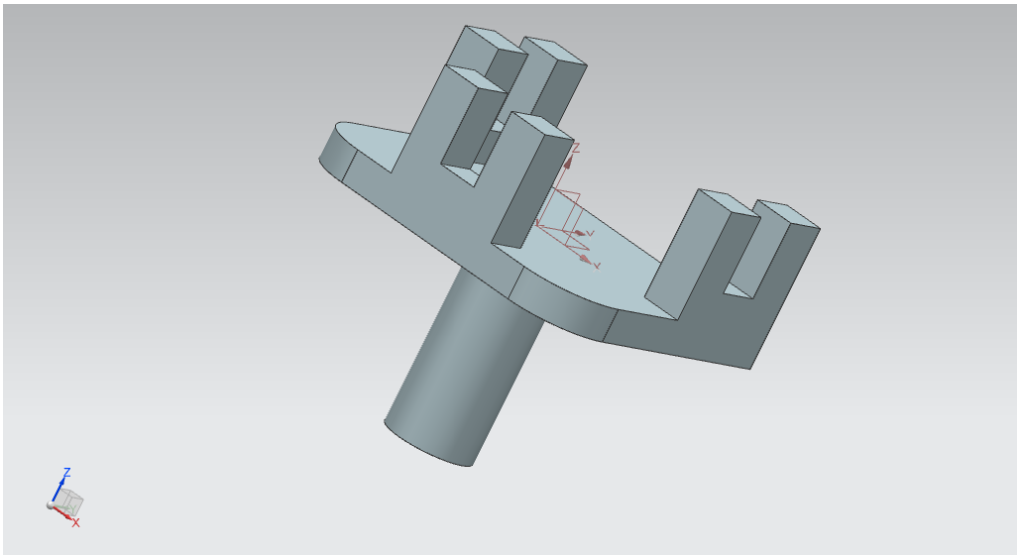


Figure 16 3D model of clutch for valve switching

- two three-way valves in series and catheter ends connecting to the donor blood bag, waste container and to the baby.

The valves are used in controlling the direction of blood flow. They allow the movement or flow of blood in three different directions. Most of the automation focuses here since every cycle will require about 4 manual turns of the valves to achieve the required flow.

Figure 17 3-way valve

3.4.2 Electronic components

a) The arduino mega 2560

The Arduino Mega 2560 is a microcontroller board based on the ATmega2560 (datasheet). It has 54 digital input/output pins (of which 14 can be used as PWM outputs), 16 analog inputs, 4 UARTs (hardware serial ports), a 16 MHz crystal oscillator, a USB connection, a power jack, an ICSP header, and a reset button. It contains everything needed to support the microcontroller; simply connected to a computer with a USB cable or powered with a AC-to-DC adapter or battery to get started. The Mega is compatible with most shields designed for the Arduino.

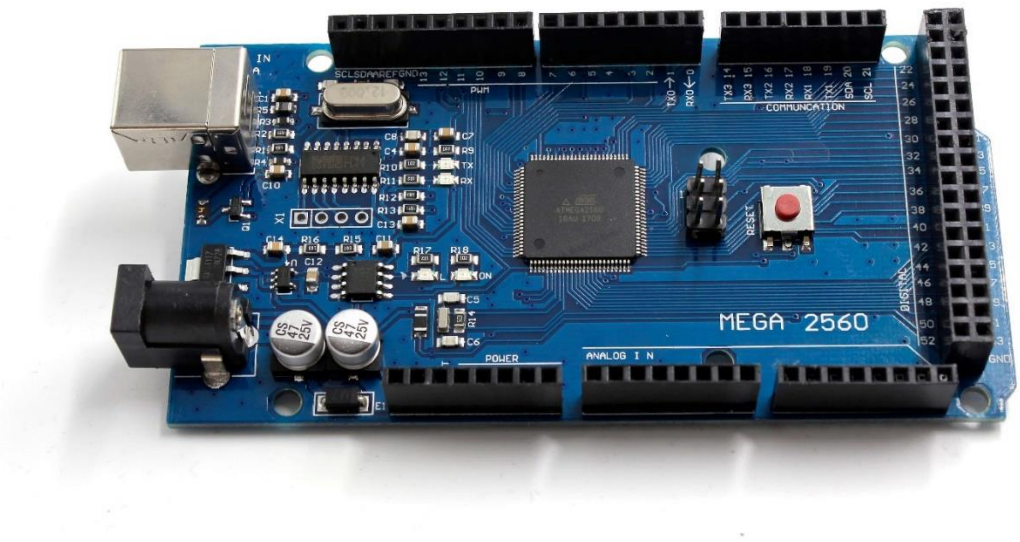


Figure 18 Arduino mega board

b) The power source

Currently, we use three power sources- 5v dc to power the Arduino microcontroller provided by a computer, a separate 6v lead acid battery which is very and readily rechargable dc to power the motor of the syringe pump and a 12v battery to power the two valve switching motors. Powering stepper motors will require high voltage input but our design takes care of that by introducing step-up transformers (CN6009) where necessary. The input 12v is stepped up to power the two motor drivers interfacing the stepper motors for the valves. The 6v is also stepped up to power the strings pump motor.

The transformers were incorporated into our design mainly to keep the input power requirement low. Also, provision has been made for the use of electricity directly from a socket through a 12v adapter to power the valve switching system.

Figure 19 6v lead acid battery

c) Liquified crystal display(lcd)

An electronic device that is used to display data and the message is known as LCD 16×2. As the name suggests, it includes 16 Columns & 2 Rows so it can display 32 characters (16×2=32) in total & every character will be made with 5×8 (40) Pixel Dots. So the total pixels within this LCD can be calculated as 32 x 40 otherwise 1280 pixels. however, the LCD 16×2 is broadly used in devices, DIY circuits, electronic projects due to less cost, programmable friendly & simple to access. The specifications of LCD 16X2 are discussed below

- The operating voltage of this display ranges from 4.7V to 5.3V
- The display bezel is 72 x 25mm
- The operating current is 1mA without a backlight
- PCB size of the module is 80L x 36W x 10H mm
- Number of columns – 16
- Number of rows – 2
- Number of LCD pins – 16
- Characters – 32
- It works in 4-bit and 8-bit modes
- Pixel box of each character is 5×8 pixel
- Font size of character is 0.125Width x 0.200height

The basic working principle of LCD is passing the light from layer to layer through modules. These modules will vibrate & line up their position on 90o that permits the polarized sheet to allow the light to pass through it.

Figure 20 LCD

d) I2c lcd adapter

I2C lcd adapter is a device containing a micro-controller PCF8574 chip. This micro-controller is a I/O expander, which communicates with other micro-controller chip with two wire communication protocol. Using this adapter anyone can control an 16x2 LCD with only two wire(SDA, SCL). It saves many pins of arduino or other micro-controller. It has an built in potentiometer for control lcd contrast. The default I2C address is 0x27. You can change this address by connecting A0, A1, A2.

Figure 21 LCD with I2c backpack

e) Keypad

The 4X4 membrane keypad has the buttons arranged in rows and columns in a 4X4 matrix. Under the buttons are membrane switches. Each switch in a row which is under a button key is

connected to another switch in the same row through an electronically conductive trace laid under the keypad buttons, and there are 4 rows in all.

Again, each switch in a column which is under a button key is connected to another switch in the same column through an electronically conductive trace laid under the keypad buttons, and there are 4 columns in all. The 4 rows and 4 columns makeup 8 pins of the 4X4 matrix keypad .

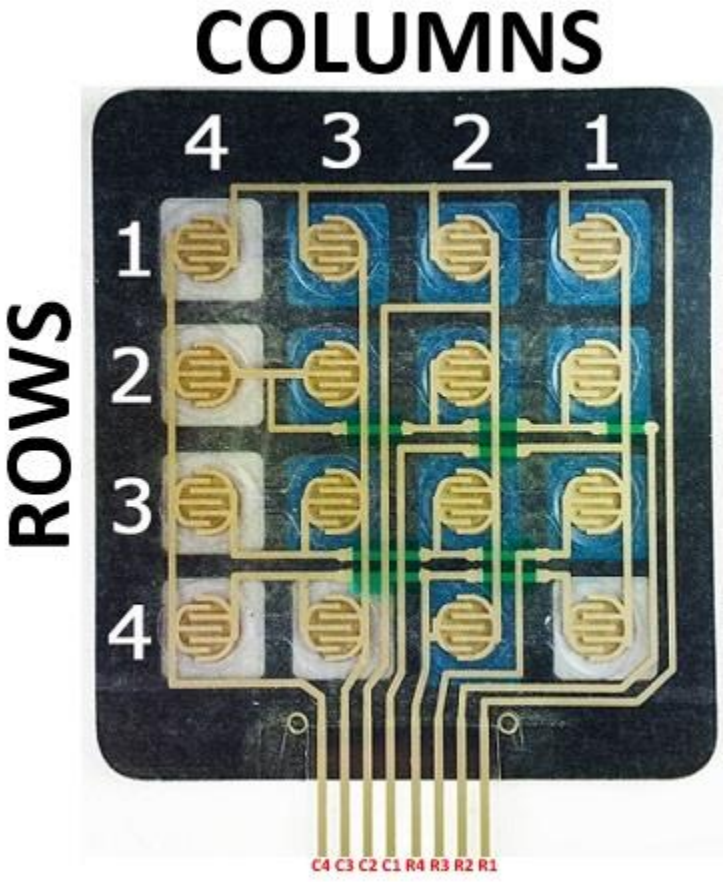


Figure 22 Rows and columns in keypad

Pressing a button joins a row and a column, thereby creating an electrical conducting path between the row and the column. See image below.

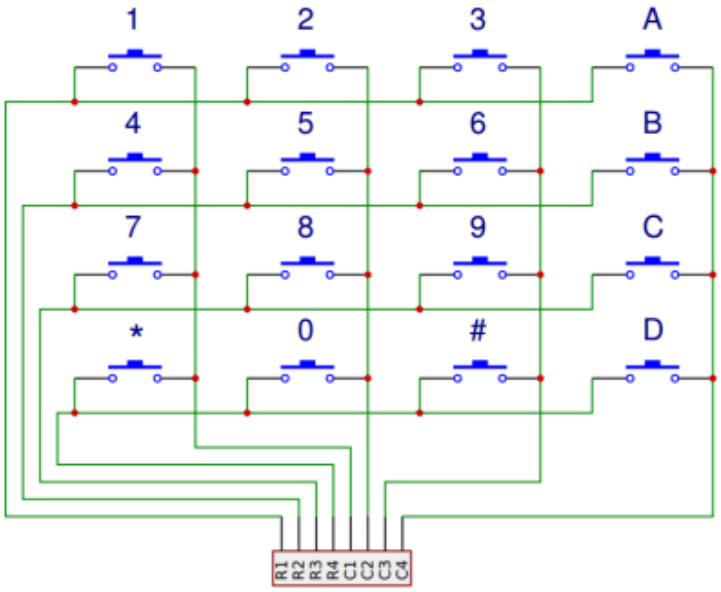


Figure 23 Schematic of the 4X4 matrix keypad

How Arduino detects pressed button

Arduino detects which button is pressed by identifying which rows and columns where joined, and here is how it happens.

- When no key/button is pressed, the Arduino “keypad.h” library code causes the row pins to go LOW and the column pins to go HIGH. See image below.

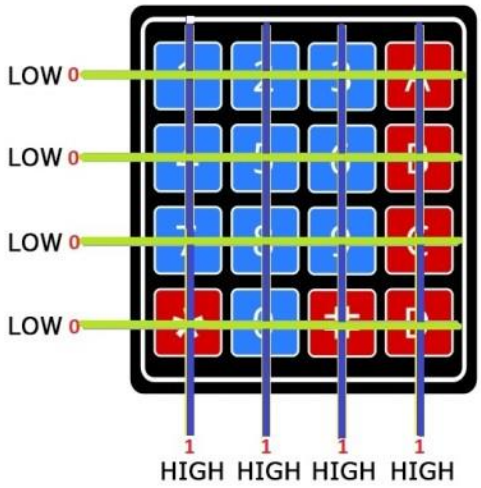


Figure 24 How Arduino detects pressed key

When a key/button is pressed, this causes a row key and a column key to be joined. Because the row pins were initially pulled LOW by the Arduino “keypad.h” library code, the particular column pin that is now in contact with a row as a result of the pressed button will be pulled LOW from its initially HIGH state. Hence, we now know the column on which the key/button was pressed. See image below.

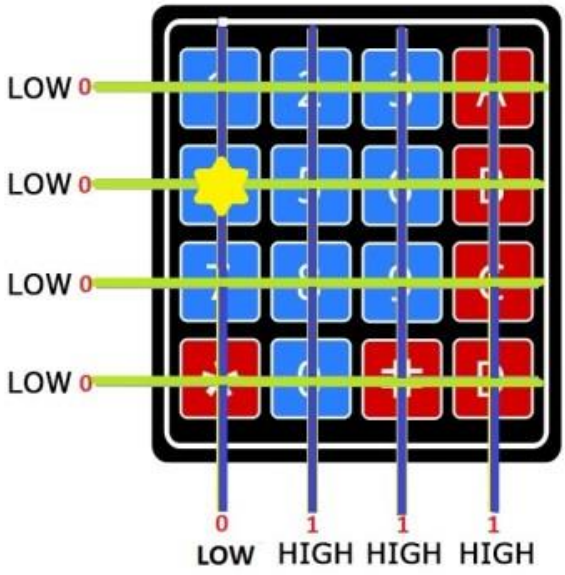


Figure 25 How Arduino detects pressed key

To identify the row that coincides with the pressed column, the Arduino with the “keypad.h” library will cause the row pins to go high sequentially and simultaneously read the column pins to note which row pin will cause a column key to go high from a LOW state.

Since all the column pins have been on a HIGH state from the beginning and has not switched state except the column that was pressed and was switched to a LOW state, it is this same pin that will switch from a LOW state to a HIGH state. With this, the Arduino now knows which row pin was pressed. By combining the row and column pins, we can identify the exact key/button that was pressed.

From the explanation above, we can say that row 2 and column 1 pins were connected when the button was pressed, hence, with this information, we can deduce that button 4 was pressed.

f) Switch

A device switch was added to the set up of design electronic components for the device to conserve energy and also to stay on

Figure 26 Switch

g) Motors shield

Stepper motors require pulse to move at specified number of steps, speed, direction and rate. A motor driver is responsible for sending these pulses. To control the bipolar stepper motor of the syringe pump, an Arduino motor shield was interfaced with the Arduino mega microcontroller.

The motor shield has channels which allows for the control of four DC motors, 2 stepper motors and 2 servo motors.It also has headers for the attachment of inputs, outputs lines. With an external power supply, the motor shield can safely supply up to 12V and 2A per motor channel or 4A to a single channel.

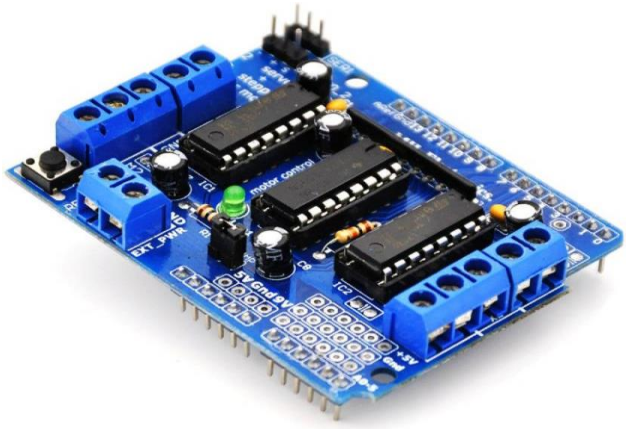


Figure 27 Motor shield

Figure 16:Arduino Motor Shield

h) Voltage boosters

This DC-DC switching boost converter is capable of driving a 4A load with excellent line and load regulation. The main switching component XL6009 IC is available in fixed output voltages

of 3.3 V, 5V, 12V, and an adjustable output version. It is an efficient switching regulator and the output efficiency is significantly higher in comparison with the popular boost regulators. At higher input voltages, the regulator operates at a switching frequency of 400kHz thus allowing the overall board size to be smaller and space-saving

This device is used to step up the supply voltage. Its output voltage is adjustable by potentiometer.

- Small size, high efficiency
- Easy to install
- Stable and reliable
- It can make the output stabilized

Features:

- Input voltage range: 3.2 to 30Vdc.
- Output voltage range: 5 to 35Vdc.
- Output rated current: 2A.
- Output maximum current: 3A (need to add heat sink).
- Pinout:

  IN+ = Input voltage

  IN- = Ground

  OUT+ = Output voltage

  OUT- = Ground
- Dimension: 41 x 20 x 14 mm.
- Weight: 12g

Figure 28 CN6009 voltage booster

i) L298N motor drivers

The L298N is a dual H-Bridge motor driver which allows speed and direction control of motors, as the name implies. A single L298N IC can drive two DC motors at the same time, and the two motors and one stepper motor and the directions can be regulated individually. Stepper motors require pulse to move at specified number of steps, speed, direction and rate. A motor driver is responsible for sending these pulses. The movement of the two stepper motors for turning the valves was regulated by L298N motor drivers.

Figure 29 L298N motor drivers

3.5 Assembly of design

3.5.1 The syringe pump.

Mechanical components used

- 3D printed parts
    - Syringe holder
    - Chassis
    - Push block
- 8mm linear shafts and bearing
- Nema 17 stepper motor
- Lead screw and nut
- Flex coupler

Assembly of the mechanical parts

The nut is placed in the pusher or carriage block which would be threaded along the lead screw to perform the task of translating the rotatory motion of the motor to linear motion which would push and pull the plunger of the syringe to form the syringe pump. Linear bearings as also placed in the pusher block for the linear shafts. The linear shafts would be inserted into the chassis and passed through the linear bearings. The linear bearings serve as guides that ensure that the carriage moves linearly in a straight line to facilitate proper plunging and pulling of the syringe.

Figure 30 Lead screw and guiding rods passed through nut and holes in carriage and chassis

A flex coupler is connected to the Nema 17 stepper motor which will provide the drive for the syringe pump to translate the rotation of the motor to the lead screw which will be inserted at the other end of the flex coupler.

The lead screw is threaded through the nut inside the push until it meets the rear of the chassis. The motor is fastened to the chassis using screws to limit its motion. The syringe adapter (holder) is put in place in the chassis and can be changed to fit the proper size of syringe.

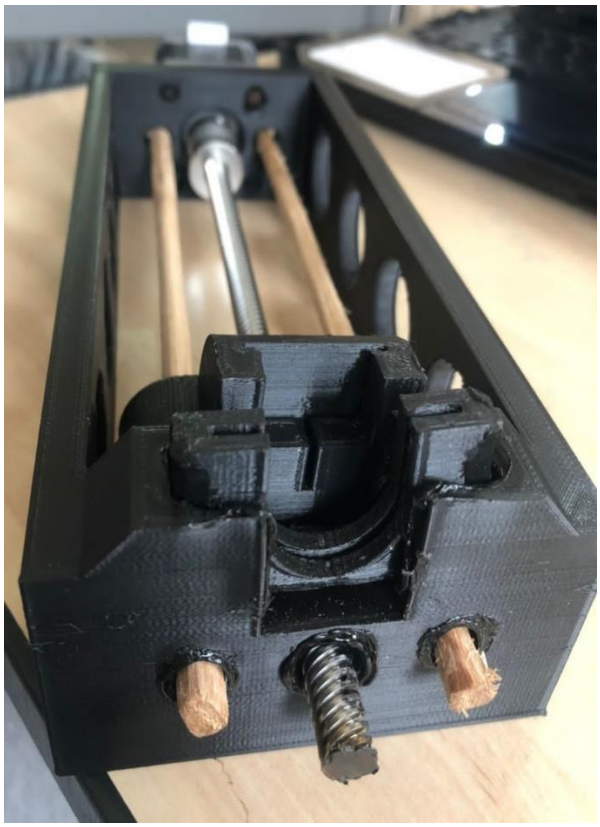


Figure 31 Images showing completed syringe pump (push and pull segment)

Electronic components used

- Arduino mega 2560
- Arduino motor shield
- 12v power supply
- Insulated wires

- USB cable
- Keypad
- LCD with I2C backpack

Connection of electronics

The Arduino mega 2560 being the main brain of the entire electronic setup must have every other component connected to it one way or the other. The mega board comes with a USB cable through which the code can be flashed onto it from a computer. Also, by connecting the mega board to the computer using the USB cable a 5v power supply can be provided to power the Arduino mega board.

The motor shield is connected by mounting it on to the mega board through the stocking headers on the Arduino mega board. The LCD with I2C backpack will have its scl and sdl connected to their respective pins on the Arduino mega board and its power connected to 5v dc vcc and 5v ground on the motor shield. The row pins of the keypad are connected to pins 50, 48, 46 and 44 and its column pins connected to pins 42, 40, 38 and 36.

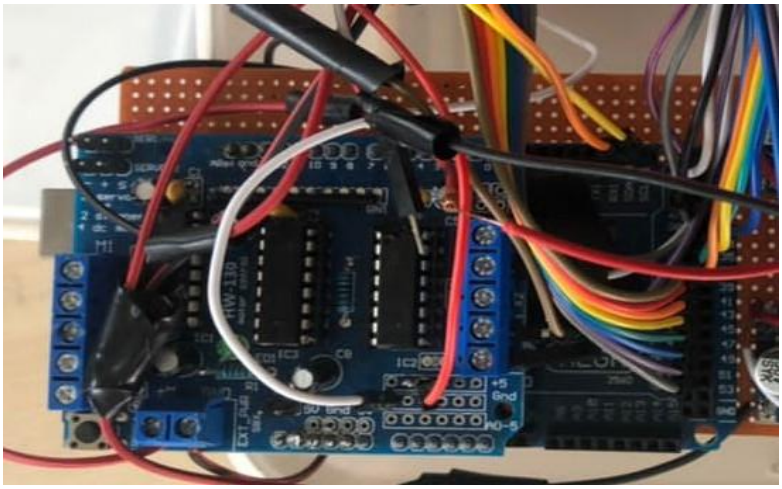


Figure 32 Motor shield mounted unto Arduino and connected to other components

The motor shield is connected to the 12v supply which will provide the power to run the motor through its M+ and M- terminals. The motor is connected to M3 and M4 terminals of the motor shield. It must however be ensured that the same coil is connected to each motor terminal. The same coil can be identified by testing continuity of the motor wires. Also for all power connections, different coloured wires are used to differentiate the vcc and ground connections and thus provide clarity. The Arduino mega board with the motor shield mounted onto it as well as the voltage boosters for the two power supplies were mounted onto a pcb board after the connections were made.

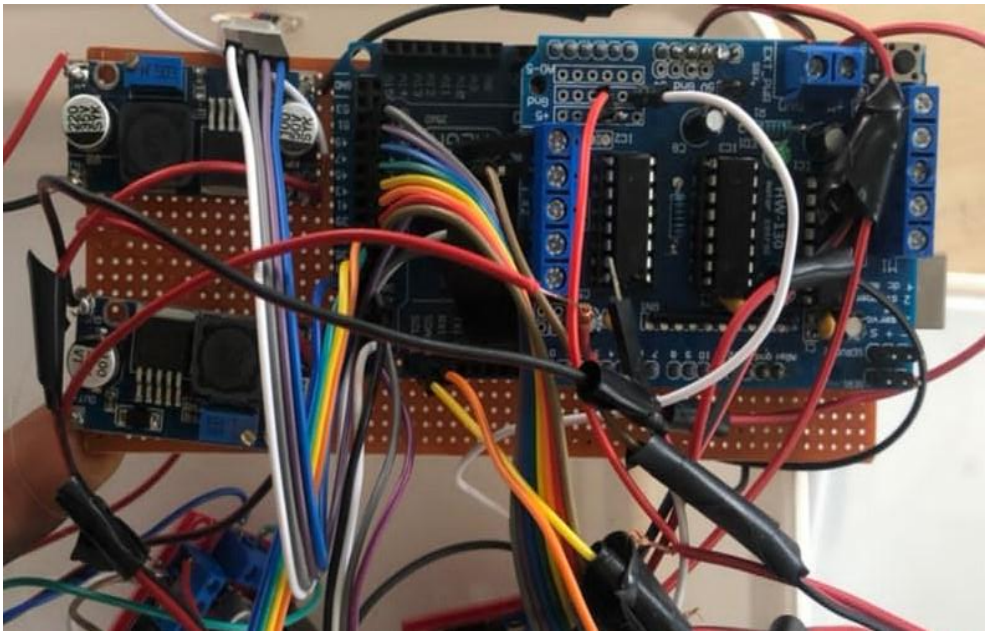


Figure 33 Arduino board, motor shield and voltage boosters mounted unto pcb

3.5.2 The valve switching system

Mechanical components used

- Nema 17 stepper motors
- Flex couplers
- 3D printed parts
- Three-way valves

Assembly of the mechanical parts

The 3d printed parts used here were designed to apply the rotatory motion of the stepper motors to the outer ends of the three way valves' handles in order to increase the torque provided by the stepper motor to turn the valves easily and effectively.

The 3d printed parts are inserted and tightened at one end of the flex coupler with the end connected unto the rotor of the stepper motor to translate the rotatory motion of the motor to turn the valves.

Figure 34 Mechanical part for switching valves

Electronic components used.

- L298 motor drivers

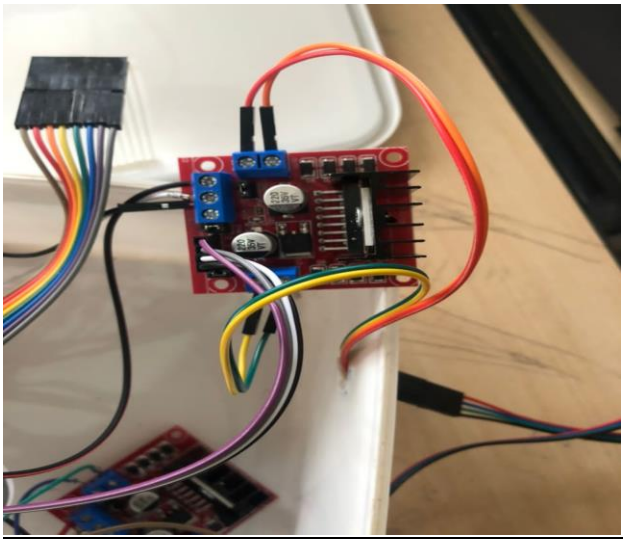
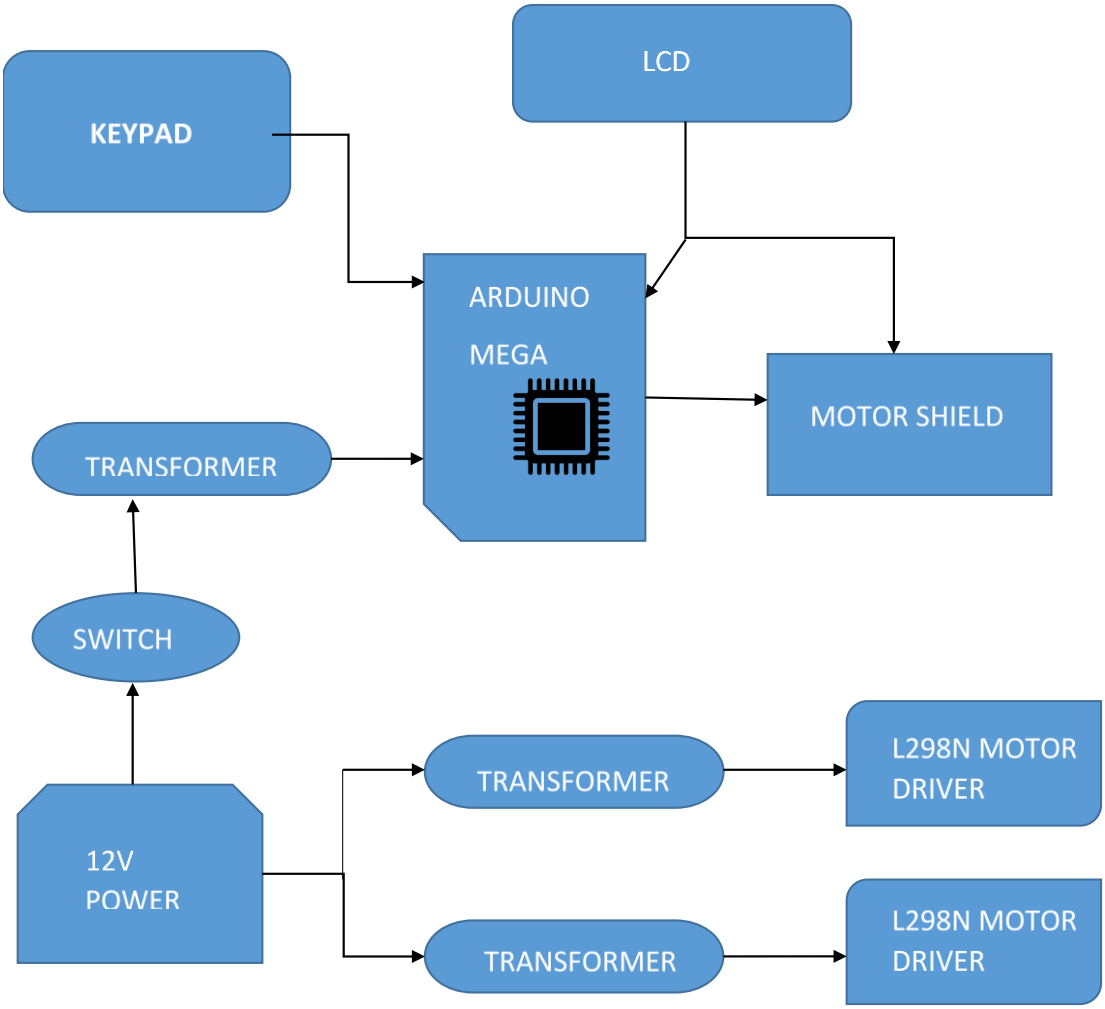


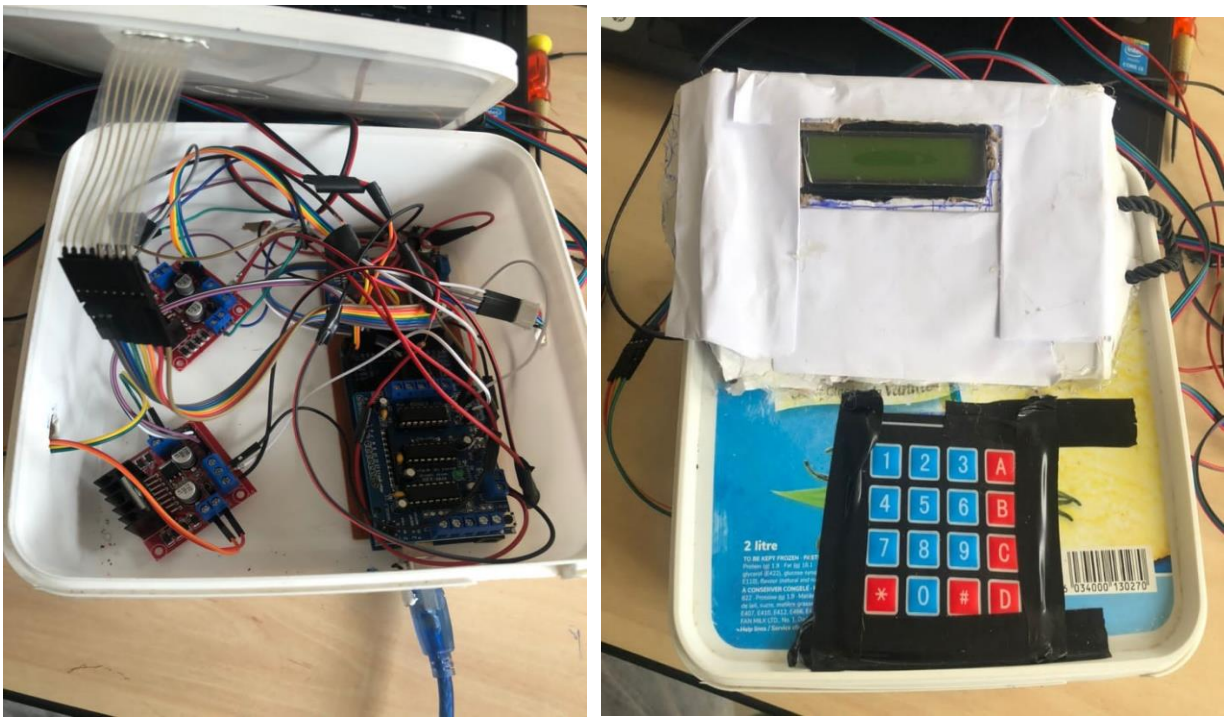
Figure 35 Connection of motor for valve switching

3.5.3 Block diagram of the connection of electronics



3.5.4 THE BUILT MODEL

After testing the components to ensure they work, they were installed into component holder to house all the electronic components. After considering the cost involved in 3D printing of fabricating a component holder, we sought for a cheaper option but equally efficient option in the form of a plastic container which customized to perform the function we intended for it.



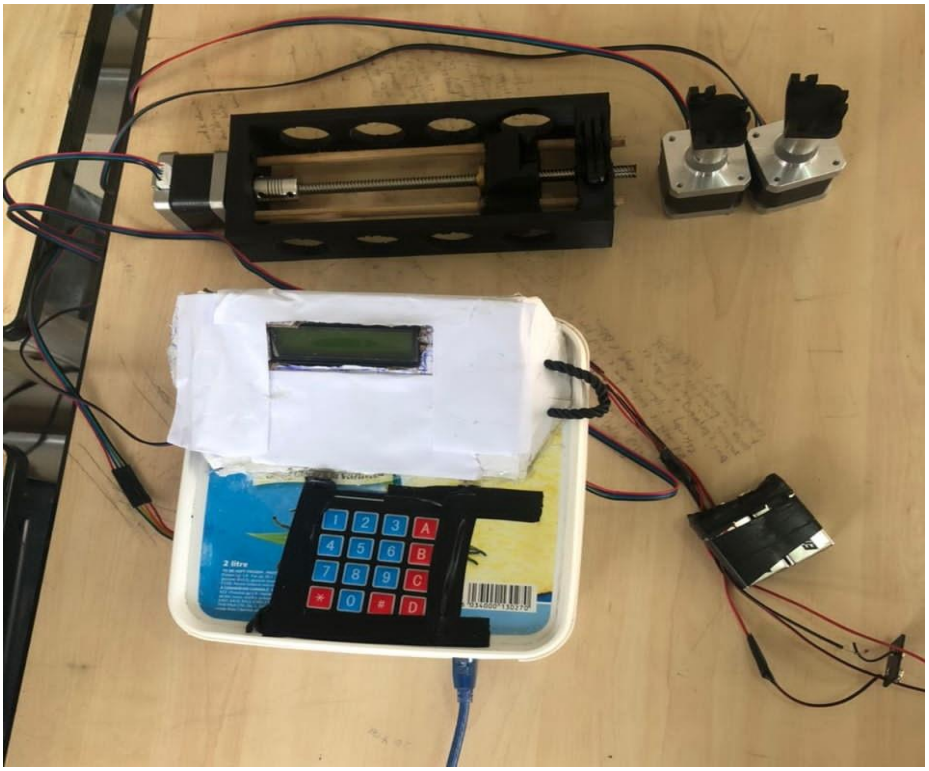


Figure 36 Images showing built model

3.5.5 Software implementation

The firmware on ANET 3.0 was written in the Arduino IDE with Arduino- C language. Most code written to Arduino microcontroller boards is in this language as it is easy to write, understand and interpret. Arduino-C has prewritten libraries that can be imported and used to control various hardware components. Some of the libraries that were included in our code to control our hardware components such as the motors, LCD and keypad are shown below;

```
#include <AFMotor.h>
#include <Stepper.h> //Include the Arduino Stepper Library
#include <Wire.h>
#include <LiquidCrystal_I2C.h>
#include <Keypad.h>
```

The <AFMotor.h> library and the <Stepper.h> library help in the control of the stepper motors. The syringe pump motor is controlled with the motor shield which works well with the <AFMotor.h> library whilst the valve switching motors are controlled with the two L298N motor drivers and thus work with the <Stepper>. The <Wire.h> library allows you the control the I2C which is used in conjunction with LCD. The <LiquidCrystal_I2C.h> library is responsible for the passing of information to the LCD. The <Keypad.h> library also helps in the keypad control.

The software has a backend written to it that collects data such as the baby's weight which will be entered into the Arduino microcontroller using a keypad. It is from this weight entered that the various parameters required for the exchange transfusion procedure are calculated. These parameters include: total blood volume for the transfusion, time for drawing blood, time for delivering blood, total number of cycles for the transfusion, syringe volume, steps required to draw and deliver blood, speed of the motor for drawing and delivering blood. These variables are represented in the code by variables that store values for the parameters listed above. The variables for our software are shown in the snippet below:

```
 //*****************Variable Definition**********
int StepsRequired;
int count;
int data_count;
float babyWeight=0;
int syringeVolume = 15;
int totalBloodVolume;
int numberOfCycles;
int minutesPerCycle;
int number_of_steps;
int number_of_revs;
float rpmDraw;
float rpmDeliver;
```

A setup code is written to the Arduino IDES setup function that displays introductory information to the user and prompts action from the user. The setup code is shown below;

```
  // put your setup code here, to
void setup() {

  Serial.begin(9600);
 lcd.init();
  lcd.init();
  lcd.backlight();
  lcd.setCursor(5,0);
  lcd.print("WELCOME");
  delay(4000);
  lcd.setCursor(5,0);
  lcd.print("ANET 3.0");
  delay(4000);
  lcd.clear();
  lcd.setCursor(1,0);
  lcd.print("BEDE , ANDREW ");
   delay(2000);
  lcd.clear();
  lcd.setCursor(3,0);
  lcd.print("and NANA");
 delay(4000);
   lcd.clear();
    lcd.setCursor(0, 0);
    lcd.print("Input weight of");
    lcd.setCursor(0, 1);
    lcd.print("baby in kg:");
}
```

The first thing displayed is a welcoming message on the LCD followed by the name of the device and the version together with our names. Delays are included after each display to allow time for the user. The user is then prompted to input baby's and the weight prompt stays on the screen until the user of the device inputs the required data i.e. weight of baby.

Figure 37 LCD displaying prompt to user

A function has been written that selects the volume of syringe that should be used for a given procedure based on the weight input and the number of steps it takes to drive the plunger in and out to accommodate

that particular syringe volume. The number of steps required to draw or pump a particular volume is determined using that volume of syringe and the result can be used to determine that of other syringe volumes. In our case we used the 10 ml syringe for these calculations, the number of steps was determined and the value gotten was used to find the number of steps for the 5ml, 15ml and 20ml syringes using ratio and proportion. To find the number of steps, we first determined or measured the distance the plunger or carriage will have to travel in order to draw a required volume. This distance is then divided by the lead of our lead screw (which was 2) to get the number of revolutions for that particular distance. For the Nema 17 motor used in the syringe pump, the number of steps per revolution is 200 steps and thus multiplying 200 by our number of revolutions we need we are able to get our number of steps

After the baby's weight is entered, it enters straight into this function to actually check if the baby's weight is within a particular range and selects a syringe volume and the number of steps. This information is displayed on the LCD. After the display on LCD, the variables syringeVolume and numberOfSteps are both initialized. A portion of the function definition is displayed in the snippet below;

```
//Function for getting Syringe Volume
int getSyringeVolume(){
  if(babyWeight < 1.5){
    lcd.clear();
    lcd.setCursor(0, 0);
    lcd.print("Use 5ml syringe");
    delay(5000);
    syringeVolume = 5;
    number_of_steps = 800;
  }
else if(babyWeight>=1.5 & babyWeight <= 2.5){
  lcd.clear();
    lcd.setCursor(0, 0);
    lcd.print("Use 10ml syringe");
    delay(5000);
  syringeVolume = 10;
  number_of_steps = 1600;
}
else if(babyWeight>2.5 & babyWeight <= 3.5){
   lcd.clear();
    lcd.setCursor(0, 0);
    lcd.print("Use 15ml syringe");
    delay(5000);
  syringeVolume = 15;
  number_of_steps = 2400;
 }
else{
   lcd.clear();
    lcd.setCursor(0, 0);
    lcd.print("Use 20ml syringe");
```

The code snippet below shows the function definition of Exchange Transfusion(), where all the necessary calculation needed for the exchange transfusion to take place is done. The first line of code in the function

definition shows the calculation for the total blood volume needed for the transfusion. To arrive at this number, the baby's weight is multiplied by 160 because we are implementing the double blood volume procedure. To determine the number of cycles, the selected syringe volume divides the total blood volume for the exchange. It must be noted that all the functions are based on the baby's weight entered. The keyword ceil is approximate the value for the number of cycles calculated in case it is a decimal value. Next thing we calculated was the number of minutes each cycle in the transfusion process will take. A cycle in the transfusion process consists of successfully drawing of blood from the baby, discard it, drawing fresh donor blood and finally delivering the blood to the baby. For the minutes each cycle takes, we can see that 120 was divided by the numberOfCycles; the reason is because the process is supposed to be done within 2 hours and the number of minutes within 2 hours is 120. In the transfusion process, drawing of blood from the baby is a bit faster than delivering new blood to the baby. However, both processes are usually very slow. A ratio was determined in order for minutesPerCycle to be shared between minsForDrawing and minsForDelivering. These ratios calculated were based on the observation of an actual exchange transfusion. For the observed transfusion, each cycle took a total of 6 mins. The time for drawing blood was 2 mins 30 seconds and time for delivering blood to the baby was 3 mins 30 seconds. On this basis, calculating for the ratios;

Ratio for drawing blood = 2.5/6 =0.41667 and

Ratio for delivering blood = 3.5/6 =0.5833

Since the time taken to draw and deliver blood to the baby vary, the motor speed for each cycle phase will differ, resulting in different revolution per minute (rpm). Rpm's for both drawing and delivering need to be calculated by dividing the number of revolutions by minsForDrawing and minsForDelivering respectively. For instance, based on the number of revolutions we had in the previous calculation and the minutes per cycle for the live transfusion we witnessed;

Rpm for drawing blood = 14.705/2.5=5.882 rpm

Rpm for delivering blood = 14.705/3.5=4.20 rpm

```
}
//***************Function for exchange transfusion*************************//
float ExchangeTransfusion(){
  //Pre-transfusion calculations
   float totalBloodVolume = babyWeight * 160;
   int numberOfCycles = ceil(totalBloodVolume/syringeVolume);
   float minutesPerCycle = 120/numberOfCycles;
   float minsForDrawing = ceil(0.4167*minutesPerCycle);
   //Minutes for drawing blood is 5/12 of the total minutes per cycle
   float minsForDelivering = ceil(0.5833*minutesPerCycle);
   //Minutes for drawing blood is 7/12 of the total minutes per cycle
   float number_of_revs = ceil(number_of_steps/200);
    int rpmDraw = number_of_revs / minsForDrawing;
    int rpmDeliver = number_of_revs / minsForDelivering;
```

A for loop was started that is responsible for performing the whole exchange transfusion process. The loop starts a count from 1 and performs the same set of instructions multiple times until the count value is

greater than the number of cycles calculated in the previous section. In the first section of the motor direction is set to move backwards which will cause the pusher block to draw blood into the syringe. At this point, the motor speed has been specified in the rpmDraw code which is already calculated for in the previous code. The number_of_steps value is also needed to give the distance the motor will move the pusher block to draw a specific volume of blood.

The second part of the code was written for discarding blood which is done after drawing blood from baby. This time, another motor comes into play (motor2), which is responsible for switching valve opening to waste bag and bad blood from the baby is discarded using motor1. This time the motor speed is set at 80 rpm, this is because discarding of blood is supposed to be done at a fast rate and 80 rpm was the highest speed our motor could move effectively without breaking. The motor direction is set to move forward to discard blood. The snippet below shows the code for the first two parts of this for loop.

```
for(count = 1; count <= numberOfCycles; count++ ) {
   //STEP 1, DRAWING BLOOD FROM THE BABY
lcd.clear();
lcd.setCursor(0,0);
lcd.print("Drawing blood");
lcd.setCursor(0,1);
lcd.print("from baby");
lcd.setCursor(10,1);
lcd.print("C" + String(count) + "/C" + String(numberOfCycles));
motor1.setSpeed(rpmDraw); // calculated rpm
motor1.step(number_of_steps, BACKWARD, DOUBLE);
 //main motor moves backwards to draw blood from baby

//STEP 2, DISCARDING BLOOD INTO WASTE BAG
lcd.clear();
lcd.setCursor(0,0);
lcd.print("Discarding blood");
lcd.setCursor(9,1);
lcd.print("C" + String(count) + "/C" + String(numberOfCycles));
// Motor2 rotates in a clockwise direction to open valve to waste bag
StepsRequired  =  -STEPS_PER_OUT_REV / 3.5;
motor2.setSpeed(1000);
motor2.step(StepsRequired);
motor1.setSpeed(35);  // 10 rpm
motor1.step(number_of_steps, FORWARD, DOUBLE);  //main motor moves backwards to draw blood from baby
```

The next section is responsible for drawing fresh blood from donor bag. Here motor2 is moved counter-clockwise and closes the opening to the waste bag. Another motor (motor3) is moved clockwise to open way to the donor bag for fresh blood to be drawn. Drawing fresh blood from the donor bag is also drawn fast and thus , the motor (motor1) speed is set at 80 rpm and is set to move backwards to draw blood from donor bag.

```
  //STEP 3, DRAWING FRESH BLOOD FROM DONOR BAG
  lcd.clear();
  lcd.setCursor(0,0);
  lcd.print("Drawing fresh");
  lcd.setCursor(0,1);
  lcd.print("blood");
  lcd.setCursor(8,1);
  lcd.print("C" + String(count) + "/C" + String(numberOfCycles));
  StepsRequired  =  STEPS_PER_OUT_REV / 3.5;
  // Motor2 rotates in a counter clockwise direction to close valve to waste bag
  motor2.setSpeed(1000);
  motor2.step(StepsRequired);
  StepsRequired  =  -STEPS_PER_OUT_REV / 3.5;
  // // Motor3 rotates in a clockwise direction to open valve to waste bag
  motor3.setSpeed(1000);
  motor3.step(StepsRequired);
  delay(200);

   motor1.setSpeed(35);  // 10 rpm
   motor1.step(number_of_steps, BACKWARD, DOUBLE);
   //main motor moves backwards to draw blood from baby
```

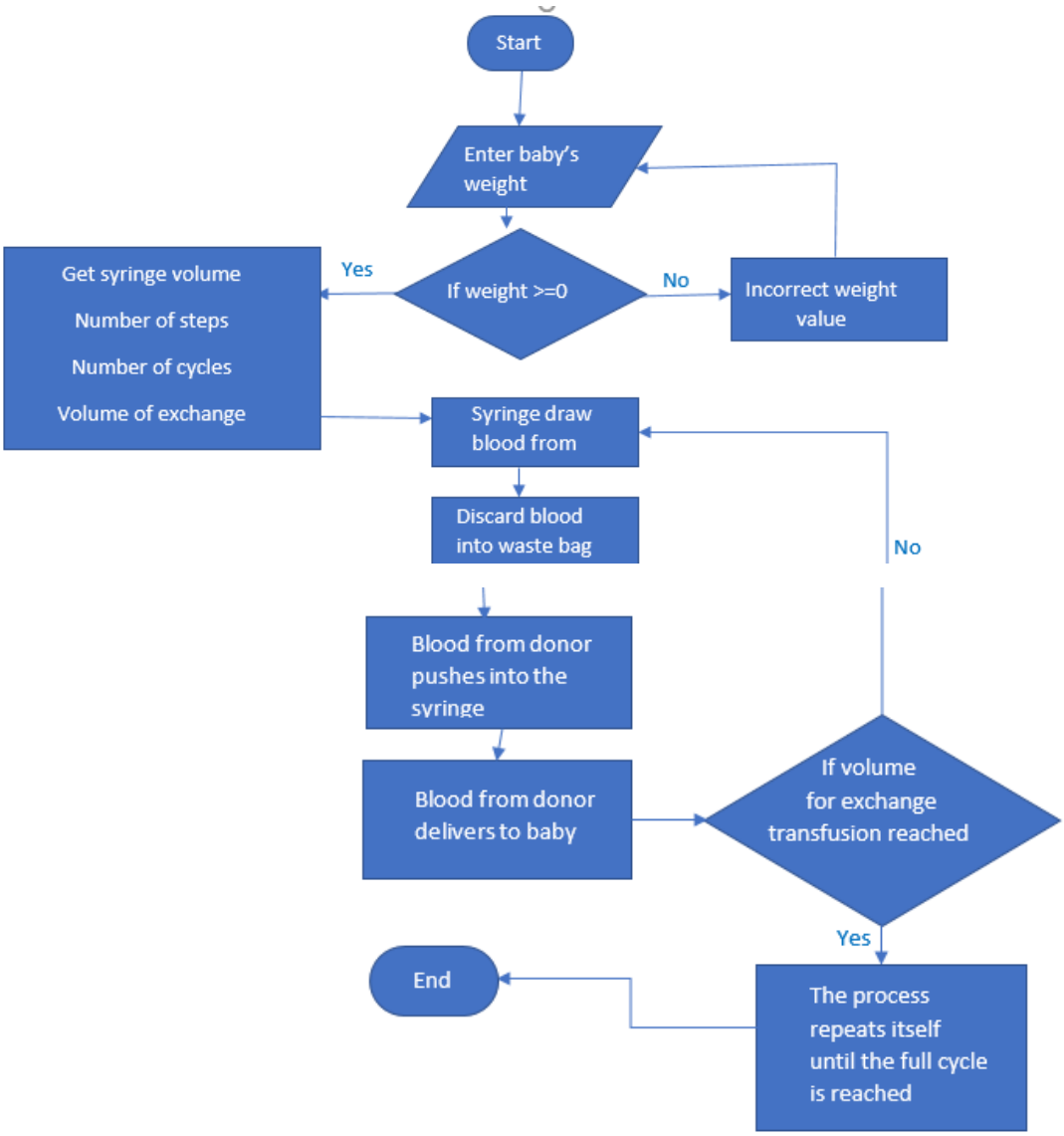
The second part of this section below is responsible for delivering fresh blood to the baby. Motor3 is moved anticlockwise in order to close the opening to the donor bag. This time all openings point to the baby and fresh blood is delivered to the baby at a speed equal to the rpmDeliver and movement is also set to ‘FORWARD’.

```
  //STEP 4, DELIVERING FRESH BLOOD TO BABY
  lcd.clear();
  lcd.setCursor(0,0);
  lcd.print("Delivering blood");
  lcd.setCursor(0,1);
  lcd.print("to baby");
  lcd.setCursor(10,1);
  lcd.print("C" + String(count) + "/C" + String(numberOfCycles));
  StepsRequired  =  STEPS_PER_OUT_REV / 3.5;
  motor3.setSpeed(1000);
  motor3.step(StepsRequired); // Motor3 rotates in a counter clockwise direction to close valve to donor bag
  motor1.setSpeed(rpmDeliver);  // 10 rpm
  motor1.step(number_of_steps, FORWARD, DOUBLE);  //main motor moves backwards to draw blood from baby
//Prompt user
  lcd.clear();
  lcd.setCursor(0,0);
  lcd.print("Numb of complete");
  lcd.setCursor(0,1);
  lcd.print("cycles:");
  lcd.setCursor(8,1);
  lcd.print( String(count) + "/" + String(numberOfCycles));
    delay(5000);
}
```

After the number of cycles intended to be done and the volume intended to be exchanged has been reached, the code has written to prompt the user that number of cycles that has been completed in case the user comes back at any time during the process. The code displays ‘Transfusion complete’ .

```
//Completion message
lcd.clear();
  lcd.setCursor(0,0);
  lcd.print("Transfusion ");
  lcd.setCursor(0,1);
  lcd.print("complete");
  lcd.setCursor(9,1);
  lcd.print(count);
    delay(5000);
```

3.5.5.1 Flow Chart Of the Process



4 CHAPTER 4
TESTING RESULTS AND DISCUSSIONS

This chapter comprise the results from tests run on ANET 3.0 and discusses these results in order to evaluate the device and draw conclusions.

4.1 Risk assessment of the device (ANET)

In performing risk analysis for ANET, a risk assessment table was mad which contained all the hazards associated with the device. A case was considered where by nothing has been done to nullify any risk while it was in use. This was done to capture every possible risk associated with the device. The table also contains a prediction of a sequence of actions or events that will occur to initiate a hazard becoming an incident and also the hazardous situation or the part of the hazard that causes harm as well as the possible harm that are likely to occur.

After all this data is collected, an analysis is done to determine the probability of harm. This probability of harm describes the possibility of harm being suffered by the patient or user and not just the presence of a hazard since not all hazardous situations will lead to harm. The severity of all hazards listed was also documented in the table and each hazard can be traced to its probability of occurrence and severity when risk control measures are to be taken.

Table 3 Completed risk assessment table for ANET

Risk Assessment Table

I. Hazards predicted from design and bench testing

Hazard	**Reasonable foreseeable sequence or combination of events**	**Hazardous Situation**	**Harm**	**Probability of occurrence**	**Severity**
Coagulation of blood	Blood clots after leaving patient body or donor bag	Thrombosis	• Pain and swelling • Stroke /heart attack • Death	Probable	Serious
Air emboli	Air bubble or foam trapped in blood line due to line – pump separation	Blood vessels blocked	• Heart attack • stroke • Respiratory failure • Death	Probable	Serious
Thrombosis	Blood clots get into the blood vessels from the blood line	Blood clots accumulate or block blood vessels	• Pain and swelling • Stroke /heart attack • Death	Probable	Serious

Endurance of device	Device ability to perform well for long periods	Device stops before procedure is completed	• Shock • Inconsistencies in operations • Death	Occasional	Serious
Ergonomic hazards (repetitive movements, improper set up)	Device not set-up correctly Blood line separation	Inaccurate measurements Air emboli Pressure altered	• Heart attacks • Strokes	Occasional	Critical
Development of Allergies	Chemical reactions in the body	Mixing of patient blood and donor blood	• Hives • Itching • Fever	Occasional	Critical
Toxicity	Reactions of foreign body being introduced into it	Foreign body could be from the introduction of needles and catheters	• Inhibition of hemoglobin • It accelerates aging	Occasional	Critical

II. Hazards associated with blood related devices and exchange transfusion

Hazard	**Reasonable foreseeable sequence or combination of events**	**Hazardous Situation**	**Harm**	**Probability of occurrence**	**Severity**
Catheter related complications	Allergy, Poor catheterization , Blood line breaks	The wrong type of catheter or catheterization used	• Thrombosis • Air emboli	Occasional	Critical
air emboli; thrombosis	Air bubble, foam or clots blocking blood vessel	Blood vessels blocked	• Heart attack • stroke • Respiratory failure • Death	Probable	Critical

Hypo or hyperthermia	Reactions to blood being exchanged	Temperature rises above normal temperature	• Fatigue • Muscle spasms • Nausea • Vomiting	Occasional	Critical
Hemodynamic (related to excess removal of injection of blood): hypo or hypertension	Inaccurate timing of blood pumping, Inaccurate, inconsistent volume drawn and pumped	Too much or too little blood drawn or pumped Blood drawn or pumped too early or too late	• Shock • Heart rate complications • Heart attack • Death	Occasional	Critical
Hypo or hyperglycemia	Inaccurate, inconsistent volume drawn and pumped	Too much or too little blood drawn or pumped	• Shock • Death	Occasional	Critical
Infection	From the exposure of the site where the exchange transfusion takes place i.e. umbilical or peripheries	Bacteria from the atmosphere could infect the place of procedure	• Fever • Difficulty in breathing • Blood in urine	Probable	Critical
Acute immune hemolytic reaction	Immune system attacks the transfused red blood cells because the donor type may not be a good match	Attacked cells release a substance into your blood	• Kidney attacks • Liver attacks	Probable	Critical
Delayed hemolytic reaction	A decrease in red blood cells	It affects the body slowly and could take up to 4 weeks to show up	• Anemia • Increased levels of jaundice	Probable	Critical
Graft vs host disease	Usually fatal ,it is more likely to affect people with severely	In this condition ,transfused white blood cells attack your bone marrow	• Leukemia • Lymphoma	Probable	Critical

	weakened immune systems				

III. General device hazards

Hazards	**Reasonable foreseeable sequence or combination of events**	**Hazardous Situation**	**Harm**	**Probability of occurrence**	**Severity**
Electrical hazards	User comes into contact with live wire, Fluids come into contact with electrical components	User is exposed to electricity	• Injury • Death	Probable	Critical
Mechanical hazards	Improper contact or entanglement to machine parts	Exposure to injurious machine parts	• Injury • Death	Probable	Critical
Misuse	Use of device or its parts for wrong purpose	Wrongful use of the device for the specific function	• Injuries • Death	Frequent	Catastrophic
Malfunctions	Software failures could cause this	It may lead to input of wrongful data which would affect proper transfusion	• Anemia • Fatigue • Weakness	Frequent	Critical
Fire or explosion	Wires may unfortunately touch due to improper wiring	Lines of wires being exposed	• Burns • Injuries	Remote	Serious

Extreme or lesser output	It happens when there is more power flowing through the equipment or less power flowing through it	Failure to adhere to proper electrical connections	• Shock • Fire	Improbable	Minor
Sharps	Needles being left too exposed	Recklessness of medical officers or users of medical devices	• Cuts • Sores	Frequent	Minor
Medication administration errors	Wrongful input of specific capacity of donor bags	Could disrupt correct organs working in the body	• Organ failures • Death	Remote	Critical
Absence of function	Device being used past it required usage or time slots	It would lead to improper	• Death • Injuries	Remote	Critical

4.2 Results from device tests

Several tests were performed on ANET 3.0 during its fabrication to verify the functioning of the various parts. The built model was tested using normal saline. Two separate bags of normal saline were used, one which dyed red to serve as the waste blood and another which was clear and served as donor blood. All the variables were manually calculated including the total blood for the transfusion, number of cycles and revolutions per minute (rpm) of the motor for each cycle among other parameters after which they were entered into the device to ensure that we were getting the right values. A timer was used to measure duration of cycles .

The bipolar stepper motor of our syringe pump was able to easily draw and pump the saline used in this trial and the stepper motors coordinated the valve switching as programmed by the microcontroller the switching was not as accurate as we expected it to be. The motors and valves needed to be held down before turning was possible.

The table below shows the data collected during our tests and this data was compared with that of ANET 2.0.

Table 4 Data collected from testing ANET 3.0 with saline

Data collection tables

Volumes per cycle

Volume Out (Withdrawn)	Volume In (Transfused)
10	10
10	10
10	10
10	10
10	10
10	10
10	10

Cumulative volumes

Volume Out (Withdrawn)	Volume In (Transfused)
10	10
20	20
30	30
40	40
50	50
60	60
70	70
80	80

Time per cycle

CYCLE	TIME TAKEN
1	4:26
2	4:28
3	4:27
4	4:28
5	4:26

5 CHAPTER 5
CONCLUSION AND RECOMMENDATIONS

5.1 CONCLUSION

The various tests performed in this project and animal trials as well as the risk analysis on ANET 2.0 brought to light important factors that affect the effectiveness of the exchange transfusion process and that are important be considered if the procedure is to be automated. ANET 3.0 was built based on those results and we attempted based on our finances and time allocated for the project to build a device that meets the needs of most of these factors. ANET 3.0 was built to offer better safety, performance and handling as an improvement from the previous editions. Although working with similar principles ANET 3.0 has a number of new additions as well as improvements in the various sections of ANET. Further additions and improvements would be made based on the findings from this project that will seek to fine tune ANET into an effective, efficient and reliable medical device to be used in various health facilities in Ghana, Africa and across the world.

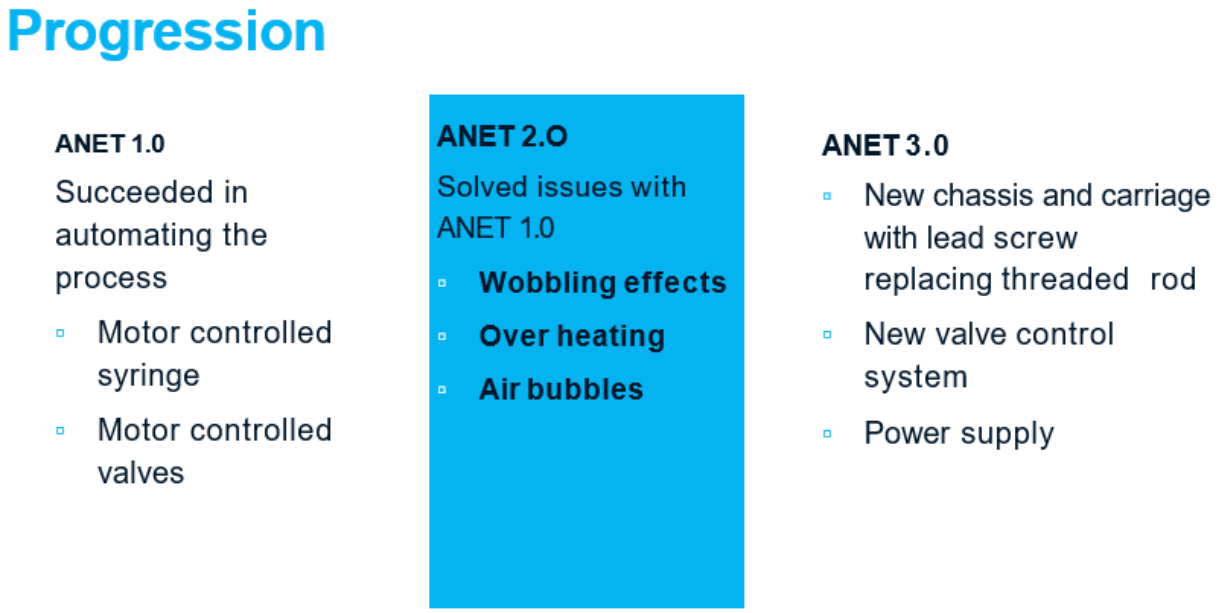


Figure 38 Progression of ANET

5.2 Recommendations

Based on results from the implementation of ANET 3.0 and testing findings were made and possible solution were established that will curb some of the limitations that still exist in ANET. It was however not feasible to implement these established solutions in our project due to financial and time constraints and thus these solutions will be suggested as recommendations for future implementation.

5.2.1 Recommendations for building device

- Heparin pump : another pump should be added to the device that would be responsible for injecting into the blood circuit while the procedure is ongoing to reduce clotting of the blood in the tubes and catheters.
- Monitoring system for blood circuit : a monitoring system should be implemented in the device that will employ the use of sensors to track the flow of blood in the blood circuitry as well as detect anomalies such as air bubbles or emboli which will make the device safer.

5.2.2 Recommendations for animal testing

- In performing future animal tests it is recommended that the test should be done with a catheter inserted directly into the umbilical vein of the test subject as this will allow easy blood flow and minimize clotting
- It is also recommended that the tests be performed on a test subject in which hyperbilirubinemia or jaundice is induced as this will serve as a proof of the clinical effective ness of the device.

5.3 Gantt chart showing the schedule of project

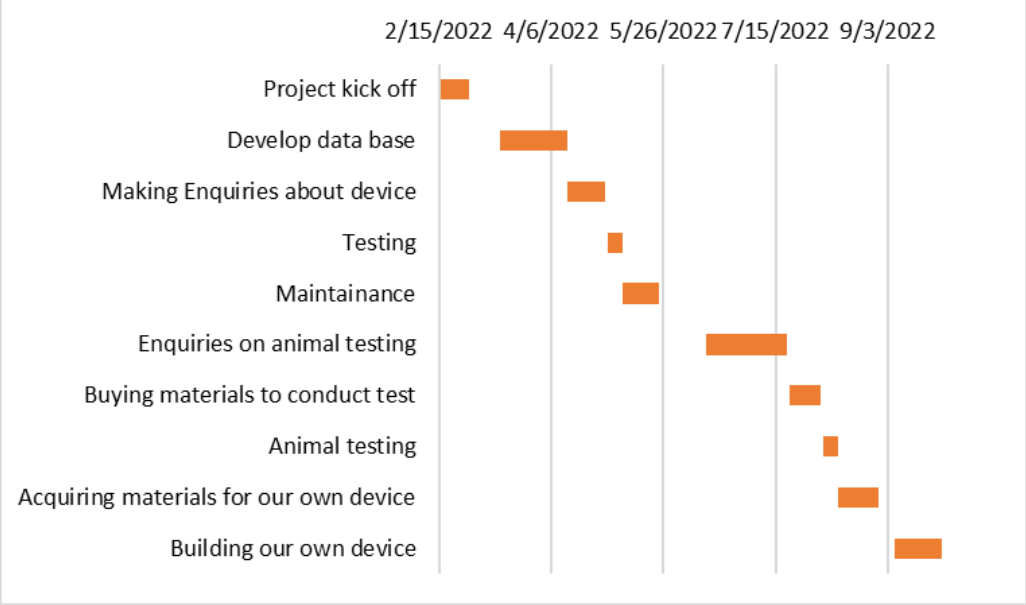


Figure 39 Gantt chart

Table 5 Data for Gantt chart

TASK	START DATE	END DATE	DURATION
Project kick off	2/15/2022	2/28/2022	13
Develop data base	3/14/2022	4/13/2022	30
Making Enquiries about device	4/13/2022	4/30/2022	17
Testing	5/1/2022	5/8/2022	7
Maintenance	5/8/2022	24-May	16
Enquiries on animal testing	6/14/2022	7/20/2022	36
Buying materials to conduct test	7/21/2022	8/4/2022	14
Animal testing	8/5/2022	8/12/2022	7
Acquiring materials for our own device	12-Aug	8/30/2022	18
Building our own device	9/6/2022	9/27/2022	21

5.4 Cost Analysis

Although this project was aimed at coming out with a device that will be affordable, we were very critical about the quality of components used in the project and only purchased from trusted sources. A few others that were to be fabricated were done locally and in managed conditions whilst still retaining high quality. A cost analysis our finances is shown in the table below;

Table 6 Cost analysis table

Component	Quantity	Budget (GH₵)	Actual (GH₵)
Arduino Mega 2560 R3	1	200	300
Bipolar stepper motor (NEMA 17)	3	300	210
28BYJ-48 Unipolar stepper motors	2	100	40
Aduino motor shield	1	30	35
L298N H Bridge Motor Controller	2	140	60
LCD & i2c	1	50	25
Keypad	1	20	10
Jumper Wires	-	20	25
Guiding rods	2	20	2
Lead screws	2	50	40
Lead acid battery	1	40	70
Energizer batteries	5	100	125
3D Printed components	-	200	305.5
Electronics housing	1	50	-
Voltage booster	2	40	50
Shipping expenses	-	250	200
Miscellaneous		250	200
Total		**GH₵1860**	**GH₵1697.5**

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Consent, “The aim of an exchange transfusion is: Haemolytic disease: Indications for exchange transfusion and FFP: Types of Red Blood Cells,” no. ext 58033.

Neli Gluzman, “Everything you need to know about jaundice in newborns”, 2019

References.

Albert Prince Kwasi Okrah, Benjamin Amanor Kisser, “Automated Neonatal Exchange Transfusion”, 2021

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