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DEPARTMENT OF COMPUTER ENGINEERING

BIOMEDICAL ENGINEERING



AUTOMATED NEONATAL EXCHANGE TRANSFUSION (ANET 4.0)

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DECLARATION

We declare that this project is our own work as a requirement for the award of a BSc. Biomedical Engineering degree, under the supervision of Mr. Prince Odame. We also declare that except where references were made and credit is duly given, the project is a result of our collective effort, ingenuity, research, and skills.

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CHAPTER ONE

INTRODUCTION

The background of the project, its relevance, scope, and objectives, and its significance to the advancement of the health sector in Ghana are discussed in this chapter.

1.1 BACKGROUND

During pregnancy, the placenta excretes bilirubin (Children's Hospital, 2023; Michael *et al.*, 2020). According to recent statistics, 80% of preterm and 60% of term neonates develop jaundice (Children's Hospital, 2023; Woodgate & Jardine, 2011), which can be attributed to the underdevelopment of organs like the liver leading to the build-up of bilirubin (unconjugated bilirubin) in the blood, other tissues, and fluids of the body of neonates. This condition is termed hyperbilirubinemia (Woodgate & Jardine, 2011). Hyperbilirubinemia is a leading cause of long-term neurodevelopmental impairment such as kernicterus and bilirubin-induced neurologic dysfunction (BIND)(Michael *et al.*, 2020). In Sub-Saharan Africa, long-term impairment following kernicterus is eight times more common than in high-income countries.

Diagnostic methods of hyperbilirubinemia include direct and indirect bilirubin levels, red blood cell (RBC) counts, blood type, and testing for Rh compatibility. Neonates whose mothers are diabetic and have Rh disease are more prone(Children's Hospital, 2023; Lee *et al.*, 1977). And hyperbilirubinemia is fairly common in nations like Ghana, where the genetic disorder glucose-6-phosphate dehydrogenase (G6PD) deficiency is very widespread. (Seneadza *et al.*, 2022). Some neonates may develop breastmilk hyperbilirubinemia, or breastfeeding hyperbilirubinemia. Benign neonatal hyperbilirubinemia is a transient and normal increase in bilirubin levels occurring in nearly all neonates. It was previously termed "physiologic jaundice". But for most neonates, this usually does not happen (Bhutani *et al.*, 2004).

Treatment methods include phototherapy, fiberoptic blanket, exchange transfusion, and ceasing breastfeeding for one or two days(Bhutani *et al.*, 2004; Children's Hospital, 2023; Duan *et al.*, 2006).A research also in China according (Duan *et al.*, 2006) to also depicts these methods of treatment. Globally, the most predominant modality is phototherapy especially when there is early detection of hyperbilirubinemia(Roelandts, 2002).

However, in severe cases of hyperbilirubinemia, usually as a result of late detection, phototherapy becomes a less effective treatment method as shown in figure 2, and considering the cost of phototherapy units, exchange transfusion becomes a more preferred approach in our part of the world (Furlan *et al.*, 2005; Roelandts, 2002). Exchange transfusion is an allogenic procedure where the neonate's blood which is contaminated with very high levels of bilirubin, is replaced with fresh blood from a donor (Ullah *et al.*, 2016). Exchange transfusion is a procedure that involves alternating giving and withdrawing blood in small amounts through a vein or artery (Bhat Y, 2007). If bilirubin levels remain high, the procedure may need to be repeated. This procedure is strictly performed in the Neonatal Intensive Care Unit (NICU) (Gartner, 2001).

The aim of the project is to design a cost-effective, time-saving workable device to make the procedure of exchange a smooth one with less human intervention for use in our part of the world.

1.2 PROBLEM STATEMENT

Neonates with serious medical issues, such as hemolytic disease (HDN), which is brought on by an incompatibility between the mother's and the baby's blood types, jaundice, anemia, or metabolic disorders, require a neonatal exchange transfusion. (Fonger *et al.*, 2014).

Although the procedure replaces a large volume of the baby's blood and is life-saving, it poses several challenges that threaten the infant's well-being and survival. Other complications can arise during or after the procedure, including bleeding, transfusion reactions, infections, and, most importantly, iron overload, which damages the infant's heart, liver, and lungs (Sabzehei *et al.*, 2015). It is crucial to control the transfusion rate carefully to prevent overloading the infant's circulatory system. The transfusion should also be performed slowly to reduce the risk of adverse reactions and complications, such as transfusion reactions, bleeding, and infections (Lee *et al.*, 1977).

It is very important that the procedure be performed accurately and consistently in order to ensure the best outcomes for the newborn, but since it takes such a long time, it is tedious and prone to human error.



Figure 1 : A neonate undergoing exchange transfusion

(Ciko *et al.*, 2010)



Figure 2 : Phototherapy used to treat a patient.

(repository, 2021)

1.3 OBJECTIVES

This project's main goal is to develop, build, and test the machine on lab subjects that automates the neonatal exchange transfusion procedure. The machine will then be used in clinical settings and intended for commercial purposes as well. All the information utilized in the manual procedure is included in the device's functionality. A motor will be programmed to move the syringe at a constant speed in order to draw and inject blood. Motors will also take the role of the doctor manually switching valves throughout the exchange operation. By doing this, human interference in the process will be eliminated. The automatic shut-off would turn the machine off when the process was complete using the alarm system.

1.3.1 SPECIFIC OBJECTIVES

The following are the project's specific goals:

1. Use programming, classical electronics, and mechanics to virtually automate the exchange transfusion procedure.
2. Include all the information from the manual procedure in our design
3. Create an educational user interface
4. Produce a workable, cost-effective effective and energy-efficient device for the public.

1.4 SCOPE OF THE PROJECT

A motor will be programmed to move the syringe at a constant speed in order to draw and inject blood. Motors will also take the role of the doctor manually switching valves throughout the exchange operation. This will almost remove all people involvement in the process.

1.5 SIGNIFICANCE OF THE PROJECT

It is impossible to overstate the importance of this effort. A device that is less dependent on humans offers a stronger assurance of reliability, precision, and efficiency. Also, many doctors and other healthcare professionals will benefit from the automation of the newborn exchange transfusion procedure.

The ordinary hospital in Ghana can buy it since its price is very modest compared to that of many other medical devices.

CHAPTER TWO

LITERATURE REVIEW

This chapter talks about the exchange transfusion as a medical procedure, principle of operation of the device and previous editions of ANET.

2.1 THE EXCHANGE TRANSFUSION PROCESS

The process involves taking aliquots of the patient's blood that are considered to be "bad blood" is taken and exchanged with aliquots of the donor's blood that are considered to be "good blood." This is what gives exchange transfusions its name; blood is taken out and replaced; there is an exchange (Kaneshiro, 2021; Ohto & Anderson, 1996).

Simple blood transfusions do not include the exchange of blood; blood is only supplied but not taken out (Underwood, 2019). Since some "old" blood and "new" blood are mixed or fused, the procedure is known as a blood transfusion. Exchange transfusions are always allogeneic, meaning that fresh, healthy blood always comes from a donor(ANDREW *et al.*, 2022).



Figure 3 : Exchange Transfusion Process

2.2 HISTORY OF NEONATAL EXCHANGE TRANSFUSION

Neonatal exchange transfusion has become a rare activity in most advanced countries but remains a frequent emergency procedure for severe hyperbilirubinemia in many underdeveloped countries, Ghana inclusive.(Underwood, 2019)

The history of NET may be traced to the Talmudic era (1st century C.E.) when the then-Jewish physicians used it as a last option for a number of ailments(Brecher, 2018). A Greek philosopher of the same era Aristotle also mentioned using it to treat jaundice (Sakhuja & Naik, 2008). Because the techniques required to assure the safe transfer of blood between donors and recipients had not yet been invented, exchange transfusions were not often offered until late in the twentieth century. Before the actual exchange transfusion procedure was developed, physicians often used a technique called 'bloodletting' to treat various medical conditions (Brecher, 2018).

This practice involved draining a patient's blood and replacing it with replacement fluids such as wine or animal milk. In 1906, the first successful exchange transfusion was performed by Dr. George Washington Crile in the United States (Brecher, 2018). Dr. Crile performed the procedure on a patient suffering from jaundice, replacing the patient's blood with stored blood from a donor(Teichler-Zallen, 2004).

The patient survived and eventually recovered from jaundice. In the following decades, exchange transfusions were further developed and refined. The approach, interchange even though it was Alexander Weiner who invented and gave the term "transfusion" its initial suggested by Dr. Bruce Robertson, a Canadian physician, in 1921(LK, 1947). The technique was applied in the therapy for children with serious burns. In the 1930s, researchers began to use the technique to treat severe anemia in premature babies (LK, 1947). A doctor from the hospital in Toronto Dr. Alfred P. Hart was the first to execute an exchange transfusion for sick children in 1925 to treat newborns with hemolytic disease (Funato & T, 1997).

It involves drawing blood from the femoral vein to replace the young child's radial artery, longitudinal sinus, or external jugular vein, or it with new donor blood through an ankle cut-down. This was how in the past they used as a process to withdraw blood from the neonate(Cogan, 1978; Spaeth & Cottrille, 1958).

Exchange transfusions have saved countless lives over the past century, and continue to be an important medical procedure used to treat a wide range of medical conditions (Elizabeth, 1975).

The need for blood exchange transfusions has decreased recently due to technological developments like the production and consumption of Rh-immunoglobulin, advancements in prenatal ultrasound, intensive phototherapy, and updated American Academy of Pediatrics (AAP) standards for hyperbilirubinemia.(Kaneshiro, 2021). The need for expertise for this procedure in most developed countries has drastically dropped. In developing countries, technological breakthroughs and simulations have evolved to improve the safety of this procedure(Murki & Kumar, 2011).

In underdeveloped countries like Ghana however, exchange transfusion remains the most used procedure because of the absence of community-based use of phototherapy, below-standard or ineffective phototherapy devices, and late recognition of high levels of bilirubin(Murki & Kumar, 2011).

2.3 RELEVANCE OF NEONATAL EXCHANGE TRANSFUSION

While the exchange transfusion procedure may be performed for infants, specifically neonates as well as adults, this project addresses neonatal exchange transfusion. Exchange transfusion is done when methods like phototherapy alone is ineffective for treating hyperbilirubinemia(Okrah & Kisser, 2021). It involves withdrawing the neonate's damaged blood and simultaneously replacing with 'fresh' donor blood, (or more specifically red blood cells (RBC) reconstituted with plasma/FFP)(Tala, 2020).

Indications of hyperbilirubinemia include severe unconjugated hyperbilirubinemia, hemolytic disease of the newborn (HDN), neonatal hemochromatosis, polycythemia, anemia, and many more.

The neonate's red blood cells are measured in hemoglobin (Hgb) or hematocrit (Hct). Hct is related to gestational age. The average Hct at birth for a term neonate is approximately 50, and approximately 40-45 for a preterm neonate.(Tala, 2020)

Hemolytic Disease of the Newborn (HDN), also called erythroblastosis fetalis is a condition where the neonate at birth, is found to have very low levels of RBC's(anemia) due to premature hemolysis

of the RBC's during pregnancy. This may be attributed to Rh or ABO incompatibility of mother and baby. At the latter part of pregnancy or during childbirth, there may be mixing of the fetus' blood and the mother's blood across the placenta(Physiology&Anatomy, 2014). When the Rhesus Factor of the mother and the fetus are different, (suppose the mother is Rh-negative and the fetus is Rh-positive.

The presence of an antigen distinguishes Rh positive and Rh negative) the body of the mother produces antibodies to fight the red blood cells of the fetus since it recognizes them as foreign bodies. This causes the breakdown of the fetus' red blood cells (hemolysis)(Teichler-Zallen, 2004). The hemolysis occurs faster than the bone marrow produces new RBCs. Exchange transfusion is done to replace the damaged RBCs of the neonate and to increase the RBC count.

Severe unconjugated hyperbilirubinemia is a condition where there are very high levels of unconjugated bilirubin in the blood of the neonate. Bilirubin in this form is fat-soluble and can cross the blood-brain barrier and cause kernicterus which can further cause neurologic impairments and to prevent this an exchange transfusion is performed on the neonate. Bilirubin is an end product of the breakdown of red blood cells(Hospital, 2005). Ideally, bilirubin should bind with albumin in order to be converted by UGT (Uridine diphosphate-glucuronosyltransferase) to form conjugated water-soluble bilirubin in the liver, then further excreted (Heirwegh & Blanckaert, 1981). But this does not happen in the body of the neonates due to the undeveloped nature of the liver, leading to a build-up of the unconjugated bilirubin in the blood of the neonate (Steventon, 2020). This leads to severe unconjugated hyperbilirubinemia or neonatal jaundice (NNJ). Exchange transfusion is done to provide fresh albumin binding sites for RBCs in the blood of neonates.

According to (RCH, 2009), the final decision to perform an exchange transfusion will be made by the Consultant Neonatologist on service, with the consent of the parents of the neonate, and will be based on the following:

- Trend of serum bilirubin levels and response to treatment
- Clinical presentation of infant (signs of bilirubin encephalopathy)
- Underlying condition

- Previous treatment at referring hospital if applicable (including in-utero management of underlying condition).



Figure 4 : Neonatal Jaundice

(Ar-Rayyan, 2020)

2.4 STEPS IN THE EXCHANGE TRANSFUSION PROCESS: SINGLE CATHETER

Blood from donors should be screened before the medical procedure starts. To avoid graft in comparison to host disease, donor blood should ideally be radioactively treated within 24 hours of transfusion. Warming the blood to body temperature is necessary. (Murki & Kumar, 2011)

1. With the catheter's tip positioned in the inferior vena cava, the catheter can typically be advanced without resistance to a length of around 8 cm in preterm infants and 11 cm in term newborns. The catheter can be removed up to approximately 3 cm in preterm and 5 cm in term if there is resistance.
2. The newborn is put on a radiant warmer or a flat incubator mattress, and their vital signs are continuously monitored.
3. It's not required to use anesthetic. To reduce discomfort and maintain a sterile field, moderate restraints, sucrose treatments, and soothing techniques are required.
4. If the newborn was fed within the previous two to three hours of the surgery, the stomach's contents are evacuated via a gastric tube.
5. The use of diapers promotes cleanliness.
6. Sterile surgical drapes are used to cover the periumbilical region after cleaning it with betadine or chlorhexidine.
7. A loose purse string is wrapped around the base of the cord to aid in hemostasis. A French size 5 or 8 umbilical venous catheter prefilled with saline and linked to a 10ml syringe is carefully

introduced into the umbilical vein to the appropriate spot. To avoid air cavitation reaching the umbilical catheter, all associations should be prefilled with saline. To avoid air embolism, the catheter or the associations should never be passed open to the air. Air embolism is a considerable risk; so, the needle should be vertical throughout the combination, and air cavitation should be avoided during the withdrawal stage. The catheter is connected to 2 three-way stopcocks or 1 four-way stopcock.

8. During the process, each aliquot should be around 5%-8% of the predicted blood volume of the neonate. Normally, 15-to-20-mL aliquots may be removed or infused at a rate of 5ml/kg/min in a term newborn kid with a body weight appropriate for gestational age. It is best to be cautious with low-birthweight and premature newborn children, and withdrawal/imbuement should be limited to 5 mL/kg. Noting that as the aliquot volume decreases, the extent of dead space volume increases, making the BET less appealing. As a result, an aliquot of 2 mL is not recommended.

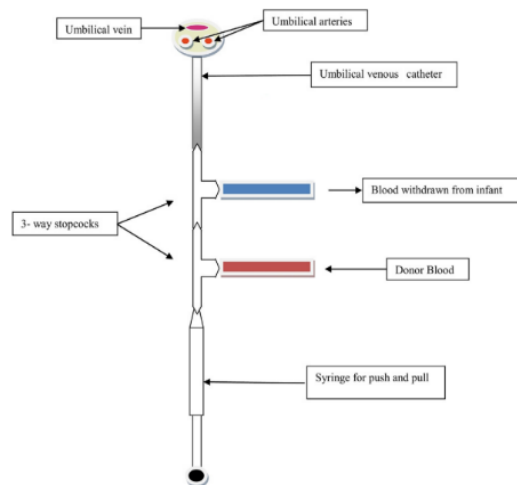


Figure 5: Flow diagram of the single catheter exchange transfusion

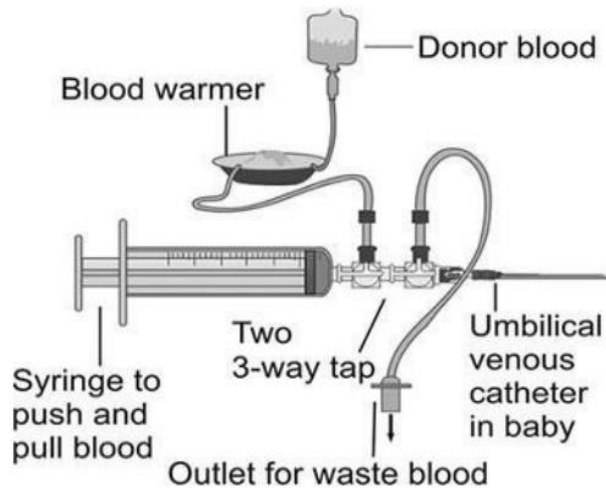


Figure 6 :Two three-way valves connected in series

(Okrah & Kissner, 2021)

2.5 EXCHANGE TECHNIQUES

The exchange techniques are the procedures or approaches to which the exchange transfusion is done.

- Single catheter pull-push technique: The umbilical vein enters the inferior vena cava just below the right atrial junction.
- Double catheter pull-push technique: This method involves inserting a catheter into both the umbilical vein and the umbilical artery.
- Substitute catheter: The substitute catheter is inserted into either a peripheral artery (typically a radial artery) or a big peripheral vein during the procedure. A big peripheral or branchial vein is usually sufficient. If the infant is critically dehydrated and the peripheral veins are compressed, it may be necessary to cannulate the jugular or femoral vein.

2.5.1 SINGLE CATHETER PULL-PUSH TECHNIQUE

One medical professional often uses this technique in exchange transfusion process without the need for an extra medical professional (Chatterjee *et al.*, 2023). It is a conventional technique that uses just one umbilical venous catheter. The series connection is terminated using a syringe, and the umbilical vein catheter is linked to two parallel three-way taps or stopcocks. Blood is removed in aliquots of 5-20 mL depending on the size of the newborn, and the correct amount of blood is subsequently restored. This is due to the fact that depending on the baby's weight, if more blood is

collected than necessary, the newborn may lose consciousness or have organ failure (Sakhuja & Naik, 2008).

Furthermore, blood is removed at a rate of 1.5–2 mL/kg/min (Doggett *et al.*, 2019). A nurse keeps track of each cycle's blood amount collected and delivered during the operation. The various vitals of the neonate are also checked periodically.



Figure 7 : Single Catheter illustration

(Starship, 2018)

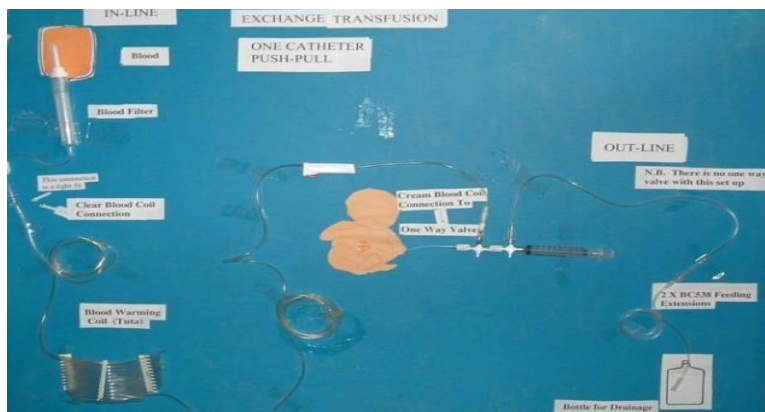


Figure 8 : One catheter push-pull

2.5.2 DOUBLE CATHETER PULL-PUSH TECHNIQUE

Two people are involved in this procedure. Here, many catheters inserted in various blood lines are used to concurrently remove and deliver equal amounts of blood. The utilized blood lines

include the umbilical artery and vein. Via the umbilical artery, blood is removed from the infant, while at the same time, blood is fed into the infant through the umbilical vein.(Doggett *et al.*, 2019)

This is also possible with other bloodlines; however arterial lines are often used for withdrawals rather than for giving out donor blood since arterial blood pressure is significantly greater than venous blood pressure. It is also called the Isovolumetric method.(Gajjar *et al.*, 2016)



Figure 9 : Double Catheter illustration

(Starship, 2018)

2.6 COMPLICATIONS OF EXCHANGE TRANSFUSION

Exchange Transfusion is regarded as a safe and successful treatment (Altunhan *et al.*, 2016), it is not without risk as in table 1. According to a study conducted (Badiee, 2007; Jackson, 1997), it was observed that the process when left untreated can cross the blood brain barrier causing a brain disorder called Kernicterus and in further cases can result in the death of neonates as well. The current guidelines for doing an exchange transfusion are based on a balance between the risks of encephalopathy and the problems linked to the treatment. Its death rates range from 0.5% to 3.3% (Bhat *et al.*, 2011). But, if the process is done extremely carefully and bilirubin levels are consistently monitored (Davutoğlu *et al.*, 2010), with the appropriate hygiene, and care, the majority of these issues may be avoided. Typically, pausing or slowing down the trade is the best way to handle these issues(Murki & Kumar, 2011; Victoria., 2018).

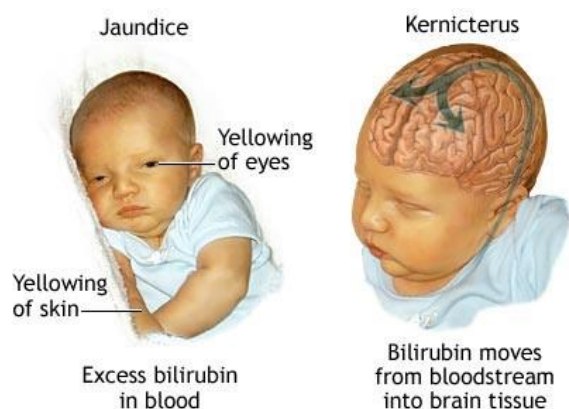


Figure 10 : Complications of Hyperbilirubinemia

Table 1 : Complication table

Complications during the procedure	Complications after the procedure
Air Embolus	Infection
Volume Imbalance	Thrombocytopenia
Hyperkalaemia	Hypoglycaemia
Arrhythmias	Blood transmitted infections
Respiratory Distresses	Hypocalcaemia
Anaemia/ Polycythaemia	Anaemia/ Polycythaemia
Acidosis	Hypernatremia

Table 2 : Complications

DONOR BLOOD	INFANT COMPLICATION	PREVENTION/TREATMENT
Old blood (high K^+ , low platelets)	Hyperkalemia, thrombocytopenia	Use blood less than 5 days old. Monitor ECG during and after procedure. Watch for signs of bleeding
Citrate blood	Hypocalcemia and hypomagnesemia	Consider 1-2 mL kg^{-1} of calcium gluconate after 50-100 mL of blood exchange in sick infants. Monitor serum calcium 2 h after an exchange. In case of unexplained arrhythmia use 2

		ml/kg of 10% calcium gluconate infusion
Cold	Hypothermia	Prewarm the blood.
High glucose	Rebound hypoglycemia	Check blood glucose 2 hours after exchange transfusion. Initiate early enteral feeds
Glucose 6-phospho dehydrogenase deficient	Increased hemolysis, rebound hyperbilirubinemia	In endemic areas screen for glucose 6-phospho dehydrogenase status of donor blood

2.5 BLOOD VOLUME CALCULATIONS

The difficulty in calculating the amount of exchange blood needed for newborns is related to how much blood is needed to raise their hemoglobin levels to an acceptable level. Nonetheless, a formula has been developed based on the supposition that the rise in hemoglobin

Throughout the operation, concentration is a linear function of volume exchange (Marsaglia & Thomas, 1971). The early stages of the blood exchange are when the change in hemoglobin concentration is largest, and it gradually decreases as the blood is exchanged.

The total volume of the cells and plasma in the circulatory system is what we refer to as blood volume (Brecher *et al.*, 1997; Gregersen & Rawson, 1959). The dilemma of whether or not the techniques for calculating plasma and cell volume include or omit these extravascular components immediately emerges because all components of the blood, including created elements, are to some extent present outside blood arteries (Brecher *et al.*, 1997; Gregersen & Rawson, 1959).

The general exchange volume parameter is given as:

The product of the total volume to be delivered and the weight of the baby which is all divided by 1kg.

Mathematically expressed as:

$$\frac{\text{Total Volume to be delivered}}{1.0kg} \times \text{weight of the baby}$$

	Weight	Exchange Volume	Total Volume of Blood
Preterm	1kg	$\frac{200ml}{1.0kg} \times 1.0 kg$	200ml
Term	2kg	$\frac{169ml}{1.0 kg} \times 2.0 kg$	320ml

According to the Table above, during the exchange operation, 200 ml and 320 ml of fluid will be given to preterm and term newborns, respectively. The exchange volume parameter provides the foundation for this computation. To calculate the number of cycles and the duration that the process will last, the formulars below are used:

$$\text{Number of cycles} = \frac{\text{Total Exchange Volume}}{\text{blood volume per cycle}}$$

$$\text{Duration} = \text{Number of Cycles} \times \text{time taken per cycle}$$

2.5.1 SINGLE VOLUME

The baby's blood volume is the same as the amount of the blood volume we estimate.

For instance, just 80ml/kg of blood volume would be needed to do a single-volume transfusion on a term. This method substitutes 60–65% of the baby's red blood volume.(Wadsworth, 2002)

Preterm or term babies mostly in the example table above, are given a total of 320ml and 200ml during the exchange procedure. (Wadsworth, 2002)

2.5.2 DOUBLE VOLUME

Double Volume Exchange Transfusion involves repeating the single volume exchange transfusion. The blood to draw from the neonate is estimated to be twice the baby's blood volume in circulation.(Mineshima *et al.*, 1998)

The blood to draw from the neonate Between 85-88% of the baby's red blood cells or blood volume are replaced.(Wadsworth, 2002)

The end part of this process is most popular and mostly used to treat newborns with chronic jaundice (hyperbilirubinemia)

The efficiency of the double volume exchange transfusion should have been twice as high as the single volume exchange transfusion, one may have predicted.

Yet this is not the case. Just a 25% average gain in efficiency is observed (i.e., from 80 to 85).

Nearly all of the baby's blood's circulation cannot be exchanged. This occurs as a result of circulation mixing the baby's blood with the blood flowing in. The double volume exchange transfusion is best when efficiency is compared to the total amount of blood that is circulated since it minimizes waste by using less time, energy, and resources while maintaining high efficiency.(Pstras *et al.*, 2021)

The amount of blood exchanged as an aliquot depends on the weight of the infant. This is because, depending on the weight of the infant, if more blood than a specific quantity is withheld, the child may lose consciousness or have organ failure. As a result, the following criterion is used to determine how much blood should be exchanged during a cycle.(Convertino, 2007)

Due to the circumstances surrounding the infant, the doctor may not strictly adhere to this and instead utilize quantities that are lower or higher.

In light of everything that has just been discussed, take into account the following: noting that the infant will get an exchange transfusion:

A premature infant with a mass of around one kilogram.

As the infant is premature, the standard quantity of blood exchange is around 200 ml per kilogram of the infant. By dividing this statistic by the baby's weight, we can determine the total volume of blood that has to be exchanged. *i.e.* $200\text{ml/kg} \times 1.0\text{kg} = 200\text{ml}$.

This suggests that a total volume exchange of around 200 ml is required. Also, because the infant weighs less than 1.5 kg, it follows that 5 ml-sized blood aliquots should be switched each cycle.

We divide the entire blood volume by the volume per cycle to determine the number of cycles necessary to exchange the complete blood volume. *i.e.* $\frac{200\text{ml}}{5\text{ml}} = 40 \text{ cycles}$

The process is carried out extremely slowly, taking 4-5 minutes every cycle, as was already said. Taking this instance into consideration, the total time for the exchange transfusion on the newborn will be equal to the time utilized each cycle times the overall number of cycles. *i.e.* $40 \text{ cycles} \times 4\text{mins cycle} = 160\text{mins} = 2 \text{ hrs } 40 \text{ min}$.

The following guidelines for exchange transfusion levels are based on the American Academy of Pediatric Guidelines and are adapted from the Department of Human Services (Victoria) Neonatal Handbook (RCH, 2009; Victoria., 2018)

Table 3 :Guidelines For Exchange Transfusion In Infants 35 Or More Weeks Of Gestation

Age (hrs)	Infants at higher risk 35-37 ⁺⁶ weeks + risk factors	Infants at medium risk ≥38 weeks + risk factors or 35-37 ⁺⁶ weeks and well	Infants at lower risk 38 weeks and well
	SBR (micromol/L)	SBR (micromol/L)	SBR (micromol/L)
Birth	200	235	270
12 hours	230	255	295
24 hours	255	280	320
48 hours	290	320	375
72 hours	315	360	405
96 hours	320	380	425
5 days	320	380	425
6 days	320	380	425
7 days	320	380	425

Table 4 : Guidelines For Exchange Transfusion In Low Birthweight Infants Based On Age

Age	Wt <1500g	Wt 1550-200g	Wt >2000g
Hours	SBR (micromol/L)	SBR (micromol/L)	SBR (micromol/L)
<24 hours	>170-255	>255	>270-310
24-28	>170-255	>255	>270-310
49-72	>170-255	>270	>290-320
>72	>255	>290	>310-340

2.6 PRINCIPLE OF OPERATION

2.6.1 BOYLE'S LAW

The automated neonatal exchange transfusion device works on the principle of **Boyle's Law**.

The automated neonatal exchange transfusion device works on the principle of Boyle's Law, the same principle applied to syringe pumps, infusion pumps, etc. Boyle's Law states that for gases, the pressure is inversely proportional to the volume. That is, $P \propto 1/V$.

The basic working principle of a syringe pump is that it converts the rotary motion of the motor in the pump to the reciprocating motion of the piston of the syringe. The syringe, which works on Boyle's Law principle is fits into the syringe pump. The motor of the syringe pump drives the movement of the piston, guided by its driver, a screw rod, and the reciprocating screw. The screw is connected to the piston in the syringe.

The syringe contains the medication to be administered. In the automatic versions, the pressure and rate are set according to the dose set, and hence the motor only acts on that amount, leading to smooth pulsating pressure. This is called the 'Thread Row Mechanism' because of the interconnection of all the parts of the machine driving one another (BiologyEye, 2023).

When the plunger of the syringe is pulled, the inside pressure, P_i decreases as the volume, V_i increases. At the same time the atmospheric pressure, P_{atm} remains greater than the inside pressure of the syringe. Inversely when the syringe is pushed, the inside pressure, P_i increases as the volume V_i decreases (Savin, 2020).

2.6.2 FLOW CHEMISTRY

The simultaneous withdrawal and delivery of blood in the automated neonatal exchange transfusion device are based on the principle of Flow Chemistry.

The concept of "flow chemistry" defines a very general range of chemical processes that occur in a continuous flowing stream, conventionally taking place in a reactor zone. The application of flow chemistry relies on the concept of pumping reagents using many reactors types to perform specific reactions. (Battilocchio & Ley, 2023) Flow chemistry depends on Stoichiometry, Residence Time, flow rate, steady rate.

2.6 PREVIOUS PROJECTS ON ANET

The idea of Automated Neonatal Exchange Transfusion started in 2020. The concept was conceived to make exchange transfusion an automated treatment method for hyperbilirubinemia.

This is because the process is a tedious and involves the intervention of the clinician which makes it prone to error.

The first project was hence named ANET 1.0. The name ANET was coined as an abbreviation of Automated Neonatal Exchange Transfusion thus using the first letter of each word of the topic.

Up until now, there have been three editions of ANET. (YIDDI *et al.*, 2020) are pioneers of this project implemented the idea in 2020 and named it ANET 1.0. (Okrah & Kisser, 2021) picked up from where (YIDDI *et al.*, 2020) left off and built ANET 2.0 using the same concept in 2021. The latest version of ANET, ANET 3.0 is an improvement of the ANET 2.0 model. It was worked on by (Agbedor *et al.*, 2022). In various generations, improvement was made on the existing model to help achieve the goal of the overall project.

Our edition, which is ANET 4.0 seeks to make ANET a workable device in healthcare centers nationwide, and globally, by addressing all challenges faced by the previous editions of ANET.

2.6.1 ANET 1.0

The whole idea of Automated Neonatal Exchange Transfusion started from here. This project involved the use of motors to control the movement of blood through valves to and from designated locations in the exchange transfusion set-up. The project would almost eliminate any human intervention in the procedure.(YIDDI *et al.*, 2020)

The automation employed a syringe pump design to control the pumping of blood in and out of the baby, and a valve control design to control the direction of blood flow. The device was designed and built to 95% completion, with some few analyses run on it. Their inability to complete the project implementation was due to the outbreak of the coronavirus pandemic.(YIDDI *et al.*, 2020)

2.6.2 ANET 2.0

Automated Neonatal Exchange Transfusion (ANET) 2.0 combined mechanics, electronics, and programming to bring the idea of reducing human interference and removing human errors into fruition.

This was accomplished using the following methods: A push and pull segment made up of a bipolar stepper motor, a lead screw, and guiding rods were employed to accomplish this function. The clockwise rotation of the stepper motor. The threaded rod moves in that direction as the motor rotates counterclockwise to provide a sucking action. The physicians' manual blood drawing and delivery procedures were replaced by this system (Okrah & Kisser, 2021).

This innovative method for switching valves that use motors driven by software that was built for the microcontroller to replace the manual switching of valves. The project synchronizes the push-pull segment and the valve control segment to carry out the procedures of blood withdrawal and donor blood replacement.(Okrah & Kisser, 2021)

Two unipolar stepper motors, two three-way valves connected in series, and a catheter end attached to the infant, the waste container, and the donor blood bag made up the valve-switching system utilized in ANET 2.0.(Okrah & Kisser, 2021)

The three-way valves that are employed in this system, however, had to be manipulated by human hands, which presented an issue for connecting the motors with them.(Okrah & Kisser, 2021)

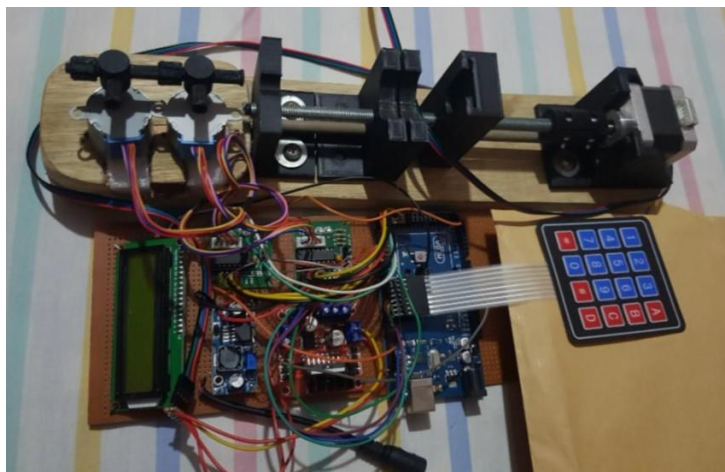


Figure 11 : Finished Design of ANET 2.0

2.6.3 ANET 3.0

The work of the automated Neonatal Exchange Transfusion version 3.0 looked at the flaws of the existing ones from ANET 1.0 and 2.0. Their objective was to also pick up from where the previous editions of ANET had ended and make the Neonatal Exchange Transfusion an automated process.(Agbedor *et al.*, 2022)

They combined mechanics, electronics, and programming to achieve this. The design of the device was a little bit different because most of the parts were 3D printed and used for the purpose without building it from scratch.(Agbedor *et al.*, 2022)

The three-way valve was manipulated by another motor in this case so the physician would not have to control it. The device was further tested on animal lab subjects.(Agbedor *et al.*, 2022)

Aside from these positive breakthroughs that ANET 3.0 was able to make, it had some challenges.

The valve was rotating as well as moving the handle. The intended purpose was for it to rotate on its own so friction is not generated. As a result of this, excess heat was generated and the device was working after a while.(Agbedor *et al.*, 2022)

Also, the push and pull block had a very rigid sense of motion in plunging.(Agbedor *et al.*, 2022)



Figure 12 : Electronics part of ANET 2.0



Figure 13 : Finished design of ANET 3.0

CHAPTER THREE

METHODOLOGY

This chapter discusses into the step-by-step procedures involved in the data acquisition, analysis process, tools, and materials used in the entire course to design the automated neonatal exchange transfusion device.

3.1 DATA COLLECTION

Primary and secondary data were used in the data collection process. Much information was gathered via conversations with ANET 2.0 and ANET 3.0 project developers. Both devices were run as well to help gather much more information needed to build ANET 4.0. The reports of these two generations of ANET were very useful in the data collection process.

The school of veterinary medicine was visited, and questions regarding the kinds of animal testing conducted there and how they were carried out were raised.

The pharmacy department's animal house was the next place to go for information on animal experiments, and there we received guidance on how to conduct our animal tests.

On the other side, secondary data came from readings such papers and journals as well as watching YouTube videos with information on the following subjects:

- I. Hyperbilirubinemia
- II. Hemolytic disease
- III. Exchange transfusion.
- IV. Anatomy of the neonate
- V. RH and ABO incompatibility
- VI. Mechanics of motors, nuts, and threaded rods
- VII. Valving technology

VIII. Bubble trap technology among others

IX. Syringe Pump Design

X. Flow Chemistry

3.2 DATA ANALYSIS

A qualitative approach was mostly used to analyze the data. This involves use of descriptive data and semi-structured observation methods in analysis. The analysis approach was influenced by brainstorming meetings and going through prior material. Our choice of animal subject for tests as well as the procedures to be used was guided by prior research on animal testing carried out on ANET-related devices such as dialysis machines as well as information gathered from officials of the veterinary medicine school and lab technicians of the pharmacy department animal house.

The shortcomings of ANET 2.0 and ANET 3.0 that would present difficulties during animal tests were identified with the help of discussions with the device's creators and bench tests on the apparatus.

3.3 DESIGN PROCESS

This project combines mechanics, electronics, and programming in order to operate the full exchange transfusion setup and run tests on it to demonstrate its usefulness.

To do this, tests will be run on the automation device's existing prototype, ANET 3.0, from which the device's shortcomings and obstacles will be determined to help with future enhancement of the device in ANET 4.0.

The present model is an improvement to one that currently exists (ANET 3.0). Our goal was to strengthen the model's strong features while addressing all of the flaws inherited from the previous models, which had both positive and negative qualities. The device's primary problems and the solutions utilized to fix them are mentioned below.

- Designing a new coupling to transfer the rotational motion of the motor to turn the valves and to rotate only the handle without rotating the valves.
- Design a power system on its own that will provide enough power for the motors so that the rotations and plunging will be done smoothly.

- Designing a cooling system to prevent the voltage boosters from overheating.

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.

The threaded rod is very stiff and this will be solved using classical electronics to affect the plunging effect. The Clinician does not get a notice when the process is done so as a solution to this a part of the code prompts the clinician when the process is done. Also, as part of this project, we will include a part to the code which will allow the clinician cancel or pause the procedure.

3.3.1 DEVICE TESTING

The goal of the initial test of the existing device is to check the mechanical parts are responding to code performing as planned, check for its clinical effectiveness, check for failures and the risk at hand, and the adverse effects that may arise in its usage. The device will be evaluated using an animal test, which often offers preliminary proof of the devices' safety, their potential performance in a live system, and the biological reaction that a living system may mount to the device.

3.3.2 ANIMAL TESTING

The use of non-human animals in medical experiments is referred to as animal testing or animal experimentation, and in this concept in vivo testing. Major advances in the treatment of diseases like breast cancer, brain injury, childhood leukemia, cystic fibrosis, multiple sclerosis, tuberculosis, and others have been made with the help of animal research.

Pacemakers, cardiac valve replacements, and anesthetics have also been developed thanks to animal research. The use of animals in testing is heavily controlled because worries about "cruelty" to animals and their humane treatment are legitimate ones.

Permission was obtained on the usage of the lab subject as a means to means of paying heed to the set rules.

3.3.3 SIGNIFICANCE OF ANIMAL TESTING

Prior to entering the clinical phase, a medical product must be thoroughly examined for safety, efficacy, and efficiency. This helps us decide what modifications need to be done before being put on the market. In order to evaluate these devices, animal experiments are frequently done.

These studies usually give preliminary proof of the devices' safety, their potential performance when used in a live system, and the biological reaction that a living system may mount against the device.

The FDA advises that animal studies for medical devices be planned with the goal of analyzing the hazards expected by the device's design, any known dangers associated with the device type, and any new concerns that may have surfaced in earlier investigations.

For instance, several skincare and cosmetic products are tested on animals to guarantee their safety, and many medical professionals and biomedical researchers support the practice since it contributes to the humane treatment of diverse animals and their safety with regard to medical device standards.

3.3.4 MAIN OBJECTIVES OF ANIMAL TESTING

This is to see the operation of the existing device, the advances, drawbacks, and additions that can be added to the device.

This helps to see the flaws of the work that was done by the previous years and to see the additions that can be added to make the device a well-improved and commercial one.

3.3.4.1 EVALUATE THE EFFICACY OF THE DEVICE OR DEMONSTRATE PROOF OF PRINCIPLE

This would entail confirming the consistency and correctness of cycle length, blood volume (aliquots) every cycle, and the entire treatment. It would also entail monitoring for any symptoms of illness during or after the procedure.

3.3.4.2 PROVIDE EVIDENCE OF SAFETY

Proof demonstrating the device's safety, including its handling and performance when compared to current automation techniques and practices. Performance and handling, device safety, physiological response, determining whether or not the device can have effects distant from the site of use (mechanical or biologic stresses), unexpected morbidity and mortality, or all observed instances of animal illness and death, and determining whether or not such events are device related are all recommendations for evaluating safety.

3.3.4.3 RISK ASSESSMENT FOR RISK MANAGEMENT

A risk is a mix of the likelihood that harm will occur and how serious that harm will be. Risk analysis and evaluation are the two steps that makeup risk assessment. The process of identifying risks and estimating the risk is known as risk analysis.

Comparing the projected risk to predetermined risk criteria, on the other hand, is the process of determining if the risk is acceptable.

Animal experiments and research are being undertaken on a variety of species. These creatures include fish and birds as well as rats, mice, rabbits, guinea pigs, dogs, primates, chimps, and orangutans. Every one of these creatures has distinctive traits and peculiarities that help researchers get the most useful results from their scientific investigations.

The most productive animals to utilize in the development of cosmetic and skin care products are rats and mice. The greatest choice would be rabbits since they have a physiology that is most similar to that of humans and because their weight is most similar to that of newborns.

The size of the gadget and its components in relation to the test subject is an additional crucial factor. The catheter, for instance, would have to fit into the blood vessels of the test subject



Figure 14 : Stages of risk assessment



Figure 15 : Risk Management Process

3.3.6 ANIMAL TEST PROCEDURE

3.3.6.1 HOW WILL THE DATA BE COLLECTED

The goal of the animal experiments is to gather information that will be used to evaluate the device and provide proof of concept and design verification. The quantities removed or transfused each cycle, the duration of each cycle, and cumulative volumes will all be recorded in order to calculate the total amount transfused.

3.3.6.2 COMPLICATIONS OF EXCHANGE TRANSFUSION

There are certain problems with exchange transfusion. Current guidelines for doing an exchange transfusion are based on a balance between the risks of encephalopathy and the problems linked to the treatment. Its death rates range between 0.5% and 3.3%.(Murki & Kumar, 2011).

But, if the process is done extremely carefully, with the appropriate hygiene, and care, the majority of these issues may be avoided. Typically, slowing down or pausing the trade is the best way to handle these issues.(Murki & Kumar, 2011)

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 were 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 related to general device use in both normal and fault conditions.

Some examples include;

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

3.3.7.1 Risk Assessment Table

The tables below are the description of the hazards associated:

Table 5 :Hazards predicted 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		
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 setup correctly Blood line separation	Inaccurate measurements Air emboli Pressure altered			
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Table 6 : Hazards associated with blood related devices and exchange transfusion

Hazard	Reasonable foreseeable sequence or combination of events	Hazardous Situations	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		

Table 7 : 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	<ul style="list-style-type: none"> • Injury • Death 		

Mechanical hazards	Improper contact or entanglement to machine parts	Exposure to injurious machine parts	<ul style="list-style-type: none"> • Injury • Death 		
Misuse	Use of device or its parts for wrong purpose				
Unforeseen malfunctions					

3.3.8. TEST WITH PREVIOUS A.N.E.T (ANET 3.0)

A clinical test was conducted for the reasons stated below;

1. To understand the general system employed in Automating Neonatal Transfusion.
2. To identify the problems encountered with the previous model.

In our version of the clinical test, we were provided with a blood sample of a California rabbit in an EDTA test tube. This provision was made by Mr. Gyan and Mr. Godwin of the Faculty of Pharmacy. The setup was made as shown in figures 13 and 14.

In the setup dyed normal saline was to serve as the donor blood, and the blood sample was provided as the waste blood from the neonate. The clinical text was partially successful. This is because the machine was in a very bad state at the time.

The leaded rod which was meant to rotate in order to move the pusher block forward and backward had been removed from the coupling which was meant to secure the threaded rod to the stepper motor. Again, the motor shield which was used with the Stepper motors provides a pulse to move at a specified number of steps, speed, direction, and rate, and would automatically go off when the procedure is started.



Figure 16 : Set up for test without the rabbits blood

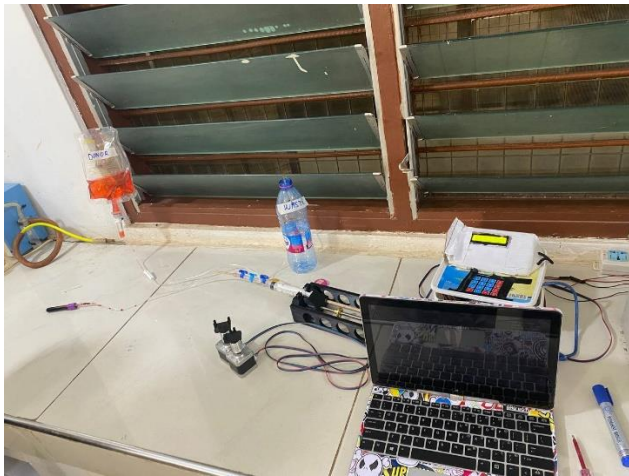


Figure 17 : Complete set up for testing

3.3.8.1 CONCLUSIONS DRAWN FROM THE TEST

The test was conducted on the recent edition of the ANET which is ANET 3.0 and from the test we realized that the pusher block could not pull the blood well due to the coupler. The lead rod removed from the coupler and as such there were not enough complete revolutions unless completed manually.

Also, the handles of the motors do not turn the valves themselves and had to be done manually so that the blood would flow through the valve to the donor blood bag and the waste blood bag for drawing and replacing respectively.

Also, issues of clotting were realized since the length of the tube was not well calculated to predict when it has to stop the draw and when to replace it.

Supply of power was one problem encountered. The power which was supplied by the energizer batteries as used by the recent generation would not power the two motors and the pusher block. At the point when the cycle of withdrawal and replacing is about to start due to inadequate power supply, the LED indicator on the motor drivers go off.

3.4 A.N.E.T. 4.0

ANET 4.0, based on the problems encountered in ANET 1.0, ANET 2.0, and ANET 3.0, as well as the results of animal trials, would differ and differ significantly from previous editions.

These new additions aim to address issues that have arisen in previous editions by utilizing classical electronics to ensure a smooth plunging effect, resolving overheating issues that have occurred in all previous generations of the ANET, and addressing numerous other issues that have been identified.

3.4.1 MECHANICAL COMPONENTS

3.4.1.1 Push and Pull Segment

This segment aims to replace clinicians' manual drawing and delivering of blood with a customized automated syringe pump.

This syringe pump consists of

- a bipolar stepper motors
- Flex coupler
- 3D printed parts

Front Support

- Hand Knob (9 mm)

Hand Knob (8 mm)

Hand Knob (7 mm)

Top Syringe Holder

Side Syringe Holder

Limit Stop

Plunger Holders

Carriage

Endstop Switch

Slider

Back support

- lead screw and nut
- 8mm guiding rods and linear bearings

The stepper motor rotates in the clockwise direction. Because of its attachment to the motor's shaft, its rotation causes the lead screw to rotate in the same direction. The pusher block, which is attached to the lead screw, moves forward in a straight line.

The linear motion is accomplished through the use of guide rods, which prevent the pusher block from moving sideways. As the pusher block advances, it pushes the plunger of the syringe, causing a pumping action. To produce a sucking action, the motor rotates counterclockwise, causing the threaded rod to rotate in the same direction. Because the pusher block's syringe holder grips the syringe tightly, it pulls the plunger of the syringe along, causing a sucking action as it moves backward. The stepper motor's continuous rotation and direction cause us to suck and pump blood into and out of the baby.

- **Stepper motor**

A stepper motor is an electric motor whose main characteristic is that its shaft rotates in steps, or by moving a fixed number of degrees.

Stepper motors produce high torque in a small package and are ideal for quick acceleration and response. It consists of a stator and a rotor.



Figure 18 : Motor

- **Flex coupler**

Couplers are used to connect two rotating shafts. In our application, the coupler connects the stepper motor's rotating shaft and the lead screw, which are inserted at opposite ends to transmit the motor's rotatory motion to the lead screw, which provides drive for the push pull segment. Misalignment of a machine's shaft can limit its performance, cause excessive vibration, high reaction loads, and accelerated wear, and frequently leads to premature equipment failure.

Flex couplers, which transmit torque while compensating for parallel, angular, and axial misalignment between drive components, can help prevent these problems. Flexible shaft couplings, when properly installed, can also reduce vibration, noise, and protect driveshaft components.



Figure 19 : Coupler

- **3d printed parts**

The whole body of the design is going to be 3D printed and these parts include;

1. Front Support
2. Hand Knob (9 mm)
3. Hand Knob (8 mm)
4. Hand Knob (7 mm)
5. Top Syringe Holder
6. Side Syringe Holder
7. Limit Stop
8. Plunger Holders

9. Carriage
10. Endstop Switch
11. Slider
12. Back support



Figure 20 : 3D parts

3.4.1.2 Automated Valve Switching Segment

The approach is to replace the physician's manual valve switching with motors that turn the valves. A program written for a microcontroller will control the motors. To successfully complete the processes of drawing out blood and replacing it with fresh donor blood, the program synchronizes the push-pull segment and the valve control segment. The valve control segment includes the following components;

- 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.

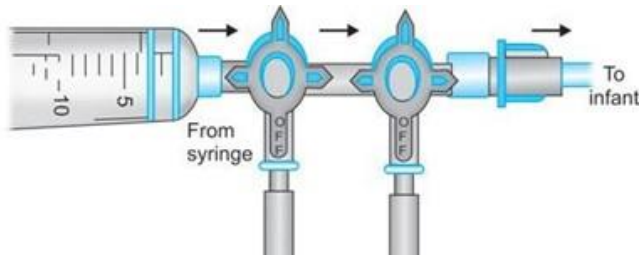


Figure 21 : A Three way valve

- **3D Printed clutch**

This is a 3D printer item that sits on top of the motor, connected to the flex coupler, and its top rests on the bottom of the valves. The outer edges of the valve are held by the 3D printed clutch, and the valves can be turned using the drive given by the stepper motor via the flex coupler.

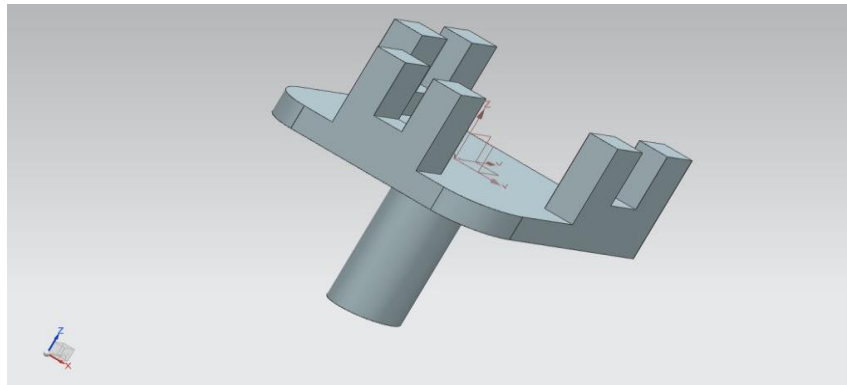


Figure 22 : A 3D clutch

- **Valve**

2 Three-way valves connected in series and catheter ends connecting to the donor blood bag, waste container and to the baby.

The valves are responsible for directing blood flow. They allow blood to travel or flow in three separate ways. The majority of the automation is concentrated here because each cycle requires around four manual valve rotations to obtain the appropriate flow.



Figure 23 : A valve

- **Lead and Screw nut.**

A lead screw shaft is a cylindrical shaft with grooves running the length of it. A mechanical linear actuator is a device that converts rotational motion to linear motion. It operates by sliding the screw and nut threads with no ball bearings in between.



Figure 24 : Lead rod



Figure 25 : A single lead rod

3.4.2 ELECTRONIC COMPONENTS

a) The arduino mega 2560

The ATmega2560-based Arduino Mega 2560 is a microcontroller board (datasheet). It contains 54 digital I/O pins (14 of which are PWM outputs), 16 analog I/O pins, 4 UARTs (hardware serial ports), a 16 MHz crystal oscillator, a USB connection, a power jack, an ICSP header, and a reset button. It comes with everything you need to support the microcontroller; simply connect it to a computer through USB or power it with an AC-to-DC adapter or battery to get started. The Mega is compatible with the majority of Arduino shields.



Figure 26 : Arduino Microcontroller

b) The Power Source.

In contrast to direct current (DC), which only travels in one direction, alternating current (AC) is an electric current that occasionally reverses direction and continuously alters its magnitude over time. Alternating current is the type of electrical energy that customers commonly use when they plug in kitchen appliances, televisions, fans, and electric lamps into a wall socket.

Alternating current is also the type of electrical energy that is delivered to companies and homes. The power source will supply a voltage to the entire system. There is an AC – DC converter that converts the AC current to the DC current and then it is stepped down to a 15V.



Figure 27 : Adapter

c) Liquified Crystal Display (LCD)

An LCD 162 is an electrical device that displays data and messages. It has 16 Columns and 2 Rows, as the name says, and can display 32 characters ($16 \times 2 = 32$) in total, with each character made up of 58 (40) Pixel Dots. As a result, the total number of pixels in this LCD is 32 \times 40, or 1280 pixels. Nonetheless, due to its low cost, programmability, and ease of access, the LCD 162 is

widely used in devices, DIY circuits, and electronic projects. The L.C.D. specifications are as follows:

- 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 operation of an LCD is to transfer light from layer to layer through modules. These modules will vibrate and align themselves at 90°, allowing light to travel through the polarized sheet.



Figure 28 : I2C Liquid Crystal Display

d) 12 LCD adapter

An I2C LCD adaptor is a device that contains a PCF8574 microcontroller chip. This microcontroller is an I/O expander that uses a two-wire communication protocol to interface with other microcontroller chips. Anybody may use this adaptor to operate a 16x2 LCD with only two wires (SDA, SCL). It saves several Arduino or other microcontroller pins.

It has a potentiometer for controlling the LCD contrast. The I2C address is 0x27 by default. Its address can be changed by connecting A0, A1, and A2.



Figure 29 : I2C LCD Adapter

e) Keypad

The buttons on the 4X4 membrane keypad are organized in rows and columns in a 4X4 matrix. Membrane switches are located beneath the buttons. Each switch in a row that is beneath a button key is linked to another switch in the same row by an electrically conductive trace put beneath the keypad buttons; there are four rows in total. Likewise, each switch in a column under a button key is linked to another switch in the same column by an electrically conductive trace buried beneath the keypad keys, and there are four columns in total. The 4X4 matrix keypad has 8 pins made up of 4 rows and 4 columns.

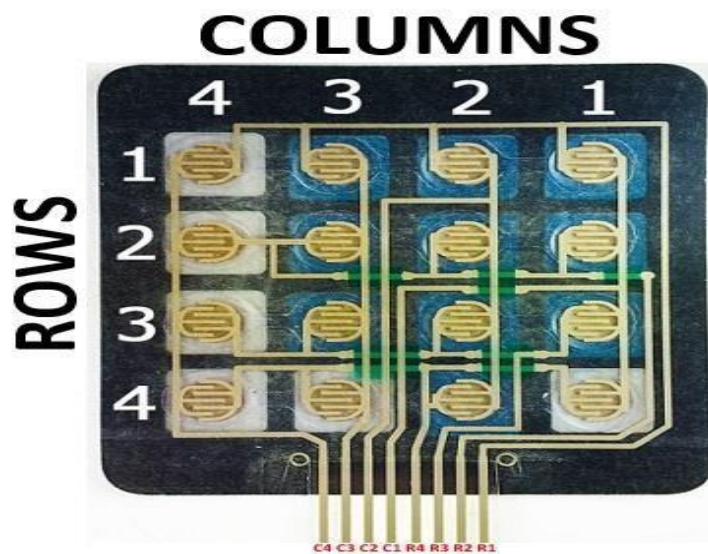


Figure 30 : Keypad

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

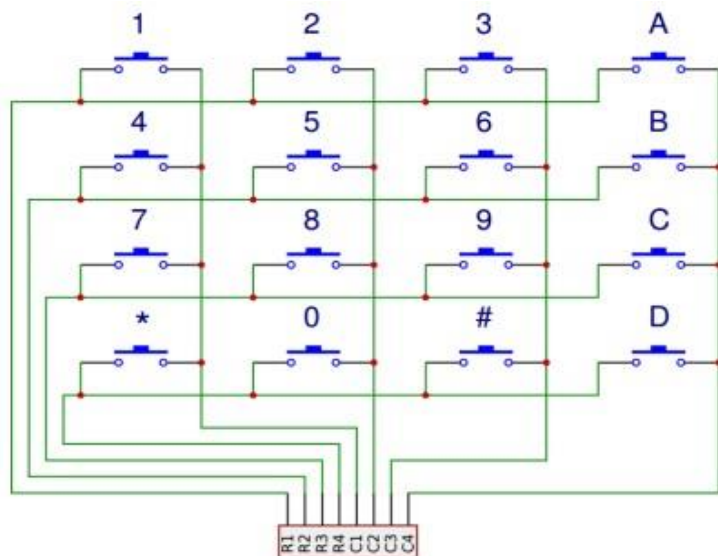


Figure 31 : Keypad pressing analysis

How Arduino detects pressed button

Here's how Arduino determines which button is pushed by determining which rows and columns are linked.

- 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.

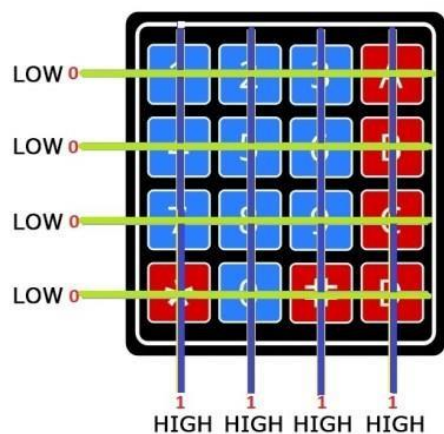


Figure 32 : Arduino detection on the keypad

When a key or button is pushed, a row key and a column key are linked. Because the row pins were initially pushed LOW by the Arduino "keypad.h" library code, any column pin that now comes into contact with a row as a result of the pressed button will be pulled LOW from its initial HIGH position.

As a result, we now know which column the key/button was pushed in. Please see the image below.

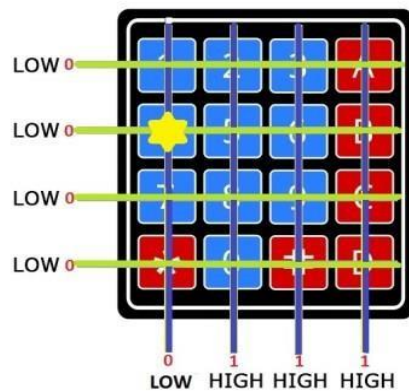


Figure 33 : Keypad

The Arduino, using the "keypad.h" library, will cause the row pins to go high consecutively while concurrently reading the column pins to determine which row pin will trigger a column key to go high from a LOW state, because all of the column pins have been on HIGH since the beginning and have not shifted state except the column that was pressed and turned to LOW, it is this same pin that will switch from LOW to HIGH. The Arduino now knows which row pin was pressed as a result of this. We can determine the specific key/button that was pressed by merging the row and column pins. 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 by toggling between on and off.



Figure 34 : A Switch

g) Motor Shield

Stepper motors need to be pulsed in order to move at a specific number of steps, speed, direction, and rate. These pulses are sent by a motor driver. An Arduino motor shield was interfaced with the Arduino mega microcontroller to drive the syringe pump's bipolar stepper motor. The motor shield provides channels for controlling four DC motors, two stepper motors, and two servo motors. It also features headers for attaching input and output lines.

The motor shield can safely deliver up to 12V and 2A per motor channel or 4A to a single channel when connected to an external power supply.

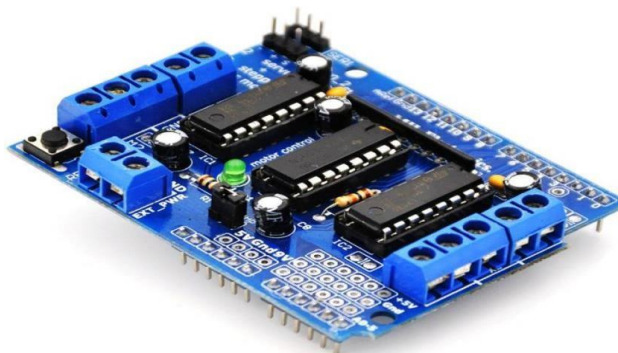


Figure 35 : Motor Shield

h) Voltage Boosters

This DC-DC switching boost converter can drive a 4A load while maintaining a good line and load control. The XL6009 IC, the main switching component, is available with fixed output voltages of 3.3 V, 5V, and 12V, as well as an adjustable output version. It is an efficient switching regulator with much better output efficiency than common boost regulators. At higher input voltages, the

regulator operates at a switching frequency of 400kHz, allowing for a lower and more space-efficient total board footprint.

This device is used to step up the supply voltage. Its output voltage is adjustable by a 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 36 : Motor Driver

f) L298N Motor Drivers

The L298N is a dual H-Bridge motor driver that, as the name indicates, provides for motor speed and direction control. A single L298N IC can drive two DC motors at the same time, and the two motors and one stepper motor, as well as their directions, may be separately controlled. Stepper motors need to be pulsed in order to move at a specific number of steps, speed, direction, and rate. These pulses are sent by a motor driver. L298N motor drivers controlled the movement of the two stepper motors used to turn the valves.



Figure 37 : L298N Motor Drivers

3.4.3 3D MODEL OF THE MECHANICAL PART

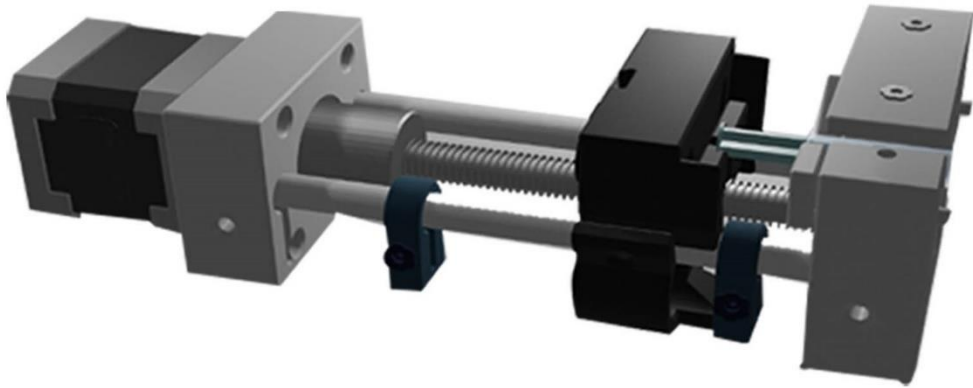


Figure 38 : 3D Model

3.4.4 BLOCK DIAGRAM OF ANET 4.0

Power is taken from the mains with a 12- volt adapter which feed the microcontroller with just the right amount of current it and voltage it requires to run. The keypad serves as the input device which is used to set the necessary parameters demanded for the procedure to be executed.

The LCD displays the vital information for the user and also tells at what stage the procedure is at a point in time. The code written on the main microcontroller for the three motors of which two controls the valve turning and one controls the pushing and pulling of the syringe plunger, are interpreted by the motor drivers which acts as an interface between the control circuit and the motor. The motor demands a large quantity of electrical current, while the controller circuit operates on low-current signals. Thus, the role of motor drivers is to convert a low-current control signal into a higher-current signal that is capable of powering the motor.

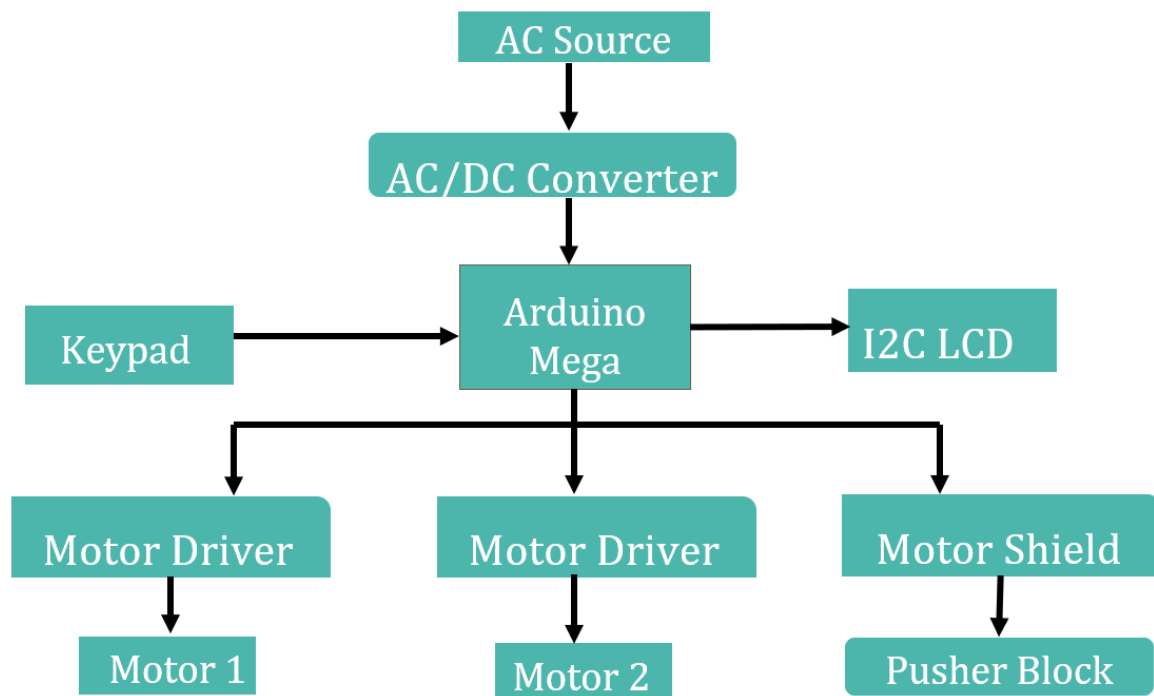


Figure 39 : Block Diagram

3.4.5 DETAILED ELECTRICAL CONNECTION OF ANET 4.0

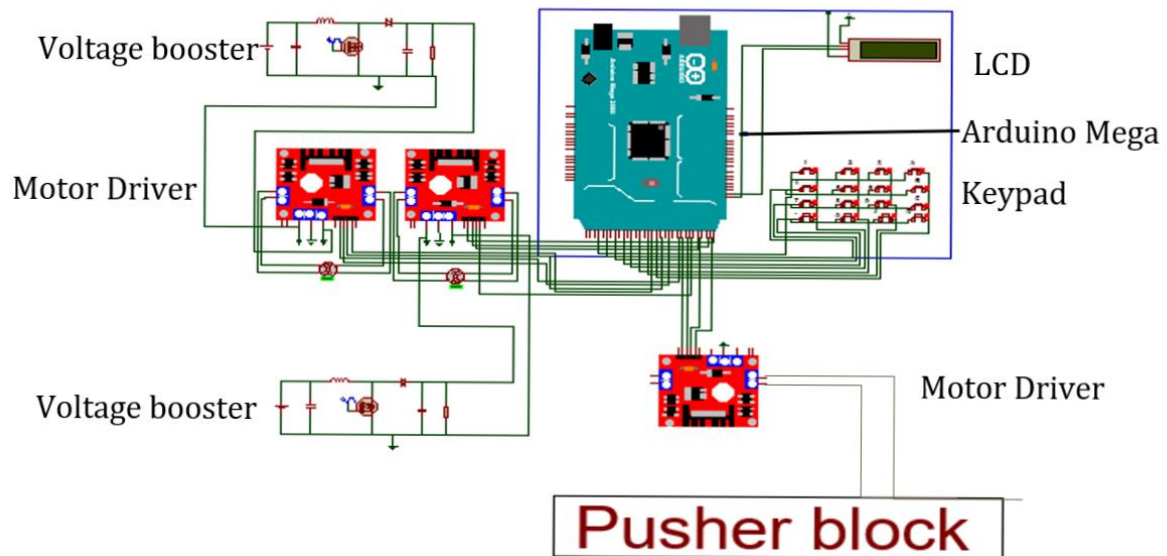


Figure 40 : Detailed electrical connection of ANET 4.0

3.4.5 SYSTEM ARCHITECTURE

The microcontroller is powered through a 12-volt adapter that provides the necessary current and voltage. Users can input required parameters through the keypad. The LCD screen displays important information and shows the current stage of the procedure. The code for the three motors (Two of the motors control valve turning, while the other controls the syringe plunger.) written on the main microcontroller is sent to the motor drivers.

The motor drivers serve as an interface between the control circuit and the motor, converting low-current signals into higher-current signals to power the motor, which requires a large amount of electrical current.

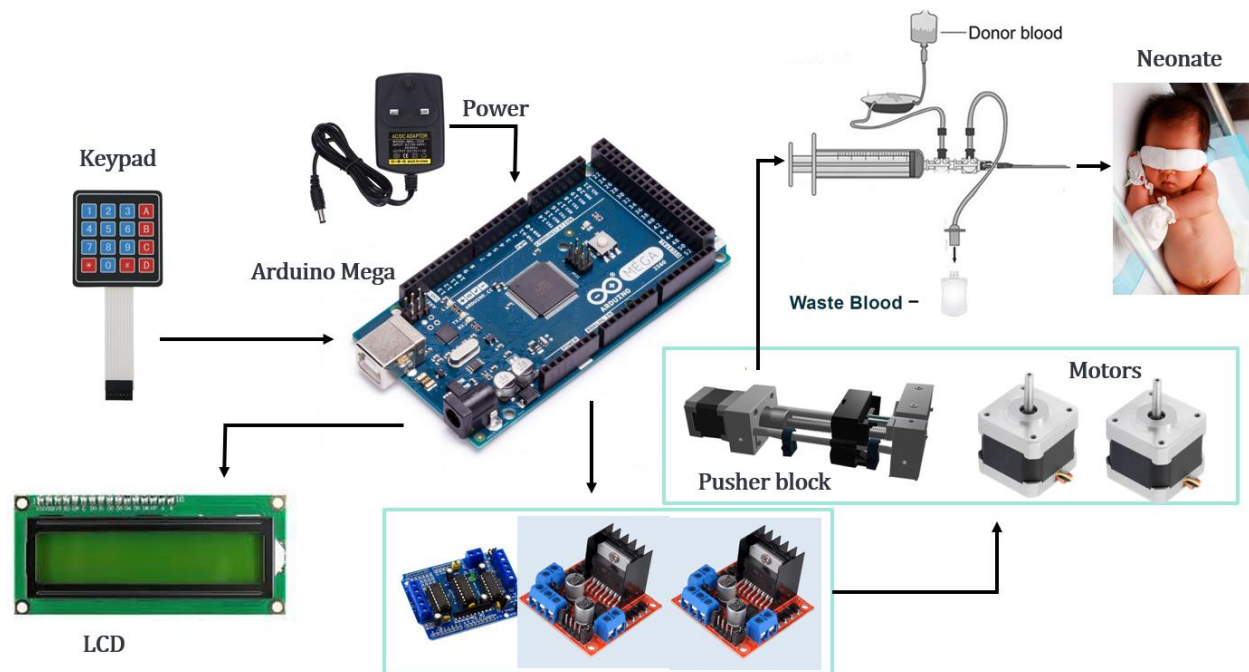


Figure 41 : System Architecture

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