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Early Stage Product Development of a New Anaesthetic Vaporizer Concept for Use in Low Resource Settings

Master's thesis in Mechanical Engineering
Supervisor: Knut Einar Aasland
January 2019

Master's thesis

NTNU
Norwegian University of Science and Technology
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ENGINEERS WITHOUT BORDERS

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Summary

For this thesis a new concept for a vaporizer for use in low and middle income countries has been examined and developed using Ulrich and Eppinger's product development methodology for concept generation and selection. The concept was presented by Prof. Fenton as an idea for making anaesthesia equipment more suitable for low resource settings.

The concept was decomposed into several subproblems, and for each subproblem a five-step concept generation method was used to generate concept solutions. Based on a concept selection phase, a few concepts were chosen for prototyping. Through an iterative process of research, systematic exploration, reflection and evaluation, and rapid prototyping, a final solution for the new vaporizer concept was proposed and prototyped.

Experimental testing was performed at St. Olavs hospital, Trondheim, to evaluate the performance of the concept. Results indicate that the prototype was functional and that it worked as intended. More testing is required to be able to compare the performance to that of other vaporizers. The concept can be made robust, easy to use, and easy to maintain and repair, to cope with the challenges regarding anaesthesia care in low and middle income countries.

Sammendrag

I denne masteroppgaven har en ny anestesifordamper for bruk i utviklingsland blitt undersøkt and utviklet ved bruk av Ulrich og Eppingers produktutviklingmetodologi for konseptgenerering og konseptvalg. Konseptet er presentert av Prof. Fenton som en ide for å gjøre anestesiutstyr mer tilgjenglig for utviklingsland.

Konseptet ble dekomponert i flere sub-problemer, og for hvert sub-problem ble en fem-stegs konseptgenereringsmetode brukt for å generere konsepter og løsnigner. Flere konsepter ble valgt for prototyping. Igjennom en iterativ prosess av søk etter løsninger, systematisk utfoskning, reflektering og evaluering, og 'rapid prototyping', ble en siste løsning for konseptet foreslått og prototypet.

Eksperimentell testing ble gjennomført ved St. Olavs hospital, Trondheim, for å evaluere konseptet. Resultatene indikerer at prototypen var funksjonell og at den fungerer som ønsket. Mer testing kreves for å kunne sammenligne fordamperens prestasjoner med andre anestesifordampere. Det er ansett som at konseptet har potensialet til å laget robust, å lages for lett bruk, og å lages for å være lett å reparere, for å kunne håndtere problemer med anestesipleie i utviklingsland.

Preface

This master's thesis is written in collaboration with Prof. Paul Fenton and Dr. Herman Lonnee. In addition, it is written as a "Master with Meaning" in collaboration with Engineers Without Boarders. The purpose is to investigate alternative solutions for a product concept presented by Prof. Fenton, and to physically prototype it. The goal is to develop a medical device usable in low and middle income countries where medical care is lacking.

We want to thank our supervisor, Knut Einar Aasland, for continuous support throughout the process, the Medical Technical department at St. Olavs for allowing testing of the prototypes, and Richard Fiedorowicz, for letting us visit his factory and business OES Medical Ltd. We would also like to thank Carlo Kriesi for helping both in the concept generation and prototyping process.

Lastly, we would also like to thank Prof. Paul Fenton and Dr. Herman Lonnee for their invaluable guidance through the field of anesthesia. This project would not have been possible without them. We are very gratefully for getting to work with experts in their field.

Oslo, 2019-01-28

Jacob Søgnen Jensen

Oslo, 2019-01-28

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Chapter 1

Introduction

1.1 Background

1.1.1 Challenges with Anesthesia Care in Low and Middle Income Countries

Meara et al. [43], from the Lancet Commission on Global Surgery, estimates that "5 billion people lack access to safe, affordable surgical and anaesthesia care when needed". Almost 17 million lives per year are lost because of conditions that are treatable with adequate surgical care [43], and the situation is most critical in low and middle income countries (LMICs). According to Boggs, the mortality rate from anaesthesia is 10 000 times higher in LMICs than in high income countries (HICs) [8]. Prof. Paul Fenton, formerly Professor and Head, Department of Anaesthesia, College of Medicine Malawi (1986-2001), experienced first hand the problems anesthesiologist in LMICs face daily.

1n 1955, Macintosh [42] wrote an article called *A plea for simplicity*, where he urged that the anaesthesia machine was too complex and too difficult to use in some countries. This sentiment was relayed by Prof. Fenton, whom in 2019, feels the same way. There are still problems with anaesthesia in LMICs, and some of these stem from complex anaesthesia machines. According to both Ulisubisya [64] and Meara et al. [43] the surgical care and anesthesia in LMICs is overlooked and receives little attention in the global medical discourse.

One of the problems related to anesthesia in LMICs is that the anesthesia machines used for inhalational anesthesia are often unusable in low resource settings. Modern anaesthesia machines are useless without a supply of electricity and pressurized gas which is unstable or lack-

ing in many LMICs [6]. One of Prof. Fentons solutions was to invent and develop an anaesthesia machine that can function without pressurized gas and for several hours without mains electricity. He called the machine the *Universal Anaesthesia Machine*, or the *UAM* [62]. Along with the UAM, the Glostavent Anaesthetic Machine is made for use in LMICs, and is also usable without mains electricity and pressurized gas. The problem of adequate surgical care is grand in scale globally, and so even with the UAM and Glostavent there are still a multitude of problems with anaesthesia care in LMICs.

A specific problem which was presented to the authors by Prof. Fenton is the draw-over vaporizer. A vaporizer is used to evaporate anesthetics so that it can be inhaled, and the draw-over type is regularly used in LMICs because it is the only commonly found vaporizer type that can function without pressurized gas. The draw-over vaporizer is not very accurate, has a tendency to over-deliver anesthetic agent at low gas flows, and is unreliable at high and low temperatures [27].

Other problems with equipment in LMICs is that it has to withstand rough use, has to have a long life span, and have low cost. Additionally, according to Prof. Fenton, to be able to sell a piece of equipment to LMICs it has to look and feel modern. John Anner, the president of East Meets West, a non-governmental organization focused on health in Asia and Africa, seem to agree. He states in a bulletin of the WHO that "Devices need to look modern, so that hospitals are proud to use them and patients feel that they are receiving the proper treatment" [70]. In one of our many conversations with Prof. Fenton, he explained that it is much easier to sell a device to LMICs if the device is usable in high income countries (HICs) as well. Often, modern machines that look good are bought or accepted as donations even if these can not be used in practice. These machines are thrown out or stowed away while old or alternative equipment is used instead. For this reason, it was important for Prof. Fenton to get the UAM CE-marked[1].

Prof. Fenton has made a concept for a new type of vaporizer he thinks can perform better than the draw-over vaporizer. It also has to be safer to use than the draw-over vaporizer. Together with Dr. Herman Lonnee, anesthesiologist at St. Olavs, Prof. Fenton contacted NTNU to see if anyone could develop and build his concept device.

The definition of LMICs used in this text is taken from The World Bank, which splits economies into four categories based on gross national income (GNI): low-income[2], lower middle-income[3],

[1] Certification mark for the European Economic Area
[2] less than $1,005
[3] between $1,006 and $3,955

upper middle-income[4], and high-income[5] [4]. When discussing LMICs, it is important to remember that the categorization is extremely broad and based entirely on economics. Even though the problem of inadequate anesthesia care is close to global, the problems that each individual country face can be vastly different. These problems depend on economic situation, social and physical environments, and a wide array of other factors. Even within a country there will be huge deviations in the standards of surgical care. When discussing LMICs in this project it is our intent to paint a general picture of a near global situation, and not to thoroughly explain the intricate individual problems that each country faces. In the literature we have researched, the term LMICs is often used even when the article discusses mostly LICs. If a country specific example is used, the country will be specified.

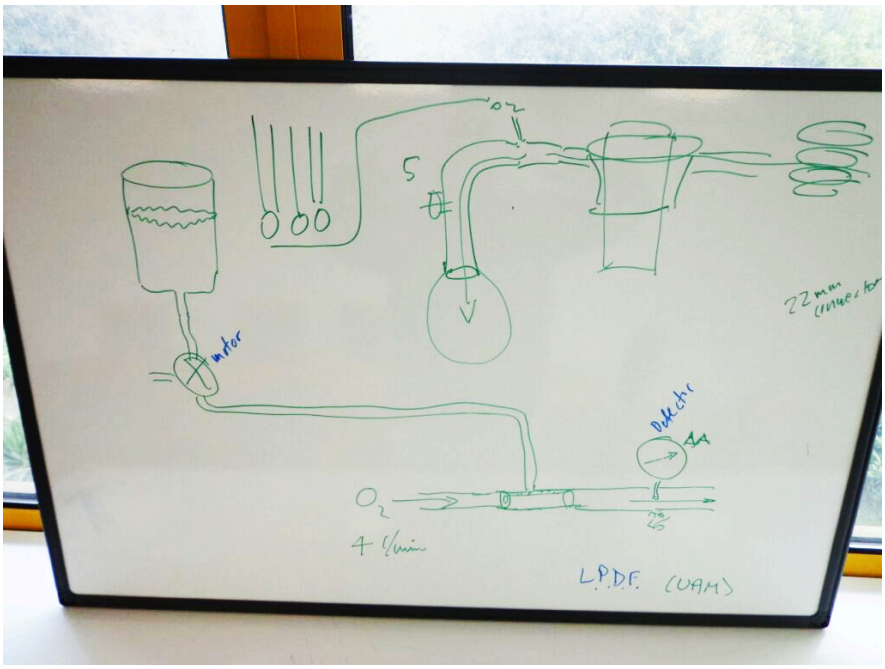
1.1.2 Fenton Concept

In October of 2017 the authors of this thesis visited Prof. Fenton at the *OES Medical Ltd* factory in Oxford, England, where the UAM is manufactured. During this visit some of the problems of anaesthesia in LMICs were presented by Prof. Fenton, and a concept for a new type of vaporizer was presented. The aim of this device is to make anaesthesia safer and simpler in LMICs as well as in HICs. After an evaluation of problems of anaesthesia in LMICs was performed for the pre-masters thesis, it was found that the main problems in LMICs with regards to vaporizers are:

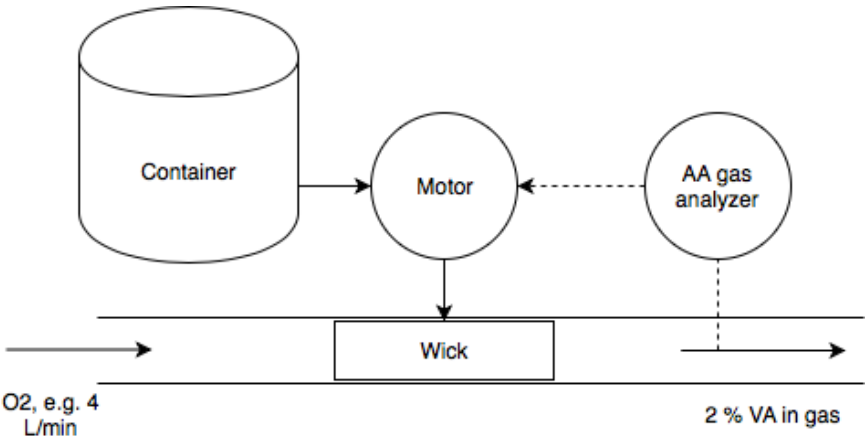
1. There is a lack of pressurized gas and unreliable electricity
2. Draw-over vaporizers are not very accurate
3. Modern vaporizers are complex, and can be hard to use in LMICs
4. Modern vaporizers are hard to repair and service without technical expertise
5. Modern vaporizers are expensive
6. In LMICs, vaporizers are handled roughly and are used in unforgiving environments

Prof. Fenton presented a concept device which is a battery powered, electronically controlled, target-controlled, direct injection type anaesthesia delivery system. It uses a closed-loop feedback system based on sensor measurements to control the concentration of the anaesthetic agent being delivered to the patient. Figure 1.1 shows the Fenton concept as presented by Prof. Fenton himself, and a redrawn flow chart for clarification purposes.

[4] between $3,956 and $12,235
[5] $12,236 or more



(a) The Fenton concept as presented by Prof. Fenton



(b) The Fenton concept, redrawn for clarification. VA stands for volatile agent, which is the anaesthesia drug

Figure 1.1: The Fenton Concept

Inhalational anaesthesia is performed by passing gas through a vaporizer and directing the gas to the patient with a breathing tube. In contemporary anaesthesia vaporizers, liquid anaesthetic agent is evaporated before being mixed with gas. For the Fenton device, the liquid anaesthetic agent is directly injected into the breathing tube, where it should spontaneously evaporate with the help of a wick [6], before being passed to the patient.

[6] A piece of material physically constructed to have a large surface area, thereby increasing the evaporation rate

The *Fenton device* consists of an anesthetic agent reservoir with an electronically controlled liquid injection mechanism, a gas analyzer, and a microcontroller. Liquid anesthetic agent will be released into the gas stream directed to the patient, where it lands on wicks and instantly evaporates. The gas, containing anesthetic agent, will flow past a gas analyzing sensor which measures the anesthetic agent concentration. Based on the sensor measurements the electronically controlled injection mechanism will self regulate. The idea is that the operator can set the concentration at e.g. 2%, and the device will self regulate the administration rate so that this target concentration will always be met.

1.2 Problem Formulation

> The goal of this thesis is to physically make the vaporizer concept presented by Prof. Fenton. This will be done by decomposing the concept into subproblems, generating alternative concept solutions, and prototyping these. Focus is directed towards a few subproblems of the Fenton concept.

The research questions are:

- R1: How can the Fenton concept solution be constructed?
- R2: How does the Fenton concept perform compared to contemporary solutions for use in LMICs, like draw-over vaporizers?
- R3: How should the Fenton concept be constructed to be usable in LMICs?

1.3 Scope

This thesis concerns the early stage product development of a new vaporizer concept developed by Prof. Fenton. From the pre-master's thesis the user needs have been identified, and product specifications have been made. This thesis will focus on the concept generation and early stage prototyping of the Fenton concept. The concept will be decomposed into subproblems, and

of the anaesthetic agent

some of these will be evaluated to find a solution that can be constructed physically. This solution will then be prototyped and tested to evaluate the performance of the Fenton concept.

It is important to note that the concept is to be developed *on order by Prof. Fenton*. The parent concept will therefore not be evaluated, and no alternative solutions will be generated for the overall idea. For the concept generation, only the most necessary subproblems will be solved. The other subproblems, which are considered solvable at a later stage, will not be investigated in this thesis. Prototyping will be performed for even fewer subsolutions.

This text will first present the theory used in this thesis. This includes the theory of anaesthesia in LMICs, the theory of the technical solutions used in the prototyping, and theory on product development. The concept generation and prototyping processes are presented chronologically as they were performed. Testing, which was performed at St. Olavs Hospital will also be presented. The thesis will end with a conclusion, where the results are presented and discussed. Limitations of the thesis and recommendations for further work will also be presented in the conclusion.

Chapter 2

Theory

This chapter will present the theory of three distinct topics. The first topic concerns anaesthesia with focus on problems concerning anaesthesia in LMCIs. This is included to give an understanding of the challenges of developing medical products for LMICs. The second topic is on the technical theory which was used in the prototyping of the Fenton concept. The last topic is the product development method which was used for this thesis.

2.1 Anaesthesia

Hore and Harley defines anesthesia as "the pharmacologically induced lack of sensation" [30, p. 3]. It is mainly used to allow the performance of painful or discomforting medical procedures. Anesthesia is divided into three main categories: general, regional, and local anesthesia. General anesthesia is achieved by intravenous induction of anesthetics, by inhalation of anesthetic gases, or by a combination of the two [63, p. 354]. Inhalational anesthesia is the most common administration technique [18, p. 67], and is the focus of this master's thesis.

For inhalational anesthesia, an anesthetic agent is inhaled by the patient [59, p. 557]. Commonly used anaesthetic agents are the volatile agents sevoflurane, desflurane, and isoflurane [71] [38], which are used because "Volatile anaesthetic agents are liquids with a low boiling point and high saturated vapour pressure (SVP) so that they evaporate easily" [59].

2.1.1 The Anaesthesia Machine

According to Ward [18, p. 67], the modern anesthesia machine or workstation is used to "accurately and continuously deliver a safe mixture of gasses and vapours for the administration of anaesthesia". There are several different types of vaporizers used for inhalational anaesthesia, and the most commonly used in HICs is the plenum type [14] [59, p. 838]. For anaesthesia machines using the plenum vaporizers, pressurized carrier gas like oxygen, air and nitrous oxide flows through pressure regulators, then through a vaporizer where the liquid anesthetic agent is evaporated and mixed with the carrier gas [59, p. 837], before being delivered to the patient. Most modern anesthesia machines operate with integrated safety features [18, p. 66] with audible alarms which are set to proper levels prior to initiation of anesthesia [15]. Figure 2.1 shows the GE Healthcare Aisys which is used at St. Olavs Hospital in Trondheim.

A breathing system is used to direct the gas to the patient [59, p. 841]. It is usually set up so that the carrier gas containing anesthetic agent flows through plastic tubing from the anesthesia machine, and into a sealed mask which is placed over the mouth and nose of the patient. Different types of breathing systems are used to ensure that volatile agents can be reused [18, p. 107-108]. A CO_2 absorber is often used to remove CO_2 from the expired gases [18]. This makes it possible to reuse the carrier gas and anaesthetic agent.

Figure 2.1: The GE Healthcare Aisys Anaesthesia Workstation

According to Dr. Lonnee [1], the carrier gas flow rate is commonly set between 2 and 10 $\frac{L}{min}$. However, low flow anaesthesia which uses flows rates of 0.5-2 $\frac{L}{min}$ is commonly used in HICs because of "economic and environmental reasons" [41]. By reducing the flow rate of gas going to the patient the amount of VA and carrier gas used is reduced [41].

Different ventilation methods are used to ensure that gas is delivered to the lungs of the patient.

[1] Personal communication

During general anesthesia, when a patient breathes by their own respiratory efforts it is said that the patient is spontaneously breathing. This mode of ventilation is also called spontaneous ventilation [37, p. 156]. If the patient needs assisted respiration it is called controlled ventilation or mechanical ventilation. For controlled ventilation the operator can either move bellows up and down or squeeze a self-inflating bag (Figure 2.2a) to ventilate the patient. Alternatively an automatic ventilator, like that shown in Figure 2.2b can be used. There are many different modes of ventilation but this topic is beyond the scope of this thesis, and will not be discussed here.

(a) Self-inflating bag

(b) Automatic ventilators used in the UAM. Photograph taken at the OES factory

Figure 2.2: Different tools used for ventilation

Vaporizers

The most commonly used vaporizers in HICs is the *plenum* vaporizer [14] [59, p. 838], wile traditionally, the *draw-over* vaporizer has been used in LMICs [5]. The physical flow of gas seen in plenum and draw-over vaporizers is very similar, but some of the internal mechanisms and components differ. For plenum vaporizers carrier gas is pushed through the vaporizer by pressure from the medical gas supply or cylinders [20], and is pressurized in the vaporizing chamber [59, p. 838] to ensure satisfactory mixing of gases. In draw-over vaporizers, pressurized gas can be used, or the gas can be drawn through the vaporizer by the pressure created by the patients spontaneous breathing. If the patient is not breathing, a similar pressure can be created with a bellow or a self-inflating bag. The pressure created by the patients spontaneous breathing is low, and because of this, draw-over vaporizers can not have a high internal resistance [72].

Because the flow rate varies with the patients spontaneous breathing, and accuracy depends on flow rate, the accuracy of draw-over vaporizers is poor [59, p. 839]. Plenum vaporizer are not usable without a source of pressurized gas, but are more accurate than draw-over vaporizers

[10] [72]. Another vaporizer is the measured flow vaporizer which is most often used with desflurane which is not used in LMICs, and will therefore not be described in this thesis. Another inhalational anaesthesia device is the AnaConDa, which uses a syringe pump to inject liquid anaesthetic agent into the breathing tube. A detailed explanation of vaporizers, including the measured flow type and AnaConDa, is included in Appendix C, Chapter 3

2.2 Problems with Anaesthesia in LMICs

Many LMICs face a multitude of medical problems, with a high incidence of disease and injury that need surgical attention [43]. According to Meara et al. [43], "an estimated 16,9 million lives (32.9% of all deaths worldwide) were lost from conditions needing surgical care [in 2010]". Even when anesthesia is available in LMICs it is often associated with a high risk. While the mortality rate from anesthesia in HICs is 0.0005-0.001%, the mortality rate in LMICs is 5-10% [8]. Both Ulisubisya [64] and Meara et al. [43] state that surgical care and anesthesia in LMICs is overlooked and receives little attention in the global medical discourse.

To administer anesthesia safely some basic factors are needed. According to Baxter et al. [6] some of these are an "adequate numbers of trained staff, reliable infrastructure, [and] functioning equipment...". These factors will be discussed in the next sections.

2.2.1 Trained staff

Maera et al. [43] state that "Human resources are the backbone of health-care delivery systems". Many countries lack adequate numbers of health-care personnel, as well as trained anesthesia workforce [16]. According to Maera et al. [43] "44% of the world's population lives in countries with a specialist surgical workforce density lower than 20 per 100 000 population, and only 28% lives in countries with a specialist surgical workforce density higher than 40 per 100 000 population". According to Prof. Fenton[2], the result of the the low numbers of physician anesthesiologist is that anesthesia is being provided by non-physician anesthesiologists and personnel with no formal education. This can result in equipment being used incorrectly.

[2]Personal communication. Oxford, England, October 2017

2.2.2 Infrastructure

The availability and reliability of clean, running water, electricity and sources of oxygen are essential factors for a hospital to be able to offer safe surgical procedures and hence, safe delivery of anesthesia [43]. In many LMICs these factors are limited and sometimes unavailable.

A lot of medical equipment and procedures require electric power to function. Therefore, a reliable and continuous supply of electricity is often necessary for providing safe surgical care and anesthesia. Examples are operating room lightning, anesthesia machines, pulse oximeters and ventilators. Kushner et al. [40], investigated essential surgical and anesthesia capacity at 132 facilities in 8 LMICs, and found that only 36% of the facilities had electricity always available, while 64% had sometimes or never electricity available. Vo et al. [68], surveyed 590 facilities in 22 LMICs about their anesthesia-related capacity, and found that 41% of the facilities had an interrupted or no available supply of electricity. In hospitals where electricity is not available a generator can be the primary source for electricity [2]. The use of a generator is not optimal since they can malfunction and require fuel to operate.

Kushner et al. [40] also found that oxygen was always available only at 21% of the facilities, and never available to 46%. Where oxygen is available, sources are mainly cylinders or oxygen concentrators. Some hospitals have oxygen concentrators that stay unused due to a lack of personnel able to repair defect machines, or because of insufficient electricity to run the machine [8] [32]. Availability of a reliable cylinder supply is a problem in countries that lack access to reliable public infrastructure [8]. If the cylinders have to be refilled, there must be adequate roads for transport of cylinders.

2.2.3 Equipment

According to Hodges et al. [32], there is a shortage of equipment in hospitals in LMICs. Vo et al. [68] estimates that 46.6% of the facilities surveyed did not have reliable access to a functioning anesthesia machine. Perry and Malkin [54] examined 112040 pieces of equipment in LMICs, and found that an average of 38.3% of equipment in these LMICs were out of service. For anesthesia machines they found an average of 32% were out of service.

Another problem is that there is a lack of personnel that know how to repair anesthesia equipment, which often breaks down or malfunctions in LMICs [54]. According to Hodges et al. [32] "only 36% of anaesthetists worked in a setting where there were individuals trained to repair

equipment". In the majority of the cases where equipment could not be repaired locally, components were sent to regional centres for repair. Perry and Malkin [54] also found that "at least 50% of [both operator and service manuals were] not found in the surveyed health systems". The result is that even if there is anesthesia equipment present at a hospital, much of it is unusable [50] [26]. Perry and Malkin [54] found that "lack of spare parts, lack of disposables and lack of required accessories" were common reasons for why equipment was out of service.

Vaporizer

Because of the poor medical situation and infrastructure in many LMICs, not all vaporizers are suitable for use. ISO has, by request from The World Health Organization (WHO), made a standard for “Anaesthetic systems for use in areas with limited logistical supplies of electricity and anaesthetic gases” [36]. ISO present four minimum criteria for anesthetic equipment designed for these countries [36].

1. Ability to function in the absence of a regular supply of compressed medical gases
2. Ability to continue to function safely when the supply of medical gases fails
3. Ability to function if mains electrical supplies are interrupted, or are subject to unpredictable increases or decreases in voltage
4. Ability to function in a challenging environment, including high temperatures, humidity, shocks, vibration, and dust

Additionally, based on conversations with Prof. Fenton and Dr. Lonnee, the authors propose that a vaporizer made for LMICs also needs to be:

5. Easy to operate and understand
6. Easy to repair for local technicians
7. Cheap to buy and maintain

Because of a lack of pressurized gas and unreliable electricity all plenum vaporizers are unusable in many LMICs. Although measured flow vaporizers are not intrinsically dependant on electricity, modern models rely on both electricity and pressurized gas to function. This is because the administration of anesthetic vapour in measured flow vaporizers is achieved most often by heating the anaesthetic agent desflurane, which requires electricity. Additionally, since desflurane is expensive, the measured flow vaporizers are not suited for, and rarely used in LMICs [44, p. 27].

The AnaConDa, which uses a syringe pump to directly inject VA into the breathing tube. Prof. Fenton has informed the authors[3] that, in his experience, the use of syringe pumps is problematic in LMICs. Syringe pumps use disposable syringes which can be hard to fill and get lost or broken. Prof. Fenton strongly recommends against including disposable equipment in medical equipment for use in LMICs. He also added that the program settings of the syringe pump drivers are not easily understood, which is a problem in emergency situations especially if the user has no formal education or experience in handling syringe drivers.

Draw-Over

The draw-over vaporizer is currently used in many LMICs because of its ability to function without pressurized gas or electricity [72]. They are robust, portable, and simple to use and understand [47]. Some models can be used both with pressurized gas or with room air, making them very versatile.

Although draw-over vaporizers are commonly used in LMICS there are some limitations to their usefulness in LMICs. In general, draw-over vaporizers are less accurate than plenum vaporizers and have a higher variability in ouput concentration when used in high temperature settings. Even though draw-over vaporizers are less complex compared to plenum vaporizers, they still malfunction and break down. Hodges et. al [32] asked anesthesiologists in Uganda about equipment at their hospital. The list below shows the responses specifically about vaporizers.

1. "... one vaporiser is stuck so the other is moved from room to room"
2. "The draw over apparatus is lying unrepaired for the last 10 years"
3. "The EMO[4] vaporiser has not been serviced for 20 years"

Anesthesia Machines made for LMICs

High-end anesthesia machines are complex, expensive, utilize advanced electronics, and are dependent of pressurized gas. They are not usable where sources of oxygen and other medical gases or electricity are unreliable or unavailable. There are a few anesthesia machines made specifically for use in LMICs that can use room air as carrier gas. Among them is the CE-marked UAM and the Diamedica Glostavent.

What distinguishes the UAM most from the high-end machines is that it can function without a continuous supply of high pressurized gases [62]. It can be used with pressurized gas if it is

[3] Email correspondence 2017-11-16
[4] An old draw-over vaporizer commonly used in LMICs

available, but if it is not or if the supply-flow fails, the machine will switch to using room air as carrier gas. When the machine is used like this the flow can be drawn through the system by use of a bellows, a self-inflating bag or by respiratory efforts of the patient.

2.2.4 Donations and Problems with Sales in LMICs

As previously mentioned, plenum vaporizers are not usable in areas where pressurized gas is sparse and electricity is not reliable. Even so, there are many plenum vaporizers in hospitals in LMICs. According to Angela Enright [24], the fact that high-end anesthesia machines are unusable in these areas, "is either unknown to, or ignored by, well-meaning donors or even purchasing agents in hospitals or ministries of health". This means that there are many hospitals in low-resource areas with high-end anesthesia equipment that is unusable because of the poor medical situation in LMICs. The term *anesthesia graveyard* and *equipment graveyard* is used to describe this situation, where perfectly fine equipment is stowed away because it is unusable for the hospital it is donated to or bought for. Figure 2.3 taken by Prof. Fenton, shows an EMO vaporizer used as a doorstop.

Dzwonczyk and Riha [22] found that 86% of the equipment examined in seven hospitals in Haiti were donated, with only 28% of all equipment working properly. Donations can even end up costing the recipient money [22]. According to Meara [43], "Hospitals often feel obligated to accept donations even when the equipment or supplies are not useful". Donated equipment is frequently donated without a service contract which means that if the equipment malfunctions or breaks down, hospitals are often left with an unusable piece of equipment [54]. Figure 2.4 shows an anaesthesia equipment graveyard.

Figure 2.3: An EMO vaporizer used as a doorstop. Photograph taken by Prof. Fenton

According to Prof. Fenton[5], anesthesiologists in LMICs often wondered why their draw-over vaporizers, which are not CE marked, were different than the ones that were used in HICs. The anesthesiologists viewed it as

[5]Personal communication. Oxford, England, October 2017

Figure 2.4: An anaesthesia equipment graveyard [61]

"a poor solution for a poor country, or that they were
used as guinea pigs" [26]. He goes on to say "In fact, any machine designated 'especially for the third world' is doomed to fail, even if works: the 'third world' may need it but it doesn't want it. Technology credentials must be internationally acceptable" [26]. This proposes a very different problem with equipment in LMICs to those discussed previously. Not only does equipment made for use in LMICs have to be usable in LMICs, but it also has to be used in HICs.

Jon Anner, the president of East Meets West[6], states that "Front-end aesthetics [of medical devices] are in fact important" [70]. Anner goes on to say that "Devices need to look modern, so that hospitals are proud to use them and patients feel that they are receiving the proper treatment".

2.3 Liquid Handling

2.3.1 Transfer of Liquids

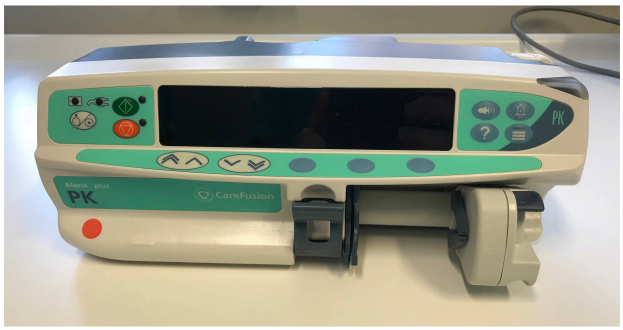
Liquid infusion is used extensively in medical application like analgesia, anaesthesia, and enteral feeding. Examples of common medical devices used for injection of liquid include syringe pumps and infusion pumps for insulin. These devices inject liquid drugs at a specific flow rate

[6] a non-governmental organization focusing among other things on health and medicine in Asia and Africa

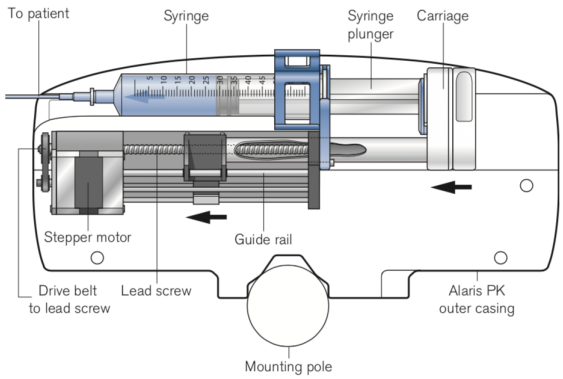
or as a volumetric bolus. The flow rate of the liquid transfer mechanism is found with the equation: Q = Crossectional area × velocity.

Syringe Pump

The syringe pump is commonly used at hospitals for analgesia, anaesthesia, and enteral feeding [18]. Figure 2.5a shows the Alaris PK Syringe Pump, which is a state of the art syringe pump, used to inject drugs intravenously at a flow rate as low as 0.1 $\frac{ml}{h}$. Figure 2.5b shows the inner mechanism of the same device.



(a) The Alaris PK. Photograph taken at St. Olavs Hospital



(b) Mechanism of the Alaris PK syringe pump [18, p. 405]

Figure 2.5: The Alaris PK syringe pump

In a syringe pump a *motor* drives a threaded rod, which is connected by a nut to a pusher [18, p. 404]. When the motor drives the threaded rod, a pusher will travel linearly down the rod driving the syringe plunger. The syringe pump injection rate depends on the motor speed, the pitch of the threaded rod, and the syringe itself [12]. The pitch of the threaded rod is the distance between two crests on a screw thread, which is equal to the distance traveled per rotation. By using a motor which can turn in small angels the distance traveled can be very small. The amount injected can be controlled by changing the motor speed, or the angular distance traveled per second by the motor. Different motors can be used to drive the syringe pump, but according to Davey and Diba [18], the stepper motor is used in most syringe pumps used at hospitals. Equation 2.2 shows the relation between the angular movement per second and the injected volume rate [13].

$$Q = \text{(Cross-sectional area of syringe)} \times \text{(velocity of plunger)} \tag{2.1}$$

$$Q = (\pi r^2) \times (pitch \times \frac{\theta}{360°}) \tag{2.2}$$

Peristaltic Pump

The peristaltic pump gets its name from the the action which also occurs when a person swallows, peristalsis. In a peristaltic pump the liquid is transported through a flexible tube by contracting waves moving through the tube [18, p. 403], as shown in Figure 2.6. The flexible tube is squeezed by rollers or cams which draw liquid from one end of the tube to the other. Since the liquid is contained in the tube and isolated from any direct contact, the peristaltic pump is especially suited for uses where the liquid should not be in direct contact with the pump mechanisms, or when the liquid should not be exposed to air [69]. Peristaltic pumps can be made with linear or circular configurations as shown in Figure 2.6. According to Davey and Diba [18, p. 403] the linear peristaltic pump is the most commonly used mechanism for infusion pumps.

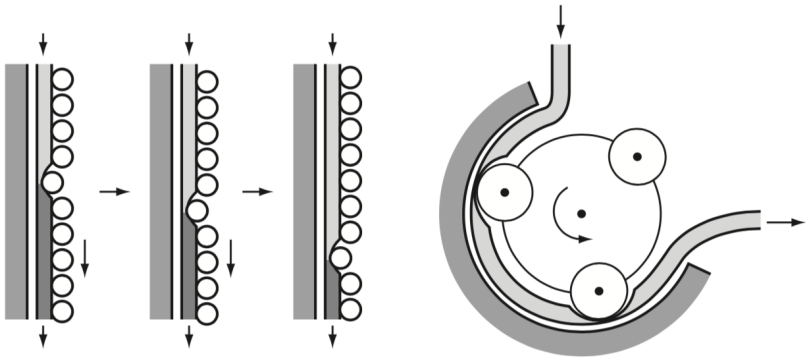


Figure 2.6: Two peristaltic pump mechanisms. Linear peristaltic pump to the left, and rotary peristaltic pump to the right [18]

2.3.2 Evaporation of Sevoflurane

Volatile agents are used for inhalational anaesthesia, and are used because they evaporate in room temperature. According to Biro P. [7] 1 ml of liquid sevoflurane is equal to 184 ml of gaseous sevoflurane. When a substance transforms from liquid to gas, energy is released to its surroundings [10]. If there is no external heat source the energy loss will cause the liquid to rapidly cool down. The temperature of the liquid substance influences the rate of evaporation [11, p. 570]. This means that as the liquid evaporates it cools down, resulting in a decrease of subsequent evaporation. To increase the rate of evaporation of the liquid we can [10]:

1. increase the temperature;

2. increase the surface area of the liquid;

3. increase the removal of vapour molecules form the liquid surface

Common plenum and draw-over vaporizers use wicks or pieces of metal or fabric mesh to increase the surface area [10]. Desflurane vaporizers use a heater to increase the temperature to the boiling point of desflurane, maximizing the evaporation rate [10]. Figure 2.7 shows three pieces of wick found inside a draw-over and a plenum vaporizer.

2.3.3 Containers for Volatile Agents

Plenum and draw-over vaporizers are often made with a container at the bottom of the device, which is lined with a mesh or wick to increase the evaporation rate. These containers can be made from metals and are sometimes lined with a protective material like Teflon to protect from degradation [18]. This includes both erosion and corrosion caused by VAs.

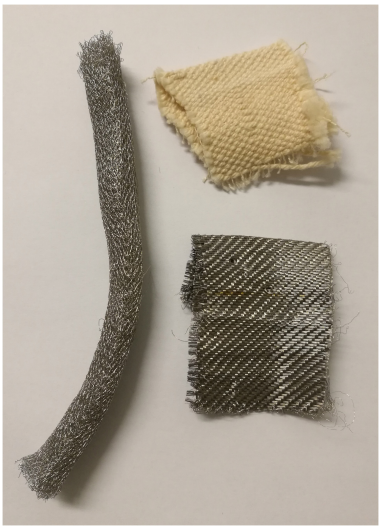


Figure 2.7: Three pieces of wick made of metal and fabric obtained from two vaporizers

To fill the anaesthetic containers different types of fillers are used. The screw fill system has historically been used and is included in several draw-over vaporizers used in LMICs [18, p. 49]. This system uses a threaded cap which can be screwed into a hole in the container [18, p. 50]. Liquid VAs can then be poured into the container. One problem with this system is that it makes it possible to use the wrong VA in a vaporizer made for use with only one VA [18, p. 50]. To combat this problem, different agent-specific filling devices, or key-fill systems, are commonly used in contemporary plenum vaporizers. This system works so that VAs are sold by the manufacturer in a bottle with a special filler. The filler can only be inserted into vaporizer fillers if the VAs are compatible. Special valves are included in the bottle which opens only when the bottle is inserted into the vaporizer container, which ensures that there is no spillage [18, p. 50]. A problem with the keyed fillers is that there are several manufacturers and types of keyed fillers, which means that if the right combination is not used the vaporizer can not be filled [18, p. 50].

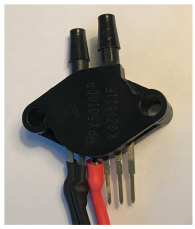
2.4 Flow Measurements

There are several ways to measure flow rates in a patient breathing tube. Mechanisms include mechanical devices like rotameters, Wright's respirometer, the axial turbine flowmeter, and digital devices like differential pressure sensors, hot wire anemometry, and ultrasonic flowmeters [18]. A technical presentation of these can be found in Chapter 2 of *Ward's Anaesthesia Equipment* by Davey and Diba [18, p. 27-39]. In this section the theory behind the differential pressure sensor, which was used to prototype the Fenton concept, will be presented.

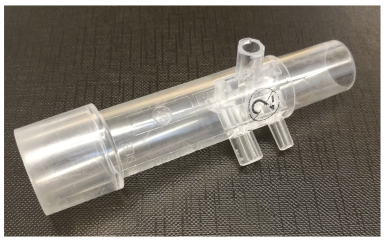
2.4.1 Differential Pressure Sensor

The piezoresistive differential pressure sensor usually include a disc which is deformed proportionally to pressure. When the disc is deformed, a voltage is generated. This voltage is proportional to the pressure experienced by the sensor, and can be read by a microprocessor. The differential pressure sensor has two measuring points and calculates the difference in pressure between them. Figure 2.8a shows a common differential pressure sensor from NXP.

To use differential pressure for flow measurement, a *flowmeter* like the GE Healthcare flowmeter showed in Figure 2.8b has to be used. A flowmeter is a hollow tube with a restrictor placed in the middle. The restrictor will create a pressure difference inside the tube which can be measured from two ports on the flowmeter. The two small ports on the bottom are used to measure the pressures, while the small port on top is used to sample gas, and is not used when only measuring the flow rate. Figure 2.8c shows a spirometer tube which is used to connect the flowmeter to the differential pressure.



(a) The MPX5010DP



(b) The GE Healthcare flowmeter

(c) The GE Healthcare spirometer tube used with the flowmeter

Figure 2.8: Components used for flow measurements using a differential pressure sensor

Depending on the type of restrictor, the flow rate is either proportional to the differential pres-

sure, or proportional to the square root of the differential pressure. The orifice and venturi types have quadratic relations, while the tubular has a proportional relation [18]. The fluid dynamics relations for the venturi type flowmeter is shown below. First, we consider the venturi effect, which states that the pressure of a fluid reduces when it enters a restriction in a tube or pipe. This can be seen in a special case of the Bernoulli equation with steady state, incompressible, inviscid flows:

$$P_1 - P_2 = \Delta P = \frac{\rho}{2}(v_2^2 - v_1^2) \tag{2.3}$$

The second equation, the mass conservation law, is used to find the flow rate:

$$Q = A_1 v_1 = A_2 v_2 \tag{2.4}$$

By solving Equation 2.3 for v_1 we get:

$$v1 = \sqrt{v_2^2 - \frac{2\Delta P}{\rho}} \tag{2.5}$$

This can be inserted into Equation 2.4 to get:

$$Q = A_1\sqrt{v_2^2 - \frac{2\Delta P}{\rho}} \tag{2.6}$$

Where:

P_n = Pressure at point
v_n = Velocity at point
Q = Flow rate
A_n = Cross-sectional area at point
ρ = Density of gas

From Equation 2.6 it can be seen that it is possible to find the flow rate through the flowmeter if the differential pressure and velocity response of the flowmeter is known [53]. The cross sectional area and the velocity response of the flowmeter, as well as the density of gas can be considered as one single constant, k, which is the *characteristic constant of the system.* It is assumed that the density of gas does not change over time.

The final equation is then:

$$Q = k \times \sqrt{\Delta P} \tag{2.7}$$

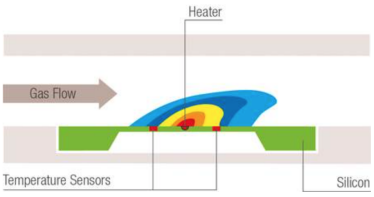
The constant can be found experimentally by recording differential pressure measurements at different flow rates and dividing the flow rates with the square root of the differential pressure [53].

2.4.2 Microthermal DPS

Figure 2.9a[7] shows a microthermal differential pressure sensor from Sensirion, which measures a temperature gradient to find the differential pressure. The setup is identical to the piezoresistive differential pressure, and the ports of the sensor is connected to the ports of a flowmeter. The majority of the gas to be measured passes through the flowmeter while a small part flows *through the sensor* from one port to the other [57]. A heater is placed inside the sensor, and two temperature sensors measure the temperature difference downstream and upstream of the heater. Depending on the temperature gradient the differential pressure can be measured. Figure 2.9b[8] shows a sketch of the mechanism inside a microthermal differential pressure sensor. The differential pressure and flow rate is again characterized by the flowmeter.

The same microthermal principle can also be supplied with in-line mass flow meters. The functional principle is the same, with the exception that the heater and sensing chip is placed *in line* with the flow as opposed to in a bypass chamber. Figure 2.9c[9] shows the SFM3200 in line flow meter by Sensirion. The mass flow meters are digital, pre-calibrated, and the accuracy is high over a large range of flows [56].

(a) The SDP810 microthermal differential pressure sensor [55]



(b) Sketch showing the mechanism of the SDP810 microthermal differential pressure sensor [55]

(c) Two Sensirion SFM3200 in line mass flow meters [56]

Figure 2.9: Microthermal sensors by Sensirion

[7] Permission for use granted by Sensirion
[8] See footnote 7
[9] See footnote 7

2.5 Gas Analysis

A gas anlayser can be used to monitor the concentration of an anaesthetic agent in the breathing tube. The most commonly used gas analysis method used in modern operating theaters is infrared absorption spectroscopy [3]. Other commonly used mechanism include refractrometry, mass spectrometry, Raman spectroscopy, photoacoustic apectrography, and piezoelectric analysers, which can be read about in articles by Garg and Gupta [29], Ali and Walker [3], Langton and Hutton [34], and Mandal [48].

2.5.1 Infrared absorption spectroscopy

VAs and gases like CO_2 absorb IR light at different wavelengths. VAs have absorption peaks between 8 and 13 μm [29]. Infrared absorption spectroscopy makes use of the Beer-Lambert law, which states that infrared absorption by a medium is proportional to the concentration of said medium [3] [29]. The gas is radiated with IR light, and a rotating *chopper* is usually included to enable transmission of specific wavelengths corresponding to the gas which is to be measured [29]. The gas absorbes some of the light at the specfic wavelength, and by comparing the absorbance of the IR light with a known reference the gas concentration can be found [3] [29].

2.5.2 Sampling

There are two ways of sampling the gas for analysis: sidestream and mainstream [29]. For sidestream sampling, gas is delivered to a sample chamber using a small sampling tube, and the gas can be returned to the patient after sampling. The sample chamber should be positioned close to the patient [29]. In mainstream sampling, the gas is analyzed directly in the breathing tube. The gas flows through a sample chamber, which is usually positioned close to the patient.

2.6 Electrical Components

In this section, the electrical components used for prototyping are presented.

2.6.1 Arduino

To enable communication between different electrical components, a microcontroller is used. The Arduino microcontroller are specifically made for prototyping and control projects [9]. The Arduino boards have several pins which are used to connect the Arduino to other components, like motors, sensors, or semiconductors. Figure 2.10 shows the Arduino Uno and Arudino Due microcontrollers. A solderless breadboard is often used to connect electrical components like resistors, motors, motor drivers, and sensors to the Arduino board. The Arudino board is supplied with a USB plug and can be connected directly to a PC. When the Arduino is connected to a computer, a program can be written in the Arduino language and uploaded to the Arudino. The program is used to give instructions to the Arduino on what to do. Examples include running a stepper motor, requesting measurements from a sensor, or performing arithmetic calculations. Connection to a computer also enables communication through what is called *serial communication* [9]. This can be used to either receive data from the Arduino visually on the computer screen or to instruct the Arduino to perform an action. The Arduino can be powered by a computer via the USB port, or by an external power supply, like a battery.

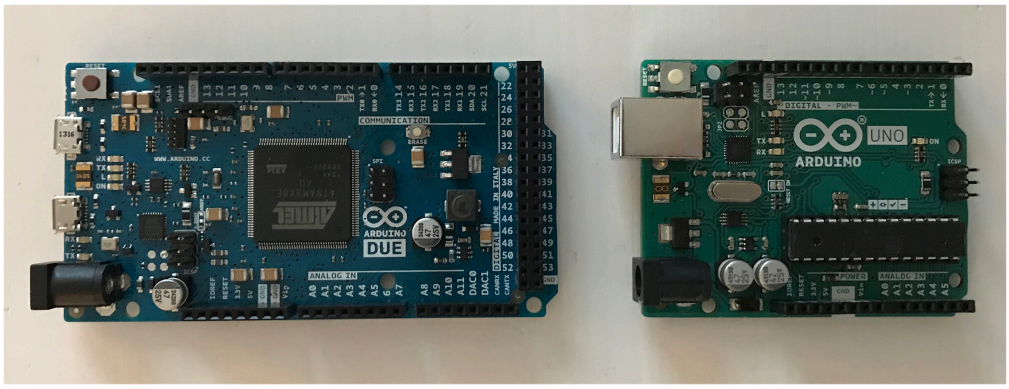


Figure 2.10: The Arduino Due to the left, and the Arduino Uno to the right

The clock speed of the microcontroller indicates how fast the program can be run [9], with the Uno having 16 MHz and the Due 84 MHz. The Arduino boards have analog pins, which are used to read analog sensors or drive analog components. The Uno can read 10-bit analog values, while the Due reads 12-bit. When an analog sensor is connected to the analog pins, the Arduino Uno board will therefore measure values between 0 and 1023 ($2^{10} = 1024$), while the Arduino Due will measure values between ($2^{12} = 4096$).

2.6.2 Stepper motor

A stepper motor is a motor where the rotational movement is performed in equal angels, or steps [9]. This means that if a stepper motor turns in 1.8 deg steps, 200 steps are needed to drive the motor through one revolution. Different stepper motors have different number of steps per revolution. *Motor drivers* are employed to drive and control the stepper motor. Some motor drivers include what is called microstepping. Microstepping is used to drive motors in semi-steps, where the angle per step is decreased so that more steps may be taken per revolution [51]. As an example, if a stepper motor with 200 steps per revolution is connected to a $\frac{1}{16}$ microstepping motor driver, the amount of steps per revolution is increased to $200 \times 16 = 3200$. Stepper motors are commonly supplied with standardized faceplates, which are called NEMA.

2.7 Product Development

2.7.1 Concept Generation Methodology

Ulrich and Eppinger state that "a good concept is sometimes poorly implemented in subsequent development phases, but a poor concept can rarely be manipulated to achieve commercial success" [65, p. 118]. A product concept is "an approximate description of the technology, working principles, and form of the product" [65, p. 118]. The concept generation phase can be performed very cheaply and quickly compared to the subsequent product development phases [65, p. 118], which can make it a very valuable part of the product development process. Different product concepts are generated based on the user needs and target specifications [65, p. 118]. To effectively use time and resources, the *expand-and-focus strategy* can be employed [65]. For this strategy, the scope is expanded and as many concepts as possible are generated, before focusing on the most promising concepts. Ulrich and Eppinger [65] present a five-step concept generation method, which is shown in the list below.

1. Clarify the problem
2. Search externally
3. Search internally
4. Explore systematically
5. Reflect on the solutions and the process

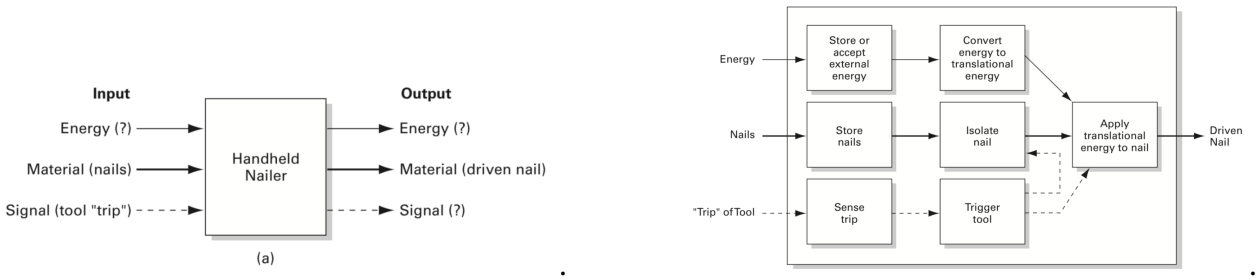
The five-step method can be used to generate product concepts for the parent concept, but also for subproblems of the product [65, p.119].

Clarifying the problem

The method begins by clarifying the problem at hand. The scope of the design problem should also be defined, either generally or specifically. A list of assumptions for the product problem can be made to ensure an equal understanding between the participants of the product development process [65, p. 121]. These assumptions can be generated from for example the user needs, the technical specifications, or by the customer.

Ulrich and Eppinger [65, p. 121] state that if the problem is complex, problem decomposition should be performed, where larger development problems are divided into simpler subproblems and evaluated separately. This is performed to be able to tackle the problems in a more focused way [65, p. 123]. There are several types of decomposition methods, including *functional decomposition* and *decomposition by key customer needs*.

Function decomposition begins by presenting the product problem as a single black box. Different lines denote different inputs and outputs, as shown in Figure 2.11a. After creating the black box and the input and output flows, the black box is divided into subproblems with different functions. The subproblems can be divided further, until the participants agree that the subproblems are simple enough to work on as a single problem. Figure 2.11b shows the function diagram.



(a) Black Box (b) Function diagram

Figure 2.11: Black box and function diagram [65, p. 122]

It is important to note that the aim of this stage is to convey the function of the subproblems, and not any technological principles or mechanisms. When the subproblems are defined, some or more of them should be picked for further evaluation. This means that some of the subproblems can be deferred for later production stages.

Search externally

After being defined, the subproblems should be researched. External research tries to find solutions to the problems by evaluating existing products or technology [65]. Both competitive products and existing solutions to similar sub-functions should be evaluated. The reason for evaluating and implementing existing solutions is that it is "usually quicker and cheaper than developing new solutions" [65, p. 124]. This way, focus can be directed towards critical subproblems for which there are no existing solutions or which are especially important for the product as whole. Sometimes, existing technology may be mated with a more creative solution, as a way of improving an existing idea [65]. This will of course not happen if the existing solution remains unknown to the product development team because of poor research.

Ulrich and Eppinger [65, p. 124-127] describe five ways of external search. *Lead user interviews*, where the first users of a product are interviewed. These users often need a solution to an existing problem long before the majority user. They can often benefit massively from product innovation. *Expert consultation*, where experts on a given field or problem are consulted in person, on the phone, or online. *Patent search*, which will exhibit technological solutions of existing technology, usually with thorough explanations and technical drawings. *Literature research*, including expert articles, white papers, instruction manuals, product announcements, and more. *Competitive benchmarking* where existing products are studied and compared can be used to compare different solutions.

Search internally

Opposing the external research phase is the internal research phase. In this step, creative solutions are generated by the product development team. It is often called brainstorming, and is a creative process where ideas are generated from the collective knowledge of the team [65]. Ulrich and Eppinger [65, p. 128] recommend four guidelines for improving the internal search phase:

1. Suspend judgement
2. Generate a lot of ideas
3. Welcome ideas that may seem infeasible
4. Use graphical and physical media

The internal search can be performed both in teams and individually. According to Ulrich and Eppinger [65, p. 128-129], research shows that performing some individual research will result

in an increased amount of concepts generated and a better quality of work. Of course, the ideas will have to be discussed and evaluated in groups to create a communal knowledge base. Additionally, it is a good way to generate creative ideas or refine ideas between members. It is especially important to remember the first guideline when working in teams. By suspending judgement, members of a team can freely think out loud and generate, perhaps infeasible ideas, which can later be refined into a well suited solution to the problem. It also makes it easier for the other members to play with and refine other members ideas without the risk of feeling that they are downplaying the original idea. The use of physical media is especially applicable when the concept has a complex form or mechanism [65, p. 128]. Physical media can then be used to communicate ideas in the product development team.

Explore systematically

After the research phase, a wide array of solutions should have been amassed. A systematic exploration can be performed to make it easier to navigate through the solutions [65].

Two tools used for systematic exploration are presented by Ulrich and Eppinger [65]. The *classification tree* is used to classify the different solutions together. An example is shown in Figure 2.12. The branches of the tree can then be pruned to remove poor ideas. The tree can sometimes expose that the team has researched and evaluated some solutions better than others [65]. If one of the branches is far larger than others, or if some branches are very small it may indicate that the group should investigate these further to look for more alternatives. Several classification trees can be made for the same concept [65].

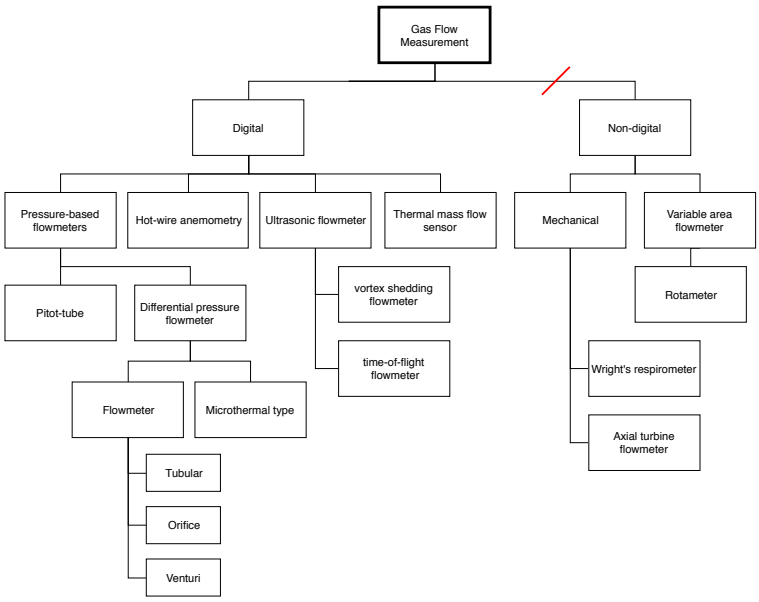


Figure 2.12: A classification tree

The *concept combination table* is used when a function is decomposed into subfunctions [65]. Several different mechanisms or solutions for the subfunctions are then listed together in a matrix. These solutions can be combined in different ways, which will result in different mechanisms. According to Ulrich and Eppinger [65], the use of concept combination tables can spark

creative thinking and forces evaluation of the concepts.

Reflect on the solutions and the process

Product development is a very iterative process, and reflection should be performed throughout. Ulrich and Eppinger [65] propose a few questions the product development team can ask themselves during the process:

- Is the team developing confidence that the solution space has been fully explored?
- Are there alternative function diagrams?
- Are there alternative ways to decompose the problem?
- Have external sources been thoroughly pursued?
- Have ideas from everyone been accepted and integrated in the process?

2.7.2 Concept Selection Methodology

Concept selection is always performed during production development [65]. Some methods are considered more effective than others. Examples of concept selection methods presented by Ulrich and Eppinger [65, p. 145] include pros and cons lists, prototyping, and decision matrices. The decision matrix is used to rate and rank the concepts by weighted criteria.

Some articles note that it may be beneficial to investigate multiple concepts, and perform the concept selection at a later date [60] [39]. This can give valuable information about the cost and customer response [17], as well as a better overview of the technical performances. This is especially true of technical products which can be evaluated quite good using virtual and analytical prototypes [17]. According to Srinivasan et al. [60], prototyping several concepts is consistent with how leading design firms like IDEO do their product development.

2.7.3 Prototyping

Ulrich and Eppinger [65] define prototype as "an approximation of the product along one or more dimensions of interest", and prototyping as "the process of developing such an approximation of the product". Using these definitions, a prototype can be an equation, a 3D model, or a physical product.

Types of Prototyping

Prototypes can be classified along two dimensions, as shown in Figure 2.13 [65]. The first dimension is whether the prototype is more physical or analytical. Physical models are created to approximate the physical product, and can for example be a cardboard or foam model, or a 3D printed fully functional mechanism. Analytical models are *models* that represent the product [65]. Examples include computer generated 3D models, computer simulations, or a mathematical equation showing the behavior of the product.

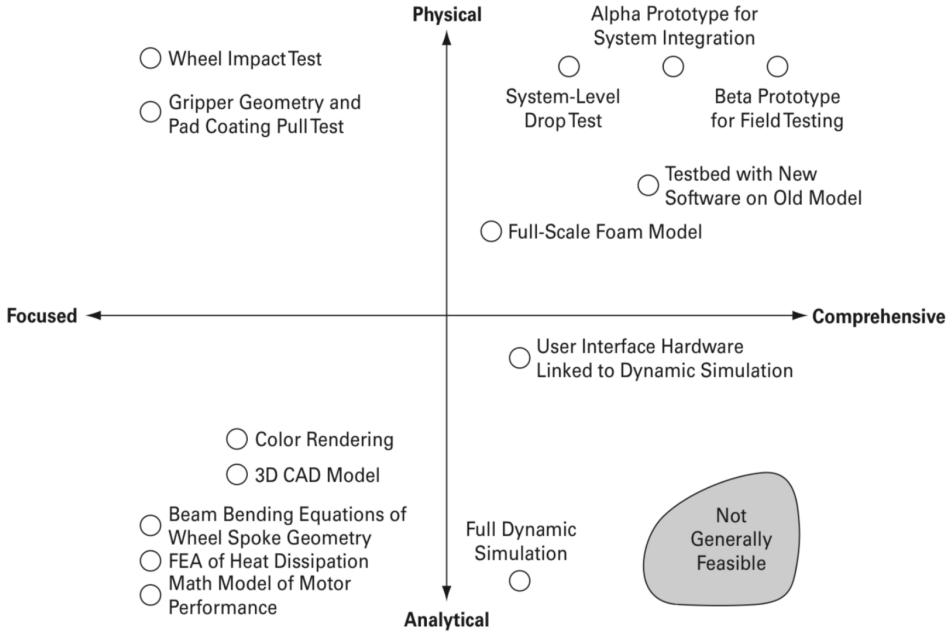


Figure 2.13: Dimensions of prototyping [65, p. 294]

The second dimension is whether the prototype is comprehensive or focused. Comprehensive prototypes show most or all of the features of the product [65]. Focused prototypes include one or a few of the features. An example of a comprehensive prototype is a beta-product used to test with actual users. Focused prototypes include computer simulations of a specific mechanisms, or a physical model of one feature of the product.

Physical prototypes are often better than analytical prototypes at uncovering uncertainties and unanticipated phenomena [65]. Analytical prototypes are, on the other hand, more flexible and are easier to modify.

Purpose of Prototyping

According to ulrich and Eppinger [65], prototypes are used for four purposes: learning, communication, integration, and as milestones.

When prototypes are made for *learning*, they are used to understand how the product works. Often, the question is used to verify whether the concept works or not, or if it meets the customer needs [65]. Prototypes can be used to answer this question, without demanding too many resources. Other prototypes are made to answer more complex questions, like how a specific component performs when subjected to testing.

Prototypes can also be made to *communicate* an idea or a concept to external participants like the user, the customer, or top management [65]. They can also be used to communicate ideas and concepts within the product development team [65] [19]. Even so, analytical models like 3D models or renderings can also be used to communicate ideas. This is particularly valuable in the early stages, since analytical models are more easily modified and do not require as high of an investment [65].

Prototypes are used to *evaluate the integration* of the system, and to ensure that the parts of a product are able to function together. Comprehensive prototypes are usually the most effective to test for integration [65].

Especially later in the prototyping process, *milestone prototypes* are used as a way to demonstrate the capabilities of the current build. It may be beneficial to test the prototypes to ensure that they are functioning as specified in the design. Milestone prototypes are commonly built later in the process, and are sometimes made to pass a specific test [65].

Late vs. Early Prototyping

Prototypes are used for different reasons depending on when in the production process they are made. Early on in the process, prototypes are used to understand how the product works, and to communicate an idea or concept to the product development team or outsiders. They are also used to encourage creative thinking [35]. Later on, the prototypes are used to validate the design and to test the solutions and to demonstrate functionality [65, p. 296]. These prototypes are more refined, and look and perform more like a finished product.

Directional and Incremental Prototyping

Elverum [23] proposes a model which explains how prototyping drives development forward. The model distinguishes between directional prototyping and incremental prototyping. Directional prototyping serves as tools for evaluating the direction the team will take forward. They are used for "good enough" assessments, to see whether an idea works or not. Incremental prototyping is performed to optimize the design without changing the overall design.

2.7.4 Prototyping Tools and Technologies

CAD and CAE

3D models, or computer aided design (CAD) can be used as tools for prototyping [65, p. 301]. CAD can is used to visualize parts of or the whole product as renderings or 3D models. Renderings are especially important for communicating an idea to someone without a background in product development or in the product field. Computer aided engineering uses numerical models to simulate and test analytical 3D models in the software.

Rapid Prototyping

Rapid prototyping is a prototyping technique which uses additive manufacturing to quickly make a prototype of a product [65]. It is used to quickly identify design flaws of a product [33] at the early stages of product development [28], and aims to reduce the time of prototyping and increase the information gained. Additive manufacturing include stereolithography, sintering and fused filament fabrication [28]. These and other 3D printing techniques are commonly used for rapid prototyping.

The Prusa i3 is an example of a budget 3D printer which uses the fused filament fabrication process, which can be used to make prototypes at a very low cost. Plastic material is extruded through a heated extruder head onto a heated metal bed. The extruder head is moved two dimensionally to create one layer of the 3D model at a time. Whenever a layer is finished, the height of the extruder is increased. The layer height can be changed in the 3D printer software, and will usually result in a better 3D print at the cost of time.

Set-based Prototypes

Set-based *prototypes*, a methodology made by Prof. Christer Elverum, can be viewed as modular prototypes which can be altered during testing[10]. The method is used to explore several concepts early in the product development process. By using this method of prototyping, the data collection can be increased even though only one prototype is created. This method is used to increase the probability that *at least one* prototype will work.

2.7.5 Planning for Prototypes

Ulrich and Eppinger [65] state that a potential pitfall in the prototyping stage is to focus energy and time on prototyping which does not add value to the product development. They propose four steps for planning for prototyping, which should reduce the risk of this problem. The list below shows the four steps.

1. Define the purpose of the prototype
2. Establish the level of approximation of the prototype
3. Outline an experimental plan
4. Create a schedule for procurement, construction, and testing

It should be decided beforehand what the *purpose* of the prototype is. Members of the production development group should list the learning, communication, and integration needs, and note whether or not the prototype is a milestone.

At this step of planning, the *level of approximation* of the finished prototype should be defined. That is, how close to the finished product is the prototype. The type of prototype should be considered - is it necessary to make a physical prototype, or will an analytical model do? Ulrich and Eppinger [65, p. 304] state that "the best prototype is the simplest prototype that will serve the purposes".

Ulrich and Eppinger [65, p. 304] state that a prototype can be viewed as an *experiment*. The experiment should therefore be planned, which includes identifying the variables of the experiment and the test protocol. It should also be noted what measurements will be taken, and a plan for post processing and analyzing of data. Some prototypes are made to give a greater insight in terms of data points. For these prototypes it is very important to plan for the experiment.

[10] Personal communication 2018-12-21

The prototyping plans should be ended by creating a *schedule*. Three dates are of special importance. First, the "bucket of parts" date, which is the day all the parts for the prototype are ready to be assembled. Second, the "smoke test" date, which is the date of the first test. Lastly, the completion date, which is the expected date that the testing is finished.

Chapter 3

Concept Generation and Selection

The five step method by Ulrich and Eppinger presented in Section 2.7.1 was used as the main concept generation method for this thesis. The method was used in two distinct ways. It was used both as a way to evaluate and characterize the parent concept, but also as a way to systematically generate concepts for the subproblems. This chapter will present the method used for both cases, and the results that followed. The method and results of the concept selection phase will also be presented, where the focus was on the liquid handling subproblem.

To better show the reader how the process was performed, the methods and results are presented in the same chapter. The product development process is presented chronologically as it was performed.

First, the parent concept was clarified and the problem was decomposed into subproblems. This will be presented as one section with method and the results of the process, with a presentation of the subproblems that were selected for further development. Then, the concept generation for the subproblems will be presented. This will be shown by first presenting how the five step method was used practically, and secondly presenting the results from the processes. In the results section, some alternative solutions that were not used are also presented. This is included to show a few of the dead-ends of the product development processes, and to highlight the decision choices. After this, the solutions were systematically explored using a combination table and qualitative evaluation. The method used for systematic exploration will be presented first, and the results second. Lastly, the concept selection method and results is presented. The results include a presentation of the recommended concept solutions.

3.1 Clarification and Decomposition of the Parent Concept

Ulrich and Eppinger's five step method begins with problem clarification. This section will present the clarification and decomposition of the *parent concept* presented by Prof. Fenton. As previously mentioned, the concept development is on order by Prof. Fenton. It is important to note that the parent concept had already been made by Prof. Fenton and was not to be modified for this thesis. The aim of the thesis was to examine *how* the Fenton concept could be solved - not to find an alternative solution to the parent concept.

3.1.1 Method

Clarification

The process of clarifying the parent concept began in the pre-master's thesis, where the user needs and target product specifications were listed in collaboration with Prof. Fenton and Dr. Lonnee. The product specification matrix was made to clearly show what the Fenton concept has to do. Because the Fenton device should be usable in both HICs and LMICs the user needs for both users were included. The product specifications were discussed with Prof. Fenton, and any assumptions for the design were noted. The assumptions were listed for two reasons. They ensure that the concept is developed as specified by Fenton, but it also ensures that the product development team are in agreement of what the restrictions of the concept are.

After listing the specifications and assumptions of the Fenton concept, a perceived problem was discovered with the concept. This was communicated to Prof. Fenton, and a solution was presented. This solution was assumed to be part of the Fenton concept for the rest of the product development. The technical specifications and assumptions made in the pre-master's thesis were subsequently modified in the master's thesis to include the ones discovered for the proposed solution.

Decomposition

The concept presented by Prof. Fenton was considered complex, and it was therefore decomposed with the intention of dividing the problem into more simple and solvable subproblems. This was done by sketching the concept as a black box and then as a function diagram. Several function diagrams were made until all essential components were covered. Prof. Fenton used technical descriptions like "motor" and "pump" in the concept presentation, which can lead

the development in a certain direction. To ensure that the development was not influenced by the descriptions, the black box and function diagrams removed these and used more neutral descriptions, like liquid injection and gas analysis.

From the function diagram the problem was decomposed into several subproblems, based on functionality. Some of these subproblems were still considered too complex to be solved as a single problem, and were split into further subproblems which could more easily be characterized. Since the Fenton concept is very complex, it was decided to focus on the ones that were most critical for the success of the Fenton concept. The selection was based on which subproblems were considered necessary to actually make a functional prototype. Two criteria were used to remove subproblems from subsequent development; subproblems were not chosen for further development if they depended on the solutions of other subproblems, or if they could easily be solved using existing products.

3.1.2 Results of the Parent Concept Clarification and Decomposition

In this section the results of the clarification process for the parent concept will be presented. A technical specifications list and an assumptions list will be presented, before showing the results of the decomposing process. The changes made to the Fenton concept will be presented first to give an overview of the actual concept that was solved for this thesis.

Initial Changes To the Fenton Concept

One of the first actions that was performed in the thesis was to solve a problem with the Fenton concept. The problem with the Fenton concept was that gas analysis was the only mechanism used to control how much liquid is to be transferred into the breathing tube. This was considered a problem, especially for the beginning of an operation when gas analysis can not be used to control the amount of liquid to transfer. It was therefore decided to investigate different ways to control the liquid transfer flow rate.

The process was performed as a concept generation phase, but was not performed using the five step model. Instead, the authors discussed the problem and consulted Prof. Fenton to clarify what the problem was. Little research was performed to evaluate how the problem could be solved using existing technology, and research was mostly performed creatively as a team. Two alternative supplementary controlling mechanism were found to be usable with the Fenton concept.

The first proposed controlling mechanism was to slowly increase the injection rate over time. When the target concentration is reached the gas analyser will take over as the main controlling mechanism.

The second proposed controlling mechanism was based on the fact that the anaesthetic gas concentration in the breathing tube should be a specified percentage. This means that the injection of liquid VA depends on the amount of oxygen or air in the breathing tube. The proposed method was to inject an amount of liquid VA proportional to the flow rate of gas in the breathing tube. This controlling mechanism necessitates the use of a mechanism capable of measuring the flow rate of gas in the breathing tube. Gas analysis would in this case be used more as a safety feature rather than the main controlling mechanism.

Figure 3.1 shows how the proportional injection would be performed. The graph assumes that a target concentration of 2% sevoflurane is used for liquid transfer. Notice that the graph uses a dual axis configuration, and that the axes are extremely different to visually show the proportional injection.

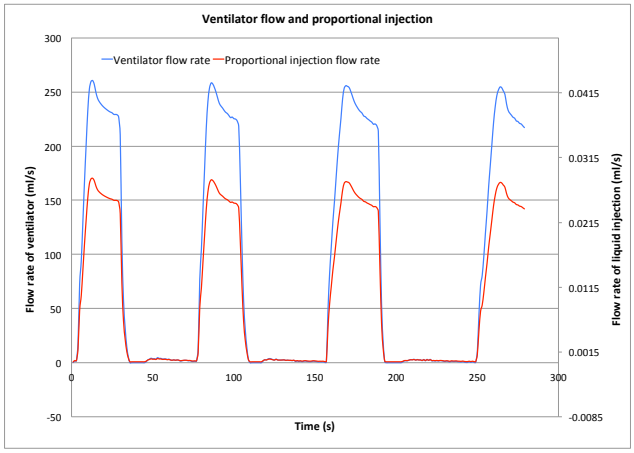


Figure 3.1: Graph showing a ventilator flow rate and a theoretical proportional flow rate

To use proportional control, a set of equations were proposed to find the *target liquid flow rate*, which is the volume of liquid needed to transfer into the breathing tube per time unit to reach the target concentration of VA. First, the target gas flow rate is found, which is the amount of VA needed to blend with the air in the breathing tube per time unit. This is found using $Q_{\text{target, gas}} = \frac{per \times Q_{\text{breath}}}{1-per}$, where per and Q_{breath} is the target percentage of VA and flow rate of gas in the breathing tube respectively. According to Biro P. [7] 1 ml of liquid sevoflurane is equal to 184 ml of gaseous sevoflurane. The constant of 184 can therefore be included in order to calculate the target volume of injection as a *liquid* and not as a gas. This thesis only concerns the use of sevoflurane, but similar constants can be found for other VAs. Equation 3.1 shows the relation between the patient breath and the target liquid flow rate.

$$Q_{\text{target, liq}} = \frac{\frac{per \times Q_{\text{breath}}}{1-per}}{184} \tag{3.1}$$

The two control methods were compared and evaluated. The benefit of the first control method is the simplicity of the setup. No calculations have to be performed, and the liquid injection is almost automatic. A problem is that the main controlling mechanism is gas analysis, which was an unknown technology to the authors. From research during the pre-master's thesis it was known that several gas analysis mechanisms have a delay of several seconds between readings. It was believed that this could create dangerous situations where the concentration could reach high levels before being automatically adjusted by the gas analysis feedback.

The main benefit of the second control method is that the system tries to reach the target concentration from the beginning of an operation, and that the injection itself is always proportional to the gas in the breathing tube. It does not rely on gas analysis to reach the target concentration, and the gas analysis can be used as a secondary controlling method. This could increase the safety of use. Another benefit is that proportional control lends itself nicely to any ventilation mode, including a patient spontaneously breathing. The system will always try to inject the proportional amount, no matter how the rhythm of patient ventilation is. It was, however considered a disadvantage to include the gas flow rate measurement mechanism, as this increases the complexity of the Fenton device as well as points of failure.

The control method of proportional injection was selected before the decomposition of the Fenton concept. Proportional injection was, for subsequent concept generation, assumed to be part of the Fenton concept. It was later believed that the selection of proportional control was performed hastily. This will be discussed in Chapter 6.

Results of Clarification and Decomposition

The product specification matrix is shown in Table 3.1. To make it easier to follow along with the concept generation of the subproblems, the specifications which pertain to one subproblem alone will be presented for that subproblem only. When these technical specifications are presented it should be noted that they were considered alongside the specification matrix for the parent concept.

Table 3.1: Product specification matrix for the Fenton concept

Metric	**Unit**	**Value**
Accurate delivery of VA	% of target	±0.5
Time from detection of too high concentration of VA to mechanical shutoff	sec	1
Weight	kg	< 10
Time to clean	s	60
Time to disassemble for maintenance	min	4
Cleanable with alcohol	binary	yes
Temperature operation range	C	-10 - 50
Time used on set up for operation	min	4
Time used on refilling	s	60
Time used to switch from mains electricity to battery	s	instant
Special tools required for maintenance	list	hex
Operational with carrier gas flow range	$\frac{L}{min}$	0.5 - 10
Percentage waste of VA	%	< 100
Battery cycle life	h	> 2
Battery life	years	5 - 15
Size	cm^3	< 100000
Instills pride	subjective	$\frac{4}{5}$
Vaporizer life time	year	5 - 15
Impact test, force until failure	Binary	To standard specification
Time to drain after use	s	60
Usable at tilted angle	degrees	-45 to +45
Battery recharging time	h	< 3
CE marking	binary	pass
Cost	$	< 10000
Intensity of visual alarms	Lumen	100-1500 [1]
Loudness of visual alarms	dB	90 - 100 [2]

The main assumptions for the Fenton concept are listed below.

- The vaporizer should be build for use with sevoflurane, but the concept should be usable with other VAs
- The vaporizer should be digital
- The vaporizer has to use gas analysis for feedback
- The vaporizer should be usable with standardized medical equipment, and should not require any special equipment to use

- The vaporizer should be portable
- The vaporiser should be easy to use
- The vaporizer should transfer *liquid* anaesthetic agent directly into the breathing tube, as opposed to the conventional way of transferring anaesthetic agent *gas* into the breathing tube
- The vaporizer should be robust
- The vaporizer should be easy to repair and maintain

Figure 3.2 shows the function diagram. It includes several functions which were not included in the original concept, but which were added after discussions with Prof. Fenton. Solid lines indicate physical movement, while dotted lines indicate information movement. The function diagram revealed the subproblems listed below. Some of the subproblems are split into several subproblems, which is indicated in the list.

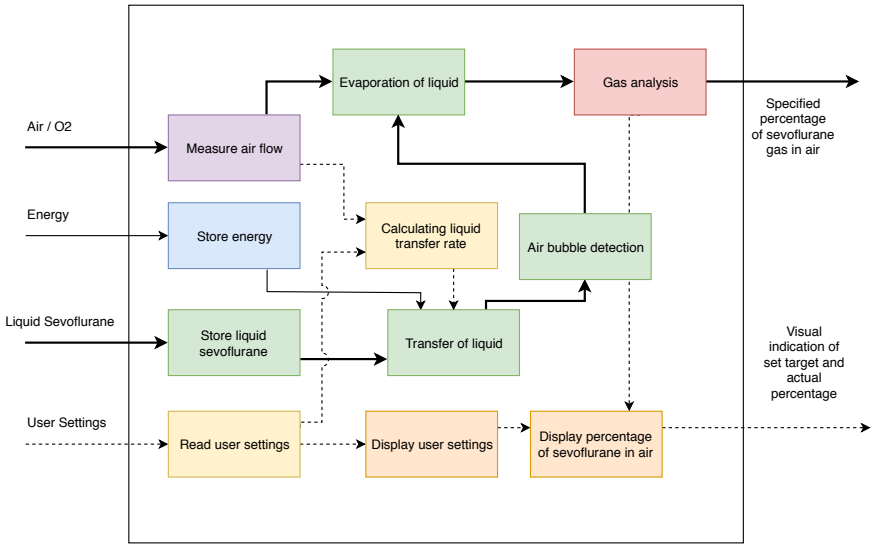


Figure 3.2: The final function diagram of the Fenton concept

1. **Measure air flow**. Flow measuring capabilities enable proportional control of the transfer rate of liquid into the breathing tube.
2. **Liquid handling**. Concerns all the handling of liquid VA.
   (a) **Transfer liquid**. The liquid VA has to be transferred to the breathing tube.
   (b) **Storage of liquid**. The liquid VA has to be stored inside the device.
   (c) **Evaporation**. The liquid VA has to be evaporated before reaching the patient.

   (d) **Air bubble detection**. To ensure a good accuracy, no air should be injected into the breathing tube.

3. **Visual feedback**. Enables the device to communicate vital information to the user.

   (a) **Display user settings**. The user has to know what percentage of VA they are specifying.

   (b) **Display concentration of sevoflurane measured by gas analysis**. The user need to know what the actual percentage in the gas going to the patient is.

4. **Store energy**. The device needs to store and translate power to the transfer liquid.

5. **Analyze gas**. This is an assumption for the Fenton concept. The liquid transfer rate should be self adjustable based on the amount of anaesthetic agent in the gas going to the patient.

6. **Read user settings**. The user should, at the very minimum, be able to adjust the target concentration.

7. **Communication**. This concerns the communication between the other subproblems. It can be viewed as all the dotted lines in the function diagram.

8. **Calculation of liquid transfer rate**. The liquid has to be transferred into the breathing tube at a specific rate, which has to be calculated based on the air flow in the breathing tube.

From the function diagram it was seen that some of the subproblems had to be solved before other. As an example, the type of power supply will directly depend on the electrical system, which means that the electrical system should be considered before the energy storage subproblem. The subproblems which were considered most urgent to solve were the liquid handling, the flow measurement, and the gas analysis.

It was also noted that some of the subproblems are readily available as existing products or solutions. The visual feedback and energy storage subproblems are readily available in many portable medical devices, as e.g. computer screens and batteries. These subproblems are therefore considered less important to develop in the early stages of the product development process.

The Fenton device is supposed to be digital, and it was assumed that a microcontroller would be used to control the device. This means that the reading of user settings, communication, and calculation of liquid transfer rate subproblems are easily solved. These were therefore not

considered for the concept generation. It should however be noted that in order to prototype and test the liquid handling subproblem, the calculations of the liquid flow rate had to be performed. The calculations were assumed to be solved using Equation 3.1. Similarly, the air bubble detection was assumed to be solvable using existing technology, and was therefore also not considered for further concept development.

A last subproblem was included in the Fenton concept, which is not easily shown using the function diagram. The subproblem concerns the problem with use of medical devices in LMICs. Special concerns and solutions have to be made to make a device such as the Fenton device, which should be usable in LMICs. For this thesis, the focus of the concept generation will be on four subproblems:

1. Liquid handling
    (a) Liquid transfer
    (b) Storage
    (c) Evaporation
2. Gas flow measurement
3. Gas analysis
4. LMIC specific concept considerations

The first three subproblems are the technical basis of the Fenton device. The liquid handling, the gas flow measurement, and the LMIC subproblems will be prototyped for this thesis, while the gas analysis subproblem will be investigated and evaluated for the concept only.

3.2 Use of Five Step Method for Subproblem Concept Generation

The five step method was used for each subproblem as a tool to generate concepts. Clarification of the subproblem was performed the same way for all subproblems. The search step was performed very differently for the subproblems, and will therefore first be presented as it was performed in general, and then it will be presented for the individual subproblems. Systematic exploration was also performed similar for all subproblems, except for the liquid handling subproblem, where a combination table was made. The general method will be presented for the

systematic exploration, as well as an explanation of how the combination table was used. Reflection on solutions and processes were done for all subproblems, and a presentation of how this was performed is presented at the end of the section.

It should be noted that product development is a very iterative process. Most of the stages were performed several times for each subproblem before generating good concepts.

3.2.1 Clarifying the problem

The first step of the five-step model is to *clarify the problem*. This was performed by first noting what the function of the subproblem was. Then, the product specifications and assumptions were listed based on the user needs, the functionality of the subproblem, and on conversations with Prof. Fenton. This step was performed in collaboration with Prof. Fenton and Dr. Lonnee. Some of the technical specifications were unknown to Prof. Fenton. Upper bound values, which indicate the maximum limit, were then proposed by Prof. Fenton based on subjective evaluation. One example of such values is the size of the mechanisms, which can be modified depending on the solutions, given that the Fenton device is *small enough to be able to sell*. Some of the technical specifications are therefore subject to change, depending on feedback from Prof. Fenton.

3.2.2 Search

The search phase was performed using the expand-and-focus strategy presented by Ulrich and Eppinger. The subproblems were searched differently, with external or internal search being emphasized depending on the subproblem. It should be mentioned that the search phase was very iterative, and that several search phases was performed for all the subproblems.

External Search

External search was performed for all the subproblems. Literature search was conducted to find scientific articles, books, patents and reviews on the topic, in order to discover technical solutions and mechanisms. Emphasis was put on researching solutions from both the field of medicine and anaesthesia, as well as other unrelated fields. This ensured that a broad range of technical solutions were researched.

Expert consultation and benchmarking was used to discover existing and commercial solutions. In some instances experts would direct the authors to research an area they believed could be used to solve the subproblem, which had not been emphasized in the original search phase. Prof. Fenton and Dr. Lonnee were used as experts on most of the subproblems, with focus on existing solutions used in medical equipment. Several professors and scientists at NTNU were also contacted with questions about different problems or solutions.

Internal Search

Internal search was performed for most of the subproblems, in order to generate new concepts solutions and ideas. In this process, brainstorming was performed using the four guidelines recommended by Ulrich and Eppinger which are listed in Section 2.7.1. The brainstorming process usually began with the authors noting ideas and concepts by use of pen and paper. Sketches were drawn and concepts were discussed in the team with the aim of increasing the amount of concepts.

For the liquid handling subproblem, the *gallery method* was used as a tool to generate new concepts. With the problem clarification fresh in mind, ideas and concepts for each problem were written down on post-it notes. These were then stuck on to a large piece of cardboard displaying the problem. It was not allowed to dismiss any ideas, and non-conventional ideas were encouraged. When the team members were running low on ideas, the post-its were evaluated by each member individually. Improvements on ideas were written down on post-its and stuck over the original idea. Sometimes an idea on the board inspired a different, but related idea, which was then hung close to the original. After a large amount of concepts had been generated these were categorized, and then placed in a two axis map, with one axis used to judge the feasibility of the concept and the other used to judge the promise of the concept. This way, the best ideas could more easily be spotted. This technique relies on subjective judgment for selection of concepts. Results from one iteration of the gallery method is shown in Figure 3.3.

Figure 3.3: The results of one gallery method iteration

For all of the subproblems, internal search was performed both individually and in groups, as recommended by Ulrich and Eppinger. The individual sessions and team sessions were used

for different purposes. The individual sessions were used to generate more concepts of better quality, and it was found that the results were often more fully fledged concepts. Team sessions were used to explore creative solutions, and through discussions with the other team member, modifications and ideas could more easily be generated. The team sessions were also used to evaluate the concepts and to ensure that both team members were in agreement of the concepts.

Physical media was used for the internal search, as recommended by Ulrich and Eppinger. Medical disposables were supplied by Dr. Lonnee, and along with cardboard and office supplies, these were extensively used for the internal search of several subproblems. The disposables included tubes, syringes, connectors and valves. Physical media was used for several reasons. First, it was used to spark creative thinking and to explore different concept solutions. Second, it was used as a way to understand the physical forms and technical mechanisms of the concepts. Third, it was used as a tool for sharing ideas and for communication between the team members.

Search for Flow Measurement

External search was conducted as a way to find existing solutions, with several of these found to be usable in the Fenton concept. A short internal search was performed, but was found to be difficult. Several concepts were generated, but none which were deemed superior to the ones found in the external search. To save time and resources, it was decided to spend less time on the internal search compared to external search.

Search for Liquid Transfer

For the liquid transfer an extensive external search was performed, both to investigate technical solutions and mechanisms, as well as commercial products. Since liquid transfer was considered one of the most important subproblem for the thesis, it was by far the most researched subproblem. A literature search was performed to find existing solutions through scientific articles, books, patents, and white papers. It was found that the topic of liquid transfer and pump technology was an extremely vast one, and a classification tree was used extensively to evaluate the space of concept solutions.

Experts consulted for the external search include Prof. Bjørn Torger Stokke, who is part of the NTNU Microfluidics Research Group and scientist Carlo Kriesi who specializes in medical product development and was at the time developing a low flow pump. Companies like Sensirion

and Braun were contacted to investigate existing commercial solutions. Dr. Lonnee and Prof. Fenton were also consulted about commonly used liquid transfer solutions in medical settings. They were also asked questions relating to the technical specifications and the feasibility of different solutions.

For the liquid transfer subproblem, it was found that the solutions were best when they were custom made for the Fenton concept, and internal search was therefore used extensively both as a way to create new ideas, but also to modify existing solutions. The gallery method was used several times to try to increase the amount of internal solutions and modifications of the external solutions. Several concepts were generated by working creatively with disposable syringes, tubes and medical connectors.

After generating concepts for all the subproblems, a few concepts were selected for further development and prototyping. The liquid transfer prototypes did not perform as expected, and it was decided to perform a second concept generation phase. The prototyping of the concepts will be presented in Chapter 4. The focus was on expert consultation, with the aim of verifying whether the liquid transfer research was going in the right direction, or if the focus had been misplaced. After a conversation with Carlo Kriesi, some new ideas were generated. One of these concepts was further developed for use in the Fenton concept.

Search for Liquid Storage

The search for liquid storage solutions began in the pre-master's thesis. At the OES factory, vaporizers had been examined at different stages of manufacturing. One plenum vaporizer and one draw-over vaporizer had been disassembled to reveal the inner mechanisms, including the container. An external search had been conducted with emphasis on existing solutions used in vaporizers. The reason for focusing on existing containers was that these are used with VAs, which was believed to influence their construction. An external search was performed for the master's thesis with focus on the technical specifications of the subproblem, like materials compatible with VAs and filling mechanisms.

However, the existing solutions could not be directly implemented in the Fenton concept. Therefore, focus was also directed to internal search for the master's thesis. Brainstorming by use of the gallery method was performed, and Dr. Lonnee was consulted about the container problem. Disposable syringes were used in the internal search to simulate containers, and tubing were used to draw liquid from the containers.

Search for Evaporation

The most commonly used evaporation mechanisms used in vaporizers had already been researched for the pre-masters thesis. From disassembling the vaporizers, and the visit to the OES factory, several solutions had been physically examined. Several of the existing solutions were believed to be usable with the Fenton concept. A new external search was performed for the master's thesis, and a short internal search was performed to generate more creative ideas. The gallery method was also employed for this subproblem. Less time was spent on the internal search, since the solutions found early in the external search were believed to be usable.

Search for Gas Analysis

Gas analysis of VAs is mostly based on physical properties of the anaesthetic agent. These physical characteristics were not previously known to the authors and are a vast topic which could not be covered in the short time span of this thesis. Internal research was therefore considered inappropriate without any knowledge of the chemistry or physics of the VAs themselves, and was not performed for the gas analysis research.

Instead, external search was performed with focus on state-of-the-art anaesthetic gas analyzers and existing commercial solutions. Several commercial products were investigated, with multiple believed to be usable with the Fenton concept. Research was also performed to find technical solutions of gas analysis of anaesthetic agents. From this technical literature search commonly used technical solutions were found, as well as some alternative and experimental solutions.

Search for LMICs

An external research was performed to find existing solutions to the problems with use of anaesthesia equipment in LMICs. Contemporary solutions for anaesthesia in LMICs, like the draw-over vaporizer were investigated and evaluated. Since both Dr. Lonnee and Prof. Fenton have worked as anaesthesiologists in LMICs they were consulted as experts on the topic.

It was found that some of the problems could be solved using existing solutions. However, internal research was also used to find more creative solutions. These ideas were subsequently presented to Dr. Lonnee and Prof. Fenton to get feedback and ideas for improvements. Cardboard and medical disposables were used to evaluate these concepts.

3.2.3 Systematic Exploration

The fourth phase *explore systematically* was used throughout the concept generation process. Several iterations were performed for all the subproblems. Classification trees were created during the search phases and were used several different ways. They were first used to categorize and classify the concept solutions. This made it easier to explore the different solutions both during and after the search phase. Secondly, as a way to narrow the focus on more promising concept classes, some of the branches were pruned. Thirdly, the classification tree was used to evaluate which areas of the concept solutions space had been adequately researched, and which had not. And lastly, the classification trees were used to spark conversations and discussions in the team. To cover more ground, several solutions or solutions classes in the classification tree were split up and researched individually by the authors. The authors would then present the main findings to the other team member before discussing and evaluating the concepts.

Classification trees were made for all the subproblems examined, but will only be presented for the liquid transfer, the flow measurement and the gas analysis subproblems. For the other subproblems, either relatively few concepts were generated or there was no evident way to classify the possible solutions found during the search phase. In these cases the classification trees did not facilitate the concept generation, and will therefore not be shown. Ulrich and Eppinger [65] states that "the concept classification tree is used to divide the entire space of possible solutions into several distinct classes that will facilitate comparison and pruning". It should be mentioned that the distinct classes in the classification trees shown in this thesis are chosen by the authors, and are not necessary the most theoretical way of classifying the different concept solutions. Since so many concept solutions were investigated in the search phases, the classification trees presented in this thesis will only show the concepts that were considered the most interesting or most promising for use with the Fenton concept.

After gathering a large amount of concepts in the internal and external research phases, the concepts were evaluated with respect to the *subproblem specification matrix* to look for any shortcomings. There were a multitude of reason *for not continuing* to research some of the concepts. The main reason was that the concept was expected to not perform to the technical specifications. Some of the technical specifications are more flexible, which meant that some subjective evaluation was required when exploring the concept space systematically. Another reason for removing some concepts from further evaluation was that the concept was thought to be too hard to prototype. This was a more practical approach, and was based on the fact that the Prof. Fenton requested a physical product delivery at the end of the thesis.

Since the liquid handling subproblem consists of three subproblems, a concept combination table was made. The combination table was used with the intention of evaluation alternative combinations of the subsolutions, and to find the best solutions to the liquid handling subproblem.

3.2.4 Reflection on the Solutions and the Process

The fifth phase *reflect on the solutions and the process* is placed last in the five step concept generation model. However, product development is iterative in nature and at different points in the process, the concept solutions and product development process were evaluated. This was performed by asking the questions proposed by Ulrich and Eppinger, as presented in Section 2.7.1.

After reflection, some rectifying activities were performed. Several classification trees were remade, research was performed on solutions that had been inadequately been researched, and more expert consultation was performed. As mentioned previously, the liquid transfer research was performed in two stages. This iteration was done because of the reflection process.

3.3 Results: Flow Measurement

3.3.1 Problem Clarification

When proportional control is used, a device capable of measuring a gas flow rate has to be included. This device will be used to measure the flow rate of gas in the breathing tube. The flow rate values will be sent to a microcontroller which will instruct a liquid transfer mechanism to transfer liquid at a proportional flow rate into the breathing tube. From the problem clarification phase the specification matrix shown in Table 3.2 was made.

Table 3.2: Flow measurement specification matrix

No.	Metric	Units	Marginal Value
1	Accurate	% of actual value	±0.2 %
2	Sampling rate	ms	< 250
3	Flow rate range of measurement	$\frac{L}{min}$	0-10
4	Size	cm^3	< 8000

3.3.2 Flow Measurement Concepts

It is assumed that the flow measurement concept can be used with N_2O, O_2 and air, and that it is robust and usable at extreme temperatures and humanities. Since the mechanism measures the breath of a patient the resistance to flow can not be very high, as this would make breathing harder for the patient. Figure 3.4 shows the classification tree with different ways to measure the flow rate of a gas. Flow measuring devices were split into the two categories *digital* and *non-digital*, and the most promising will be presented below.

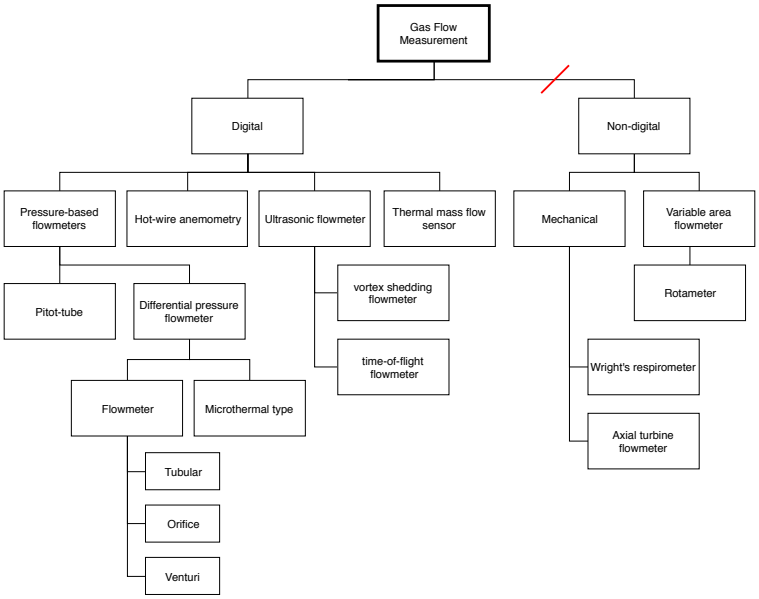


Figure 3.4: Classification tree for flow measurement subproblem

Mechanical and Non-digital Measuring Devices

Mechanical flow measurement devices include the Wright's respirometer and the turbine flowmeter. These devices have a physical mechanism inside the tube where gas is flowing which rotates proportional to the flow rate [18]. These mechanical devices can be modified for digital capabilities. After some evaluation it was decided to exclude the digitized mechanical devices since they also include more uncertainties. The extra step of digitization was considered unnecessary for use in the Fenton device, since other digital sensors were readily available. Another problem with the mechanical devices is that they are often sensitive to humidity, and are relatively inaccurate because of inertia problems.

Another non-electrical measuring device is the rotameter which is commonly included in commercial anaesthesia machines [18]. The rotameter consists of a bobbit placed inside a tapered

glass cylinder tube which the gas flow passes through. The bobbit floats at a specific height in the tube depending on the flow rate. The same reasoning as for the mechanical devices was used to exclude this device from further development.

Hot Wire Anemometry

Hot wire anemometry measures a change in the resistance of a heated wire placed inside a tube which the gas flows through [18]. The change in resistance is proportional to the flow rate. They are fast and very sensitive to changes in flow rate. There is also a very low resistance to flow in the sensor, which means that it can be used with a patient breath. However, the rate of heat loss is dependant on the density, viscosity, and specific heat of the gas, which means that the sensor has to be calibrated for specific gases and humidity. It was therefore believed that the hot wire anemometry method would be unsuitable for use in LMICs, where the use of VAs depends on availability and where humidity can be extremely varying.

Differential Pressure Sensor

The most interesting type of flow measuring device was the *differential pressure sensor*. It can measure large flow ranges, is relatively cheap, and is easy to set up. The accuracy depends on the flowmeter and type of differential pressure sensor, but there are several solutions which are very precise and are used in contemporary medical devices. There are several flowmeters on the market which have low resistance to flow, which means that the mechanism can be included in the Fenton device. The flowmeter should be a reusable type, but it may also be necessary to make it easy to change flowmeters in case they break or fail to function.

The microthermal differential pressure sensors have similar characteristics to the commonly used piezoresistant differential pressure sensors, and the flowmeter setup is identical. They may even be better suited for the Fenton device because of their inclusion of a heater which creates an extra stability in the system.

3.4 Results: Liquid Anaesthetic Agent Handling

In this section, the clarification and results of the liquid handling subproblem will be presented. The subproblem consists of liquid storage, liquid transfer, and evaporation, all of which will be presented individually.

3.4.1 Results: Liquid Storage

3.4.1.1 Problem clarification

The liquid storage should be able to hold liquid VA. The liquid inside the storage system will be transferred from the storage system into the breathing tube in one of two ways. Liquid can either be drawn out using a liquid transfer mechanism which will subsequently transfer the liquid into the breathing tube, or liquid can be pushed out of the storage system and directly into the breathing tube. The storage system has to be closed to the atmosphere to ensure that the liquid does not evaporate. It also has to ensure that no vacuum is created when liquid is removed from the storage. The specification matrix is shown in 3.3.

Table 3.3: Liquid storage specification matrix

Metric	Units	Value
Storage volume	ml	100-200
Time to drain	s	60
Time to refill	s	60
Leakage	Binary	No
Usable at tilted angel	degrees	-45 to +45

The upper bound of the volume was recommended by Dr. Lonnee and is included to ensure that the draining of the device does not take too long. The lower bound is chosen so that the storage device should not have to be filled too often. It should also ensure that less VA is wasted.

Some assumptions were also made for the storage design. It should be easy to fill, robust, and sturdy. It has to be compatible with one or more VAs. Resistance to liquid draw must be as low as possible to ensure that the system does not create any backpressure or vacuum. No special equipment should be needed for filling or handling, but a *keyed filler* may be needed for commercial success in HICs. A liquid level indicator has to be included to show how much liquid is left in the storage system.

3.4.1.2 Liquid Storage Concepts

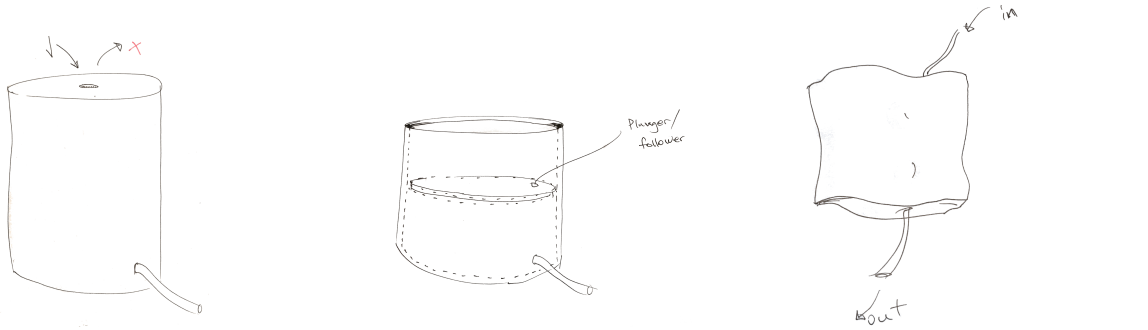
The external research revealed some solutions which are used in contemporary vaporizers. Most of these were cylinders made of a metal material coated with a protective layer to inhibit degradation. However, since most of these containers are open, these solutions could not directly be implemented in the Fenton concept. Additionally, these vaporizer containers are not designed to have liquid drawn or pushed out.

Figure 3.5 shows a few sketches of the most promising containers generated during the internal research. Figure 3.5a shows a simple cylindrical container with a one-way valve on the filling cap and a connection point at the bottom where liquid should be withdrawn. The concept is called the *valve container*, and the one-way valve has two functions. First, it enables the container to be constructed as a closed container, which ensures that the evaporated liquid does not escape from the container. Secondly, when liquid is being drawn from a closed container a vacuum is created inside the container. The valve ensures that air is being drawn into the container when liquid is drawn out of it, and no vacuum is created. The valve container concept also enables filling of the container during an operation, even while liquid is being drawn from it. The container can be fitted with both a *screw fill system* and a keyed filler. This concept was assumed to be possible to build, and there was no consideration of how to construct the valve or the filling mechanism, since several such solutions were found to already exist.

Dr. Lonnee noted a problem with this concept. When liquid is being drawn out of the container, and air is being drawn in, the VA will evaporate and a portion of the container will be filled with gas. Whenever the container has to be drained or if the anaesthetic agent has to be changed the gas has to be discarded somewhere. This could be problematic, not only because the disposal of VAs is regulated in many countries, but also because VAs are considered hazardous to medical personnel and bad for the environment.

However, to mitigate the problem proposed by Dr. Lonnee, the container shown in Figure 3.5b was designed. The container includes a *plunger* which follows the level of liquid. By including this plunger the VA will not evaporate inside the container and the liquid can easily be drained. However, this concept was tested using disposable syringes, and it was discovered that the resistance of the plunger can be relatively high, which can cause the withdrawal of liquid to become more difficult. Dr. Lonnee stated that glass syringes usually have very low resistance to draw, and it proposed that a low resistance material could be used to make a container if this concept were to be used. One problem with this container concept is that it would be harder to refill compared to the valve container, due to the plunger. To make it easier to fill, a mechanism could be included which opens the container to the atmosphere when the container is empty, which allows the plunger to be withdrawn using an actuator, and the container to be filled.

Figure 3.5c shows a sketch of a flexible bag container. The idea was that the container is similar to an IV bag. Any empty space in the vaporizer could be made to fit the plastic bag. However, it is unknown how robust these bags can be made and the bag would possibly have to be filled under pressure. This idea was considered less promising for use in LMICs.



(a) Container with a valve (b) Container with plunger (c) A flexible bag container

Figure 3.5: Different container concepts

Figure 3.6 shows the the double container concept. The proposed solutions uses two containers instead of one. One is fastened inside the device, and the other is removable. A connection has to be included between the two containers, to ensure that the they are securely fastened together. The connection should also include a mechanism, like a ball check valve, to ensure that liquid only moves in one direction. Using this double container concept, the fastened container can always hold liquid, even when the removable container is being refilled. The inside container should be constructed as either the container with a valve or a plunger. A similar system is included in the Aladin cassette vaporizer which is presented in Appendix C, Chapter 2.

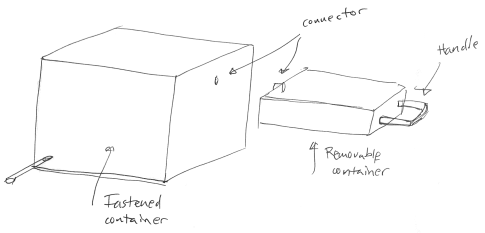


Figure 3.6: The double container concept

For the liquid level indicator, a glass sight hole is usually included in contemporary vaporizers. A similar solutions can be used with all the proposed concepts. Another solutions is to use a liquid level sensor, which are also readily available.

3.4.2 Results: Liquid Transfer

3.4.2.1 Problem Clarification

The aim of the liquid transfer solution is to remove liquid from the storage system and transfer it into the breathing tube. The flow rate has to be extremely low to get the correct concentration of VA in the breathing tube. Table 3.4 shows the target specification matrix for this subproblem. It is assumed that the liquid transfer mechanism has to be compatible with VAs.

Table 3.4: Liquid transfer specification matrix

Metric	Units	Value
Accurate	% deviation from target	±0.2 %
Low flow rates	$\frac{\mu L}{s}$	0-40
Size of mechanism	cm^3	< 3000
Usable with low viscosity fluids	$\frac{Pa*s}{cP}$	$\frac{1.276*10^{-5}}{0.01276}$
Time between injection pulses	ms	< 20

3.4.2.2 Liquid Transfer Concepts

Figure 3.7 shows the classification tree created during the research phase. The most common liquid transfer mechanisms are pumps, which are usually categorized into positive displacement pumps and kinetic pumps [69]. After some research it was found that positive displacement pumps are more suited when there is a need for low flow, constant flow, and accurate and repeatable flow measurements [69]. A decision was therefore made to prune the kinetic pump branch. Similarly, the microfluidic pump category was pruned because these were considered too complex, too difficult to repair, and expensive. There was also no real benefit to using them over similar macro concepts.

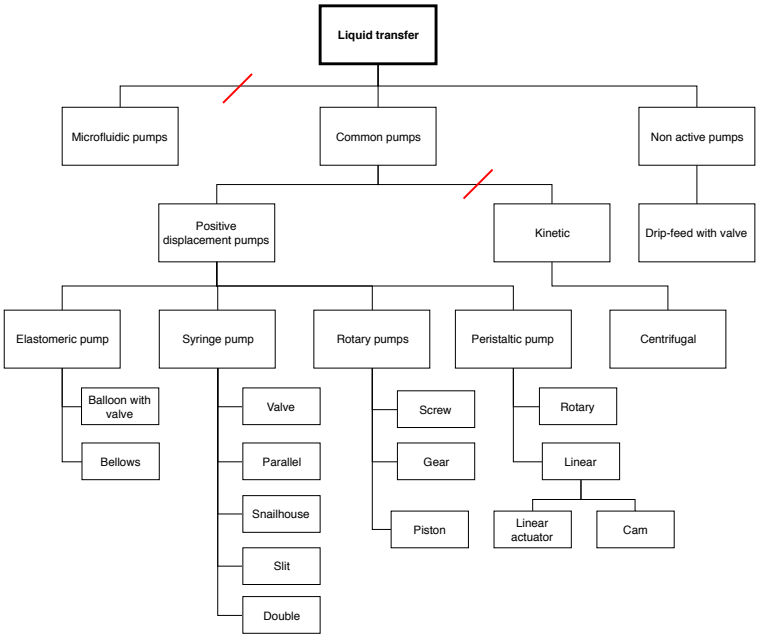


Figure 3.7: Liquid transfer classification tree

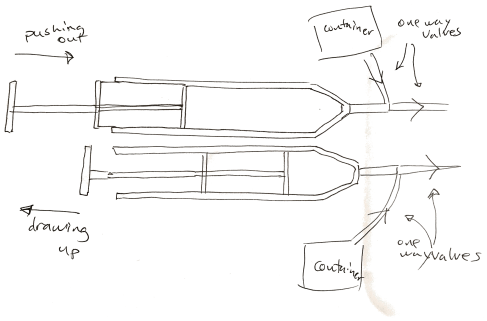
Syringe Pump

The syringe pump was considered interesting because of its ability to continuously inject liquid at very low flows, and because the principle is relatively simple. If a stepper motor is used to

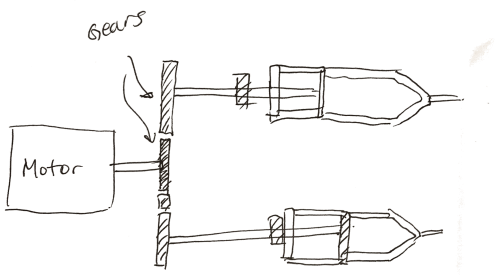
drive the threaded rod, the injection can be very smooth and continuous. Although medical syringe pumps commonly use disposables, it should be possible to design and construct a syringe pump where the syringes are integrated into the device. This will circumvent the problem with using disposables in LMICs mentioned in Section 2.2.3.

A problem with conventional syringe pumps is that they are filled by either drawing liquid by hand or by reversing the direction of travel of the plunger. The first method is problematic because it requires the use of disposables and human interaction, while the second is problematic because driving in reverse takes a relatively long time. A normal syringe pump can not inject liquid while being filled. By the time the syringe is filled, the concentration of VA in the breathing tube may have decreased substantially.

Some alternative syringe pump concepts were generated in the internal research phase which were specifically generated to be easier to fill. Figure 3.8a and 3.8b shows a sketch of the *parallel pump*. The concept uses two syringes placed in parallel and a gear system to drive the syringes. The gear system is included so that the two plungers are driving in opposite directions when the motor is driven. This means that the pump is able to simultaneously inject liquid from one of the syringes and draw liquid from the storage system with the other one.



(a) Sketch of the parallel syringe pump showing the liquid flow



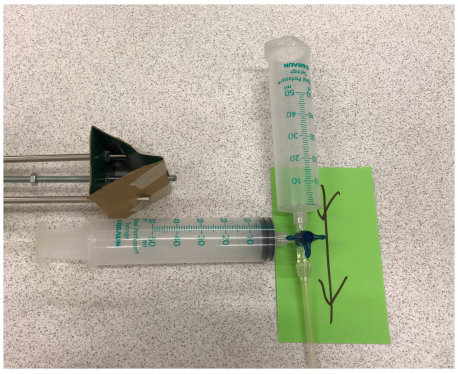
(b) Sketch of the parallel syringe pump showing the gears

Figure 3.8: Parallel syringe pump concepts

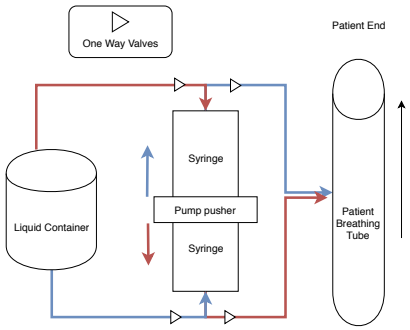
Another concept is the *valve syringe pump*, which is shown as a physical model in Figure 3.9a. This concept uses a small syringe pump which is connected to two one-way valves. The one-way valves are shown as arrows on a post-it note, and are used to direct the flow of liquid. When the syringe plunger is drawn back liquid is drawn from the storage system through a one-way valve, and when the syringe plunger is pushed down liquid is injected into the breathing tube. The idea is that liquid is injected when the patient is breathing in, and liquid is drawn from the storage system when the patient is breathing out. This would would work similarly to a piston

pump, but should be able to inject liquid more continuously and at very low flow rates.

Another syringe pump concept was generated, called the double syringe pump. Instead of placing two syringes in parallel, the two syringes can be placed plunger to plunger. When the motor is driving the pusher, one syringe injects liquid while the other one draws liquid from the storage system. Figure 3.9b shows the *double syringe pump* concept as a flowchart, with arrows and colors showing the direction of the plungers and liquid flow.



(a) Physical layout of the valve syringe pump made with medical disposables



(b) Flow chart of the double pump liquid movement

Figure 3.9: Syringe pump concepts

Peristaltic Pump

The peristaltic pump was considered interesting because of its small size and easy mechanism. One design of a small peristaltic pump was found in the external search where the pump was designed to be fastened onto a stepper motor. The peristaltic pump has the benefit of always keeping the liquid contained inside the tube [69, p. 21]. This means that the construction of the pump does not have to consider the corrosive and degrative nature of VAs, given that a compatible tube is used. One problem with the peristaltic pump is that the liquid is ejected in pulses. This characteristic can however be reduced by using several tubes that are squeezed in an offset pattern causing small amounts of liquid to be ejected alternately [58].

Drip Feed

The original concept by Prof. Fenton was to have a drip feed system. The system uses a simple container to hold VA, and the injection is driven by gravity and regulated by a valve. The concept can be small in size, and by using a valve the power consumption should be lower compared to a motor driven mechanism [25] like the syringe pumps.

3.4.3 Results: Evaporation

3.4.3.1 Clarification

The liquid VA has to evaporate as quickly as possible upon entering the breathing tube. If the evaporation rate is slower than the liquid injection rate, liquid VA will pool up inside the breathing tube and the target concentration will not be met. It was originally assumed by Prof. Fenton that the liquid VA would evaporate spontaneously as it was injected into the breathing tube. An evaporation mechanism is still included to increase the evaporation rate, as the evaporation has to occur instantaneously.

Only one technical specification was listed for the evaporation subproblem - the time to evaporate had to be less than two seconds. It was assumed that the evaporation mechanism had to have a low resistance to flow, to ensure that the patient is comfortably breathing. If the mechanism is in physical contact with VA it has to be constructed in a material which is compatible with VA.

3.4.3.2 Evaporation Concepts

The most common mechanism included for increased evaporation of anaesthetic agents is a wick or mesh. Desflurane vaporizers include a heaters which maximizes the evaporation rate. The AnaConDa includes a long porous *evaporation rod* which the liquid VA flows through [46]. The liquid flows through the vaporizer and exits as very small particles which should instantaneously evaporate.

There is also a device called a nebulizer, which is used to create aerosols of water droplets for use in humidifiers [18]. Using a nebulizer, liquid is directed into the path of a jet stream of gas which splits the liquid into droplets. An anvil is placed downstream of the jet stream, and when the liquid hits the anvil, it will split the larger particles into smaller ones. This could be similarly used to split the liquid anaesthetic agent droplets. Another idea was to have several injection points in the breathing tube. If each of these points have their separate wicks and heaters the evaporation rate should increase drastically.

One idea generated during the internal research was to use a sprayer mechanism at the injection point in the breathing tube. This way, a thin mist of VA can be sprayed into the breathing tube which should evaporate more easily. The mechanism was proposed to be like that of a nasal spray. If a heat source is placed close to the injection point it should be possible to keep the evaporation rate stable.

During the prototyping phase, a humidifier was used at the Medical Technical department at St. Olavs. This device supplies humidified air to patients with difficulty of breathing. When this machine is used, *heated breathing tubes* can be used to keep the temperature of the humidified air stable, which ensures patient comfort [21]. It was theorized that the evaporation rate may be kept stable by including heated breathing tubes inside the machine and around the injection point.

It was also noted that the evaporation rate will increase with an increase in the removal of vapour molecules form the liquid surface. If liquid were to pool up in the breathing tube, a mechanism could be included to remove the evaporated gas from the surrounding liquid VA. One such concept is to include a small fan inside the breathing tube, which would keep the gas moving at all times, even when the patient is not breathing.

3.4.4 Results: Systematic Exploration of Liquid Handling Subproblem

The combination table for the liquid handling subproblem is shown in Table 3.5. Several different solutions are shown which have not been previously discussed. These are included since they were considered the most promising alternatives at the time. Less promising concepts are not included because of space considerations. Concepts written in italics were generated internally. The double syringe pump is included last in the list since this was added during the second iteration of concept generation.

Table 3.5: Combination Table for the Liquid Handling Subproblem

Liquid Storage	**Liquid Transfer**	**Evaporation**
Container with valve	Syringe pump	Metal wick
Container with follower	*Slit syringe pump*	Plastic wick
Double container	Parallel syringe pump	Fabric wick
Elastic bag	Valve syringe pump	Nebulizer
VA bottle with adapter	*Balloon with valve*	Heater
	Linear peristaltic pump	Heated breathing tube
	Rotary peristaltic pump	*Spray*
	Elastomeric pump	Fan
	Snail house pump	
	Gravity feed with valve	
	Drip feed with valve	
	Double syringe pump	
	Bellows pump	

Several combinations were made, and several concepts were generated for the liquid handling subproblem. To make it easier for the reader to follow subsequent product development, the four concepts which were *later* selected for further development are presented below. It should be noted that only the liquid transfer concepts were prototyped, as these were viewed as the most critical component of the liquid handling.

The first concept combination consists of the rotary peristaltic pump using alternating pumping, with the double container, and a wick and heater evaporation mechanism. Because the peristaltic pump will eject liquid in pulses, it was believed that placing a heater around the tube going into the breathing tube, the liquid would evaporate even before exiting the tube. This would smooth out the pulsating characteristic. The peristaltic pump was itself considered a contender because of its small size, easy setup, and relatively easy handling.

The second concept combination consists of the drip feed, the IV bag container concept, and a nebulizer. The IV bag container would be placed high inside the Fenton device, to ensure that the pressure crated by gravitation would be high. A valve controls the injection rate of liquid. A nebulizer was proposed for the evaporation mechanism as it is believed that the drip-feed concept will eject liquid in drops. The nebulizer should be placed by the injecting point, and will ensure that the drops are split instantaneously when exiting from the injection point.

The third concept combination consists of the valve syringe pump, the double container, and a wick. This was considered easy to use and setup, and could easily be made to inject liquid continuously. By injecting liquid when the patient is inspiring and drawing liquid when the patient is expiring, the valve syringe pump can inject liquid continuously.

The fourth concept combination consists of the parallel syringe pump, the double container, and a wick. This was considered a relatively simple setup which could drive the liquid injection continuously.

The four liquid transfer concepts were subsequently prototyped as one of the methods in the concept selection phase. From these, two were chosen for further prototyping, before a second concept generation iteration was performed. During this iteration, the concept of the double syringe pump was generated. This concept was also placed in the concept combination table, and it was found that this concept would be best suited along with the double container and wick.

As can be seen from the combinations some mechanisms were considered much better than the others for the storage and container subproblems. The double container with a fastened

valve or plunger container was considered the best concept for the liquid storage subproblem. For the evaporation mechanism, it was noted that several of the mechanisms could be used simultaneously. As an example, the evaporation mechanism can consist of a sprayer, which sprays a thin mist onto a metal wick, which is heated by an electrical heater. A heated tube can also be used to keep the evaporation stable. The limiting factor is cost and complexity. By increasing the amount of mechanisms the cost of maintenance and repair will increase, and there are more points of failure. This should be carefully considered, especially for use in LMICs where all of these problems are considered more critical. The evaporation mechanism should therefore be chosen on the basis of the cheapest and least complex system that *gets the job done*. A simple metal wick was therefore chosen as the first choice for the evaporation mechanism if there seemed to be no need for any specialized evaporation mechanism for use with the other liquid handling solutions.

3.5 Results: Gas Analysis

3.5.1 Clarification

The Fenton concept aims to keep the concentration of VA in the breathing tube stable at the target concentration by using gas analysis as feedback control to the injection mechanism. Whenever the gas analyser detects a deviation from the target concentration the injection rate is adjusted correspondingly. The gas analysis target specifications are shown in Table 3.6. It is assumed that the gas analysis solutions is usable with all common VAs.

Table 3.6: Gas analysis specification matrix

No.	Metric	Units	Marginal Value
1	Accurate	%	±0.2 %
2	Fast sampling rate	ms	< 500

Figure 3.10 shows the classification tree made during the research phase. A table with the technique, principle and limitations of commonly used VA analysis mechanisms was found in the scientific article *Analysis of Oxygen, Anaesthesia Agent and Flows in Anaesthesia Machine* by Garg and Gupta [29]. This table was used in conjunction with other scientific articles to evaluate the most promising mechanisms.

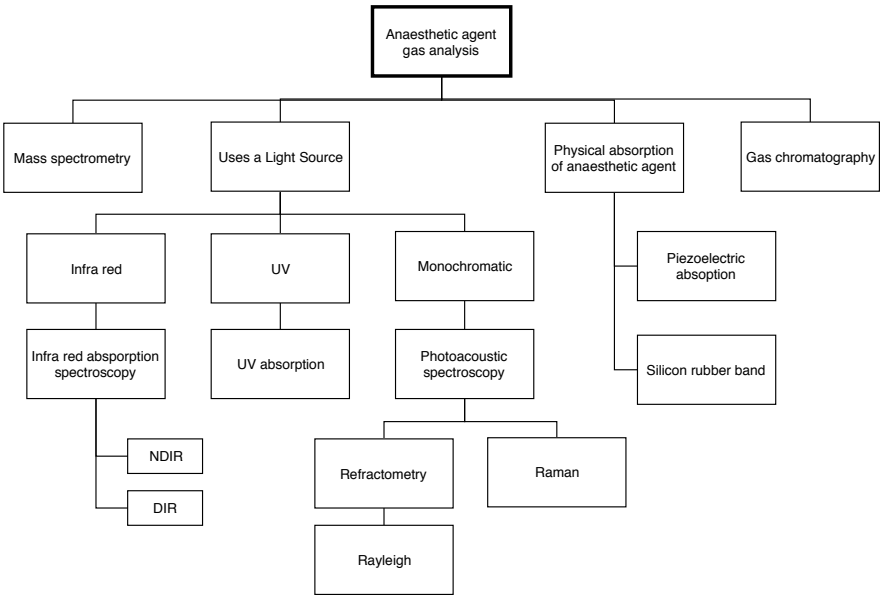


Figure 3.10: Gas analysis classification tree

3.5.2 Gas Analysis Concepts

Infrared absorption spectroscopy was in the end believed to be best suited for use with the Fenton concept. The method is precise, has a fast response rate and can detect several VAs. It can also detect other gases like carbondioxide and oxygen. This is beneficial both because it is useful information for the the medical personnel during an operation, but also because it will increase the attractiveness of the device in HICs.

One other interesting mechanism which was considered is Raman scattering, where a laser beam is pointed at the gas, energy is absorbed by the gas and then released with a different wavelength. The absorption of the laser light is measured using a light sensor and is proportional to the gas concentration [29]. It has a fast response rate, is accurate, and can measure several VAs. However, the use of a laser beam means that the power consumption is high.

Several mechanisms is presented in the whitepaper *Anaesthesia Gas Monitoring: Evolution of a de facto Standard of Care* [1], written by the gas analyser manufacturer Masimo. One of these mechanisms was used in the earliest commercially available gas analysers - the North American Dräger Narko-Test. A silicone rubber band is placed in line of the gas flow. It is fastened to a lever and tensioned. When anaesthetic agent passes over the rubber band it is relaxed, and the relaxation can be measured by the tension on the lever. From this measurement the concentration of VA can be found. This mechanism was only accurate between 0 and 3 %. The mechanism was considered interesting for use in the Fenton concept because of its simple form factor and

mechanism. It was however considered too dangerous and unsuitable for use in the Fenton concept because of the low range of accuracy.

Some commercially available gas analyzers were found online. These include the Masimo IRMA AX+ mainstream gas analyzer, the ISA AX+ sidestream gas analyzer, and the Artema AION Argentum sidestream gas analyzer. All uses *nondispersive infrared sensor* (NDIR) gas analysis. The first two are very small, with the IRMA AX+ weighing 25 grams. The third is also relatively small with dimensions of around 90x69x34 mm [45]. Artema was contacted, and stated that the AION Argentum is available for around 10000 NOK, with an additional 10000 NOK for an obligatory evaluation kit. This is considered a good price for use in the Fenton device. No price was found for the Masimo ISA AX+. It should be mentioned that it is believed that the most expensive piece of technical equipment used in the Fenton device is the gas analyzer. It was important for Prof. Fenton to find a solution which was not too expensive.

Both sidestream and mainstream sampling were considered for use in the Fenton device. By using mainstream sampling the Fenton device can be made smaller. However, with sidestream sampling it may be possible to analyze the gas at two or more points in the breathing tube. In addition, it may be possible to alternate between sampling the gas at different points. Sampling could for example be performed both before entering and after exiting the Fenton device. This could make it easier to enable a circle system with reuse of VA.

The problem of gas analysis was considered quite complex, with several considerations of anaesthetic agents and placement of sampling, which is important for patient safety. It was believed that to properly investigate the gas analysis solutions a great amount of time and resources had to be input into the search phase. It was therefore decided to direct focus towards the other subproblems.

3.6 Results: Design for LMICs

3.6.1 Problem Clarification

For a vaporizer to be useful in LMCIs it should be usable without mains electricity and pressurised gas. These problems are solved by the Fenton concept itself, which does not require power or pressurised gas to function. A separate subproblem concerns the general design of medical equipment for use in LMICs. The list below presents three of the main problems with

the medical situation in LMICs, along with the specifications the Fenton device has to fulfill to mitigate the problems.

1. **There is a problem with a lack of repair personnel in LMICs**. Donated equipment does not carry service manuals which make them even harder for local maintenance crew to repair. The device should be designed to be *easy to repair and maintain*.
2. **There is a lack of educated medical personnel in LMICs**. Since contemporary medical devices often are complex to operate, several mistakes can easily be made during an operation. To ensure that the device is not used incorrectly the design should make it *easy to use*.
3. **The physical and environmental conditions in LMICs is harsh**. Contemporary medical equipment is therefore often unusable. The device should be designed for *robust use*.

From research into the three problems it was seen that the first point could be solved creatively, while the two last points on the list could more easily be solved using existing technology. Less focus was therefore spent on the last two points.

3.6.2 Design for LMICs Concepts

Design for Easy Repair and Maintenance

To make the Fenton device more easy to repair and maintain, a concept was generated internally. The solution is to make the Fenton concept device as a modular box where different mechanisms are kept in separate boxes which fit together in a larger enclosure. This way, each, separate mechanism can easily by examined without damaging any other part of the device. If one of the mechanisms fail or break down the modules can easily and more cheaply be replaced.

The modular boxes concept is made so that the different boxes can be connected to a breathing tube. This way, the air or oxygen going to the patient passes through the modular boxes one by one. Electrical connectors are included on the outside of the boxes which make contact with electrical connectors on the enclosure. This ensures that the boxes can communicate with each other. It also ensures that the device has to have all the modules installed for it to function, as a safety feature. Bolts should be used to fasten lids to the modular boxes and the boxes to the enclosure. This ensures that the modular boxes wont get lost or unintentionally removed.

Figure 3.11 shows a sketch of an idea to ensure that the modular boxes are placed in the correct space inside the enclosure. By color coding the boxes and including indentations the boxes can be made to only fit inside the correct hole. The idea was communicated to Prof. Fenton who thought it was a good idea, and agreed that it could be beneficial in the maintenance and repair stage of the device [3].

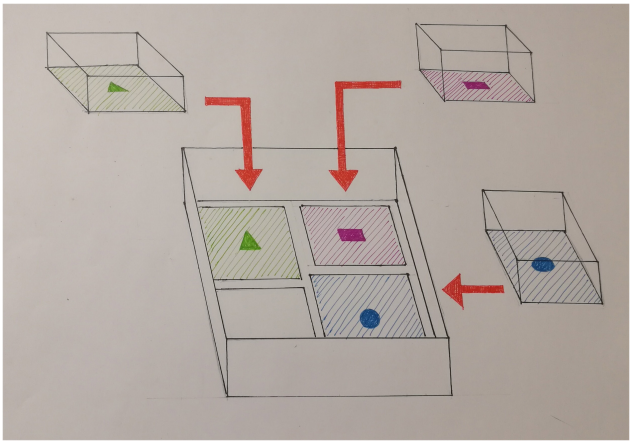


Figure 3.11: The modular concept, displaying the color coding

Design for Ease of Use

A few different aspects were considered to keep the vaporizer easy to use:

1. **Simple mechanisms**. This mostly concerns the mechanisms the user will interact with, like the container, exterior connection points to the breathing tube, and the interface.
2. **Few mechanisms**. According to Prof. Fenton and Dr. Lonnee, many of the functions on contemporary anesthesia machines are not used for routine operations. Fewer mechanisms and functions means less points of failure.
3. **Physical design specifically made for ease of use**. The physical design should be performed to make the machine easy to use. This especially concerns the interface, which should be simple and easy to understand.

Employing simpler and fewer mechanisms should be considered throughout the product development process. The list below shows the main functions of the interface as specified by Prof. Fenton. The first four make up a bare-bones interface, with the fifth being thought of as an extra feature.

1. A way to specify target concentration
2. A way to visually verify which *target concentration* is set
3. Visual feedback from gas analyzer, displaying the *actual concentration*
4. A way to show whether the device is connected to mains electricity or battery, with an indication of how much battery power is left

[3] Email communication, 2018-12-01

5. Visual feedback of the breath or air flow going to the patient

To make it easier to use, the design should use as little text as possible and instead rely on numbers, graphs, colors and lights. It is also important to include non textual alarms and indicators, like visual LED alarms, sound alarms, and for example visual liquid level indicators. By including a screw fill system, the filling should be made easy. However, it is noted that a keyed filler may be needed to ensure that the correct VA is used, and that the device is usable in HICs, where keyed fillers are virtually required for use.

Design for Robust Use and Harsh Environmental Conditions

To enable use in as many LMICs as possible, the specifications shown below are very important.

1. Usable at extreme temperatures
2. Usable in high humidity settings
3. Should be robust enough to withstand rough physical use
4. Should be portable, and tiltable when transported
5. No specialized tools needed for use or maintenance

It should be noted that the category of LMICs is very broad, and that the environmental challenges differ greatly between them. The main proposed solution to the problem of environmental conditions is robust construction. This includes use of non corrosive materials, electrical components which are compatible with harsh conditions, and gaskets to seal the inner part of the modular boxes from the environment.

Figure 3.12: The Panasonic Toughbook [66]

The problem of rough use should be solvable by constructing the device as robustly as possible. This can be solved using high strength metals, and materials like rubber which should increase the physical shock resistance. The mechanisms and modular boxes also have to be securely fastened to the enclosure to ensure that the device can be handled roughly. Robust devices are commonly found in military, offshore, and military medical equipment. Several examples were

found which use a combination of physical design and materials to ensure that the device is usable in a rough use setting. Figure 3.12 shows a Panasonic Toughbook, a computer made specifically for use in harsh environments.

The parts which are in direct contact with VA will have to be made of materials which are usable with the VA. The materials should also be made to ensure that there is no corrosion or other degradation of the system. Baxter Healthcare, the producer of sevoflurane, states that "sevoflurane is not corrosive to stainless steel, brass, aluminium, nickel-plated brass, chrome-plated brass or copper beryllium" [31]. These materials should therefore be considered.

3.7 Systematic Exploration of the Concept Solutions

3.7.1 Method

A concept combination table was made to evaluate the different combinations of the subsolutions. It was found that the differential pressure sensor and infrared absorption concepts were considered the best solutions for the flow measurement and gas analysis subproblems. There were no combinations where it was seen as beneficial to choose another solution for these two subproblems. However, several of the liquid handling solutions were believed to be usable in the Fenton concept, and different combinations were evaluated in the team.

3.7.2 Results

A concept combination table was made, and several concept combinations were initially considered for further development. Since the gas analysis and flow measurement solutions were the same for these concept combinations, the only difference between the combinations was the solution of the liquid handling subproblem. The table is therefore not shown. All concept combinations are to be made with the solutions presented in Section 3.6 pertaining to the subproblem regarding use of the device in LMICs. The solutions are listed below.

1. A modular system to enable easy repair and maintenance
2. A well designed physical form and visual interface with emphasis on communication to make the device easy to use

3. A robust design to combat challenges of harsh environmental conditions and rough physical use

For all the concept combinations the functionality is virtually the same. The flow rate of the gas in the breathing tube is measured by a differential pressure sensor and a flowmeter, and the flow rate of the liquid is calculated by a microcontroller based on this measurement. Downstream of the injection point a mainstream infrared absorption spectroscopy gas analyser measures the concentration of VA and regulates the injection flow rate.

3.8 Concept Selection

3.8.1 Method

A concept selection phase was performed to evaluate the concepts and find the optimal solution. Since the gas analysis and flow measurement subsolutions were the same for all the concept combinations the concept selection mostly concerned the liquid handling solutions. Even then, the most differentiating sub-component was the *liquid transfer*, and the selection pertained mostly to this subproblem. Two methods were used to help select the best solutions: a pros and cons list and prototyping. Since the product development was at an early stage it was believed to be best to use prototyping as a concept selection method, as proposed by Srinivasan et. al [60].

A pros and cons list was initially used to quickly and easily compare and evaluate the different concepts. The concepts were evaluated in terms of a few aspects. First, it was evaluated whether the concept fulfilled the technical specifications and user needs. Secondly, several concepts were compared to remove the ones that were believed to have the worst performance. Thirdly, it was discussed whether the concept could be prototyped. Based on these criteria four concepts were deemed to be the best.

These liquid transfer solutions of the concepts were then prototyped and qualitatively tested, before making a decision on which to develop further. The reason for using prototyping as a concept selection method was because it was believed to be more easy to qualitatively evaluate and compare the different concepts as physical prototypes. Some of the concepts that were prototyped for the concept selection phase were then *selected* for further development.

After further prototyping these concepts, it was found that they performed worse than expected.

A second iteration of the concept generation was therefore performed. Several new concept were generated and all the concept were qualitatively and subjectively evaluated in the team.

3.8.2 Results

The pros and cons list is presented in Table 3.7. Only the four concepts that were selected for further prototyping and the double syringe pump are presented due to space considerations. After prototyping these as part of the concept selection phase, the valve syringe pump and peristaltic pump were selected for further development. The double syringe pump concept was generated in the second iteration of concept generation. This concept was believed to be the most promising liquid transfer concept, and was therefore selected alongside the IR gas analyser and differential pressure sensor for use in the Fenton concept. The final selection was therefore based on qualitative and subjective evaluation of all the concepts.

It should be noted that the process of concept selection was a iterative one. Several pros and cons lists were made and several team evaluations were had, both for the individual subsolutions and the concept combinations. Even after prototyping, several new concepts were generated which were then evaluated and chosen for selection. One example was the valve container concept which was generated while prototyping, and was heavily inspired by the use of disposable syringes in the prototyping phase.

3.8.3 Presentation of the Final Concept

The final concept uses the double syringe pump with the double container and wick as the liquid handling solution. It is assumed that a microcontroller will be used to control a stepper motor which is used to drive the double syringe pump. The differential pressure sensor is used alongside a flowmeter to measure the flow rate of gas passing through the breathing tube. The microcontroller will use proportional control to drive the stepper motor of the double syringe pump, which will draw liquid from the valve container and inject a proportional amount of liquid into the breathing tube at the same time. The IR gas analyser is used to measure the concentration of gas and send feedback to adjust the liquid injection flow rate.

A 3D model of a proposed design is shown in Figure 3.13a. The touch screen is designed to be tiltable. Visual alarms are shown with LEDs and auditory alarms are included via speakers on either side of the screen. A rotary knob is included for easy adjustment of the target concentra-

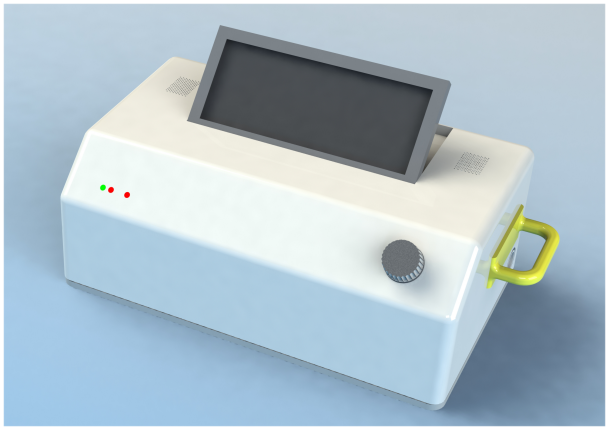
Table 3.7: Liquid transfer pros and cons list

Concept	Pros	Cons
Valve syringe pump Double container Wick	Continuous flow Simple mechanism Capable of low flows Precise	Cant pump while filling syringe Complex operation (breath by breath)
Parallel syringe pump Double container Wick	Continuous flow Fillable while pumping Simple mechanism Capable of low flows Precise Easy to control	Hard to prototype pump
Rotary peristaltic pump Double container Wick + heater	Small Simple mechanism Easy to prototype	Pulsating injection Not precise enough Harder to use with proportional control
Drip feed IV bag container Nebulizer	Low power consumption Small size Simple mechanism	Not continuous flow Hard to control Hard to fill IV bag Nebulizer is complex Complex setup of IV bag
Double syringe pump Double container Wick	Continuous flow Fillable while pumping Simple mechanism Capable of low flows Precise Easy to control	

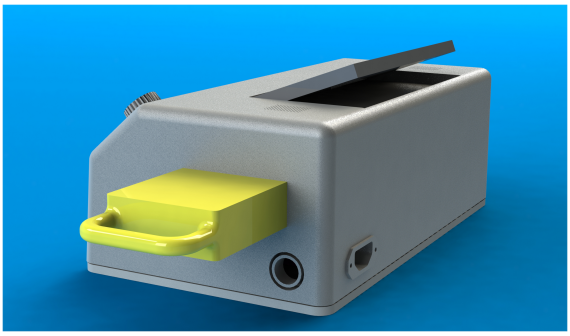
tion. The double container is shown with the removable container modelled in a yellow color. A glass sight hole is included on the back of the device to indicate how much liquid VA is left in the container. A screw fill system is included in the removable container to enable easy filling. Two breathing tube connectors are included on either side of the device, and a breathing tube which passes through the modular boxes is included inside the device.

Figure 3.13c shows the 3D model with the enclosure raised, showing the modular boxes. These are shown in different colors, which indicate the placement inside the enclosure. Figure 3.13b shows the vaporizer with the removable container taken out of the vaporizer for filling. Figure 3.14 shows a sketch of the modular boxes concept, with emphasis on visualizing the technical

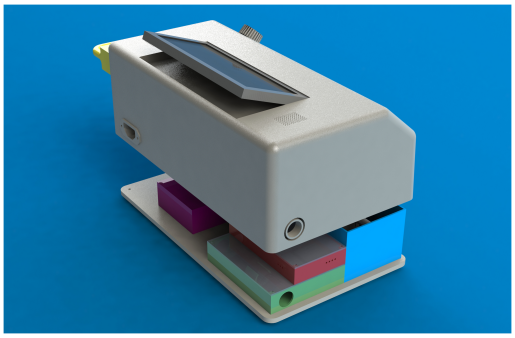
solutions and the flow of gas though the concept. It should be noted that this sketch shows the actual physical setup of the concept, and not a function diagram. The dotted lines show physical electrical wires and solid lines show physical connections. Machine bolts are chosen to fasten both the modular boxes and enclosure, to ensure that the boxes are securely fastened and not mistakenly removed.



(a) The proposed vaporizer concept, front view



(b) The proposed vaporizer concept, back view, showing the removable container halfway removed



(c) The vaporizer with the enclosure lifted, displaying the modular concept

Figure 3.13: The proposed vaporizer concept

The concept is relatively flexible regarding changes and modifications. This means that several of the features of the concept can be changed without negatively influencing the other features. Examples are that the wick can be exchanged for a sprayer and heater, or that the double syringe pump can be changed to a parallel pump or a peristaltic pump.

It should be remembered that the concept can be physically designed many different ways. One alternative design is shown in Figure 3.15. As mentioned in Section 2.2.4, the front-end aesthetics of devices sold to LMICs are important. It is therefore noted that the designs shown for the Fenton concept are not made with this in mind, and were rather simply made to clarify and

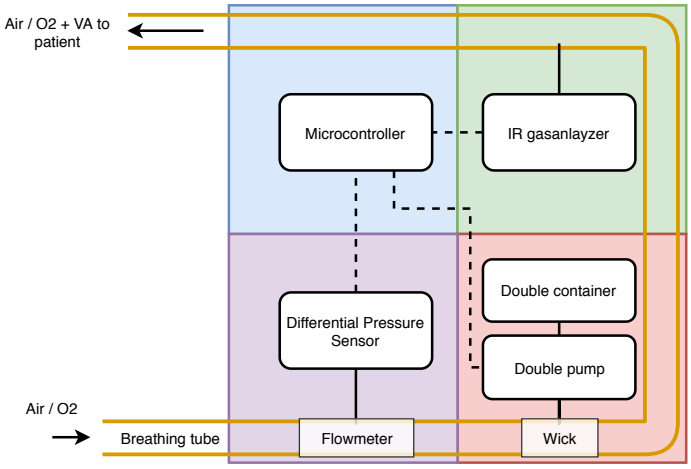


Figure 3.14: The modular box concept, showing the direction of flow through the boxes

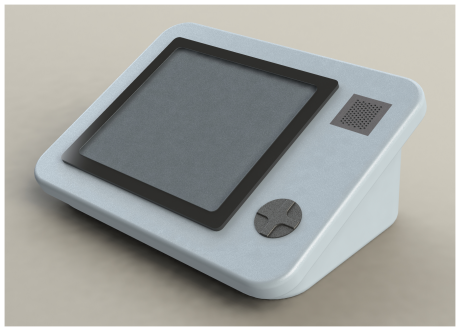


Figure 3.15: A second proposed design for the vaporizer

communicate the concept to Prof. Fenton. The physical device should be designed by actual designers with focus on design for use in LMICs and front-end aesthetics.

Chapter 4

Prototyping

Prototyping was used both as a way to generate and select concepts, but also as a way to understand, verify and test the concept solutions. This chapter will first examine the tools and techniques that were used for the prototyping and how they were used to make the prototypes. Then, the overall method of how the prototyping process was performed will be described. Lastly, the prototyping process and results will be systematically presented.

4.1 Method: Prototyping

4.1.1 Techniques and Tools Used for Prototyping

In Chapter 2, different prototyping tools and techniques were presented. This section will describe how these were used for the prototyping process of this thesis.

3D Design

As a way to prototype the concepts, computer aided design (CAD) and 3D printing was used. The CAD program *SolidWorks* was used to make most of the 3D models, while *Fusion 360* was used because of its ability to share 3D models online between the authors. The 3D designs often consisted of several different parts or components. These could then be assembled in an *assembly*. Simulations were performed by simply simulate motion or movement of a mechanism. This was performed to visualise motion and movement, and was used to verify a design or to communicate ideas more easily between the authors.

Rapid prototyping

Rapid prototyping was used as a way to rapidly make physical models which could be tested. It was not decided beforehand how much of the system would be prototyped using 3D printing, but rather decided on a case by case basis. Components for the prototypes were 3D printed using a Prusa i3 3D printer, like the one shown in Figure 4.1. The material used for printing was polylactic acid (PLA) and polyethylene terephthalate (PET).

The final double syringe pump prototype was printed in an acrylic material using the 3D printer Objet Alaris 30 at Troll Labs at NTNU, which uses a layer height of 28 microns. The acrylic material is harder than the materials used with the Prusa i3, and also has a glossier finish. The print quality of the Objet Alaris 30 printer is far better compared to the Prusa i3.

Figure 4.1: The Prusa i3 3D printer [67]

The authors had little experience with 3D printing before writing this thesis. It was quickly realized that it was very important to carefully consider the 3D model before 3D printing it. Since the components of the pump concepts had to be screwed or bolted together, it was important to ensure that they were designed correctly. Several draft prints, with less demanding 3D printer settings were made for most components to verify that the dimensions and design was correct before printing with the correct settings. The draft setting prints take a considerably less amount of time to print. 3D printing made it very easy to prototype the different pumps, and allowed functioning devices to be built quickly. Since the 3D prints are based on CAD models, the print could easily be modified to quickly test alternative solutions.

Prototyping Using Standardized Medical Equipment

Medical disposables were supplied by Dr. Lonnee. They were used to help with the prototyping of the liquid handling and flow measurement subproblem, and were used to rapidly make functional prototypes. The disposables used include syringes, tubes, valves, different connectors, breathing tubes, and flowmeters. Most of the tubes, syringes and valves use the standardized Luer lock connection system. The system ensures a leak-free connection between the female and male mating parts. Luer lock connectors were extensively used in the prototyping as it made it easy to mix and match tubings and disposables. Some additional syringes and connectors were also used, which have the Luer slip systems. The ends of the Luer slip are tapered and

can be tightly inserted into the Luer lock connectors to create a sealed fit. They are however not securely fastened like the Luer lock system. Figure 4.2 shows a few of the disposables used in this thesis, and Figure 4.3 shows two syringes, one with a Luer lock and one with a Luer slip.

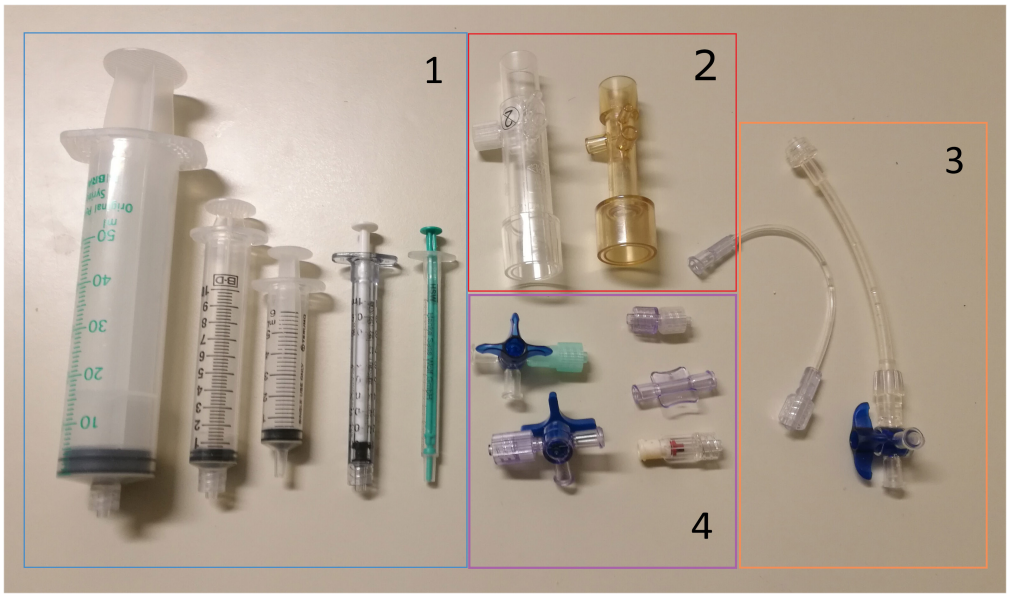


Figure 4.2: Disposables used for concept generation and prototyping. 1: different syringes. 2: flowmeters, 3: three-way stopcock and a Luer lock extension, 4: small Luer lock connectors

Figure 4.4 shows a one-way valve and a three-way connector. These were used extensively, both as tools for creating creative concepts and ideating, and as components of the actual concept prototypes. The valve was used to ensure that there was no backflow, and to direct the flow in different ways. The three-way connector also includes a valve which can be turned by hand, which changes the direction of flow. These connector were also used to direct the liquid flow, and to connect different tubes to each other. The breathing tubes used are made to ISO standard 80369. They have tapered ends which means they can be inserted into each other, keeping the connection sealed.

Other Tools

Two devices were used to test the flow measurement prototypes and the proportional control systems. The Laerdal Silicone Resuscitator, shown in Figure 4.5a, was used. It is a hand operated device which can be collapsed in order to eject air, and will self inflate when pressure is released. The continuous positive airway pressure (CPAP) machine is a medical device used to help patients breathe by ejecting a continuous flow of air to the patient. The CPAP, shown in Figure 4.5b, was borrowed by the Medical Technical department at St. Olavs. Since the CPAP

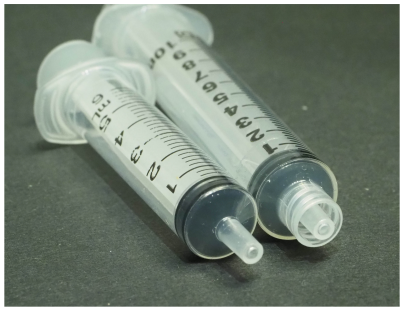


Figure 4.3: Luer connectors on syringes. Luer slip to the left, Luer lock to the right.

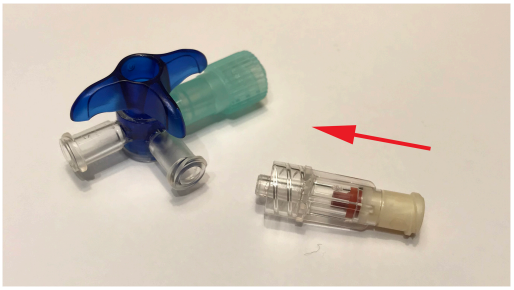


Figure 4.4: The three-way stopcock connector and one-way valve, with an arrow indicating direction of flow through the valve.

was digital and the flow rate could be adjusted, it was especially useful when a known flow rate was needed for testing.

(a) The Laerdal bag. Air is expired through the top by collapsing the silicone bag

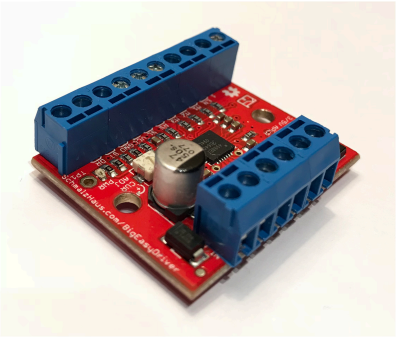
(b) The CPAP machine

Figure 4.5: Tools used to test the flow measurement prototype

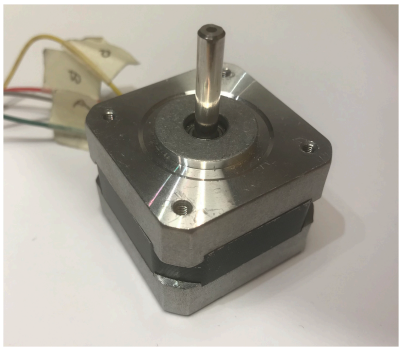
The CAD program Fritzing was used to make analytical models and circuit diagrams of the electrical circuits before physically making them. Fritzing has a library of stock components which were used to model the different prototypes.

To enable communication between the liquid transfer and flow measurement prototype, the Arudino Uno and Arudino Due microcontrollers were used. They were used to drive stepper motors, read sensor values, and perform arithmetic calculations.The use of the Arduino was considered a practical approach, which was based on the fact that the Arduino was previously

known to the authors. Figure 4.6b shows the stepper motor used for prototyping, and Figure 4.6a shows the *Big Easy Driver* motor driver which was used to drive the stepper motor.



(a) The *Big Easy Driver*, stepper motor driver



(b) The stepper motor used for prototyping

Figure 4.6: Electrical components used for prototyping

4.1.2 Prototyping Process

The prototyping phase overlapped with the concept generation phase. The flow measuring subproblem was investigated first and the prototyping of this system was started earlier than for the liquid handling and LMICs subproblems. This meant that the first functional flow measurement prototype was finished when the first few liquid handling prototypes were made. This made it possible to test the two systems together and to test the integration of the two systems quite early on. Although the microcontroller was used to drive motors used in the liquid transfer pump solutions, the presentation of the microcontroller and motor setup is included in the flow measurement prototyping section. This is done because the actual prototyping using the microcontroller, motor, and proportional control was performed while prototyping the flow measurement concept. Several programs were written and continuously modified throughout the process, both for the liquid handling and flow measurement prototypes.

Figure 4.7 shows a timeline designed after the prototyping methodology by Prof. Elverum described in Section 2.7.3. It shows the different prototypes in a roughly chronological order and shows whether the prototypes were directional or incremental. As is seen, most of the prototypes made early on were direction, and were made to evaluate whether the concept was to be used or not. Later on in the prototyping process, incremental prototypes were made more extensively. The incremental prototypes were the ones which were considered modifications of a directional prototype.

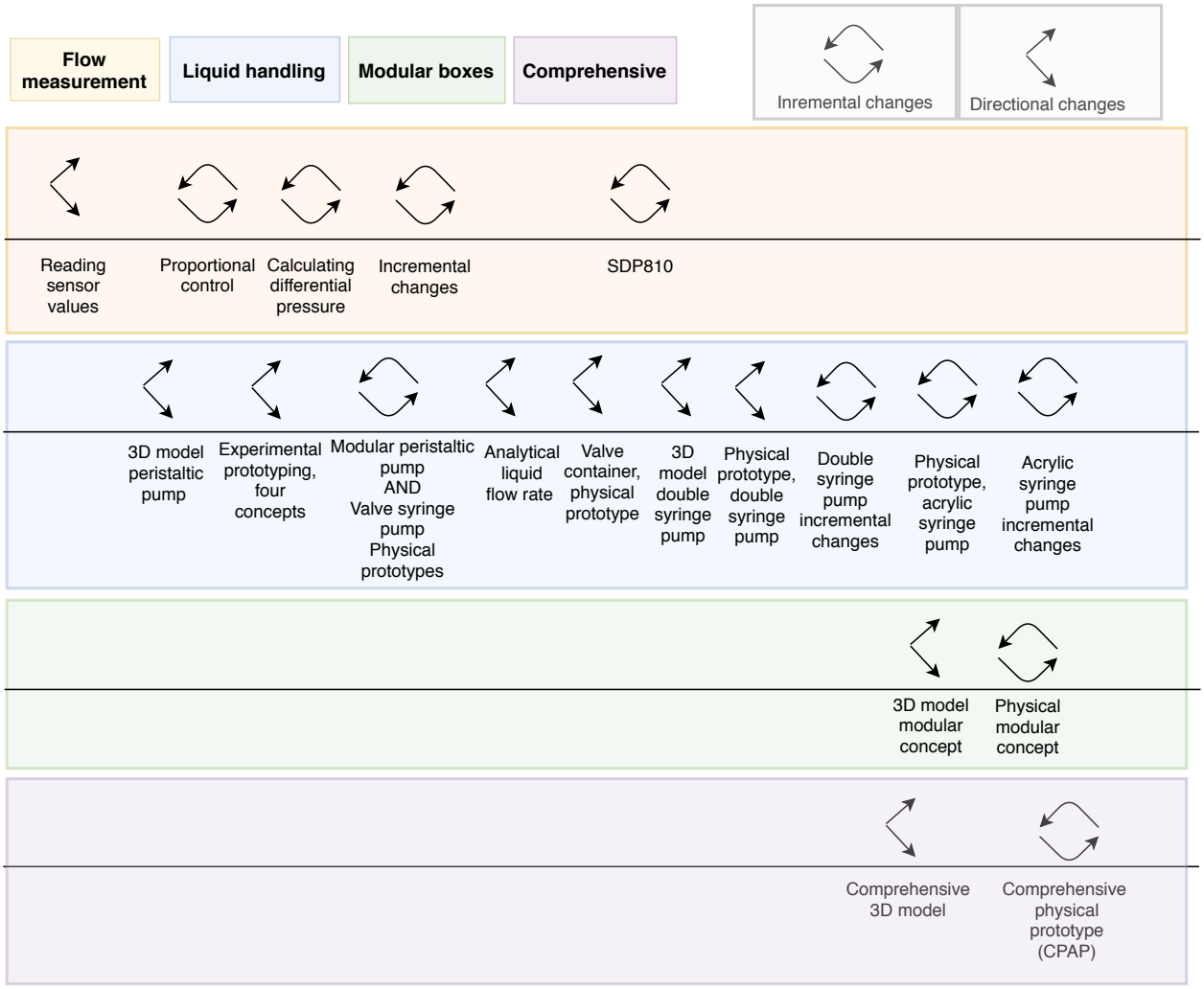


Figure 4.7: The prototyping timeline

Prototyping was performed using the methodology presented by Ulrich and Eppinger. *Planning* was systematically performed, by first defining the purpose of the prototype in the team. Second, the level of approximation was noted, and a decision to make a physical or analytical prototype was made. Third, an experimental plan was made, along with a test design. And fourth, a schedule was made to indicate how long the prototyping should take.

At the beginning of the thesis, Prof. Fenton requested a physical prototype. To meet this request, a practical prototyping approach was undertaken. This meant that some of the prototyping considerations were based on how to prototype quickly. Some examples include the use of the Arduino, the GE flowmeter, and the disposables, which were all used to rapidly generate prototypes rather than being used because they were best suited for the prototype.

Since so many prototypes and incremental changes were made for this thesis, it was decided to

present both the method and results of prototyping in the same chapter. The following sections will present the prototypes that were made and tested in this thesis. For each prototype, the prototyping phase will be presented systematically by presenting the planning, execution, and results of the prototyping.

Because this thesis concerns early stage development the approximation for most of the prototypes was very low. Although the approximation is different between the prototypes, since it was low for all prototypes, it will not be presented in the planning section of the prototypes. It should be noted that the approximation was noted during the actual prototyping process.

The *planning* section will present the plan that was made for the prototypes, including the purpose of the prototype, the experimental plan, and the schedule. Schedules were made for all prototypes, and most of the prototypes could be prototyped and evaluated in a very short amount of time. More time was however spent on incremental changes. It was sometimes assumed that incremental changes would have to be performed, and this time was then included in the schedule. Other times, the incremental changes were performed out of necessity, and these were not scheduled for. Incremental changes include programming changes and reprinting of 3D models. The schedules are included in the planning section for the prototyping to give an overview of how the prototyping process was performed.

The *execution* section will present how the prototype was actually prototyped. This section will show whether there were any unforeseen events and how these were subsequently handled. Additional considerations and prototyping which was not planned for will also be presented in this section.

The *results* section will present the results gained by the prototype. Some of the prototypes were directional, and were made to answer a yes or no question. Others were made specifically to test one part of the system. The results from both types of prototypes are discussed in this section. Results discussed in this section are the direct results of the prototype and experimentation as described in the planning section. If prototypes were modified for other reasons than those discussed in planning, a separate section is included called *Incremental Changes*.

4.2 Prototyping of Flow Measurement Subproblem

The prototyping of the flow measurement concept was performed using the Arduino microcontroller, electrical components, and a flowmeter and spirometer tube. Both physical and analyti-

cal prototypes had to be made, with most of the prototyping concerning the programming of the microcontroller. For the flow measurement subproblem, the behaviour of the communication between the sensor, microcontroller, and motor was considered the main unknowns. Prototypes were made to investigate these areas and test the prototype to validate the concept. All the prototypes involved programming of the microcontroller. This process was highly iterative, with changes being performed between testing for all the prototypes.

The flowmeter used for the prototyping was the GE healthcare flow sensor along with the spirometer tube shown in Figure 4.8. Because a flowmeter was used, the characteristic curve and constant had to be found. After a functional prototype had been made, several tests were performed to find this characteristic constant. The constant was subsequently added to the Arduino program used for proportional control. The flowmeter characterization tests were performed as a practical necessity in order to actually use the flowmeter that was available for use. The tests are described in Section 5.2. A conscious decision was made to also use these tests to improve the Arduino program, and programming was performed both before, during, and after testing.

Figure 4.8: The flowmeter and spirometer tube setup

4.2.1 Prototype 1: Reading sensor values

Planning

The purpose of the first prototype was to verify whether the Arduino could read values from a differential pressure sensor. A physical prototype would have to be made to test the possibility of reading.

Since the microcontroller and a similar sensor had previously been used by the authors, it was decided to spend two days on the prototype, with assembly and physical prototyping being performed on the first day and testing on the second day.

The experimental plan was:

1. Assemble all components for the physical model
2. Make the physical setup by connecting the sensor to the Arduino
3. Write a program which reads sensor values in raw voltage data
4. Verify the system by reading raw sensor values

Execution

There was no differential pressure sensor readily available, so a *pressure sensor* was used as a placeholder while waiting for a shipment of the correct type. The wiring for this sensor is the exact same as for the differential pressure sensor and is shown in the datasheet for both sensors. The sensor was connected to the Arudino and a very short program was written to read the voltage of one of the analog pins of the Arduino. Several program changes were made while testing, which was performed by blowing into the port of the pressure sensor and reading the values measured by the Arduino on a computer.

Results

Figure 4.9 shows the first physical setup of the *differential pressure sensor* hooked up to the Arduino. Testing showed that the system was able to read sensor values.

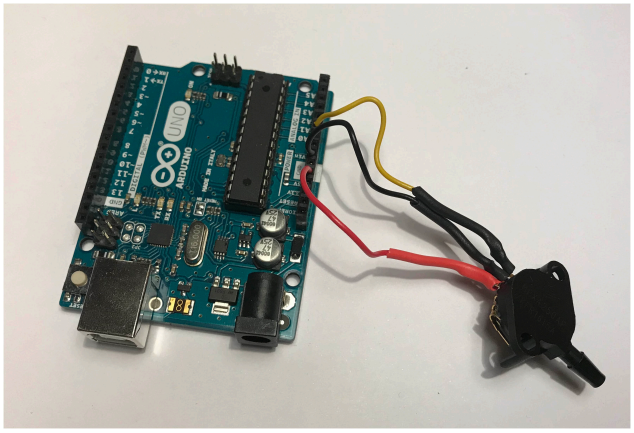


Figure 4.9: The first Arduino and sensor setup

4.2.2 Prototype 2: Proportional control

Planning

The second prototype was made to verify that sensor values could be used to control a mechanism. At this time, the liquid transfer concept had not been selected, but the peristaltic pump

and syringe pump were considered, so it was decided to use a stepper motor which both of these employ. This time, an analytical prototype would be made in Fritzing before physical prototyping on a breadboard.

This prototype included the physical setup and programming of a stepper motor, which was not known to the authors. Because of this, it was decided to spend six days on the prototype, with the first two days being spent on assembly of components. Two more days would be spent on the initial prototyping, and two days on prototyping and iterative changes to the program.

The experimental plan was:

1. Visualize the system using Fritzing
2. Breadboard the prototype
3. Write a program which reads sensor values and drives the motor depending on the values
4. Validate the system by qualitative inspection

Execution

Prototyping began with assembly of components, which included the components used for the last prototype, the L298n H-bridge motor driver, a unipolar stepper motor, and a 12 V battery made from eight AA batteries in series. A Fritzing diagram was made using library components. Physical prototyping was performed as shown in the Fritzing schematic, and the Arduino was programmed. The programs were all tested by blowing air into the port of the sensor and feeling the rotation of the motor shaft. Again, several programs were written while testing.

Results

Figure 4.10 shows a Fritzing model of the setup. Testing showed that the motor was rotating dependant on the sensor values.

4.2.3 Prototype 3: Calculating the differential pressure

Planning

Since the sensor measurements would be used to drive the stepper motor, the delay between the calculations and driving of the motor had to be minimized. If the delay is too long, proportional control is not unusable. The third prototype was made with the purpose of verifying if the

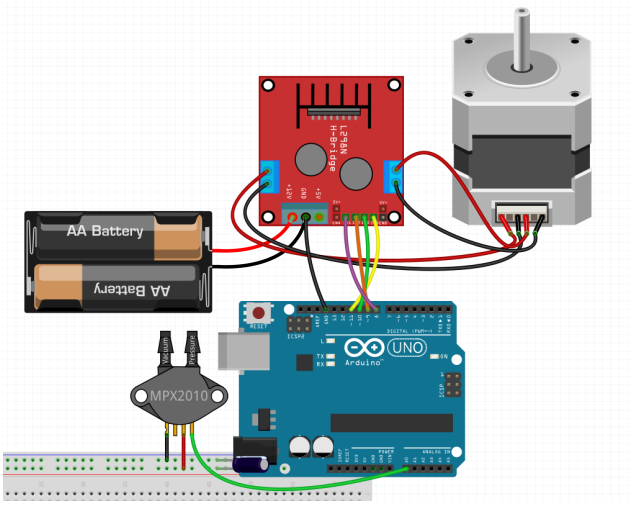


Figure 4.10: The Fritzing diagram made for the second prototype

calculations could be performed quick enough with the Arduino setup. At this time the differential pressure sensor had arrived, and it was decided to make a prototype with the new sensor and to program the microcontroller to convert the raw voltage measurements to a differential pressure. It was also planned to setup the flowmeter, and to test the differential pressure sensor connected to the flowmeter, by subjecting the flowmeter to a flow rate of air using the Laerdal bag.

All the components were readily available, and the only prototyping would be to swap the differential pressure sensor with the pressure sensor, and program the calculations. It was decided to use four days on the prototyping, with one day to physically set up and write the first program. The last three days would be spent on testing the system and iterative programming changes.

The experimental plan was:

1. Make a physical prototype of the flow measurement system
2. Program the calculations
3. Test the prototype

Execution

The MPX5010DP differential pressure sensor was used for this prototype. The datasheet for the MPX5010DP shows a linear relation between the measured voltage and the differential pressure: $\frac{\frac{\text{Sensor value}}{1023} - 0.04}{0.09}$. The value of 1023 is included to convert the measured sensor value to a raw voltage, as explained in Section 2.6. The relation was included in the program. Most of the prototyping was spent on programming of the calculation.

Testing was first performed by blowing air into one of the ports of the differential pressure sensor and checking if the calculations were performed as programmed. Then, the differential pressure sensor was connected to the flowmeter and subjected to a flow of gas. The differential pressure was then graphed in real time to verify that the sensor measured the flow. Motor speed was verified by touching the motor shaft.

Results

Testing showed that the sensor was able to measure the flow of air through the flowmeter in real time. However, the motor speed was very slow at the beginning and end of every injection of air, which resulted in the motor rotating in granular steps. It was not known how, or whether this would impact the system.

Incremental Changes

From research into the L298n motor driver, it was discovered that this driver does not drive the stepper motor efficiently. A dedicated stepper motor driver would be more efficient, easier to set up, and can drive the stepper motor in microsteps. The L298n was therefore substituted with a *Big Easy Driver* which has $\frac{1}{16}$ microstepping capabilities, which enabled the motor to turn 3200 steps per revolution. This solved the problem of granular stepping.

Another problem with the system was that the differential pressure sensor displayed values higher than zero when the ports were submitted to the same pressure. The MPX5010DP datasheet was examined, and it was discovered that the MPX differential pressure sensors should be calibrated before use. The program was rewritten to include a *zero-calibration function* as specified in an application note from NXP Semiconductors [52]. The function samples 32 values at zero value conditions and subtracts this value from the subsequent measurements. This function took several days to write and to verify.

From the tests with the Laerdal bag it could also be seen that the resolution of the sensor was quite low, which means that the range between possible measurements is high. It was decided to hook up a 16 bit analog-to-digital converter (ADC) to the Arduino and route the differential pressure sensor through it. The 16 bit ADC reduced the resolution from 9.76 $\frac{Pa}{unit}$ to 0.375 $\frac{Pa}{unit}$. It was also decided to hook the sensor up to an RC filter, which was believed to stabilize the output. Figure 4.11 shows the last wiring of the flow measurement setup with the Arduino Uno, MPX5010DP, stepper motor, ADC, filter, and Big Easy Driver. The components were later fastened to a 3D printed box with bolts. This was done to more easily work with the components

while testing, but also because the MPX5010DP datasheet recommends fastening the sensor for better measurement performance.

After the prototype was finished a test was performed to characterize the flowmeter using a ventilator at St. Olavs. Although the *ventilator test* did not result in any characterization of the flowmeter, it did however verify that the output from the sensor followed the ventilator flow, as shown in Figure 4.12. The same graph was shown on the ventilator screen, which meant that the system was at least set up correctly. Additionally, the graph shows that the zero-calibration function worked as intended.

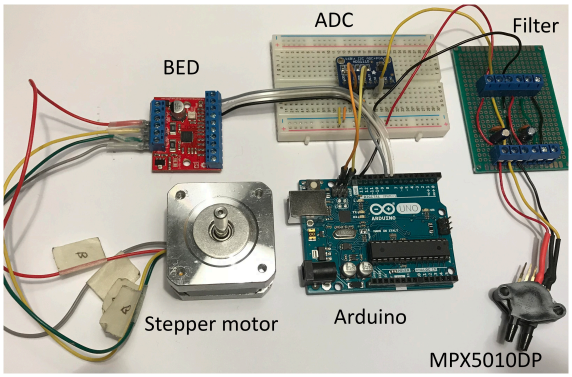


Figure 4.11: The final MPX5010DP setup

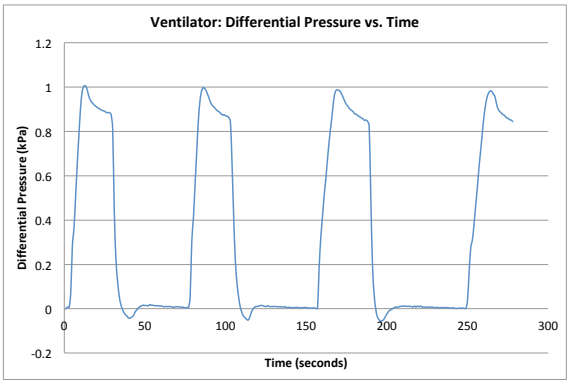


Figure 4.12: The measured output from a ventilator flow

4.2.4 Prototype 4: SDP810

Planning

The SDP810 differential pressure sensor had been purchased early in the prototyping process. This sensor is based on the microthermal principle presented in Section 2.4, and has a upper bound of 500 Pa, and a resolution of $0.02\frac{Pa}{unit}$. It was believed that the SDP810 was better than the MPX5010DP, both because the resolution is lower, and because it is digital and does not need an ADC or a filter to be usable. A prototype of the flow measurement system using the SDP810 was to be made, with the purpose of directly comparing it to the MPX5010DP.

The SDP810 communicates with the Arduino using the I^2C protocol, which is used for communication between microcontrollers and integrated circuits. Since the I^2C protocol was unknown to the authors, it was decided to first research how to correctly set up the SDP810 with the Arduino, before writing the code and building a physical model. It was decided to use a week on this prototype, since it was not known how long it would take to research the I^2C setup. All

components were assembled, so only the physical setup, programming, and testing had to be performed. Testing was planned to be performed at the next flowmeter characterization test.

The experimental plan was:

1. Research the I^2C protocol and how the SDP810 can be set up
2. Breadboard the electronic system
3. Program the Arduino to read sensor values and calculate the differential pressure
4. Compare the performance of the SDP810 to the MPX5010DP when performing the next flowmeter characterization test

Execution

The SDP810 was setup as specified in the datasheet, using two 10 kΩ resistors to enable correct communication thought the I^2C protocol. Like the MPX5010DP, the SDP810 sensor displays a linear characteristic between the measured voltage and differential pressure. A program was written which instructs the SDP810 to either take average or continuous measurements. A flowmeter test using a humidifier was used to verify the SDP810 prototype. The test is described in Section 5.2.

Results

Figure 4.13 shows the physical setup of the SDP810. Compared to the MPX5010DP the setup was simpler. Testing was performed using the same method as for the MPX5010DP, with the SDP810 hooked up to the flowmeter via the spirometer tube. The results showed that the SDP810 and MPX5010DP sensors measured different values, and it was later believed that the SDP810 was incorrectly setup. However, it was also found that the stability of the SDP810 was better than the MPX5010DP. This, and the fact that it was simpler to handle made it of interest to use the SDP810 for the testing at St. Olavs.

A subsequent test was performed by subjecting the SDP810 and different MPX sensors to a CPAP flow and comparing the results. It was discovered that the spirometer tube was not compatible with the SDP810, and that by changing the spirometer tube with two short plastic tubes the SDP810 was functional. Figure 4.14 shows the SDP810 connected to the flowmeter via plastic tubes.

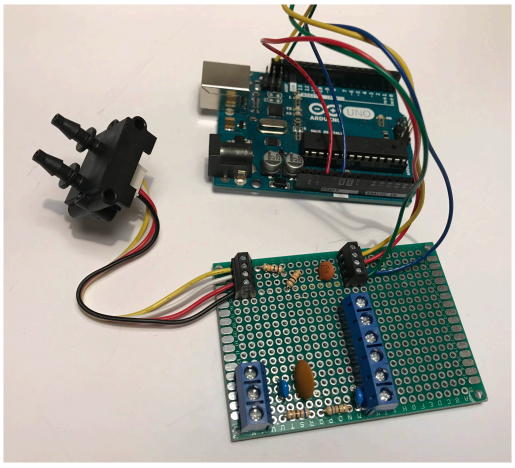


Figure 4.13: The SDP810 connected to the Arduino, via two resistors

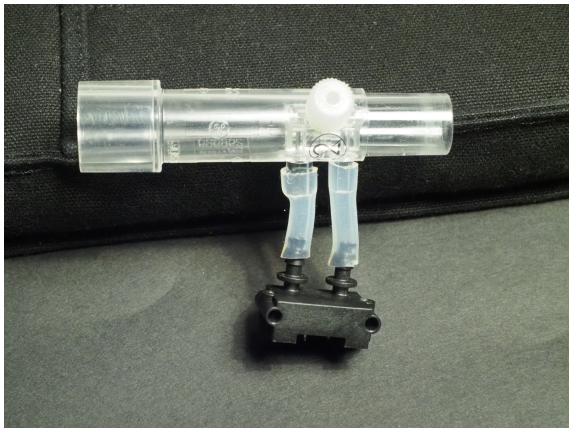


Figure 4.14: The SDP810 connected to the flowmeter ports via plastic tubes

4.3 Prototyping of Liquid Handling Subproblem

Two distinct prototyping phases were performed for the liquid handling subproblem. The first phase was *prototyping used as a method of concept selection*. This phase was performed with no focus on approximation, and with more focus on improving the concepts. No detailed schedule was made for these prototypes, but it was decided to not spend more than two weeks on the prototypes made for concept selection. The schedules will not be presented in the text for these prototypes. Qualitative evaluation of the prototypes were used to select the best concepts. These prototypes were made simultaneously to the prototyping of the flow measurement concept.

The second phase was prototyping of the concepts that had been selected in the concept selection phase. These are the *valve syringe pump*, the *peristaltic pump*, and the *double syringe pump*. These were prototyped with the intention of testing the concept and presenting it to Prof. Fenton.

4.3.1 Prototype 1: Peristaltic Pump 3D Model

Planning

To help with the concept selection of liquid transfer concepts it was decided to 3D model a peristaltic pump, which had been designed in the internal search. The pump was designed to be screwed onto a NEMA 17 stepper motor.

The purpose of the prototype was to get an understanding of the principles of the mechanisms of the concepts, and to investigate how the concept would perform. It would also be used to communicate ideas in the product development team. The prototype was entirely analytical and focused. Testing would be performed by constraining the parts in a CAD program, and simulating the movements of the mechanism in the CAD program.

The experimental plan was:

1. Make a peristaltic pump 3D model using CAD
2. Test the rotational mechanism in the software

Execution

The 3D model of the pump and the NEMA 17 stepper motor was made using Fusion 360. By designing the peristaltic pump around the face plate of the motor, some of the dimensions of the physical design were already constrained. By use of different assemble commands in Fusion, the parts could be connected so the mechanism of the pump could be visualized. The pump house would be fastened to the motor face plate, while the rotor would be jointed to the shaft of the motor and fixed inside the pump house. The rollers would be jointed to the rotor so they could rotate about their own axis.

Results

Figure 4.15 shows the peristaltic pump 3D model. The pump design consists of a *pump house*, one *rotor* and four *rollers*, which are shown as blue, green, and yellow components respectively. The mechanism worked analytically, and the peristaltic pump was considered viable for further development.

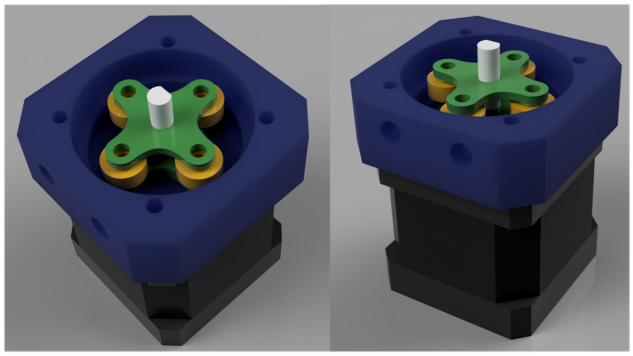


Figure 4.15: Two views of the peristaltic pump 3D model, shown with the pump house fastened to a NEMA 17 stepper motor.

4.3.2 Prototype 2: Experimental Physical Prototyping of Several Pumps

To help with the concept selection it was decided to physically prototype several of the concepts simultaneously. Four concepts were chosen for prototyping; the valve syringe pump, the parallel syringe pump, the peristaltic pump, and the drip feed.

Planning

The purpose of the prototyping was to evaluate qualitatively whether the concept solutions could be used in the Fenton concept. Selection would be based on subjective and qualitative evaluation of the physical prototypes.

The peristaltic pump would be physically prototyped by 3D printing the 3D model. The 3D prints, liquid tubings and a stepper motor would have to be assembled for testing. A simple open source 3D model of a syringe pump had been found during the external research, and it was decided to 3D print this pump and use the medical disposables to set up both the valve syringe pump and the parallel pump concept. For the parallel pump, gears would be 3D modelled and printed. The drip feed mechanism would be prototyped by using a disposable syringe with the plunger removed. A finger could be placed over the exit hole to simulate a valve opening and closing.

The experimental plan was:

1. Syringe Pumps
   (a) 3D print the syringe pump model
   (b) 3D print the gears
   (c) Assemble all components
   (d) Physically prototype the syringe pump concepts using medical disposables
   (e) Verify the concept visually
2. Peristaltic Pump
   (a) 3D print the peristaltic pump model
   (b) Assemble all liquid tubings
   (c) Physically prototype the peristaltic pump
   (d) Verify the concept visually
3. Valve Controlled Drip Feed
   (a) Physically prototype the drip-feed concept with medical disposables
   (b) Verify the concept visually

Execution

The prototyping began with 3D printing of the peristaltic pump and the syringe pump. Since this was the authors first experience with 3D printing several of the peristaltic pump components had to be reprinted due to poor design. The open source syringe pump model was printed correctly, but the model turned out to not function with the disposable syringes that were available. Modifications were made to the model before 3D printing the new components. While redesigning and subsequently printing the models, the other components needed for prototyping were assembled. For the syringe pump one rotary bearing, two linear bearings, two smooth rods, one threaded rod, one coupler, and one stepper motor was needed. A NEMA 17 stepper motor had previously been used with the flow measurement prototypes. To use the syringe pumps, the threaded rod had to be connected to the motor shaft. A *coupler* was not available at NTNU, and it was instead decided to 3D model and 3D print a motor shaft coupler.

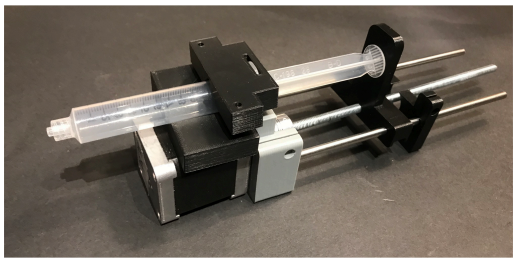
Both the syringe pumps and the peristaltic pump were tested by driving the pumps at different speeds of the motor. For the syringe pumps, the syringes were filled with water by hand an placed in the pump. For the peristaltic pump, a paper cup filled with water served as a container. One end of the plastic tube was placed in the water and the other end in an empty cup. Visual inspection was used to evaluate the performance of the pumps.

The drip feed mechanism was tested by removing the plunger from a syringe, and filling the syringe with water. A finger was used to simulate a digitally controlled valve, and the performance was evaluated with visual inspection.

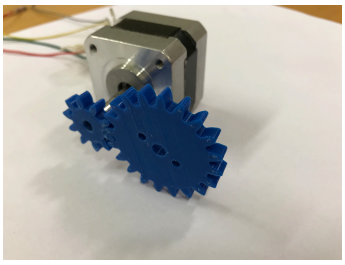
Results

Figure 4.16a, Figure 4.16b, Figure 4.16c, and Figure 4.16d shows the valve syringe pump, the gears used for the parallel syringe pump, the peristaltic pump, and the drip feed mechanism respectively.

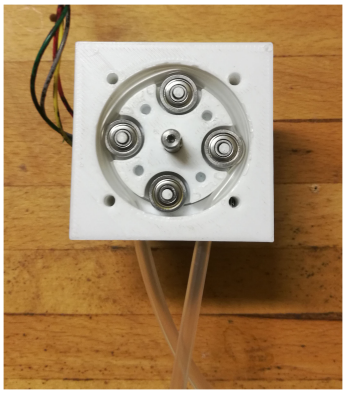
Figure 4.17 shows a 3D model of the valve syringe pump, with the components colored to visually differentiate them. In the following text the green part is known as the *pusher*, the red part is known as the *pump end*, the yellow part is known as the *syringe clamp*, and the blue part is known as the *motor end*. The valve syringe pump was able to inject liquid at different speeds, and it could visibly be verified that the flow rate was both continuous and dependant on the motor speed. The valve syringe pump was not tested with valves as these were not available at the time of prototyping.



(a) The valve syringe pump prototype. Notice that the photograph shows a 10 ml syringe which was not available at the time of prototyping



(b) The gears used for the parallel syringe pump prototype



(c) The peristaltic pump prototype

(d) The drip-feed prototype

Figure 4.16: Prototypes made for concept selection phase

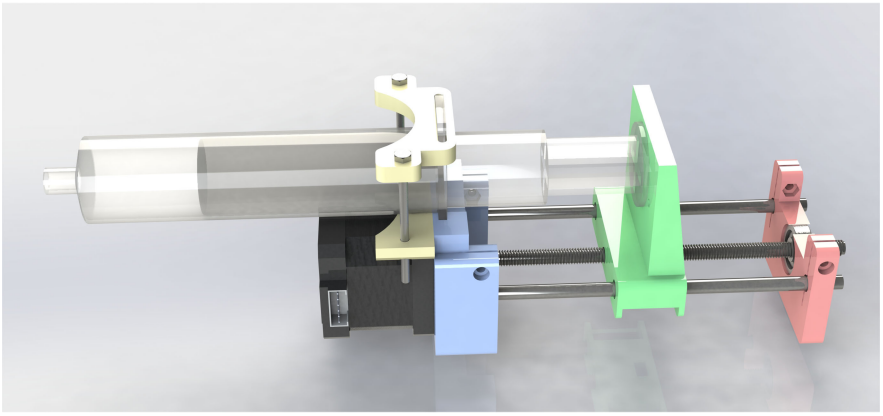


Figure 4.17: 3D model of the valve syringe pump

The parallel syringe pump was unable to function properly. This was caused by the 3D printed gears. The gears could be driven by the motor when not connected to anything. However, when they were connected to the threaded rod, the motor stopped several times. It is believed that the problem was either that the motor had a very low torque, or that the gear system was too poorly designed.

The original peristaltic pump design did not work, and the motor would not run properly. It was believed that this was because the pressure on the tube by the rotor was too high. Another problem was that the tubes that were used in the prototype were made of a stiff plastic material, which made it harder for the rotors to squeeze them. Several redesigns had to be made to get the prototype to work. In the end the peristaltic pump was made to pump water. However, as expected, the flow was pulsating.

The drip feed mechanism worked as intended. It was possible to control the flow rate by placing a finger over the tip of the open syringe. However, it was believed that the valve would have to open and close very quickly to correctly regulate the flow rate. Additionally, the syringe tip was believed to be too wide to be able to inject liquid at the lowest flow rates required. Even when the syringe tip was opened for a very short amount of time, a relatively large amount of water was ejected.

The valve syringe pump was considered the best current solution. The peristaltic pump was also considered interesting, mostly because of its very small size and easy setup. It was speculated that the injection of the peristaltic pump could be made less pulsating by designing a better peristaltic pump, by using a plastic tubing with a smaller inner diameter, and by testing the offset configuration mentioned in Section 3.4.2. These two concepts were selected in the concept selection phase for further development.

4.3.3 Prototype 3: Modular peristaltic

Planning

The original peristaltic pump design was made for use with a specific size of plastic tube. During testing of the pump the motor got stuck several times due to high pressure between the rollers on the rotor and the walls. It was therefore decided to make a better design of the peristaltic pump.

Several types of plastic tube with different outer diameters had at this point been found at NTNU and some purchased online. To test all the tubes several pumps would have to be printed with different sizes between the rotors and walls. Additionally, from the research into peristaltic pumps it was known that the flow rate depends on how much of the liquid tubing is pushed down. It would therefore be beneficial to also test the same tubes but with different distances between the rotors and walls. This would also necessitate several pump designs.

The purpose of this prototype was to evaluate the performance of the peristaltic pump concept, and to evaluate how the distance between the walls and bearings would impact the pumping. Even though the set-based prototypes methodology is developed to be used with a top-down approach, it was decided to design a *set-based prototype* of the peristaltic pump concept. By designing the peristaltic pump so that it could be fitted with different size rotors, the distance between the rotor and walls could be easily changed while testing. The set-based prototype would consist of a *ramp* instead of the pump house. The ramp would reduce the printing time, in addition to enable more easy fitting of the different rotors.

Prototyping of the peristaltic pump and valve syringe pump was performed at the same time. The schedule was therefore similar, with a finish date for both within two weeks. The first week would be used on assembly and physical setup, while the second week would be spent on testing and analysis.modular

The experimental plan was:

1. Make a 3D model of the redesigned peristaltic pump
2. Make the different 3D models for the rotors
3. 3D print the peristaltic pump ramp, rollers, and different size rotors
4. Set up the peristaltic pump with different tubes and rotors
5. Test the system with water
6. Analysis by visual inspection

Execution

The existing 3D model was modified to make the set-based prototype. One ramp, four plastic rollers, and several rotors of different sizes were printed. The printing was quite rapid, and testing with the first rotor could be started while the other ones were printing. The length of the rotor arms were easily changed in the CAD program, and could be printed in around fifteen minutes. Testing was performed by running the motor with different rotor sizes and different tubes. The performance was evaluated qualitatively and subjectively.

Results

Figure 4.18 shows the peristaltic pump setup and some of the different rotors which were printed to test different distances between the walls and bearings. It was found that the pressure on the tube had to be much smaller than anticipated. Several of the new tubes performed better than

the one used in the first prototype. The tubes obtained for this test were made of different materials like latex and silicone, and were specifically made for use in peristaltic pumps. Use of these tubes made the motor run much smoother. However, the pumping was still ejecting liquid in pulses. Even when the best combination of liquid tubing and rotor was used, the pulses were too large to enable low flow. The idea of offset liquid injection was evaluated, but it was believed that the pulses would still be too large.

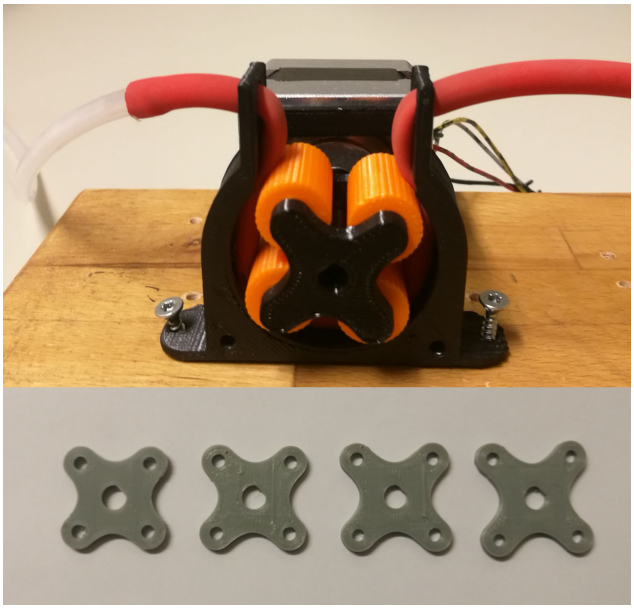


Figure 4.18: The modular peristaltic pump setup and rotors

4.3.4 Prototype 4: Valve syringe pump

Planning

Since not all components needed to fully verify the valve syringe pump concept were available for the first prototype of the concept, it was decided to make a new prototype with the purpose of evaluating the valve setup. The main questions revolving around how the pump would work during filling from the container and if this could be solved using of one-way valves. To test the valve concept a three-way connector would have to be connected to the syringe, with one one-way valve placed between the container and the syringe, and another on the outlet side.

As previously mentioned the valve syringe pump was planned to be prototyped at the same time as the peristaltic pump. The schedule was the same.

The experimental plan was:

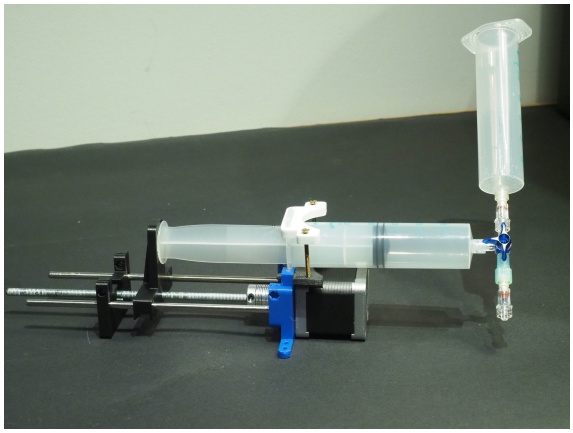
1. Modify the 3D model
2. 3D Print the 3D model
3. Assemble components for the valve syringe pump and container
4. Set up the valve syringe pump with medical disposables
5. Test the forwards and backwards motion of the pump

Execution

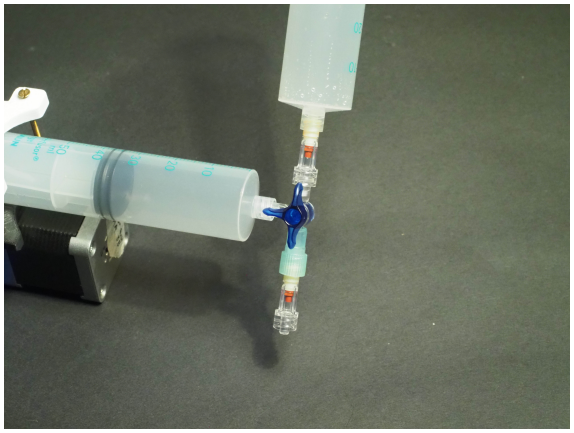
The 3D model was modified to include a fastener for the syringe plunger. This way the direction of travel could be reversed and liquid could be drawn from the container. A physical model was constructed, and one-way valves and three-way connectors were set up to make the valve concept. Two one-way valves were used to direct the flow of liquid through the system. Two containers were tested; a 50 ml syringe, and a 50 ml syringe with the plunger removed.

Results

Figure 4.19a shows the physical prototype of the valve syringe pump with a 50 ml syringe, and an open syringe used as a container. Figure 4.19b shows the three-way connector and one-way valve setup which directs the liquid from the container, to the syringe, and then to the breathing tube. Testing showed that injection of liquid worked correctly with the valve system. The direction of flow was controlled by the valves, and liquid could be drawn from the container.



(a) The valve syringe pump setup with the new fastener designed for use with the 50 ml syringe



(b) The valve setup

Figure 4.19: The valve syringe pump and valve setup

However, the syringe container with a plunger was not usable. When the motor was running backwards and the syringe was drawing water from the container, the pressure created in the syringe container was too high. After stopping the drawing of liquid the container plunger would

still travel downwards. To keep the pressure at an adequate level the reversing had to be performed at a very low motor speed. This meant that filling around 15 ml took several minutes. According to Dr. Lonnee, glass syringe have a very low resistance, and could possibly be used for the prototype. However, no glass syringes were available for use. The open container did not experience any problems with pressure build up, but even at the fastest motor speed the filling of 15 ml took around half a minute.

It was believed that the open container could be used, but it would not be usable with sevoflurane, as evaporated VA would escape the container. After questioning Dr. Lonnee about the problem a design was made of a container consisting of a syringe house with a tapered plunger cap with a one-way valve. This would mean that the liquid would not leak out of the container, but that air could be drawn into the container. This container is the valve container presented in Section 3.4.1.

4.3.5 Prototype 5: Analytical flow rate prototype

Planning

It was decided to make an analytical prototype with purpose of finding the flow rate range of the valve syringe pump and to evaluate which parameters the flow rate depends on. This would be prototyped using Excel. Since the prototype was purely analytical and relatively straight forward it was believed that the prototyping would take a few hours at most. No assembly was needed, so prototyping was to begin straight away.

The experimental plan was:

1. Make an Excel sheet with the equations
2. Analyse how flow rate depends on the parameters

Execution

The *actual liquid flow rate* of the syringe pump depends on the motor speed, pitch, and syringe inner diameter, and is shown in Equation 4.1. The aim of proportional control is to inject an amount of liquid that is equal to the *target liquid flow rate*, which depends on the target concentration of sevoflurane, the type of VA, and the patient breath. This is shown in Equation 4.2. By equating the two equations, Equation 4.3 is obtained, which relates the motor speed to the other variables.

It should be noted that the value 3200 is the steps per rotation taken by the stepper motor, given that microstepping is set to 16. This value is multiplied by the distance traveled per rotation, which corresponds to the pitch which then has units of $\frac{mm}{rotation}$. The factor 0.001 is included so that the units are correct, with area having the unit of mm, and the Q_{breath} having unit of $\frac{ml}{s}$. The motor speed has the unit *steps per second*.

$$Q_{\text{actual}} = \text{Area}_{\text{syringe}} * \text{Distance per sec} = (\pi \times r^2) \times pitch \times \frac{\text{Motor speed}}{3200} \tag{4.1}$$

$$Q_{\text{target}} = \frac{(\frac{\text{target percentage} \times \text{patient breath flow rate}}{1-\text{target percentage}})}{\text{VA conversion factor}} = \frac{\frac{per \times b}{1-per}}{c} \tag{4.2}$$

$$\text{Motor Speed} = \frac{3200 \times per \times b}{(1-per) \times (c \times \pi \times r^2 \times pitch \times 0.001)} \tag{4.3}$$

The three assumptions listed below were made for further evaluation:

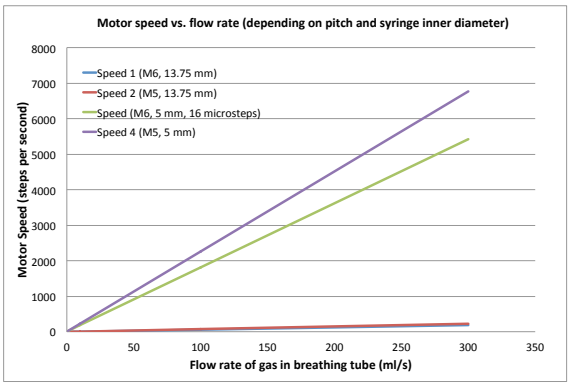
1. The VA sevoflurane is used, and the conversion factor is 184 $\frac{ml}{ml}$
2. The patient breath flow rate is between 0 and 300 $\frac{ml}{s}$
3. The motor is theoretically unstable at steps over 1000, because of the Arduino stepper library that was used, but there was no noticeable instability under 4000 steps per sec

The equations were included in an Excel sheet, and the parameters listed. Graphs were made to evaluate how the flow rate depends on different parameter changes. Since no small syringe was available at the time, an assumed inner diameter of 5 mm was used to evaluate the changes in motor speed. Dr. Lonnee stated that syringes of that size were available at St. Olavs if they were needed.

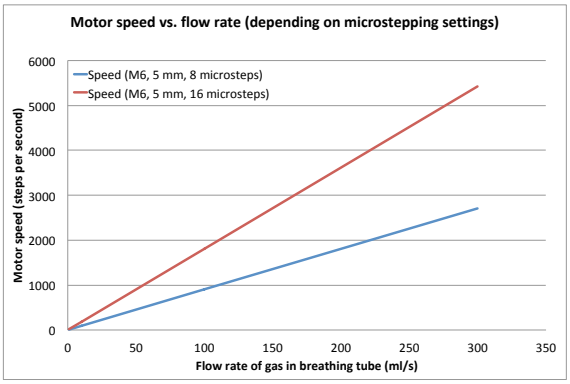
Results

From the equation it can be seen that the motor speed of the syringe pump depends on four variables: the inner area of the syringe, the target concentration of VA, the distance traveled per second, and the patient breath. The distance traveled per second is determined by the pitch and the stepper motor settings. Since the Big Easy Driver was used at this point, it was possible to change the amount of steps per rotation from 200 to 400, 800, 1600, or 3200. A larger value of microstepping means that more steps have to be taken per rotation, but also that the injection is smoother.

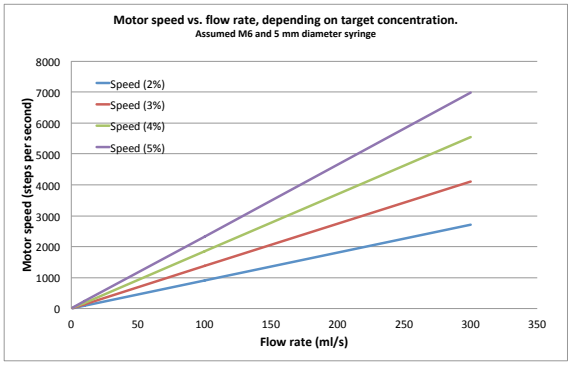
Figure 4.20a shows the motor speeds dependency on inner diameter of the syringe and pitch. As is seen, the motor speed and liquid flow rate depends more heavily on the syringe diameter. However, the step values are very high for higher gas flow rates. Figure 4.20b shows the dependency of microstep values when assuming the use of an M6 threaded rod and a small syringe. 8 microsteps results in step values below 4000, and was deemed best suited for the smaller syringe sizes. Figure 4.20c shows the dependency of target concentration, again assuming the use of an M6 threaded rod and a small syringe. An increase in target concentration necessitates larger step values. The current syringe pump can inject up to 3%, but the target can be increased further by changing the microstep values. It should be noted that the patient breath flow rate was assumed. If the patient breath flow rate is lower than 300 $\frac{ml}{s}$, higher concentrations can be obtained. Based on the results of the analytical prototype it was found that a smaller syringe than the 50 ml should be used.



(a) Graph showing motor speed dependency on pitch and syringe inner diameter



(b) Graph showing motor speed dependency on microsteps



(c) Graph showing motor speed dependency on target concentration

Figure 4.20: Graphs showing the relations between motor speed and different parameters

It should be mentioned that the equations used for proportional control are theoretical. The equations were included in the Arduino program to drive the pumps using proportional control. Because of this, a test was performed to evaluate the *actual liquid flow rate*. The test is presented in Section 5.1.

4.3.6 Prototype 6: Valve Container

Planning

The valve container presented in Section 4.3.4 was to be physically prototyped, with the purpose of verifying that it was functional. The prototype would be 3D modelled, but this was performed only to be able to 3D print the concept. It was therefore considered a physical prototype.

The design for the prototype had already been made on paper. 3D modelling was scheduled to be finished on the day, 3D printing was scheduled to be performed over night, and testing would be performed the next day.

The experimental plan was:

1. Make a 3D model of the cap
2. 3D print the cap
3. Test the concept by drawing liquid from the container, and holding it upside down

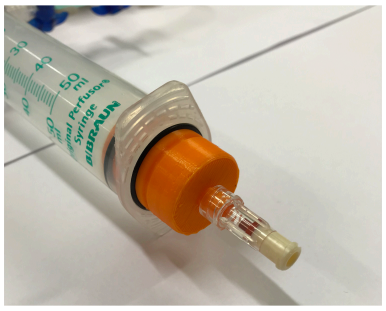
Execution

The valve container cap was 3D printed. Figure 4.21c shows the first 3D printed cap, which has visible grooves indicating poor 3D printing quality. It was decided to make the cap using o-rings, to ensure a tight seal between the print and syringe house. The 3D model was modified so that o-rings could be inserted. Several iterations were performed of 3D modeling and 3D printing, and the schedule was not met. Total prototyping time was five days.

Results

Figure 4.21a and 4.21b shows the finished cap for the valve container and the cap inserted into the 50 ml syringe. The cap was shown to be water tight, and air was drawn into the pump while drawing liquid from the container.

(a) The finished cap with o-rings and a one-way valve



(b) The valve container

(c) The cap showing visible grooves, indicating poor printing quality

Figure 4.21: The final valve container prototype

4.3.7 Prototype 7: Double pump 3D model

At this point, several liquid transfer concepts had been prototyped, and the peristaltic pump and valve syringe pump had been chosen in the concept selection phase. However, the valve syringe pump still had problems drawing liquid from the container and the peristaltic pump ejected liquid non-continuously. After the second iteration of concept generation the double syringe pump was selected for further development and prototyping.

Planning

It was decided to first make a 3D model of the double syringe pump. The purpose was to further evaluate and verify the double syringe pump concept. To more easily communicate the concept to Prof. Fenton, a plan was made to make a flow chart to show the liquid movement through the system. This prototype would be analytical. It was decided to spend four days on 3D modelling the pump, with focus on final assembly in SolidWorks to ensure that the pump would be ready for printing. The flow chart was expected to be drawn in a few hours at most.

The experimental plan was:

1. Make the double syringe pump 3D model
2. Create an assembly with the 3D models and 3D models of syringes
3. Create the flow chart

Execution

The 3D model of the double syringe pump was performed by modifying the existing syringe pump model. A new end piece which could hold a 50 ml syringe was modelled. The pusher was made to hold two syringe plungers.

The flow chart was designed in the web-based program *draw.io*. After the pump assembly was examined it was decided to set up the liquid tubing and syringes as they would be in the double pump. This was not planned for during the prototype planning, but it was decided that getting a physical overview of the liquid tubing could help visualize the system and possible problems.

Results

The 3D model indicated that the double pump was a viable solution for the liquid transfer system. It could in theory easily draw liquid from the container, and the double pump configuration would enable continuous injection. Figure 4.22 shows the 3D model of the pump with two 50 ml syringes fastened.

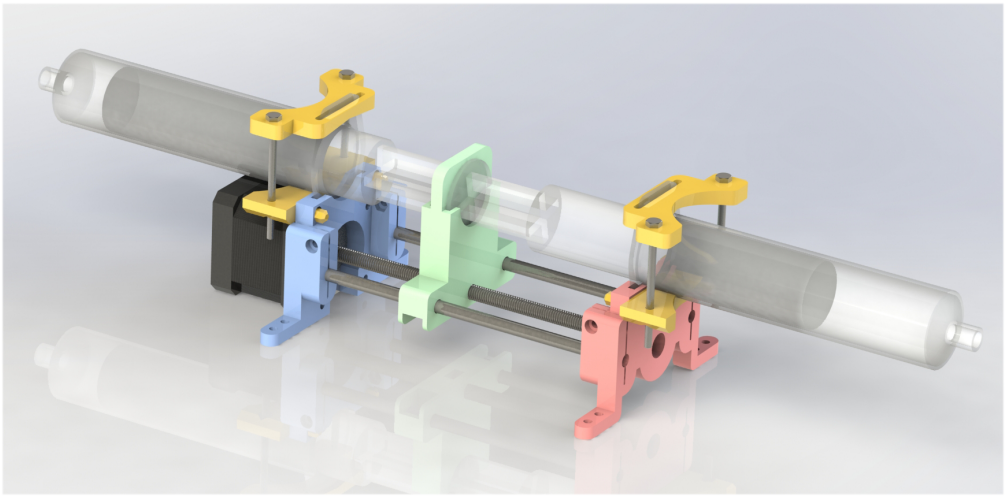
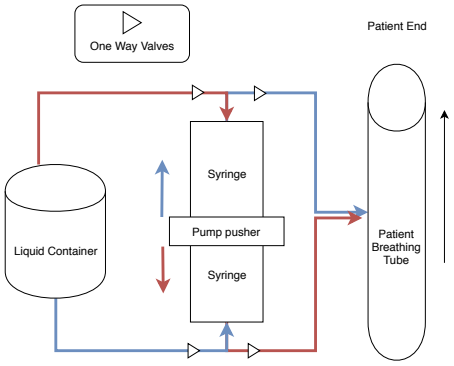
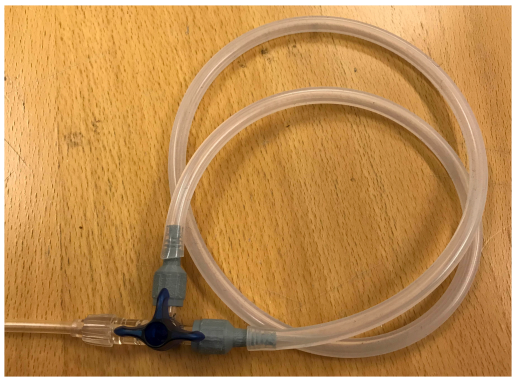


Figure 4.22: The double syringe pump 3D model

The flow chart is shown in Figure 4.23a. It could be seen with the flow chart and the physical tube setup that one connections between the liquid tubings required a female to female Luer lock. This type of connector was not available at the time, but Dr. Lonnee later supplied one tube with female to female Luer lock gas sample tube. The tube was too long and stiff, which resulted in high pressure in the tube and no liquid getting drawn out from the chamber. It was decided to print two *female Luer lock to tapered ends* and connect them with liquid tubing, as shown in Figure 4.23b.



(a) The double syringe pump flow chart, showing the liquid flow through the system



(b) The female to female luer lock prototype, shown with the two female connectors connected to the male ports on a three-way connector

Figure 4.23: The flow chart prototype and female to female Luer lock 3D printed solution

4.3.8 Prototype 8: PLA double pump

Planning

The double syringe pump was to be 3D printed, with the purpose of verifying the physical design. This would be performed by setting up the double syringe pump and connecting it to the previously prototyped valve container. Medical disposables would be used to connect the container and the double pump, and the mechanism would be tested by driving the motor at different speeds.

A schedule was made, and the prototype was planned to be finished within six days. It was assumed that the prototyping would be performed iteratively, with modifications being made to the 3D prints after testing. Four days was scheduled for iterative 3D modelling and 3D printing, and two days for testing and analysis.

The experimental plan was:

1. 3D print the components
2. Assemble all other components
3. Set up of physical prototype using medical disposables
4. Test the pump by driving at different speeds

Execution

After 3D printing the pump, the container and medical disposables were set up. These were connected to the double syringe pump, and testing was performed by running the motor at different speeds.

Results

Figure 4.24 shows the double syringe pump prototype. The pump was printed in a PLA material and will be referred to as the *PLA pump* in the rest of the text. Testing showed that the PLA pump worked, and that liquid could be drawn from the container with one syringe and injected simultaneously by the other. Liquid was continuously injected even while changing the direction of travel. The 3D printed female Luer lock to tapered ends worked, but it was decided to also purchase a few female to female Luer locks from *Qosina.com*. Most of the time spent on prototyping was spent on the Arduino program, rather than the physical double syringe pump. Several functions were written to enable easy use of the pump.

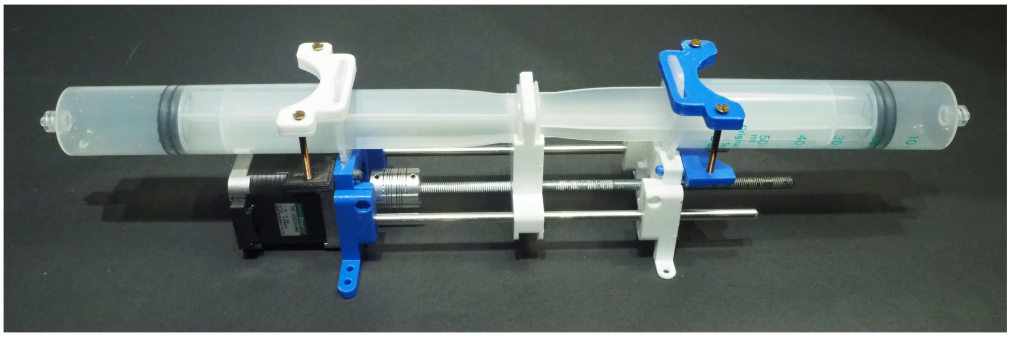


Figure 4.24: The PLA syringe pump prototype

Incremental Changes

A few problems were discovered with the system after testing, which are listed below:

1. The flow rate was too high using the 50 ml syringes
2. The system kept dripping *after* the pump had stopped
3. The pump was not injecting liquid continuously for low speeds. The liquid flow was rather injected as drops.
4. The pusher was traveling down the threaded rod with an eccentricity and was moving erratically.
5. The nuts and linear bearings used in the pusher were slightly loose in their holes. This could cause a delay when changing direction.

The first problem was solved by changing the 50 ml syringes with smaller Braun syringes with Luer slip connectors. To test the syringes in the PLA pump, a small modular syringe holder was printed. This was done to save time, since printing a new motor faceplate and PLA pump end would take around four to six hours compared to twenty minutes for the syringe holder. This method allowed rapid testing of the syringes.

From the analytical Excel prototype it could be seen that the flow rate depended mostly on the inner diameter of the syringe. Several other syringes were therefore obtained which were also tested using this same modular setup. Figure 4.25 shows a few of the modular syringe holders that were made for this prototype. The newly found syringes includes a smaller 1 ml Luer slip syringe, and the BD 1 ml Luer lock syringe. BD was contacted[1], and the diameter of the Luer lock syringes were found to be between 4.623 and 4.775 mm. This syringe was used for subsequent prototyping and testing, and the diameter was added to the Arudino program.

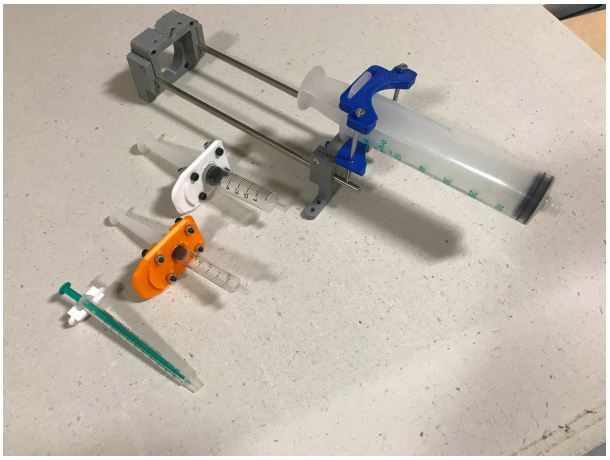


Figure 4.25: Some of the modular syringe holders

The second problem was believed to be caused by a pressure buildup in the system, and was solved by using a smaller syringe and shorter liquid tubings.

The third problem was communicated to Dr. Lonnee who stated that the problem may not be as critical as expected. Since VA have lower viscosity and droplet sizes the dripping injection may not be as pronounced when using sevoflurane. VAs also evaporate in room temperature, so the injection may behave differently for sevoflurane. Dr. Lonnee supplied epidural catheter tubes which are very thin and have several small holes at the end point. He believed that the dripping may not be as pronounced using these tubes. Figure 4.26 shows an epidural catheter connected to the 1 ml Luer lock syringe. A test was performed to characterize the behaviour of sevoflurane, and is presented in Section 5.1.2. Carlo Kriesi was also consulted, and stated that the dripping characteristic can be removed by ensuring that the injection tip is in contact with the wick.

The fourth problem was assumed to be caused by the threaded rod not being stiff enough, and because there was a slight bend in the rod. This was fixed by using an M6 threaded rod with a

[1] Email communication: 2018-11-14

higher tensile strength.

The fifth problem was solved by including a locket that can be screwed on to the pusher to ensure that the nuts and bearings are tightly fastened. This ensures that neither the nuts nor the bearings move when the pump is driven. This system is shown in Figure 4.27.

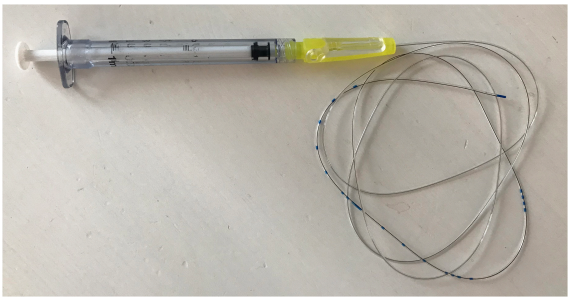


Figure 4.26: The epidural catheter tube connected to the 1 ml Luer lock syringe

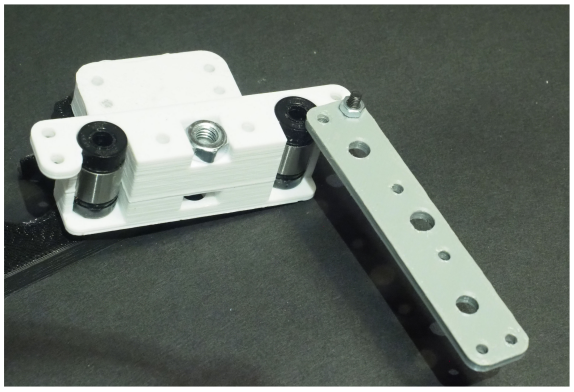


Figure 4.27: The locket system

The incremental changes made for this prototype were extensive, especially for the double syringe pump components which were printed several times with small modifications. An example of such changes and an explanation of this process is presented in Appendix B, Section B.2.

After the prototyping of the PLA double pump, a prototype was made with the purpose of investigating a modified double syringe pump concept that was made to make the pump smaller. This prototype did not contribute to the overall product development. A presentation of the prototype is presented in Appendix B, Section B.1.

4.3.9 Prototype 9: Acrylic Double Pump

Planning

It was assumed that the *accuracy* and *stability* of the double syringe pump could be increased by making a more massive prototype with more precise tolerances. A prototype was planned to be made using the Objet Alaris 30 3D printer at Troll Labs, with the purpose of investigating the performance of the improved pump, and comparing it to the PLA pump. To compare the two pumps a *pressure test* would be performed.

The physical prototype would be made by sending the 3D models to Carlo Kriesi for 3D printing. The 3D printer was available on the day of requesting access to the 3D printer, and the pump

was scheduled to be printed on the day. It was only possible to print the pump this one time. The schedule was therefore short, with two more days spent on testing and analysis.

The experimental plan was:

1. Modify any 3D models and get the pump ready for printing
2. Print the pump at Troll Labs
3. Set up the physical pump with medical disposables
4. Test the system in a pressure test

Execution

The 3D model was modified before printing. Some of the changes were cosmetic, like indentations for bolt heads, while other were made to increase performance, like including a locket on both sides of the pusher as opposed to only one.

By connecting the syringe to a three-way connector, and directing a plastic tube from one port to the MPX5010DP differential pressure sensor, the pressure changes in the tube could be recorded. The zero-condition values were not the same for all tests, so the tests do *not* show the actual pressure in the system, but rather the changes of pressure when the syringe pump is run.

Results

Figure 4.28 shows the results from the pressure test performed with both the acrylic pump and the PLA pump. The results showed that the pressure changes are similar between the two pumps when injecting water into thin air, with similar pulsations of the graph which indicate dripping. However, when injecting water onto paper, which was used to simulate a wick, the acrylic pump is seem to pump much smoother. Figure 4.29 shows the acrylic pump.

Incremental Changes

A few problem with the double syringe pump were subsequently discovered. These are listed below.

1. The double pump was shaking when driving. This was caused by the stepper motor, and had been noticed for the previous pumps, but no action had been taken.
2. The motor would sometimes stop or act erratically. It was theorized that this was because of too low torque.

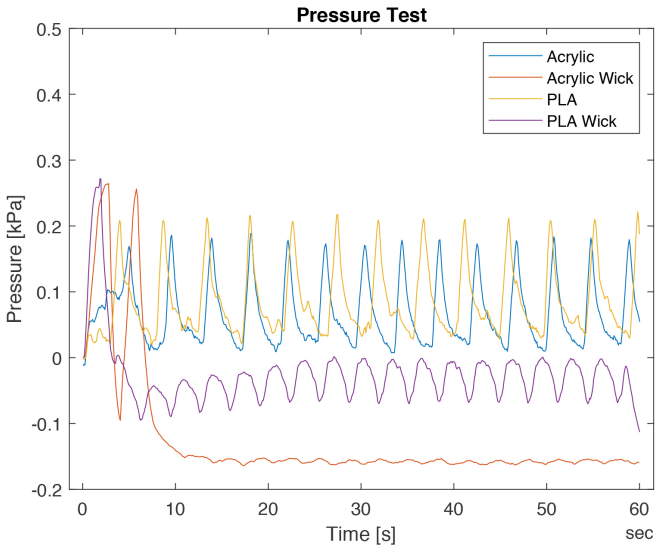


Figure 4.28: Results from the pressure tests

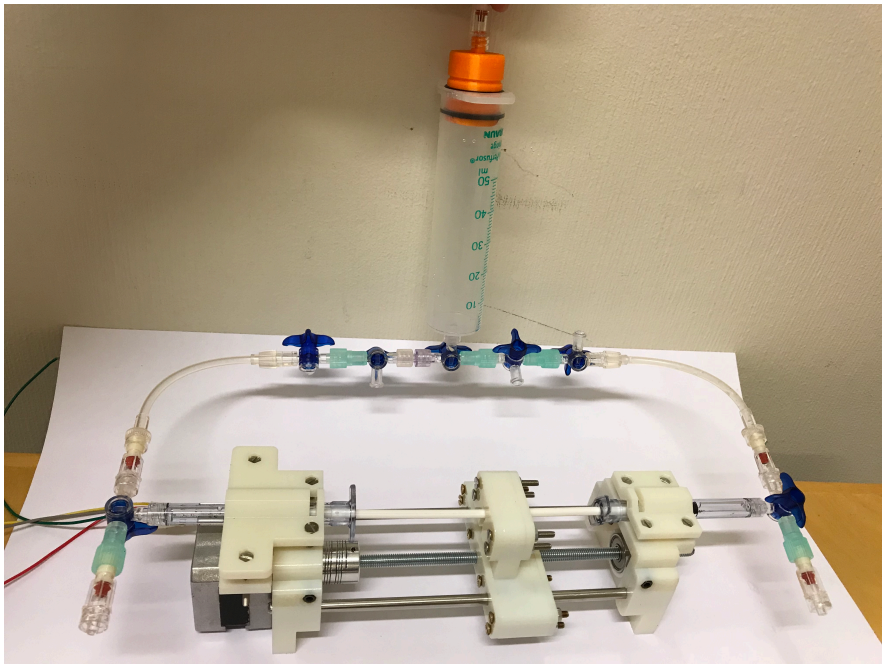


Figure 4.29: The acrylic double syringe pump prototype printed at Troll Labs, shown with tubes and the valve container.

The first problem was solved by mounting the pump onto a massive piece of wood. This ensured that the system was stable. The second problem was solved by using a stepper motor with a torque of 0.37 Nm, compared to the first with a torque of 0.16 Nm. This was the last physical liquid handling prototype. Several changes were later made to the liquid medical disposables setup, and to the program of the Arduino, and will be described in Section 4.5.

4.4 Modular Box, Proof of Concept Prototype

The modular concept was prototyped a few times at the end of the thesis. These prototypes were made to clearly communicate the concept to Prof. Fenton in order to get proper feedback. It was clear that not much more could be gained from prototyping this concept, so less focus was spent on this subproblem.

4.4.1 Prototype 1: 3D model boxes

Planning

A 3D model of the modular box concept was to be made to communicate the idea to Prof. Fenton, and to communicate ideas between the authors. The prototype was completely analytical and very focused. The prototype was planned to be finished in one day, with the 3D modeling consisting of making simple square boxes.

The experimental plan was:

1. To create a 3D model of the modular system in SolidWorks
2. Make an assembly of the 3D models next to each other

Execution

It was decided to place components inside the boxes, and part files for the Arduino, MPX5010DP, ADS1115, and Big Easy Driver were all downloaded online. The battery and gas analyzer were modelled as black boxes, with dimensions based on the *RRC2054* and the *Artema AION* respectively.

Results

The prototype is shown in Figure 4.30. Two of the modular boxes, the flow box and CPU box, were made to include the components physically used for prototyping. The flow box contains the differential pressure sensor, filter, and ADC. The CPU box contains the Arudino and Big Easy Driver. Several setups were made by moving the 3D models around. Thought was put into how the boxes should communicate with each other, and how the breathing tube should be positioned inside the box. In the end it was believed that this concept has promise, and that it

should be evaluated further at a later date. Renderings were sent to Prof. Fenton and an answer was received with encouragements to continue pursuing the modular concept.

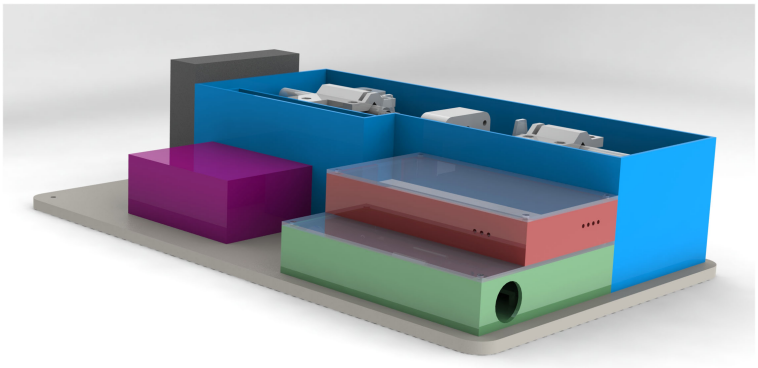


Figure 4.30: 3D model of the modular concept

4.4.2 Prototype 2: 3D Print Modular Boxes

Planning

The modular boxes were to be 3D printed to evaluate how the concept would perform in real life. It was especially of interest to investigate how the CPU and flow box would integrate together, with wires between them. This was a physical prototype, and testing would be performed by qualitatively evaluating the 3D prints after using them for testing at St. Olavs. Five days was scheduled for this prototype, with the assumption that the boxes would have to be 3D printed iteratively.

The experimental plan was:

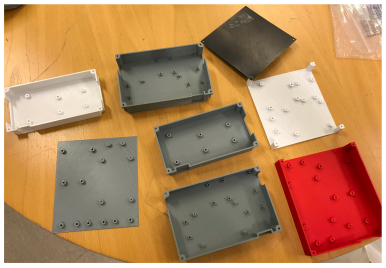
1. Print both modular boxes
2. Use them for further prototyping and testing

Execution

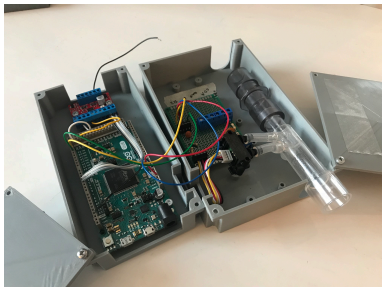
The first 3D prints were printed with rough printer settings and no walls or locket to save time, and ensure that the layout for the components was modelled correctly. Later prints were made to include lockets, screw holes, and wire handles.

Results

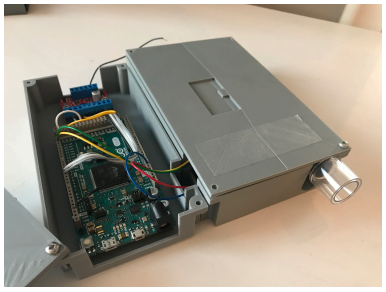
Figure 4.31a shows several modular boxes. Changes and modifications were made to improve the concept. The final physical modular boxes are shown in Figure 4.31b and Figure 4.31c. Notice how the flowmeter protrudes out of the box in Figure 4.31c, making it easy to connect to a breathing tube. The system was evaluated and it was believed that the concept would be usable in the Fenton device.



(a) Several modular boxes at different stages of prototyping



(b) The final modular box prototype, with the internals showing



(c) The final modular box prototype, with the lid closed over the flow box

Figure 4.31: The modular boxes

4.5 Comprehensive, Integration Prototypes

Comprehensive prototypes were made to ensure that the different subsolutions could be integrated together, and to communicate concepts to Dr. Lonnee and Prof. Fenton. For this section the comprehensive prototypes are presented, with the second comprehensive being the physical prototype used for testing at St. Olavs. The iterative changes made between the St. Olavs tests are also presented in this section.

4.5.1 Prototype 1: Comprehensive CAD Model

Planning

A comprehensive 3D model was to be made, with the intention of communicating the whole concept to Prof. Fenton. The model was planned to include all the previous prototypes as well as an outer shell. It would be modelled to show different aspects of the design, like portability, alarms, and screens, and also the concepts, like the modular boxes concept and the double

container concept. Six days was scheduled for this prototype. The first five would be spent on making the 3D model and design of the encasing. The last day would be spent on making renderings and sending them to Prof. Fenton.

The experimental plan was:

1. Assemble already made components in a 3D assembly file
2. Model the other components
3. Make renderings

Execution

An encasing for the device was quickly designed. The outer shell was modeled with a tiltable touch screen, rotary knob, and LED lights and speakers for alarms. A square shaped fastened container, and a removable container was modelled. Since all the other 3D models were readily available, the prototype was simply finished by including these in the assembly model.

Results

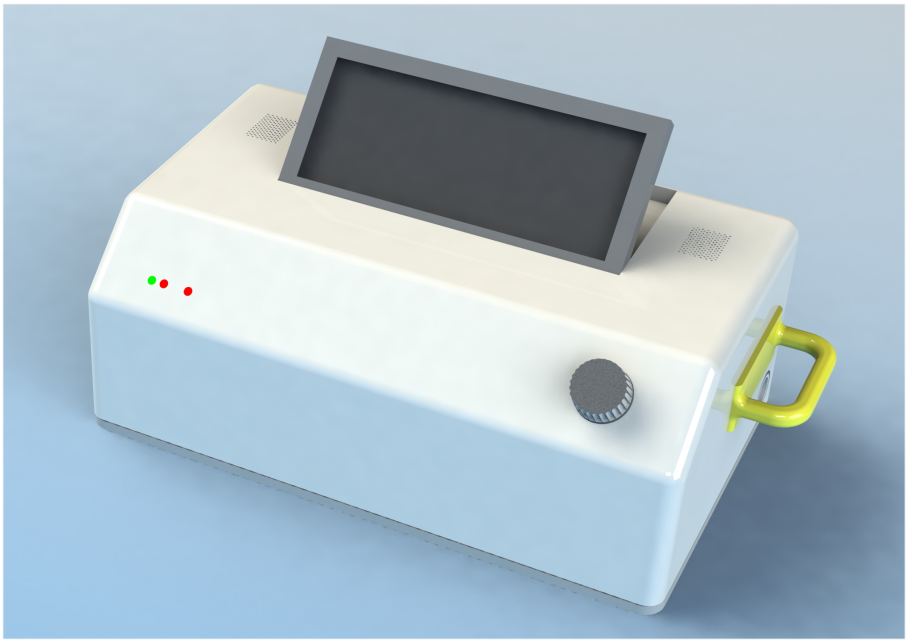
Figure 4.32a and Figure 4.32b shows the front and back side of the final 3D prototype. Figure 4.32c shows the same prototype with the top encasing lifted, showing the modular system inside the box. The modular boxes are placed in the bottom of the device, with different colors to differentiate them from each other. Renderings were sent to Prof. Fenton and positive feedback was received.

4.5.2 Prototype 2: Comprehensive Physical Prototype

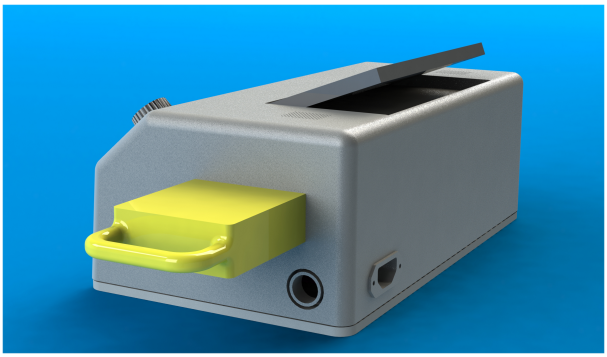
Planning

A comprehensive physical prototype was to be made to evaluate the integration of the prototypes and concepts, and to evaluate the performance of proportional control. This would include both modular boxes, the acrylic double pump complete with the valve container and wick, and the flow measurement system.

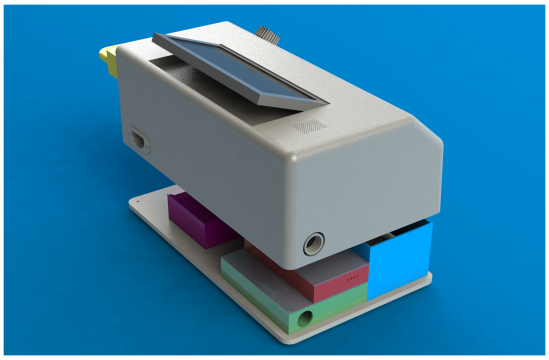
Testing was planned to be performed using the CPAP and driving the acrylic pump using proportional control. It was also very important to evaluate the integration of the programming. Previously, separate programs had been made for the different prototypes. For this comprehensive prototype, the different programs would be merged into one. Since the prototype was to



(a) The comprehensive 3D model



(b) Side view of the concept showing the removable container



(c) Side view of the concept, showing the modular boxes inside

Figure 4.32: The comprehensive 3D model

be tested at St. Olavs using sevoflurane the program had to be written to include some extra functionality.

In order to inject the liquid sevoflurane, the tube going from the double syringe pump would have to be inserted into the breathing tube. For the final concept, it was assumed that this could be solved by designing a breathing tube with a tube going into it. However, to be able to test the prototype, an alternative way of injecting liquid into the breathing tube had to be investigated. A few alternative concept designs had been made throughout the previous prototyping stages which would be tested with this comprehensive prototype.

It was assumed that this prototype would be very iterative, with several small changes made to

the both the Arudino program and the physical setup. Five days was planned for the prototype, with the first day being used to assemble the components and physical prototyping. The rest of the time would be spent on testing and modifications.

The experimental plan was:

1. Assemble all components
2. Set up the physical prototype
3. Write a designated program for the St. Olavs test
4. Test the system using the CPAP

Execution

All the components were readily available. The modular boxes were connected with wires, the acrylic pump connected to the Arduino, and the flowmeter connected to the breathing tube, the SDP810, and the MPX5010DP. Testing was performed after discovering how to correctly set up the SDP810 sensor. The breathing tube from the CPAP was connected to the flowmeter, and a set flow rate was injected into the prototype. Proportional control was verified by injecting different flow rates and letting the Arduino write out the motor speed. The actual motor speed was verified by calculating the theoretical motor speed by hand. Figure 4.33 shows how the CPAP was connected to two different flowmeters which were connected to the MPX5010DP and SDP810 sensors. The injection point solution was made using a breathing tube connector with a rubber insert, through which epidural tubes could be inserted.

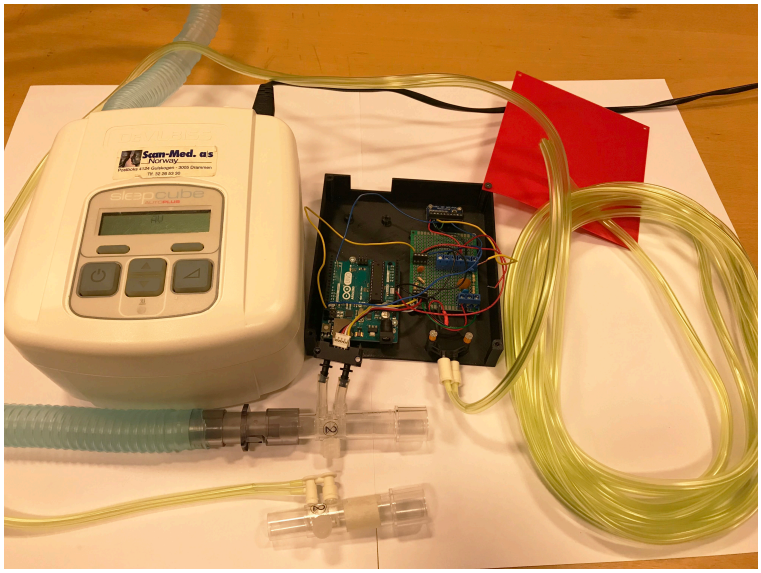


Figure 4.33: The flow measurement setup for the CPAP test

A new program was written, and most of the prototyping was spent on this. Several new functions were included which were meant to be used when testing at St. Olavs. This included the priming function and proportional control function, which are presented in Appendix B, Section B.4.

Results

Testing showed that the prototypes integrated well, and that proportional control worked. The program was written to first perform priming manually by driving the motor back and forth, and drawing liquid into the tubes. Then, the proportional control function would begin, where the pusher moves in one direction for a set distance before returning the other way. Program flow control with keypresses worked well. Figure 4.34 shows a flow schematic of the Arduino code of the prototype. Main functions are shown in a red color, serial command requests are shown in blue, and flow control is shown in orange. Not all functions are shown, and there are some differences between the actual program and the flow schematic.

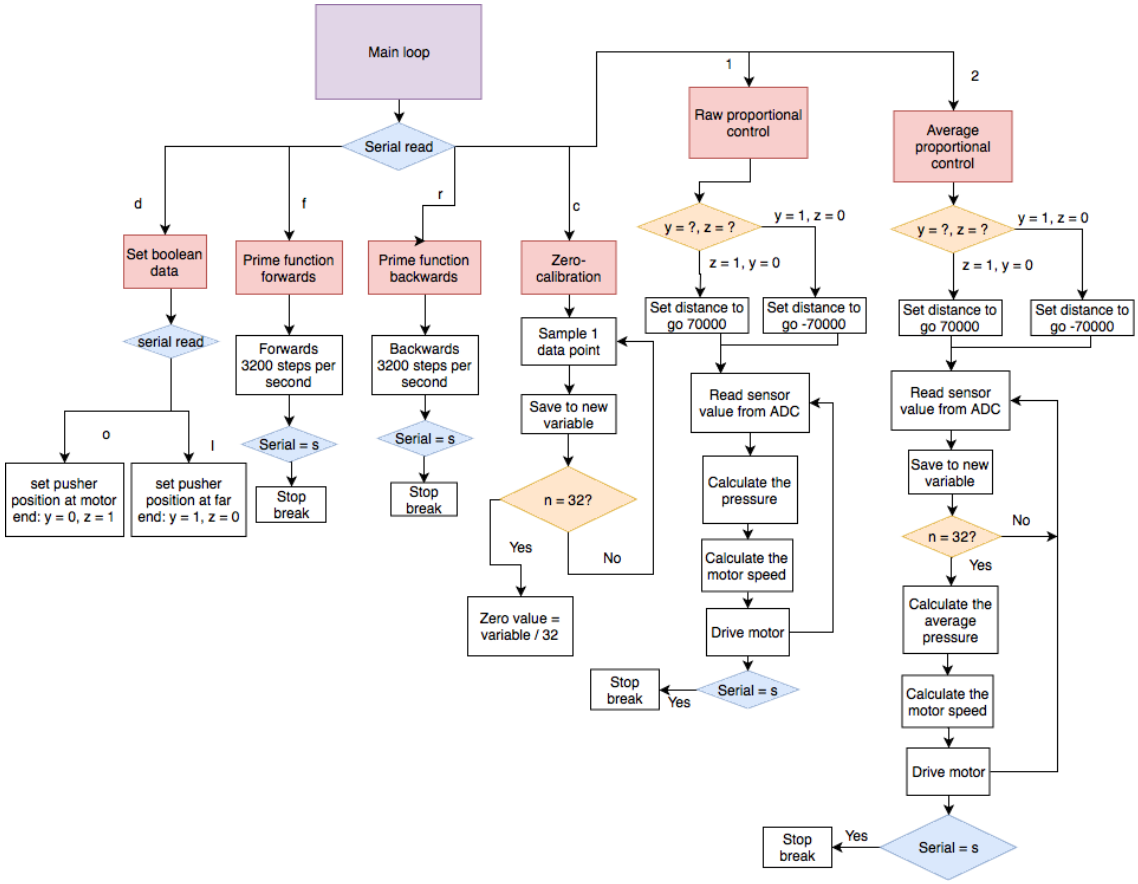


Figure 4.34: Flow chart for the final Arduino program

The injection point solution is shown in Figure 4.35. It was believed to be tight enough to be used in an experimental test. A wick could be placed inside the connector.

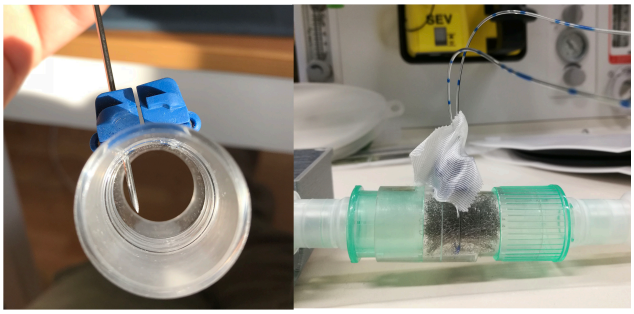


Figure 4.35: The injection point. Left panel shows how a syringe was used to make a small hole in the rubber. Right panel shows the injection point with two epidural tubes inserted into the breathing tube

Incremental Changes of the Prototype After Tests at St. Olavs

A few changes were made to the comprehensive prototype after the tests at St. Olavs. Since there was believed to be a leakage due to the use of too many three-way connectors, changes were made to the liquid tubing setup. To minimize the use of connectors, two valve containers were included, one for each syringe. This meant that the last setup used two three-way connectors and four one-way valves. The physical setup of the double syringe pump used for the third and last test at St. Olavs is shown in Figure 4.36.

Due to poor motor control, which manifested itself in erratic and unstable motor performance, changes was made to both the programming and physical microcontroller setup. The physical change was to swap the Arduino Uno for the Arudino Due, in order to increase the clock speed from 16 MHz to 84 MHz which meant that the program could be read faster. The code was changed to include more stepper motor commands, which ensured a slight increase in motor performance. A separate function was included to control how often the flow measurement was requested. By reducing the amount of requests from one request per iteration through the *while loop*, to one request per 125 ms, a drastic performance change was notices.

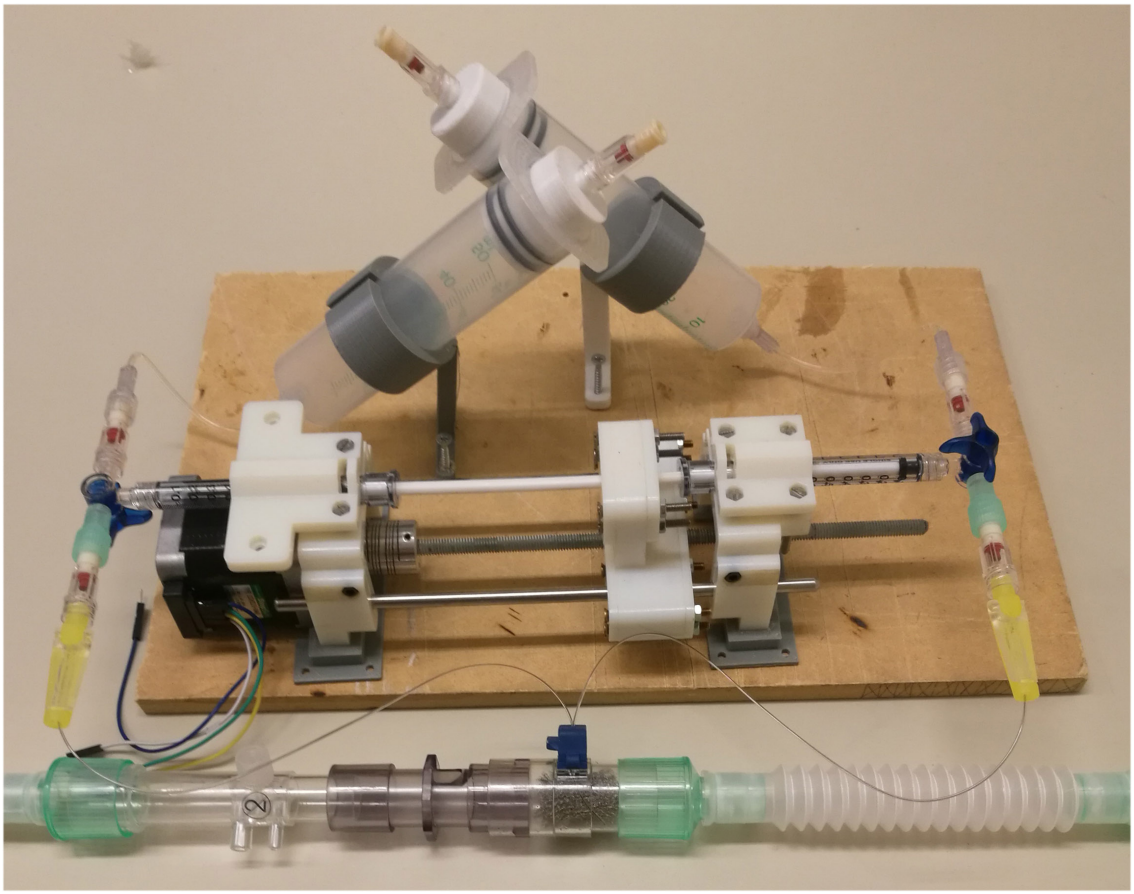


Figure 4.36: The physical setup of the last prototype used for testing at St. Olavs

Chapter 5

Testing

Four distinct tests were performed for this thesis:

1. The double syringe pumps were tested to characterize the liquid injection flow rate.
2. Sevoflurane was tested to characterize the behaviour.
3. The flowmeter was tested to characterize the relation between the differential pressure and flow rate. This was performed as a prerequisite for actually being able to use the GE Healthcare flowmeter to measure flow rates.
4. The final prototype was tested at St. Olavs to qualitatively evaluate the performance of the concept.

5.1 Testing of Liquid Handling

Two tests were performed to answer different questions concerning the liquid handling. The first test was performed to verify that the actual flow rate of the double pump complied with the theoretical flow rate, which was used as an assumption when programming the proportional control. The second test was performed to evaluate the behaviour of sevoflurane, since the behaviour was unknown to the authors. This was performed because there was some problems with the liquid dripping when using the double pump, as described in Section 4.3.8. It was also performed to help generate new ideas and concepts specifically for use with sevoflurane.

5.1.1 Liquid Flow Rate Test

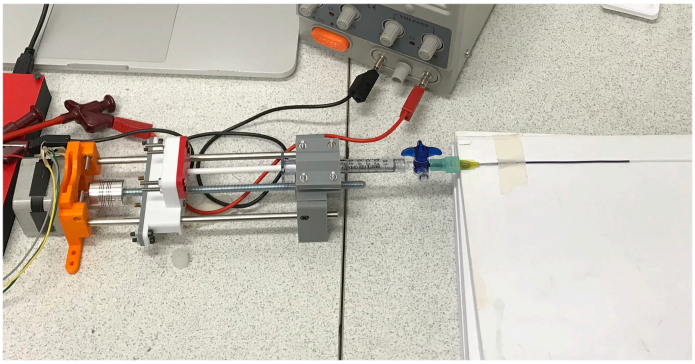
Method

At the beginning of prototyping the syringe pump, it was assumed that the actual flow rate complied with the theoretical flow rate, given that the calculations were performed correctly. Tests using water as liquid media were performed to verify that this was the case. Since a dedicated liquid flowmeter was not available for use, a liquid test design had to be made. The tests were performed by running the PLA syringe pump at a specific speed for a specified time interval. The volume of the ejected liquid was then measured and divided by the time interval to find the flow rate. Three different techniques were used to measure the ejected volumes. The first test was performed using a measuring cylinder with a grading division of 0.1 ml. However, the grading division was too large to characterize the low flows of the syringe pump. No further tests were therefore performed using the measuring cylinder.

The second test was performed using an analytical balance and weighing the ejected liquid. The high-resolution *Mettler Toledo Classic Plus AB204-S* analytical balance with a readability of 0.1 mg was used. The setup is shown in Figure 5.1, with a tube going from the pump to a measuring boat inside the analytical balance. Since the purpose of the test was to investigate the flow rate in means of $\frac{ml}{s}$, the weight of the ejected water was converted to milliliters using the formula: $V = \frac{m}{\rho}$, where V is the volume, m is the mass of the ejected water, and ρ is the density of water at the time of testing. The temperature of the water was measured to find the correct density.

Figure 5.1: The setup for the analytical balance test

To verify the test results from the analytical balance a third volume measuring technique was used. For this test a droplet of colored water was injected into a 0.86 mm plastic tube via a three-way connector. The pump was driven, injecting non-colored water into the tube, and the length of travel of the colored water was recorded using a caliper. The volume of the ejected liquid was found using the formula: $V = \pi r^2 \times l$, where V is volume, r is the radius of the tube, and l is the length of travel. Figure 5.2a shows the test setup, while Figure 5.2b shows a closeup of the tube with colored water.



(a) The setup for the analytical balance test

(b) The setup for the length test

Figure 5.2: Setup for the liquid flow rate tests

Results

Figure 5.3 shows the theoretical flow rate for the PLA syringe pump and the actual flow rate curves obtained from the tests. The results from the analytical balance and length tests indicate that the actual flow rate complies with the theoretical test. Both tests show deviations from the theoretical straight line, but on either side. Based on the test results is was concluded that the theoretical flow rate could be employed in the proportional control Arduino program.

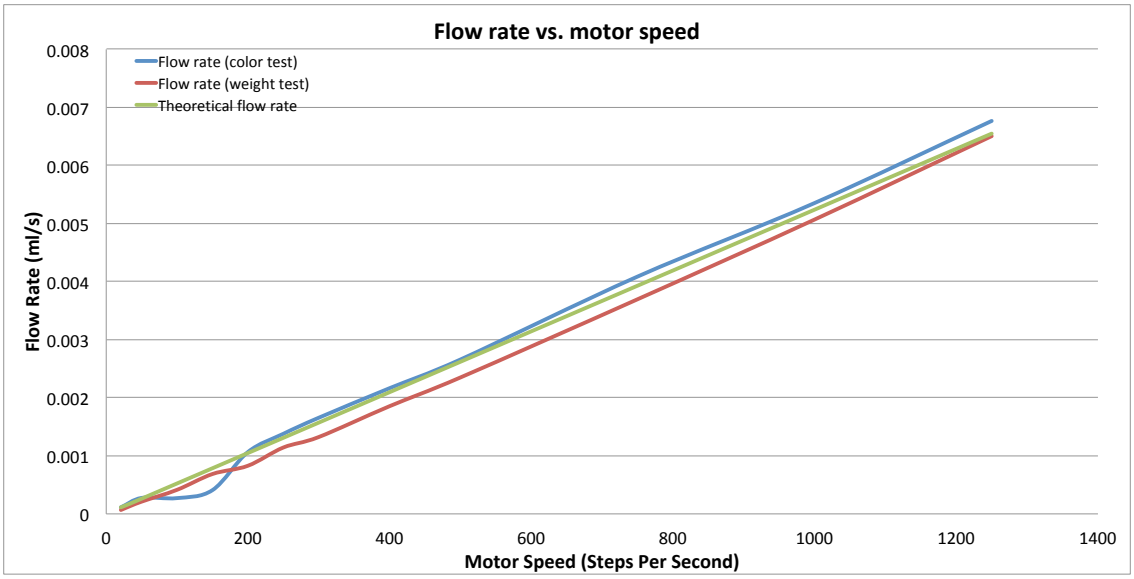


Figure 5.3: Results from flow rate tests

5.1.2 Sevoflurane Behaviour Test

Method

The purpose of this test was to investigate the behaviour of the anaesthetic agent sevoflurane. It was of interest to investigate how it evaporates in room temperature and how the PLA syringe pump behaved when used with sevoflurane. In addition, it was desirable to investigate if the problem with dripping, which was described in Section 4.3.8, could be reduced and if the output flow would be more continuous with use of a volatile anaesthetic agent.

Due to the anaesthetic effects of sevoflurane, the test was performed in a fume hood at St. Olavs under supervision of Dr. Lonnee. For this test the PLA pump was used with a 1 ml syringe and an epidural catheter. The syringe was manually filled with sevoflurane by Dr. Lonnee, and clamped to the pump. First, a test was performed by ejecting sevoflurane onto a glass petri dish and a piece of paper. The piece of paper was used to simulate a wick. Another test was performed to evaluate how the patient breath through the breathing tube would influence the evaporation rate. A Laerdal bag was used to direct a flow over the injection point, simulating a patient breath. Figure 5.4 shows the petri dish with paper on top, the epidural used for injection, and the tip of the Laerdal bag. The tests were filmed using a camera phone. After the tests the time of evaporation was evaluated using the video.

Figure 5.4: The sevoflurane testing setup

Results

Several behaviours were noted, and are listed below:

1. Without paper, liquid would pool up in the petri dish before evaporating. With use of paper, the evaporation rate was increased drastically.
2. Evaporation was quicker if the liquid was subjected to a gas flow. Time to evaporate was reduced from 10 to 4 seconds.
3. The droplet size of sevoflurane was visually verified to be smaller than water.

4. The flow rate was more continuous compared to water. Comparisons were made using the same motor speeds.
5. No dripping was experienced when the epidural tip was touching the paper.

From the tests it was found that a wick would probably be necessary for satisfactory evaporation. It was also believed that the dripping problems experienced with the PLA pump could be mitigated by ensuring that the tube tip going into the breathing tube was in contact with the wick.

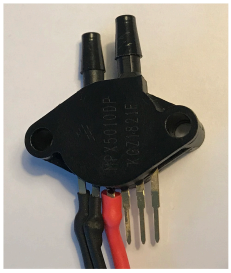
5.2 Flow Measurement Tests

Method

The solution to the subproblem of flow measurement was a differential pressure sensor and a flowmeter. To be able to use this system, the characteristic constant of the GE Healthcare flowmeter had to be investigated. This constant is used to calculate the flow rate of gas from the differential pressure, as is shown in Section 2.4. By measuring the differential pressure when the flowmeter is subjected to a known, constant flow rate of air, the known flow rate can be plotted against the square root of the differential pressure. It is expected to find a linear curve, which follows the equation: $Q = k \times \sqrt{\Delta P}$, where Q is the flow rate, k the characteristic constant, and ΔP the differential pressure. The constant can then be found by dividing the flow rate by the square root of the differential pressure. Two different devices were used to eject a constant, adjustable, known flow rate; a humidifier and a gas blender.

Two tests were performed using the *Airvo 2* humidifier, which is used to supply humidified air to patients with hard of breathing. The tests were performed only with the MPX5010DP sensor. Two tests were also performed using the gas blender. For the first test the SDP810 sensor was used alone, while the last test was performed using the MPX5010DP, the MPX5004DP, and the SDP810 sensors. The reason for performing the last test using all the sensors was to compare and verify the results between the different sensors. The in-line mass flow sensor Sensirion SFM3200 was used as a reference flow meter for all tests. Figure 5.5 shows the MPX5010DP, the SDP810, and the SFM3200. The physical setup was the same for all the tests. The GE Healthcare flowmeter was hooked up to the differential pressure sensors through the spirometer ports using a spirometer tube, as shown in Figure 5.6.

A breathing tube was connected from the gas flow device to the flowmeter. Measurements were



(a) The MPX5010DP

(b) The SDP810

(c) The SFM3200

Figure 5.5: The sensors used to measure differential pressure and flow rate

Figure 5.6: The flowmeter test setup, showing the MPX5010DP ports and flowmeter ports connected to the spirometer tube

taken using the computer program MATLAB, which was set up to record the measurements over a specified time interval. For the tests using the MPX sensors three measurements were taken per flow rate. For all the measurements the values were averaged over time, and the three tests were averaged. The first averaging ensures smooth sampling, while the second averaging ensures better accuracy in the test [49]. Both MATLAB and Excel were used for post-processing of the data. The characteristic constant was found by dividing the flow rate measured by the SFM3200 with the differential pressure values.

It should be noted that the in-line mass flow sensor SFM3200 was assumed to measure the correct flow. This was later verified by comparing the measured values with the ones shown on the *rotameter* of the gas blender, which was known to be correct. Small iterative changes were made both to the physical design and the Arduino program between tests.

Results of the Flowmeter Characterization

Figure 5.7 shows the results from the first two humidifier tests, and the first gas blender test. As is seen, the two MPX5010DP measurements gave relatively similar curves, while the SDP810 gave a different, less steep curve. Several reasons were theorized for why this could occur, and are listed below.

1. The sensors may be set up different or incorrect, which could results in a faulty sensor reading.
2. The temperature and humidity were different between the tests. Since the SFM3200 output has to be multiplied with a compensation factor which depends on the humidity and temperature the results are unknown.
3. The set up for the two humidifier test were poor at best. The gas tube connected to the spirometer was curled up, and not laid out straight. This could cause the gas flow to become more turbulent, which should have an impact on the spirometer characteristics.

The fourth and last test was performed to try to find the reason for the difference in results between the SDP810 and MPX5010DP. It was of interest to use the SDP810 for the tests at St. Olavs, because it was believed to be more stable, and did not require a filter or ADC to function. Figure 5.8 shows the results from the last gas blender test.

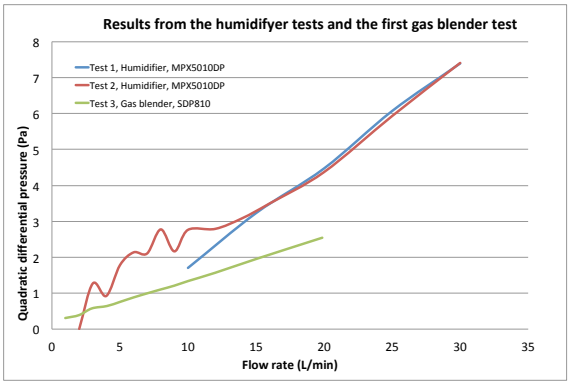


Figure 5.7: Results from the first two humidifier tests and the first gas blender test

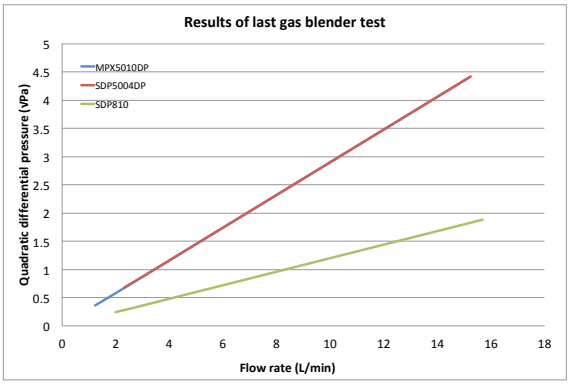


Figure 5.8: Results from the second gas blender test

First of, it should be noted that the gas blender tests seem to be much more stable compared to the humidifier tests. It is also seen that the MPX5010DP and MPX5004DP sensors gave similar curves, while the SDP810 sensor gave another curve entirely. Because both MPX sensors complied with each other, it was assumed that it was the SDP810 sensor which was set up incorrectly. The MPX values were therefore used to find the characteristic constant which was 55.5.

The constant that was used in the Arduino program was however set to be $k_{\text{Arduino}} = \frac{1}{k}$, which was 0.018. As mentioned in Section 4.2.4 the SDP810 was subsequently found to function correctly when used with plastic tubes instead of with the spirometer tube. Since the characteristic constant only depends on the type of flowmeter, it was assumed that the SDP810 was able to measure the correct flow rate using the same constant.

5.3 Testing of the Whole System at St. Olavs

The purpose of the tests was to evaluate the performance of the different concepts and subsolutions which had been prototyped. It was also of interest to verify that proportional control could be used to reach the target concentration. It should be noted that the test was performed more as an experiment on the prototype rather than a scientific test. The experiments were performed to qualitatively evaluate the performance of the prototype. There were several reasons for not performing a strictly scientific test, some of which are listed below.

1. The time available for testing was restricted to four hours per session. The physical setup of the test took about an hour
2. The amount of tests were limited to three times
3. The notification that testing could be performed was given on the day of testing
4. The machine and equipment available at St. Olavs was previously unknown to the authors, and Dr. Lonnee was needed to set up the breathing system
5. The handling and filling of sevoflurane was performed by Dr. Lonnee, with restrictions on how often the prototype could be refilled

The test of the final concept was performed at St. Olavs using sevoflurane. Testing was performed at an operation theatre with Dr. Lonnee present to ensure that the machines were used correctly and to ensure safe use of the sevoflurane. The GE Healthcare Aisys CS anaesthesia machine was used to setup a breathing circuit, to deliver a ventilator gas flow, and to analyze the gas downstream of the injection point. It was found that the gas analyser updates the measured concentration every two seconds.

Three tests were performed, but for the first two the setup was incorrect. The incorrect setup is shown as a sketch in Figure 5.9, where the breathing tube exits the Aisys, passes through the concept prototype, and enters the Aisys again. This was a problem since the Aisys automatically

uses a circle breathing system where CO_2 is absorbed, and sevoflurane is reused. This means that the gas passing through the prototype was a mixture of O_2 and sevoflurane. The concept was not designed to be used with a circle breathing system, which rendered these tests unusable. However, for these tests a few problems were noticed. First, the motor was found to behave erratically, and was believed to be due to poor programming and motor control. Second, there was believed to be a leakage somewhere in the tube set up. These problems were subsequently solved, as explained in Section 4.5.2.

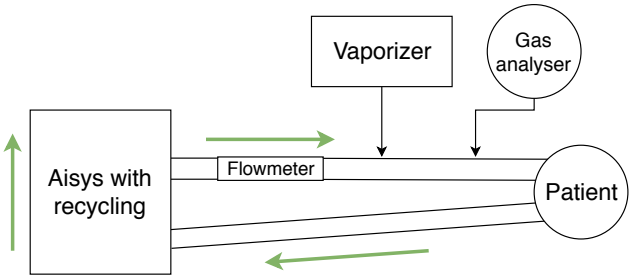


Figure 5.9: The wrong test setup

5.3.1 The Test

Method

The breathing tube setup is shown as a sketch in Figure 5.10. The Aisys was used to inspire a flow, and the breathing tube from the machine was connected to the flowmeter of the prototype. A Laerdal bag was used to simulate a patient breath instead of the ventilator from the Aisys. The gas from the Laerdal bag passed through the flowmeter, and liquid was injected into the breathing tube just downstream of the flowmeter. A test lung was used to simluate the lungs of a patient. The gas containing sevoflurane passed into the lungs, and were expired by the lungt directly into the gas absorber canister, by Sedana Medical, which shown in Figure 5.11. The absorber uses a charcoal filter to remove sevoflurane, and is used with the AnaConDa to absorb VAs. By using the absorber there was no recycling of VA in the system. The concentration of sevoflurane was measured by the Aisys gas analyzer, and could be seen on the anaesthesia machine screen. The Arduino program included a speed factor, which could be used to change the amount of injected liquid. If the speed factor was set to 0.5, 50% of the target concentration would be injected. This was included to rapidly change the liquid flow rate during the tests.

An initial test was performed using a continuous air flow from the Aisys, without moving the Laerdal bag. The rest of the tests were performed using a Laerdal bag as the ventilation mode.

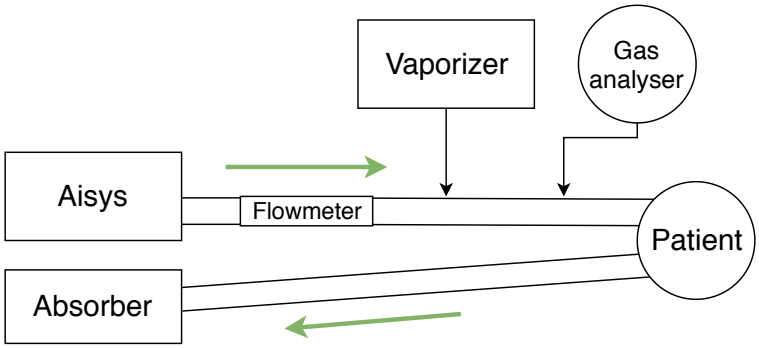


Figure 5.10: The correct breathing tube setup

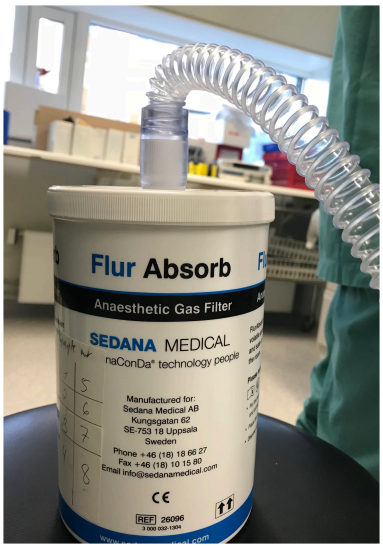


Figure 5.11: The Sedana Medical Flur Absorber

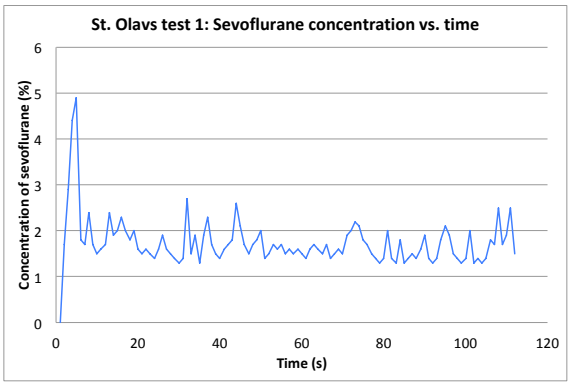
This is closest to the actual application in LMICs. To log the results, the gas analyser screen was filmed using a camera phone. This way the peak values could be correctly logged after the test. Because of time restrictions, several shorter tests were performed using this setup. The first test was logged for five minutes, with subsequent tests taking thirty seconds to one minute. The reason for doing several short tests instead of one long was to test several wicks and program variables like speed factor and target concentration. Four tests were performed, with different speed factors, target concentrations, and wicks as shown in Table 5.1.

Table 5.1: Data for the four Laerdal bag tests

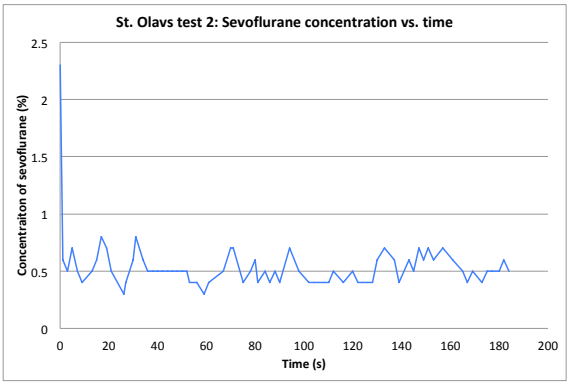
Test #	Wick type	Target concentration (%)
Test 1	Fabric	2
Test 2	Metal	0.5
Test 3	Fabric	1
Test 4	Metal	1

Results

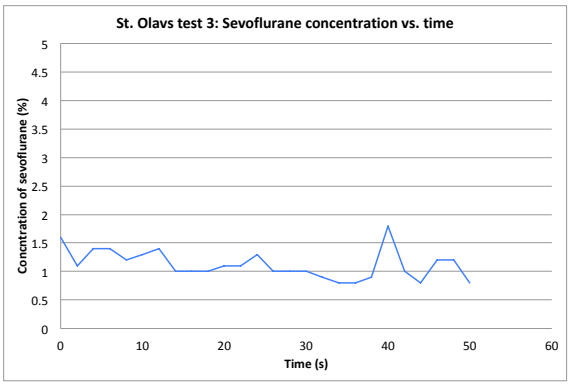
For the first test, using a continuous flow, the pump was found to inject a proportional amount of sevoflurane. Figure 5.12a, 5.12b, 5.12c, and 5.12d shows the results from Laerdal bag test one, two, three, and four respectively. The first test was started when the concentration of sevoflurane in the breathing tube was 0%. From the figure, it is seen how rapidly the concentration begins to fluctuate around the target concentration. Test one also shows some large fluctuations and jumps in concentration. These happened whenever the Laerdal bag was moved more



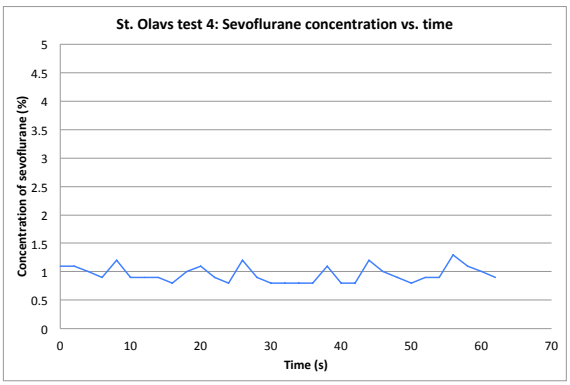
(a) Results from the first test



(b) Results from the second test



(c) Results from the third test



(d) Results from the fourth test

Figure 5.12: Results from testing at St. Olavs

slowly. When the Laerdal bag was not moved, the concentration quickly increased to between 4 and 5%. This indicates that the system is very sensitive to changes in flow rate, and that the system is injecting even when there is no flow detected. This should be solvable by ensuring that the liquid injection stops instantaneously when there is no detected flow.

When using the metal wick there was a high loss of heat which could noticeably be felt when touching the plastic tube. This was not as pronounced when using the fabric mesh. This indicated that the evaporation rate was higher when using the metal wick. However, the heat loss would greatly decrease the subsequent evaporation rate.

From the test results it could be seen that the concentration fluctuated within $\pm 0.2\%$ of the target concentration. It is believed that the accuracy can be increased by improving the system, but that this test shows that the Fenton system, and proportional control *can* function. Some of the reasons for the poor accuracy are listed below.

1. The evaporation was not optimal. The breathing tube was still very cold to touch after about a minute of injection.

2. The sevoflurane may not be sufficiently mixed with the air before getting sampled by the gas analyzer. The gas analyzer was placed quite close to the injection point, which could cause large jumps in concentration. This could be fixed in subsequent testing by increasing the length of breathing tube before the sampling point.

The short test times are a big uncertainty, and it is not known how the prototype would perform over time. In any case, the concentration would probably decrease because of the poor evaporation performance.

Chapter 6

Discussion

This section will present a discussion of the two product development phases: concept generation and prototyping. First, the general product development process will be discussed, then the concept generation method and results, then the prototyping method and results.

6.1 General Product Development

Since the development of the concept was on order by Prof. Fenton, and the parent concept was not to be evaluated or modified throughout the product development process, the scope of possible solutions was limited. It was also evident that some of the subproblems could be solved using existing technology. It is noted that the subproblems did not impact one another. As an example, the choice of liquid handling solutions does not impact which type of gas analyser that should be used. This meant that the general concept selection was driven by finding the optimal solutions to the subproblems, rather than finding a tailor made solution for the Fenton concept.

Following the problem decomposition, a few of the subproblems were chosen for further product development. The focus was broad, with subproblems concerning vastly different fields, like gas analysis of VA and pump technology. This meant that a lot of information had to be amassed through the search phases. In the end, it is believed that the search was satisfactory for the early stage product development, but it is also noted that the broad focus had an impact on the concept generation. In prospective, some subproblems probably suffered from too little research, and thus hastily selection of solutions.

The use of a *New Product Development* methodology like *Fuzzy Front End* was investigated at

the start of the thesis. However, since these methodologies focus heavily on user contact and interaction, and the authors only had access to Prof. Fenton and Dr. Lonnee, this was decided against. Additionally, it was believed that Prof. Fenton, at least in part, had performed some of the steps of a new product development methodology, including the *idea generation*. Instead, the methodology presented by Ulrich and Eppinger was used, with particular attention to communicating and discussing ideas and concepts with Prof. Fenton and Dr. Lonnee.

Prof. Fenton and Dr. Lonnee were contacted throughout the product development process, both to present different concept solutions, but also as a way to get a better understanding of the problem and their input to the solutions generated. Prof. Fenton often presented additional problems of anaesthesia care in LMICs, and it was clear that the topic is very large and complex. Sometimes, Dr. Lonnee and Prof. Fenton presented opposing views, which were very beneficial, as it highlighted which areas to research further.

6.2 Concept Generation and Selection

Before decomposing the Fenton concept, the method of proportional control was presented to Prof. Fenton, and it was stated that this was the best solution. However, it is possible that the control method was selected hastily, and that a more systematic approach would have resulted in a better concept.

Concept generation began with the problem clarification. This process was performed in collaboration with Prof. Fenton, and most of the technical specifications and assumptions were specified together with him. Since the product development is in the early stages it is believed that some of the specifications were unnecessarily included, and that most should be revisited in upcoming iterations of the product development.

Both external and internal search was performed for most subproblems. Focus was directed towards external search if it was known from previous research that the problem could be solved using existing technology, or if the solutions were considered to be technically complicated. Internal search was harder to perform, and therefore less effective, for the more technical problems. The amount of research needed to internally solve the technical problems related to e.g. gas analysis and flow measurement, were believed to require too much time and resources to be doable within the available time frame. Internal search was however applied to other subproblems, like liquid transfer and storage, which seemed to benefit more from creative solutions. The use of medical disposables in the internal search heavily influenced the concept generation

for several subproblems, as it was very useful in order to generate more creative ideas. The use of medical disposables was especially well suited for team work, as it made communication and sharing of ideas more easy. It also allowed the authors to explain the physical concepts more concisely.

The product development team worked both individually and together. It was found that the individual concept generation allowed the creation of more realistic and fleshed out concepts. Team work and brainstorming in the team was found to be useful for a couple of reasons. It was successfully used to generate a high amount of concepts, and was used to more creatively explore thoughts and ideas. This was especially suited for use with the expand-and-focus strategy. Modifications of concept were made and discussed in the group which aided creative concept generation. It was found that performing an individual research before discussing the findings in the team were beneficial to the overall results, which is in agreement with what is presented by Ulrich and Eppinger [65, p. 128-129].

Classification trees were made for all the subproblems. Some were larger than others, and some were used more than others. The liquid transfer and flow measurement classification trees were used the most, where there were a high number of researched concepts. Since the topics were so large in scope, it was very beneficial to get an overview, and by pruning some branches it was easier to direct the concept generation process. For some of the other subproblems, like liquid storage, there were simply not many solutions that were found or concept generated. This meant that the tree was very small, and there seemed to be very little benefit from using it. It may however also indicate that some of these subproblems were inadequately researched.

The concept combination table was used twice in this thesis, once for the liquid handling concept and once for the overall concept. Since many of the solutions were supported by existing technology, and the subsolutions did not depend on each other, the concept combination method seemed to be unnecessary. Most of the combinations were selected based on which subsolutions were deemed the best individually, rather than picking subsolutions that were especially suited with each other. However, with that said, several combinations like the drip-feed liquid handling concept were generated because the subsolutions seemed to compliment each other. These combinations were not presented because of space considerations and because they were considered poorer alternatives than the ones that were presented.

The selection of the concepts was based on pros and cons lists, subjective evaluation, and prototyping. It should be noted that the pros and cons list method relies on both objective and subjective evaluation. Most of the subproblems had clear technical specifications which were

used to *exclude* solutions from further product development if they did not fulfil them. Because of the subjective nature of subjective evaluation, prototyping was preferred as concept selection method. This prototyping was performed with two distinct purposes. First, the concepts were physically evaluated, which was found to be a great way to characterize the performance and usability of the concepts. Secondly, the physical prototyping enabled more creative concept generation and modification of the concepts chosen for prototyping. Several features were added to the concepts in the early prototyping phase.

In addition to pros and cons lists and prototyping, Ulrich and Eppinger present a two-step methodology for concept selection consisting of a concept screening and a concept scoring phase. For each phase a decision matrix is made, which is used to rate and rank different concepts, to help with an objective evaluation and selection of concepts. None of these phases were performed for this thesis, and concepts ended up being chosen based on more subjective evaluations. Since a second concept generation phase had to be performed for the liquid handling subproblem, it is believed that a more objective evaluation would have been advantageous, especially for this problem.

The final concept fulfils the current technical specifications and assumptions made in collaboration with Prof. Fenton. Several concepts were generated during the generation phase, and many are believed to be viable solutions for the Fenton concept.

Although the final concept was presented with the *new* modular boxes solution, specially designed with considerations to repair and maintenance in LMICs, the concept is not yet ready for use in LMICs. The alternative solutions mentioned in Section 3.6 concerning material and design for easy use should be considered for further development. It is also believed that the design of the Fenton device should be performed by a designer. The design for use in LMICs should be considered both when further developing the current solutions, as well as when investigating the other subproblems.

6.3 Prototyping

The final prototype was tested at St. Olavs and was shown to function. Proportional control was used to inject a proportional amount of sevoflurane into the breathing tube. Several special considerations had to be taken when physically prototyping a device for use with a medical drug like sevoflurane. This included making the functional valve container, the tube setup, and the construction for the injection point. Several concepts were generated while prototyping,

and it was found that prototyping was a great way to creatively explore different concepts and solutions.

Because Prof. Fenton had requested a physical product, focus was put into prototyping as many prototypes a possible and to use a practical approach when prototyping. This meant that some of the prototypes were made from readily available material, like the valve container, and that some of the solutions were not further developed because they were considered difficult and time-consumable to prototype. A result of this was that the parallel pump was not selected for further prototyping, while the double pump was. Since the double pump and parallel pump concepts are very similar, the only difference is the gear setup, it is possible that this practical approach of basing further prototyping on how easy the prototyping is can have resulted in sub-optimal solutions.

Some of the prototypes were made with experimentation in mind. Some of these include the set-based peristaltic pump, the valve container, and the drip-feed mechanism. These were all made with the intention of qualitatively evaluating the concepts by playing around with different configurations and prototyping creatively with modifications made iteratively, as a way to improve the concepts. Scheduling was not as strict for these prototypes, as it was quite hard to schedule for creative ideation using prototypes. It is believed that all of the mentioned prototypes benefited from this type of prototyping. However, some other creative prototypes, like the offset pump, were found to not contribute to the overall product development. It is believed that this is due to poor planning and scheduling.

The prototypes were continuously tested, which ended up stealing time from the product development process. The flow measurement system was tested to find the characteristic constant of the flowmeter, and the liquid handling was tested to verify that the flow rate was correct. These tests were also performed with a practical approach, in that they had to be performed to make the prototypes usable. The time spent on testing the flowmeter and liquid flow rate far exceeded what was expected when planning the tests. Since so many tests were performed, a conscious decision was made to spend time on the programming of the microcontroller before and after these tests.

Programming of the microcontroller was performed for the flow measurement and liquid handling prototyping. A functional prototype of the proportional control program was made within weeks of starting the thesis, and the rest of the time was spent making iterative changes and optimizing the program. It is believed that the programming of the Arduino was sufficient for the early stage product development, but it is noted that the program could have been written

more efficiently by actual programmers.

Rapid prototyping was used throughout the prototyping. It allowed rapid modification of prototypes, and made it easy to practically prototype the liquid handling concepts. Most of the concepts had to be tested to evaluate them, and the prototyping was characterized by physical modeling. Sometimes, the analytical models were sufficient to evaluate a concept. The analytical models were also used to great effect when communicating with Prof. Fenton.

6.4 Limitations of the Study

The product development methodology presented by Ulrich and Eppinger [65] was used as the main method for this thesis. Several other methodologies exist, and if the methodology used was unsuited for this problem the results may be sub-optimal.

Both authors have no previous knowledge of neither anaesthesia or problems concerning anaesthesia in LMICs. This lack of knowledge meant that the authors had to rely on Prof. Fenton for guidance. Focus was therefore directed to finding solutions for the subproblems, rather than the parent concept solution itself, which may not be the optimal one.

The time available for the thesis limited the amount of research. Even so, the scope of the thesis was extremely broad, and several subproblems were selected for concept generation and prototyping. The flow measurement and liquid handling subproblems were considered the critical subproblems that *had* to be solved first. Because of the time restrictions, the broad scope meant that some of the subproblems might have been inadequately researched, and the selection may have been performed too hastily.

Because the resources were not available to perform a scientific test, the testing at St. Olavs was performed more as an experiment. This meant that the performance of the Fenton concept prototype could not be adequately characterized.

Chapter 7

Conclusion

This thesis has presented the early stage concept generation and prototyping of a new type of digital vaporizer proposed by Prof. Fenton. The Fenton concept was decomposed into several subproblems which were evaluated and prototyped using product development methodology. The early stage prototyping was used to evaluate how the concept behaved. Experimental testing was performed at St. Olavs to qualitatively evaluate the concept. Results were presented to Prof. Fenton for further product development considerations.

The concept generation was performed using the five step model presented by Ulrich and Eppinger. Through use of the method, the concept was decomposed into subproblems which were evaluated to find alternative solutions. Research was performed to find both existing technology and new, creative concepts. The proposed concept solution is supposed to inject liquid anaesthetic agent proportional to the breathing of a patient. A gas analyser is used to adjust the injection rate based on the concentration of anaesthetic agent in the breathing tube. Several other feasible concept solutions were generated, and it is believed that several solutions can be made.

Prototyping was performed as a way to select concepts, to generate new concepts, to modify existing concepts, and to evaluate the concepts. Because of time restrictions, gas analysis was included only in the concept generation phase and not in the prototyping phase. Several functional prototypes were made using rapid prototyping, and micrcontroller and electrical components. These were tested and evaluated, and a comprehensive prototype was made to evaluate the proposed concept solution generated in the concept generation phase.

Final testing was performed at St. Olavs using the anaesthetic agent sevoflurane, and results

indicate that the concept is feasible and that the prototype was functional. Since testing with sevoflurane requires testing permits, the tests were performed with Dr. Lonnee. Further testing is required to characterize the prototype performance.

In this thesis, one alternative concept solution has been proposed for the Fenton concept. Since the Fenton concept was not evaluated in its entirety and the proposed solution only concerns some of the subproblems, we conclude that research question one has been answered in part. The second research question can at the time not be answered conclusively. It is believed that the prototype has to be developed further, and tested to qualitatively examine the performance and compare it to the draw-over vaporizer performance. Based on test results, the prototype performed close to the performance of a draw-over vaporizer, with an accuracy of ± 0.5%. It is believed that the accuracy of the Fenton concept can be improved through better construction of the current solution and with the inclusion of a gas analyser. The third research question has also been answered in part. A few solutions, like the modular concept and robust construction, have been proposed to make the Fenton concept usable in LMICs. It is believed that the concept has potential to be used in LMICs, given that further product development focuses on ease of use, robustness, and general usability for LMICs.

7.1 Recommendations for Further Work

The Fenton concept was decomposed into subproblem, of which only a few were chosen for concept generation and prototyping. Going forward, more of the subproblems should be evaluated. It is proposed that this should be performed as quickly as possible, to ensure that the existing and new subsolutions are usable with each other. Gas analysis is considered the most urgent subproblem to investigate.

Testing was performed qualitatively and experimentally. Further testing should be performed, both of the current prototype and of a new prototype with a gas analyser. It is considered especially important to evaluate whether gas analysis can be used as feedback to adjust the injection rate of liquid anaesthetic agent.

Most of the solutions generated in this concept did not consider design for use in LMICs. It is proposed that further evaluation is performed on the existing solutions to design them better for use in LMICs. The existing solutions should be investigated to find ways to creatively design the physical form of the liquid handling concept and flow measurement concept to include robust design and materials. Product development of the subproblems that were not consid-

ered for this thesis should heavily investigate the possibilities of design for use in LMICs. This particularly concerns the interface, battery, and physical design of the Fenton device.

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Appendix A

Acronyms

VA Volatile agents

LMIC Low and middle income countries

HIC High income countries

UAM Universal Anaesthesia Machine

BED Big Easy Driver

Appendix B

Appendix

Additional Information on the Master's Thesis

B.1 Prototype: Offset Pump

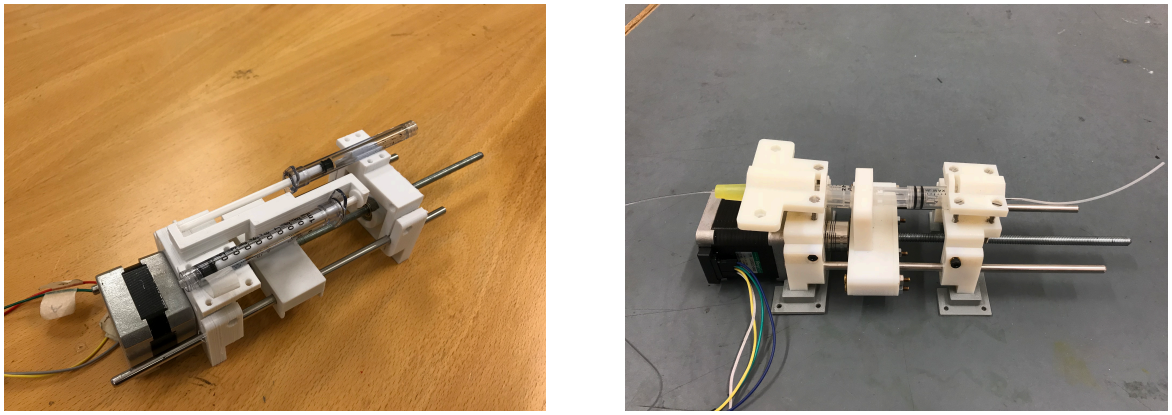
Planning

While prototyping the double syringe pump, it was noticed that the pump was relatively large. A few alternative designs were made with the intention of making the system smaller. It was decided to 3D model and 3D print one of the alternatives.

The purpose of this prototype was to verify that the alternative concept could work. It was also prototyped to show Prof. Fenton that the pump could be made smaller. The purpose was therefore both learning and communication. Both the 3D model and the physical model were considered the same prototype. It was decided to not prioritize this prototype, but to rather make it as quick as possible. The final prototype was planned to be finished within five days with most of the time spent on it while other prototypes were 3D printed. Testing would be performed by a qualitative evaluation of the pump.

The experimental plan was:

1. Make the 3D model of the concept
2. 3D print the pump
3. Evaluate the pump qualitatively



(a) The offset double syringe pump (b) Double pump with the Animas cartridge

Figure B.1: The offset syringe pump and Animas syringe pump

Execution

The 3D model was made by modifying the PLA double syringe pump model and was finished in about one day. 3D printing was also fast, with the printer settings set to draft mode with a layer height of 0.3 mm. It was decided to only 3D print three of the components, which meant that syringes could not be mounted to the pump. The prototype was worked on intermittently. A large pause was taken from the prototyping while working on the double syringe pump and testing of the flow rate range.

Results

Figure B.1a shows the *offset double syringe pump*. The pump was specifically made for the 1 ml Luer lock syringe, which are quite long. By offsetting the pusher, the syringes can be placed more in parallel, which will shorten the length of the pump.

At a later date, another way to decrease the size of the pump was found. The design is shown in Figure B.1b. The pump uses the 2 ml Animas cartridge which were obtained at the Medical Technical department. The Animas cartridge has a plunger that can be completely pushed into the cartridge house. By using this cartridge the pump could be made even smaller than the offset pump. In the end, it was decided that there was not very much to be gained from making the pump slightly shorter. There are other ways of decreasing the size of the pump, which can be more thoroughly investigated at a later time.

B.2 Incremental Changes in Prototyping

Several iterative changes were made most of the prototypes. For the flow measurement this mostly concerned the programming of the microcontroller. For the liquid handling, incremental changes were made to the 3D model and 3D prints of the liquid transfer concepts, in order to improve the performance.

As an example, Figure B.2 shows some of the changes made to the the pusher. First, the pusher was made to simply push the plunger of a syringe. This was made to test the pushing, with no regard to pulling the plunger back. To speed up the printing process, the pusher was made thinner than the original design. The pusher was then made to hold *two* 50 ml syringes so that the plunger could be pulled back. The third pusher is made with screw holes, so that plastic pieces can be fastened over the plunger. Six holes are included so that several different plastic holders can be fastened. The different holders were used to test the different syringe sizes. Up until this point, the pusher was around 10 mm thick, which meant that it could be 3D printed very quickly. These pushers were used *without* any linear bearings. This was only done to speed up the prototyping process. The fourth pusher has the thickness increased to make place for the linear bearings. The fifth pusher includes one locket to tighten the screws. This also made it very easy to change the linear bearings. The sixth iteration shortened the pusher height. At this time the 1 ml Luer lock syringe was chosen, and the height was lowered to reduce unnecessary printing time. Similar changes were also performed to the double syringe pump *motor face* and *end piece*.

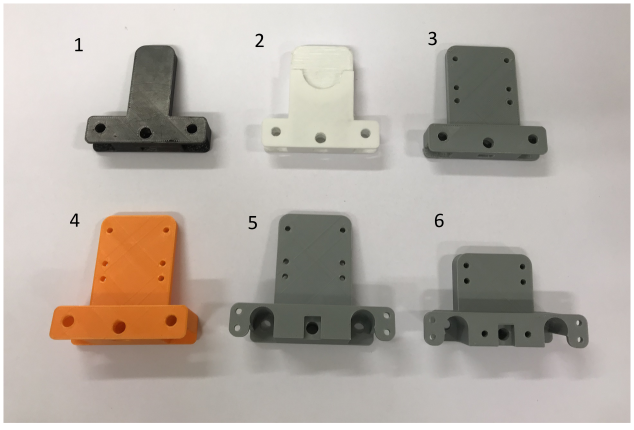


Figure B.2: Changes made to the pusher design from the very beginning of prototyping to the end

B.3 Pressure Testing of the Double Pumps

Testing was performed by connecting the liquid tube to a differential pressure sensor. A three way connector was used to connect the syringe tip to the MPX5010DP differential pressure sensor and a different liquid tubes. This enabled the MPX5010DP to record the *pressure changes* in the system. The zero-condition values were not the same for all tests, so the tests do *not* show the actual pressure in the system, but rather the changes of pressure when the syringe pump is run.

Results

Figure B.3 shows the results from the pressure test performed with both the acrylic pump and the PLA pump. The graphs show the pressure inside the liquid tubings tested for different cases. Again, it is noted that the pressures were not zero-calibrated before testing and the graphs do *not* show the actual pressures in the tube but rather the pressure changes when pumping.

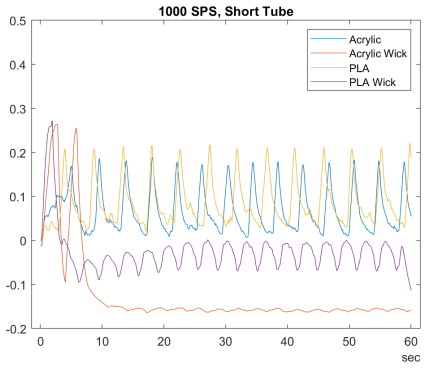


Figure B.3: Results from the pressure tests

The figure shows the pressure for both the PLA pump and the acrylic pump, when water is injected directly into air without anything touching the tip, and when water is injected onto a piece of tissue paper, simulating the function of a wick. It can be seen that there is very little difference between the two pumps when pumping into thin air. The graph shows that pressure builds up before falling down again. This was consistent with drips dropping from the tubing tip. It is not known whether this is caused by capillary action and surface tension or by the linear movement of the system. For the tests with the tip touching the paper the pumping is much smoother using the acrylic pump compared to the PLA pump. While the PLA pump still shows some pulsating injection the acrylic pump injection is almost completely continuous. It is therefore believed that the acrylic pump moves more smoothly. It was also beneficial to again verify that the wick helps smooth injection.

B.4 Arduino Program

The final Arduin program was used for the tests at St. Olavs. A priming function was included, which would be used at the beginning of an operation. The function was semi-manual, and when it is run it moves the pusher in one direction until the key 's' is pressed on the keyboard. This way, the priming could be controlled during the testing.

The main function was set up so that the pusher would move in one direction, and when it reached the other end it would reverse and go the other way. This could also be stopped by pressing 's'. To ensure that the pusher starts moving in the right direction after stopping the pump a system of Boolean operators was used so that the pump would always know which end it was at. It was found that moving the pusher 70000 steps was a good amount for the pusher to reach the other end of the pump without crashing into it. The program would set the current position of the motor to 0 when it was at either end of the pump, and instruct the motor to turn 70000 steps before reversing.

Appendix C

Pre Master's Thesis

NTNU
Norwegian University of
Science and Technology

Evaluation of a New Anesthetic Vaporizer Concept

Tuva Kristine Østby

Jacob Søgnen Jensen

December 2017

PROJECT THESIS

Department of Mechanical and Industrial Engineering

Norwegian University of Science and Technology

Supervisor: Knut Einar Aasland

Preface

This project paper is written as a part of the study program Mechanical Engineering, and Product Development and Materials Engineering at the Norwegian University of Science and Technology. It was carried out during the autumn semester of 2017, and will be continued in a Master's thesis.

Trondheim, 2017-12-13

Tuva Kristine Østby

Trondheim, 2017-12-13

Jacob Søgnen Jensen

Acknowledgment

First, we would like to thank our supervisor, Knut Einar Aasland, for continuous support throughout the process.

We would also like to thank Dr. Paul Fenton and Dr. Herman Lonnee for their invaluable guidance through the field of anesthesia. This project would not have been possible without them. We are very gratefully for getting to work with experts in their field.

Lastly, we would like to thank Richard Fiedorowicz, for letting us visit his factory. The visit was both exciting and valuable for our understanding of anesthesia equipment.

T.Ø & J.J.

Summary and Conclusions

In this project, two topics have been thoroughly researched. The anesthetic vaporizer used for inhalational anesthesia, and the current situation with anesthetic care in low and middle income countries. Based on the research, an evaluation of a new vaporizer concept was performed.

From a technical standpoint, it is possible to make the device. In theory, the device is also possible to use in low and middle income countries. No conclusion is drawn as to the performance or the cost of the device, or to the practical usability in low and middle income countries.

Contents

Chapter 1

Introduction

1.1 Challenges with Anesthesia Care in Low and Middle Income Countries

Meara et al. [45], from the Lancet Commission on Global Surgery, estimates that "5 billion people lack access to safe, affordable surgical and anaesthesia care when needed". Almost 17 million lives per year are lost because of conditions that are treatable with adequate surgical care [45]. Dr. Paul Fenton, formerly Professor and Head, Department of Anaesthesia, College of Medicine Malawi (1986-2001), experienced first hand the problems anesthesiologist in low and middle income countries (LMICs) face daily. This project has been a collaboration with Dr. Paul Fenton and Dr. Herman Lonnee, anesthesiologist at St. Olavs.

One of the problems related to anesthesia in LMICs is that the anesthesia machines used for inhalational anesthesia are often unusable in LMICs. Modern anesthesia machines are useless without a supply of electricity and pressurized gas which is unstable or lacking in many LMICs [8]. One of Dr. Fentons solution was to invent and develop an anesthesia machine that can function without pressurized gas and for several hours without mains electricity. He called the machine the *Universal Anaesthesia Machine*, or the *UAM* [72]. The problem of adequate surgical care is grand in scale globally, and so even with the UAM there are still a multitude of problems with anesthesia care in LMICs.

A specific problem which was presented to us by Dr. Fenton is the draw-over vaporizer. A vaporizer is used to evaporate anesthetics so that it can be inhaled, and the draw-over type is regularly used in LMICs because it is the only commonly found vaporizer type that can function without pressurized gas. The draw-over vaporizer is not very accurate, has a tendency to over-deliver anesthetic agent at low gas flows, and is unreliable at high and low temperatures [28].

Other problems with equipment in LMICs is that it has to withstand rough use, have a long life span, and have a low cost. Additionally, according to Dr. Fenton, to be able to sell a piece of equipment to LMICs it has to look and feel modern. John Anner, the president of East Meets West, a non-governmental organization focused on health in Asia and Africa, seem to agree. He states in a bulletin of the WHO that "Devices need to look modern, so that hospitals are proud to use them and patients feel that they are receiving the proper treatment" [80]. In one of our many conversations with Dr. Fenton, he explained that it is much easier to sell a device to LMICs if the device is usable in high income countries (HICs) as well. Often, modern machines that look good are bought or accepted as donations even if these can not be used in practice. These machines are thrown out or stowed away while old or alternative equipment is used instead. This is why it was very important for Dr. Fenton to get the UAM CE-marked[1].

Dr. Fenton has made a concept for a new type of vaporizer he thinks can perform better than the draw-over vaporizer. It would have to be accurate, safe, and saleable. Together with Dr. Herman Lonnee, Dr. Fenton contacted NTNU to see if anyone could develop and build his concept device.

The definition of LMICs used in this text is taken from The World Bank, which splits economies into four categories based on gross national income (GNI): low-income[2], lower middle-income[3], upper middle-income[4], and high-income[5] [6]. When discussing LMICs, it is important to remember that the categorization is extremely broad and based entirely on

[1] Certification mark for the European Economic Area
[2] less than $1,005
[3] between $1,006 and $3,955
[4] between $3,956 and $12,235
[5] $12,236 or more

economics. Even though the problem of inadequate anesthesia care is close to global, the problems that each individual country face can be vastly different. These problems depend on economic situation, social and physical environments, and a wide array of other factors. Even within a country there will be huge deviations in the standards of surgical care. When discussing LMICs in this project it is our intent to paint a general picture of a near global situation, and not to thoroughly explain the intricate individual problems that each country faces. In the literature we have researched, the term LMICs is often used even when the article discusses mostly LICs. If a country specific example is used, the country will be specified.

1.2 Problem Formulation

> The goal of this project is to research anesthetic vaporizers and the challenges associated with anesthesia care in LMICs, and to evaluate a new vaporizer concept by Dr. Fenton, to see if it is possible to make it and if it could be usable in LMICs.

The project will begin with a broad research phase where two topics will be researched:

- Inhalational anesthetic vaporizers
- The situation of anesthesia care in LMICs

After the research phase, the concept by Dr. Fenton will be presented and evaluated to see if:

- It is possible to make the device
- It is possible to use it in LMICs

The device will be compared with the draw-over vaporizer which is currently used in LMICs and the AnaConDa which in theory can be used in LMICs, to see if the device can compete with it. Although the device should be usable and marketable in HICs as well, this project will only evaluate the usability of the concept in LMICs. Based on the evaluation,

recommendations will be given on whether the device should be developed further.

1.3 Method

Several different methods were used to increase our understanding of the medical problems that LMICs face. We spoke to Dr. Paul Fenton and Dr. Herman Lonnee, anesthesiologists who have both worked in LMICs. A large literature search on the current medical situation in LMICs was performed. To be able to evaluate the concept device presented by Dr. Fenton, a separate literature search on commonly used inhalational drug delivery systems was performed to get a technical understanding of existing solutions. The concept device was evaluated using product development methods, and compared with vaporizers currently used in LMICs.

The project began with a meeting with Dr. Herman Lonnee. We were introduced to the problems of anesthesia in LMICs and to a concept for a new type of vaporizer created by Dr. Paul Fenton. Lonnee showed us around in an operating theatre at St. Olavs hospital. We were shown a high-end anesthesia machine connected to a breathing circuit, and were explained the basic principles behind anesthesia. Lonnee also donated some anesthesia equipment that could be disassembled to examine the internal mechanisms. The donation included two different vaporizers, another delivery device called the AnaConDa, as well as an old anesthesia machine.

Since we had no prior insights into the field of anesthesia Dr. Lonnee and Dr. Fenton supplied us with articles from academic journals and chapters from books on anesthesia. They have both worked with anesthesia in different LMICs, and first hand accounts of their experiences were also very helpful. It gave us a more vivid and clear overview of the problems with anesthesia in these countries. During these conversations, phrases and words used in the field of anesthesia was picked up, and used in further research. To further familiarize ourselves with the subject of anesthesia and vaporizers, a literature search was conducted.

Literature Search

When researching a complex topic like anesthetic vaporizers it is important to use good quality sources. We used the NTNU literature search database ORIA [56] extensively in our research phase. Although results from ORIA and other databases often overlap, some results are exclusive to specific databases. Therefore, we used a selection of other databases, like Scopus/Elsevier and MEDLINE/PubMed. Some specific literature search examples and important considerations for our searches are included in Appendix B, Section B.1.

Visit to OES Medical

When planning the project we were invited to Oxford, England, for a visit to a factory that manufactures anesthesia equipment. The business visited was OES Medical, run by Managing Director Richard Fiedorowicz. In addition to manufacturing high-end equipment for western use, they manufacture the Universal Anesthesia Machine (UAM) for Gradian Health, which was developed by Dr. Fenton. We were given a tour of the factory with the possibility to speak to staff freely. We learned a lot about the technical challenges of anesthesia equipment manufacturing. At the factory Dr. Fenton presented his concept, and we discussed the benefits and challenges of the concept.

The visit was very productive, and we left with a better comprehension of the development and manufacturing of anesthesia equipment. The insights we got, especially into the different vaporizers they manufacture as well as the technical electrical system they develop were truly invaluable.

Concept Research and Development

Our planned project is to evaluate if the concept device can be made, and if it can be usable in LMICs. Before evaluating the concept, it will have to be more narrowly specified. Therefore, further concept development will be performed. The concept development model explained in the book Product Design and Development, by Ulrich and Eppinger [77] was used.

Ulrich and Eppinger [77, p. 14] presents a *product development process*, which consists of: planning, concept development, system-level design, detail design, testing and refinement, and production ramp-up. The phase that this project will focus on is the concept development phase. Ulrich and Eppinger lists several activities that can be undertaken in this phase, which are shown in Figure 1.1. It is important to mention that all activities in the concept development phase are iterative in nature. This means that any phase may be performed multiple times to achieve a good result. The two activities this project will look at are:

1. Identifying customer needs
2. Concept generation

The second activity in this list has already been done by Dr. Fenton, so our case is slightly different than a normal concept development case. Instead of generating the concept based on the customer needs and target specification, as is normal, the concept presented by Dr. Fenton will be measured against the customer needs to see if it suitable for use in LMICs. The concept will also be evaluated in terms of feasibility, that is if it is possible to build a working device.

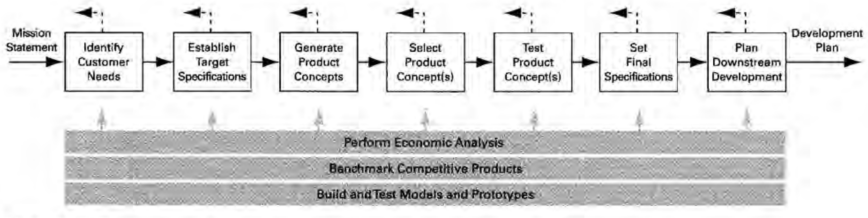


Figure 1.1: The concept development process

Chapter 2

Anesthesia

To understand the principles of an anesthetic vaporizer it is useful to first know what anesthesia is, and how it works. Hore and Harley defines anesthesia as "the pharmacologically induced lack of sensation" [33, p. 3]. It is mainly used to allow the performance of painful or discomforting medical procedures. Anesthesia is divided into three main categories: general, regional, and local anesthesia. General anesthesia is achieved by intravenous induction of anesthetics, by inhalation of anesthetic gases, or by a combination of the two [73, p. 354]. Inhalational anesthesia is the most common administration technique [18, p. 67]. This project will focus on inhalational anesthesia.

2.1 Inhalational Anesthetics and Gases

For inhalational anesthesia, an anesthetic agent is inhaled by the patient [66, p. 557]. The most commonly used anesthetic agents in HIC are the volatile agents sevoflurane, desflurane and isoflurane [81] [40]. According to Smith [66] "Volatile anaesthetic agents are liquids with a low boiling point and high saturated vapour pressure (SVP) so that they evaporate easily". Another volatile agent, halothane, is often used in LMICs because of low cost compared to other volatile agents [46, p. 27]. Although diethyl ether is no longer used in modern anesthetic practice for safety reasons, it is still used in LMICs due to low cost [46, p. 27].

Because of the high potency of modern agents, the anesthetic agent vapour has to be diluted with what is called a carrier gas, which is often a mix of air, oxygen and nitrous oxide [18, p. 42]. The carrier gas mixes with anesthetic vapour in the anesthesia machine, and is delivered to the patient through a breathing system. The use of nitrous oxide will be discussed briefly in Appendix B, Section B.2.

When the carrier gas mixes with anesthetic vapour, the volume percent of the carrier gases is reduced. Since a certain amount of oxygen is crucial to keep a patient alive, including a proportion of pure oxygen as the carrier gas is favoured. It is possible to use ambient air as carrier gas, but since the oxygen concentration in air is 21 vol.% [75], care must be taken to avoid delivery of a gas mixture with an inadequate amount of oxygen. To ensure the oxygen concentration in the gas mix, an oxygen analyzer should be used. It will alert the operator when a lower oxygen limit is reached [52].

According to Dr. Lonne[1], *fresh gas flow* is used to describe the mixture of anesthetic agent vapour and the carrier gasses.

2.2 The Anesthesia Machine

According to Ward [18, p. 67], the modern anesthesia machine is used to "accurately and continuously deliver a safe mixture of gasses and vapours for the administration of anaesthesia". The dilution of anesthetic agent vapour with carrier gas takes place in an anesthesia machine. Modern anesthesia machines, like the Astra 3i shown in Figure 2.1, depend on a continuous flow of high pressurized carrier gas to function [18, p. 68-69]. Carrier gas is fed into the machine from cylinders or from a piped supply. Some hospitals use oxygen concentrators which extract oxygen from room air [18, p. 1]. There are some anesthesia machines, like the already mentioned UAM, that can use room air as carrier gas.

From the supply connection of the back of the machine the carrier gas flows through pressure regulators [32]. The pressure regulators ensure that high pressure from the supply is reduced

[1]Email correspondence 2017-12-10

Figure 2.1: The OES Medical Astra 3i [49]

to a constant, low operating pressure, so that no high-pressurized gas will reach the patient or damage the machine [32]. Gas flow measurements and control devices are also present [65]. Further, the gas flows through a vaporizer. The function of the vaporizer is to evaporate the liquid anesthetic agent and to mix it with the carrier gas [66, p. 837]. How the carrier gas is mixed with the anesthetic vapour differs between different types of vaporizers, and will be discussed in Chapter 3.

Vaporizer are either permanently mounted to what is called the backbar of the machine, or mounted with a manifold system, with the latter being more common in modern machines [18, p. 81-83]. In modern manifold systems, vaporizer are detachable, which enables for easy removal and replacement with different vaporizer models. Depending on the model, an anesthesia machine can be fitted with one or several vaporizers. The manifold is often fitted with a *safety interlock system* which ensures that only one vaporizer is used at a time. After mixing with anesthetic vapour, the fresh gas flow exits the machine and flows into a breathing system.

Most modern anesthesia machines operate with integrated safety features [18, p. 66] with

audible alarms which are set to proper levels prior to initiation of anesthesia [13]. An example is the oxygen failure warning device, which activates if the pressure of the supply reaches a critical level [30]. As mentioned previously, an oxygen analyzer can be used to ensure a proper amount of oxygen is being delivered to the patient [70] [13].

2.3 Breathing system

A breathing system is used to direct the gas to the patient [66, p. 841]. It is usually set up so that the carrier gas containing anesthetic agent flows through plastic tubing from the anesthesia machine, and into a sealed mask connected to the patient. The modern breathing systems used with anesthesia machines can be categorized as *rebreathing*, and *non-rebreathing* [66, p. 841-842] [18, p. 107-108]. According to Ward [18, p. 107], it is normal to define rebreathing as rebreathing of any of the expired gases, including CO_2, water vapour, anesthetic agent and oxygen. Which system is used depends on availability of equipment, and the preference of the anesthesiologist.

Because the expired gas from the patient contains CO_2 and anesthetic agent, rebreathing of CO_2 should be avoided. In a rebreathing circuit, rebreathing of exhaled gas is possible, but can be avoided by using high fresh gas flow rates to flush out the expired gas [18, p. 108].

Non-rebreathing circuits are set up so that rebreathing of CO_2 is prevented, either with a non-rebreathing valve or with a CO_2 absorber [18, p. 107-108]. A non-rebreathing valve will direct the expired gas away from the patient and out of the breathing system, leaving the inspiratory limb free from expired gas. If a CO_2 absorber is placed in the breathing circuit, CO_2 is removed from the expired gases. This enables the reuse of expired anesthetic agent and oxygen, and is used in the circle system, which will be discussed in Section 2.3. This reuse of anesthetic agent and oxygen should *not* be confused with re-breathing of expired gases. The difference is that the expired gas has to be modified, with the CO_2 absorber to be reusable.

Low-flow Anesthesia and the Circle system

According to Baum [7], "low-flow anaesthesia has become the acknowledged method of performing inhalational anaesthesia". Lucangelo et al. [44] echoes this sentiment that low-flow anesthesia is increasing in popularity, and explains that it is because of "economic and environmental reasons". Some advantages to low-flow anesthesia is heat and moisture conservation, which is beneficial for the patient, and less anesthetic agent and gas consumption [5]. Both advantages scale with lower flows.

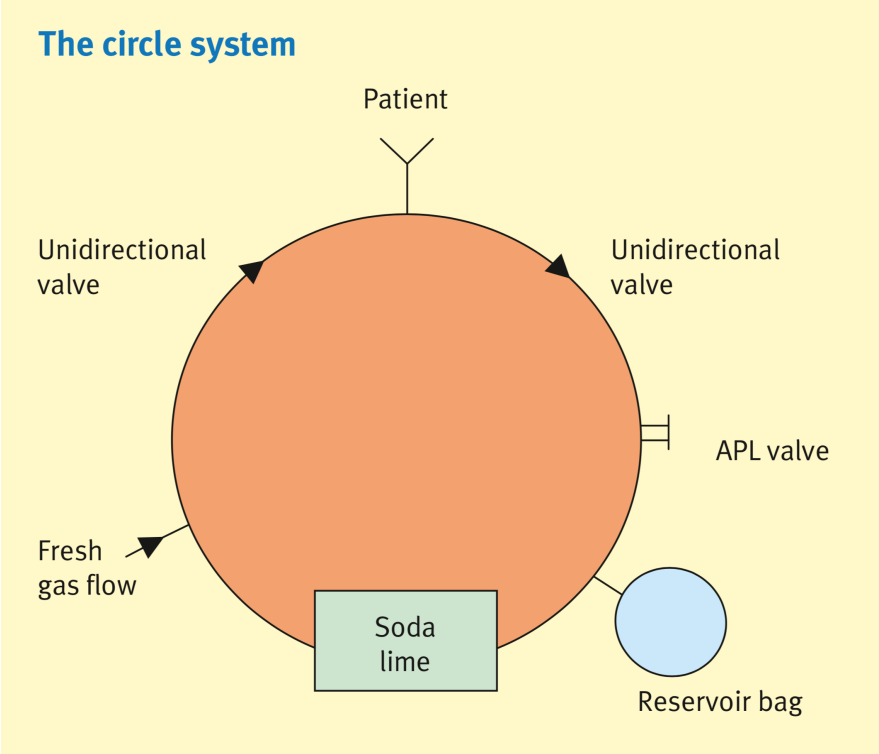


Figure 2.2: Schematic of the circle system [15]

One type of breathing system that enables the use of low-flow anesthesia, is the *circle system*. A schematic of the system is shown in Figure 2.2. As the name implies, the circle system is a breathing system where the components are arranged in a circle. When the patient expires, the gas passes through a CO_2 absorber that removes CO_2 from the gas[2]. The rest of the gas is now mostly O_2 and anesthetic agent, which flows through the circle breathing system and back to the patient. This means that expired anesthetic agent and carrier gas is recycled in

[2]The CO_2 is absorbed by what is called soda lime

(a) Bellows being operated [72]

(b) Self-inflating bag [4]

(c) The Penlon AV9000 ventilator [18, p. 303]

Figure 2.3: Three ways to ventilate a patient

the circle system. It is possible to use what is called a *closed flow system*, where the flow rates are as low as the patient uptake [18, p. 127]. Some of the reasons for using a circle system is that it enables the use of low-flow anesthesia, and by recycling the anesthetic agent it offers economical and environmental benefits.

Ventilation

According to Jackson et al. [38, p. 156], "Ventilation is the process by which gases get to the alveoli of the lungs". During general anesthesia, when a patient breathes by their own respiratory efforts it is said that the patient is spontaneously breathing. This mode of ventilation is also called spontaneous ventilation [38, p. 156]. If the patient needs assisted respiration it is called controlled ventilation or mechanical ventilation. For controlled ventilation the operator can either move bellows up and down (Figure 2.3a) or squeeze a self-inflating bag (Figure 2.3b) to ventilate the patient. Alternatively an automatic ventilator, like that shown in Figure 2.3c can be used. There are many different modes of ventilation but they will not be discussed here.

As mentioned, some anesthesia machines can function without a supply of pressurized gas, and only by use of ambient room air [18, p. 486]. Air is then drawn into the system and

through the vaporizer based on patient demand. To enable air to flow through the system, a pressure must be created on the patient site. This can be achieved by spontaneous breathing or by use of a bellows, a self-inflating bag, or an automatic ventilator if electricity is available. This mode of operation can be called a demand system. In contrast, when pressurized gas is used to push the flow through the system it can be called a continuous-flow system.

Chapter 3

Anesthetic Vaporizers

A vaporizer is used to administer inhalational anesthetics to a patient. The purpose of the vaporizer is to evaporate liquid anesthetic agent, and in some way administer this vapour into the gas stream directed to the patient [66, p. 837]. The vaporizer has to be accurate and reliable, with an adjustable output concentration to ensure that the patient gets a "clinically useful concentration" of anesthetic agent [12] [10].

Some alternatives to the traditional vaporizer have been developed. A few of these drug delivery systems will be examined. They are all based on the principle of direct injection of anesthetic agent into the breathing system, and are included because the concept device by Dr. Fenton is also a direct injection system. Although it can be argued that these alternative systems are not true vaporizers since no evaporation occurs inside the device, this text will denote them as such[1].

3.1 Vapour and Gas Theory

To understand the mechanisms of an anesthetic vaporizer, it is useful to first understand the mechanisms of evaporation. According to Smith et al. [66] "vapour is formed from a liquid by evaporation". During evaporation, a fraction of molecules of a substance will escape its

[1]Other articles on the subject also denote these devices as vaporizers

liquid phase becoming vapour [10], and a fraction of the vapour molecules will reverse back to its liquid phase. A substance is said to be *saturated* when the same number of molecules enter and leave the liquid phase [10]. The area in a vaporizer where the anesthetic agent evaporates is called the vaporizing chamber. Modern anesthetic agents are liquid at room temperature but evaporate easily [66, p. 560].

In a closed container like a vaporizer the vapour exerts a pressure on the container walls. If the substance is saturated the pressure is known as the saturated vapour pressure (SVP). The SVP depends on temperature [11, p. 571-572], and if the temperature is known it is possible to find the SVP.

When a substance transforms from liquid to gas, energy is released to its surroundings [10]. If there is no external heat source the energy loss will cause the liquid to rapidly cool down. The temperature of the liquid substance influences the rate of evaporation [11, p. 570]. This means that as the liquid evaporates it cools down, resulting in a decrease of subsequent evaporation. To increase the rate of evaporation of the liquid we can [10]:

1. increase the temperature;
2. increase the surface area of the liquid;
3. increase the removal of vapour molecules form the liquid surface

When the SVP is known, it is possible to calculate the concentration of anesthetic vapour in the vaporizing chamber [10]:

$$\text{Gas concentration} = \frac{\text{Vapour pressure}}{\text{Ambient pressure}}$$

As an example, in atmospheric pressure conditions, the SVP for sevoflurane at 20 °C is 21.3 kPa, which results in a gas concentration in the vaporizing chamber of:

$\text{Gas concentration} = \frac{21.3}{101.3} = 21\%$

Clinically useful concentrations are between 0.5% and 8% sevoflurane in oxygen [26]. 21% is far too high, and the anesthetic agent vapour in the vaporizing chamber has to be diluted to

be usable in a clinical setting. There are two principle types of vaporizers that use different mechanisms to dilute the concentration [12]:

- Variable bypass vaporizers
- Measured flow vaporizers

3.2 Variable Bypass Vaporizers

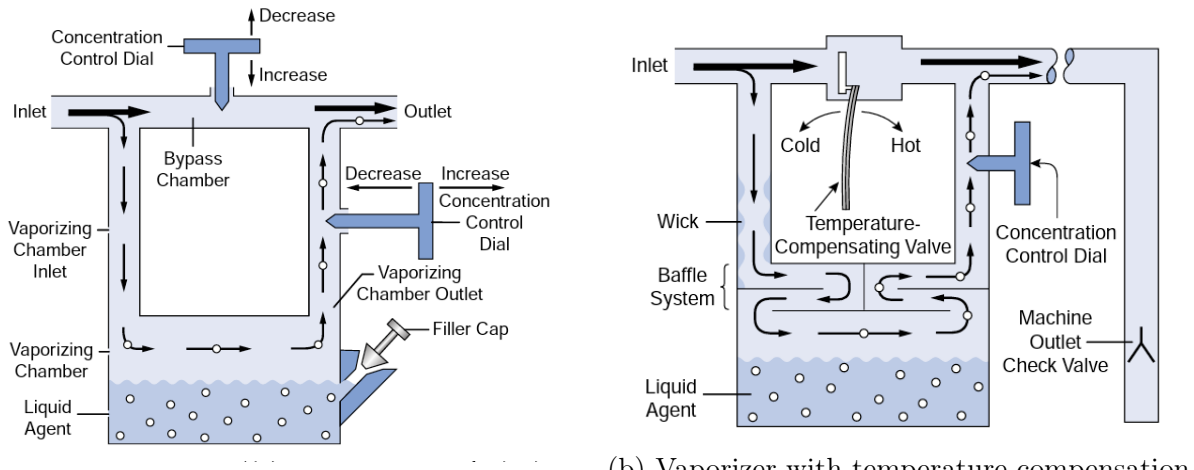
There are two main types of variable bypass vaporizers: the *plenum* vaporizer, and the *draw-over* vaporizer. The physical flow of gas seen in plenum and draw-over vaporizers is very similar, but some of the internal mechanisms and components differ. The plenum vaporizer is the most common type [12] [66, p. 838] and is more accurate than the draw-over [10] [82]. While the plenum vaporizer is dependent on pressurized gas to function, the draw-over vaporizers can function without it and is most useful in areas where pressurized gas is not available [10] [82]. Plenum and draw-over vaporizer will be explained in detail in Subsection 3.2.1 and Subsection 3.2.3 respectively. A separate explanation of plenum vaporizers with electronic control is included in Subsection 3.2.2.

Variable Bypass Vaporizer Components

There are several different variable bypass vaporizer models, all of which are different in some way or another. What follows here is a description of a generic variable bypass vaporizer, which is shown in Figure 3.1a.

Variable bypass vaporizers have one inlet for the carrier gas, and one outlet for the fresh gas flow. The vaporizer unit has a vaporizing chamber, where the evaporation of liquid anesthetic agent occurs, and a bypass chamber where a portion of the carrier gas simply flows through.

Liquid anesthetic agent is filled through a filler port and flows from the port into the vaporizing chamber. Usually a small sight glass is located on the vaporizing chamber, and gives a visual indication of how full the vaporizer is [11, p. 574]. Some vaporizers are made to



(a) Vaporizer without temperature compensation

(b) Vaporizer with temperature compensation

Figure 3.1: Variable bypass, with and without temperature compensation [11, p.571-572]

be used with a specific anesthetic agent and are therefore called agent specific vaporizers. These often have some kind of keyed filler port, which ensures that the right anesthetic agent is used [19] [12]. A concentration control dial is used to specify the target concentration of anesthetic agent wanted in the fresh gas flow going to the patient.

Depending on the model and type of vaporizer, they can include different components and mechanisms that are used to stabilize the output concentration. Some of these components are temperature compensators, wicks, and baffles, all of which are shown in Figure 3.1b. These components will be discussed further in Subsection 3.2.

Method of Action

In a variable bypass vaporizer the carrier gas flowing into the vaporizers is split into two separate streams inside the vaporizer [12] [19]. This can be seen in Figure 3.1. One stream passes through the vaporizing chamber, where it gets enriched with anesthetic agent vapour. The other stream flows through the bypass chamber, bypassing the vaporizing chamber completely. Downstream of the two chambers the streams connect and mix. This is the mixture that is delivered to the patient.

The output concentration of anesthetic is determined by the relative amount of the carrier gas

that flows through each chamber [19] [12]. The concentration control dial controls a variable restrictor that determines the splitting ratio of the streams [12]. For electronically controlled vaporizers the output concentration can be typed into a computer that electronically regulates the variable restrictor.

Physical Properties that Influence Output

There are several factors that influence the output concentration in variable bypass vaporizers. Some important factors will be explained below.

Temperature

A variable bypass vaporizer will experience changes in temperature because of fluctuations in ambient temperature, or because of the energy loss during evaporation [10] [82]. The gas concentration in the vaporizing chamber depends on SVP, and since the SVP depends on the temperature, a decrease in temperature will cause a decrease in output concentration. Two mechanisms are used to try to combat this problem: *temperature stabilization*, and *temperature compensation*.

Temperature stabilization is achieved with a heat sink [82], which is normally a solid mass made of a dense "material with high specific heat capacity" [10], or a hollow container containing such a material. A material with high specific heat capacity will experience less temperature change during evaporation compared to a material with low specific heat capacity [11, p. 571]. The material used for the vaporizer body should also have a high thermal conductivity which is an indication of how well the substance conducts heat. A material with higher thermal conductivity maintains "a more uniform internal temperature" [11, p. 571]. An example of a vaporizer with temperature stabilization is the Oxford Miniature Vaporiser (OMV), which is shown in Figure 3.3. It has a chamber with water and ethylene glycol in the base, which acts as a heat sink [18, p. 59].

Temperature compensation is achieved by increasing the proportion of carrier gas through the vaporizing chamber, which increases the amount of vapour picked up. This actively

compensates for the decreased concentration of anesthetic vapour in the vaporizing chamber due to the cooling of liquid agent. Figure 3.1b shows a generic variable bypass vaporizer with a temperature compensating valve, which increases or decreases the proportion of flow through the bypass chamber, depending on temperature. Several different temperature compensating mechanisms are used in different vaporizers.

Temperature compensation can be achieved both through physical as well as computer controlled mechanisms [82]. In computer controlled temperature compensation the gas flow through the two chambers is simply regulated electronically.

Gas Flow Rate

The anesthetic output concentration depends on the gas flow rate through the vaporizer [10]. At high flow rates the anesthetic agent may not evaporate quick enough. The gas leaving the vaporizing chamber may not be fully saturated with vapour, which results in a drop in output concentration [19]. To ensure adequate vaporization most plenum and some draw-over vaporizers include *wicks* and *baffles*, which increase vaporization efficiency. Wicks can be made from metals, fabrics or synthetic materials [18, p. 48]. As an example, the Diamedica vaporizer has a stainless steel mesh wick. When the liquid anesthetic flows in and around the wicks, the agent is spread out over a larger surface area which increases vaporization efficiency [19], as explained in Section 3.1. Baffles are channels direct the carrier gas closer to the wicks and liquid anesthetic which increases the amount of vapour picked up during high gas flows.

At low flow rates the resistance produced by the variable restrictor will increase [10]. The flow will then take the path of least resistance and more gas will flow through the bypass chamber, which decreases the output concentration [66, p. 839]. This is a problem in draw-over vaporizers [66, p. 839].

Backpressure (The Pumping Effect)

This phenomenon occurs when gas is pushed backwards from the patient side, reversing through the vaporizer [19]. This can cause already saturated gas to flow back, and during the next inspiration, flow through the bypass chamber. The effect is an increase in the output concentration. The pumping effect is largest at low flows. It can be prevented by the use of a one-way valve, a long inlet to the vaporizing chamber, or by having the bypass and vaporizing chambers of equal sizes.

Pressurizing effect

The pressurizing effect is caused by compression of fresh gas during controlled ventilation [19]. When the pressure is released the compressed gas expands. The amount of anesthetic agent in the gas is the same as when the gas is compressed, so the net result is a dilution in output concentration. The effect is largest at high flows.

Hazards and Safety Measures

The use of vaporizers is associated with some risks [11, p. 573-574]. Some of these include misfilling, tipping, using vaporizers in parallel, over- and underfilling of liquid anesthetic, leaks, and electronic failure. Modern vaporizers often include safety mechanisms like keyed fillers that only allow filling from agent specific containers [11, p. 573] and color coding of vaporizers and anesthetic agents, which minimize the risk of misfilling. A more detailed discussion about the hazards associated with vaporizers is presented in Appendix B, Section B.3.

3.2.1 Plenum Vaporizers

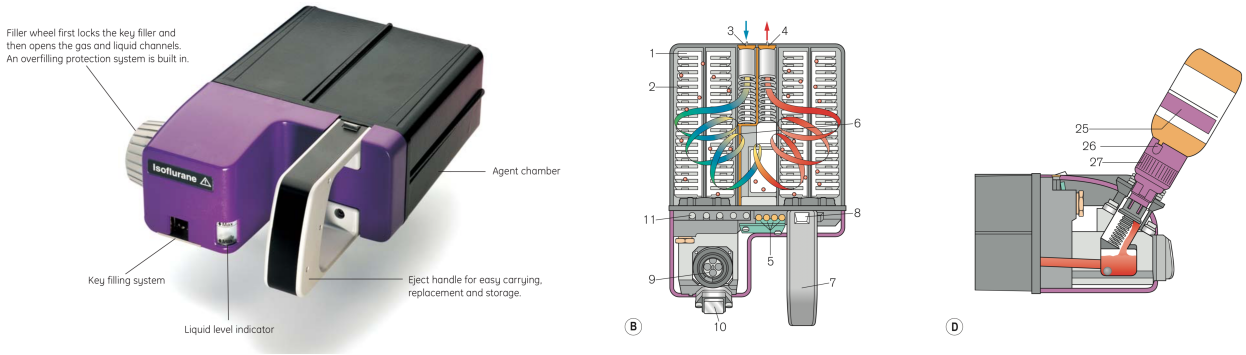
Plenum vaporizers are the most common type of vaporizer found in hospitals [12] [66, p. 838]. They are used with continuous-flow anesthetic workstations. The carrier gas is pushed through the vaporizer by pressure from the medical gas supply or cylinders [19], and is

pressurized in the vaporizing chamber [66, p. 838]. At low gas flows gas may pass along the top of the vaporizing chamber, where it does not pick up enough of the anesthetic vapour. By pressurizing the carrier gas in the vaporizer, the density of the gas is increased which solves this problem of unsatisfactory mixing [66, p. 838] [18, p. 46].

The resistance in a plenum vaporizer is high [12], which means that if the pressure driving the gas is too low, it will not be able to pass through the vaporizer. Plenum vaporizer can therefore not be used without a source of pressurized gas. Most plenum vaporizers are temperature compensated and stabilized, include wicks and baffles to increase the vaporization rate, and are calibrated for a specific anesthetic agent [12]. Plenum vaporizers are more accurate than draw-over vaporizers [10] [82].

3.2.2 Plenum Vaporizers with Electronic Control

Contemporary plenum vaporizers can be electronically controlled. This means that a microcontroller can register physical quantities like temperature, pressure, flow rate and adjust the proportion of flow through the bypass and vaporizing chamber accordingly.



(a) The Aladin Cassette [17]

(b) Internal mechanisms [18, p. 57]

Figure 3.2: The Aladin Cassette

One example of an electronically controlled plenum vaporizer is the Aladin Cassette from GE Healthcare. The Aladin Cassette is shown in Figure 3.2a and 3.2b. A microcontroller is located inside the anesthesia machine, while the vaporizing chamber is a standalone cassette that contains the anesthetic agent [12]. In this system, sensors measure the gas flow, temperature, and the pressure inside the cassette. The concentration output is regulated by a

throttle valve [82]. By measuring the temperature, it is possible to accurately calculate the pressure in the cassette, which is used to calculate the anesthetic agent concentration in the gas [10].

Computer controlled vaporizers are often very accurate. According to the manufacturer, the accuracy of the Aladin Cassette (5% concentration) is "± 0.15% v/v or ± 10% (whichever is greater)" [34]. ± 0.15% v/v means that the concentration will be within ± 0.15% of the target concentration, e.g. 0.85-1.15% if the target is 1%. ± 10% means that the concentration will be between 4.5% and 5.5%, with a target of 5%.

Electronically controlled machines often include safety measures that can not be included in non-electronic vaporizers. For example, in the Aladin Cassette, an alarm message can appear when only 10% of liquid anesthetic agent is left in the vaporizer [12]. The Aladin Cassettes also has one-way valves, which means that the cassettes can be tilted without leakage [82] [12]. It also has a dedicated chamber where the carrier gas and the saturated vapour mixes, which solves the problem of backpressure [10]. Plenum vaporizers with electronic control do not work without electricity or pressurized gas [12].

3.2.3 Draw-Over Vaporizers

In draw-over vaporizers, gas can be drawn through the vaporizer by the pressure created by the patients spontaneous breathing. If the patient is not breathing, a similar pressure can be created with a bellow or a self-inflating bag. The pressure created by the patients spontaneous breathing is low, and because of this, draw-over vaporizers can not have a high internal resistance [82]. Because the flow rate varies with the patients spontaneous breathing, and accuracy depends on flow rate, the accuracy of draw-over vaporizers is poor [66, p. 839]. The OMV, a simple draw-over vaporizer, is shown in Figure 3.3 and Figure B.1 in Appendix B. The Diamedica Vaporiser is shown in Figure 3.4.

Depending on the vaporizer model, draw-over vaporizers can be temperature compensated, have wicks, have baffles, or have some form of temperature stabilization like a heat sink. Some models, like the Diamedica Draw-Over Vaporizer (DDV) and the OMV, can function as both

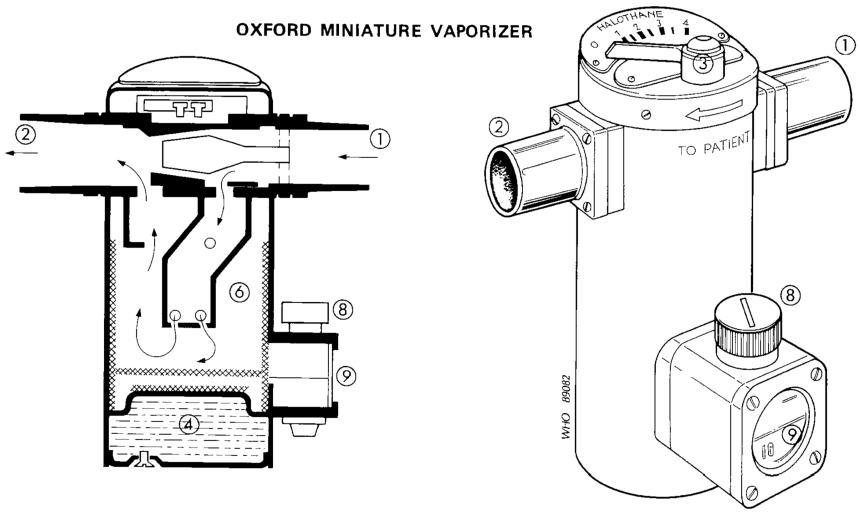


Figure 3.3: The Oxford Miniature Vaporizer [21]

Figure 3.4: The Diamedica Vaporiser [20]

plenum and draw-over vaporizers, which means that they can be used both with and without pressurized gas [24]. Because the resistance has be kept low in draw-over vaporizers, features like wicks and baffels can not be very complex, and are less effective than their equivalent in plenum vaporizers [10]. In contrast to plenum vaporizers, the vaporizing chamber in a draw-over vaporizer is not pressurized. This means that some gas can pass along the top without picking up any agent vapour [66, p. 838].

According to Dhulked et al. [19] draw-over vaporizers are "robust, portable and better suited for field anesthesia". Some draw-over vaporizers, like the OMV and DDV, have smaller agent capacities than most plenum vaporizers. This means they may have to be topped up during use, which increases the risk of spilling. The OMV has the smallest capacity of 50 ml, while

the DDV has a capacity of 150 ml [24]. Topping up agent during operation will destabilize the output concentration, because the newly added agent has a different temperature than the agent already in the vaporizer [24].

As mention before draw-over vaporizers are less accurate compared to plenum vaporizers [10]. English et al. [24] compared the accuracy of the DDV and the OMV. The team found that, with dial settings of 1-4%, 17% of the DDV tests and 40% of the OMV tests had a real output concentration 0.5% more or less than the target agent concentration[2]. They also found larger deviations from set concentration when using controlled ventilation, with some deviations larger than 1%. According to Ambrisko and Klide [3], it is recommended that vaporizers are accurate within 0.2%. This gives an idea of the poor accuracy achieved with draw-over vaporizers.

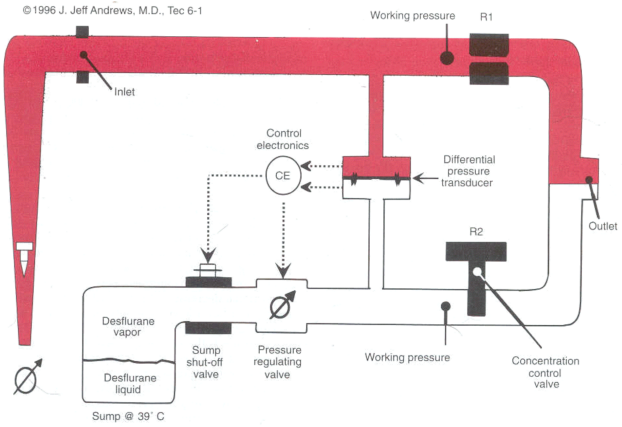
3.3 Measured Flow Vaporizers

The other main category of commonly used vaporizers is the measured flow vaporizer. It can be used with common volatile agents, like sevoflurane and isoflurane, but also works with desflurane which because of its physical properties can not be used with variable bypass vaporizers [7]. Many measured flow vaporizers are therefore made specifically for use with desflurane [12].

Measured flow vaporizers work by directly injecting anesthetic agent vapour into the carrier gas directed to the patient [12], and can therefore be seen as a "gas/vapour blender" [10]. Usually, there are two parallel gas streams. The carrier gas stream going to the patient, and a separate stream that carries anesthetic agent vapour. The stream containing anesthetic agent is administered directly into the carrier gas [10]. To administer the right concentration of anesthetic agent, the injection rate of the anesthetic agent vapour is adjusted to match the carrier gas flow rate [19]. A variable restrictor controls how much anesthetic agent vapour is administered into the carrier gas stream [18, p. 60].

[2]E.g. with a target concentration of 2%, the output concentration can be 1.5-2.5%

(a) The Tec 6



(b) Internal mechanisms of the Tec 6

Figure 3.5: The Datex-Ohmeda Tec 6 [1]

The Datex-Ohmeda TEC 6 vaporizer, which is specifically made for use with desflurane, is shown in Figure 3.5. In this model a differential pressure sensor measures the pressures from both streams. From this it can calculate any change in the carrier gas flow rate. As mentioned, the output concentration going to the patient depends on the ratio between the flow rates of the two stream. This means that the vaporizer can use the measured carrier gas flow rate to calculate the administration rate of the vapour needed to reach the target concentration. This mechanism also allows the vaporizer to automatically adjust the administration rate in case of fluctuation in the carrier gas flow rate. The mechanism is used both to *reach* the target concentration, but also to *stabilize* the output concentration.

In contrast to variable bypass vaporizers, measured flow vaporizers are not temperature dependant. Usually, anesthetic agent in measured flow vaporizers is either heated like in the Tec 6 [11, p. 574], or pressurized and heated like in the Dräger DIVA cassette [48] [18, p. 63]. Any temperature decrease will have little impact on the agent output concentration. Backpressure and the pressurizing effect are not experienced in measured flow vaporizers.

As with variable bypass vaporizers there are hazards related with the use of measured flow vaporizers. There is a risk of misfilling, overfilling, underfilling, and leaks. Modern measured

flow vaporizers often include safety mechanisms like keyed fillers and one-way filler valves. Most measured flow vaporizers are electronically controlled, which have an inherent risk of failure. The inclusion of electronic control often increase the amount of safety features like alarms and automatic shut off if any tilting is experienced [18, p. 60-63].

3.4 Alternative and Experimental Delivery Concepts

There are several other experimental and alternative drug delivery systems for inhalation anesthesia. Three such systems will be explained here, and since they all use what is called target-controlled infusion (TCI) an explanation of this will be presented first.

3.4.1 Target-Controlled Infusion

Target-controlled infusion (TCI) is defined by Ward [18, p. 408] as "a system whereby a computer controls the rate of infusion of a drug to achieve (in as short a time as possible) and maintain any given target concentration". It was first used in intravenous anesthesia with a syringe pump [68], but it can be employed in inhalational anesthesia. It is used in plenum vaporizers like the Aladin Cassettes [61], in measured flow vaporizers like the DIVA [48], and in direct injection of anesthetic agent into the breathing circuit [7]. The latter will be explained in Subsection 3.4.2.

There are several terms used to describe the system of target-controlled drug delivery. According to Egan and Talmage [23], some normal terms used are "computer-controlled infusion pump (CCIP), computer-assisted continuous infusion (CACI), target-controlled infusion (TCI), computer assisted titration of IV anesthesia (CATIA) and model-based drug delivery".

The TCI method is based on pharmacokinetic and pharmacodynamic models to administer anesthetic agent [23] [78]. These models are based on the drug or anesthetic, and its behaviour in a general population [23]. The model is programmed into the anesthesia delivery unit, and the administration rate is adjusted throughout based on the computer model. To administer

the right amount of agent the patient weight, and sometimes sex, age and height has to be input into the computer [18, p. 408].

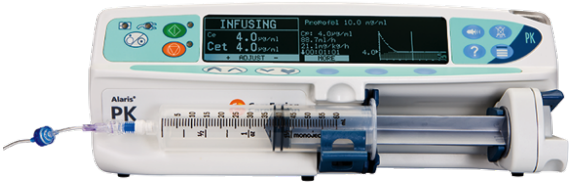
TCI can be used with an open-loop system with no feedback from the patient, or a closed-loop system with feedback [23]. In an open-loop system, the only parameter adjusting the infusion rate is the computer model. In a closed-loop system, a measurement of the effect of the drug in the patient is registered by the TCI unit which adjusts infusion rate accordingly. One measurement of drug effect is called Bispectral Index (BIS), and is a "measurement of hypnotic depth" [69]. Locher et al. [43] found that closed-loop control, isoflurane inhalational infusion, using BIS "performed significantly better than manual control". The Drager Zeus anesthesia machine uses TCI of vapour with "electronic gas and anesthetic agent flow control with closed-loop control system" [48].

Potdar et al. [61] found that less anesthetic agent is used in the GE Healthcare Aisys anesthesia machine during TCI operation compared to manual operation. This decreases cost and pollution. A machine using TCI will self adjust and will therefore require fewer adjustments by the anesthesiologist, which will allow the anesthesiologist to focus on the patient [44].

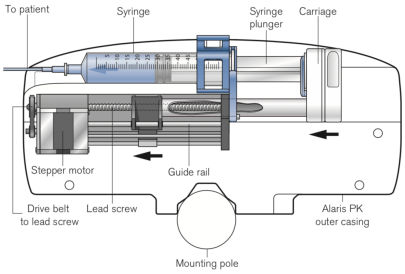
Although the accuracy of TCI systems often surpasses that of manual control systems, the TCI system can never be more accurate than the administration model it uses [23]. Because the administration models are based on the behaviour of a specific drug in a general population, it will always be different in a single patient. Of course, since a syringe pump uses TCI, any system using a syringe pump will experience all benefits as well as problems associated with TCI.

3.4.2 Direct Injection of Anesthetic into the Breathing Circuit

Baum [7] discusses the use of a syringe pump for direct injection of anesthetic into the breathing circuit. The system uses a motor driven syringe pump like the one seen in Figure 3.6, an oxygen supply, a ventilator, and a closed re-breathing circle system. The syringe pump simply injects anesthetic agent at a rate controlled by a TCI model directly into the



(a) Aleris^{TM} PK [47]



(b) Internal mechanisms [18, p. 405]

Figure 3.6: The Aleris^{TM} PK Syringe Pump

breathing circuit.

One advantage of this system is that the administration of anesthetic agent is independent of fresh gas flow, which results in a quicker response to changes in administration of anesthetic agent [7]. On the other hand, to get a rapid decrease in concentration the carrier gas flow rate will have to be increased to flush out the anaesthetic vapour in the breathing circuit. It is possible to use low-flow anesthesia with this system [7].

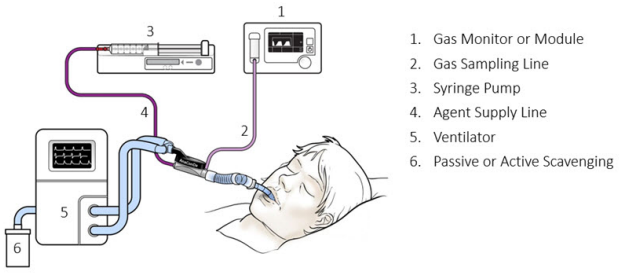
According to Baum [7], there is a "lack of precise control of the gas composition circulating within the breathing system", which is disadvantageous. As a safety measurement against misdosage a gas monitoring system has to be used with this system.

AnaConDa

The method of direct injection of volatile agent into the breathing circuit is also used in the *Anaesthetic Conserving Device*, or *AnaConDa*. As the name suggests it aims to minimize the use of anesthetic agent. The AnaConDa unit, and a recommended set up is shown in Figure 3.7a and Figure 3.7b respectively.

The unit contains a bacteria filter, moisture exchanger, and a layer of activated carbon fibers [50]. A syringe pump pumps anesthetic agent into the AnaConDa, which is positioned between the patient and the carrier gas flow inlet. There is a small vaporizer inside the AnaConDa where the liquid anesthetic evaporates. Carrier gas is directed through the AnaConDa picking up the anesthetic vapour which is inhaled by the patient. When the patient

(a) The AnaConDa unit [50]



(b) Typical set up for the AnaConDa [50]

Figure 3.7: AnaConDa

expires, the excess anesthetic agent not taken up by the patient attaches to the activated carbon fibers. This excess vapour is picked up again during the next inspiration [67] [64] [50]. Because of this ability to pick up expired anesthetic agent, agent consumption is lowered [67]. A study by Nishiyama et al. [54] found that the AnaConDa used 4 times less sevoflurane compared to a conventional vaporizer when administering a 2% concentration.

The output concentration from the AnaConDa depends on the syringe pump rate [67]. Because the anesthetic agent is administered in liquid form the output concentration does not depend on temperature. According to Soro [67] the AnaConDa "has been used safely since 2004 for the administration of inhalation anesthetics to sedate critical care patients...". Soro also found that the accuracy of the AnaConDa is "in the range of that of the target-controlled infusion systems used in intravenous infusion", which is commonly used in modern hospitals. The AnaConDa device is not intended for multiple uses, and has to be replaced at least every 24 hours [50]. This increases cost of use as well as waste.

SomnoSuite

The last drug delivery device that will be discussed is the Kent Scientific SomnoSuite (Figure 3.8). Because the device is meant for use with mice and rats [63], the discussion will be brief.

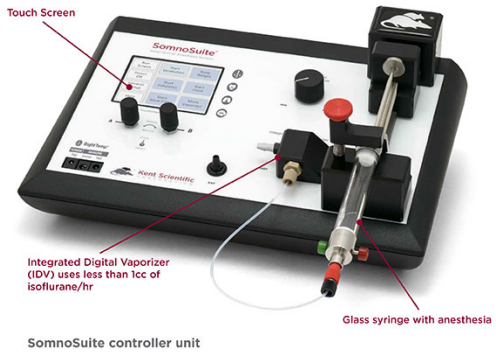


Figure 3.8: The SomnoSuite [63]

The reason for including this device is that it is very closely related to the concept by Dr. Fenton, which will be evaluated in Section 5.2.

The SomnoSuite uses an electronically controlled syringe pump which feeds liquid anesthetic into what the maker calls an integrated digital vaporizer [16]. From this vaporizer the gas containing anesthetic agent flows to the rodent. The amount administered is based on the weight of the animal. The unit can be used with either pressurized gas or room air with an internal pump. SomnoSuite continuously measures the gas flow and from this a microcontroller uses the ideal gas law to calculate the amount of anesthetic gas being used. The system uses a feedback loop where the microcontroller registers the anesthetic gas measurement, and calculates what the rate of administration of anesthetic has to be to constantly maintain the target concentration. It is made specifically for low flows and a study funded by Kent Scientific showed that the device is more precise and uses less anesthetic agent than a traditional vaporizer [16].

Chapter 4

The Medical Situation in LMICs

Because the vaporizer concept by Dr. Fenton is supposed to be usable in LMICs, it is very important to understand the challenges associated with anesthesia care in LMICs. In this section a short summary of the general situation concerning medical care and anesthesia in LMICs will be presented. Since one of the challenges in this project is the evaluation of a new vaporizer concept for use in LMICs a separate section about *vaporizer use in LMICs* will be presented.

Many LMICs face a multitude of medical problems, with a high incidence of disease and injury that need surgical attention [45]. According to Meara et al. [45], "an estimated 16,9 million lives (32.9% of all deaths worldwide) were lost from conditions needing surgical care [in 2010]". Even when anesthesia is available in LMICs it is often associated with a high risk. While the mortality rate from anesthesia in HICs is 0.0005-0.001%, the mortality rate in LMICs is 5-10% [9]. Both Ulisubisya [76] and Meara et al. [45] state that surgical care and anesthesia is overlooked and receives little attention in the global medical discourse.

To administer anesthesia safely some basic factors are needed. According to Baxter et al. [8] some of these are an "adequate numbers of trained staff, reliable infrastructure, functioning equipment, and the availability of essential drugs". The next sections will discuss these factors in LMICs.

4.1 Anesthetics

One big difference with anesthesia between HIC and LMICs is the use of different anesthetics. While sevoflurane, isoflurane and desflurane are the currently most used inhalational anesthetics in HICs, halothane and ether are the only agents available in many LMICs [46, p. 27]. Because of unfavorable side effects and other hazards related to the use of halothane and ether, these agents have been replaced by other agents in more resourced countries. Factors influencing the low availability of anesthetic agents in LMICs are among other things cost, unreliable deliveries, and transport issues [46, p. 27]. Hodges et al. [35] analyzed the anesthesia service in Uganda, and found that ether was always available to 68% of the 91 anesthesia providers surveyed, while halothane was only always available to 38%. Another study by Baxter et al. about the anesthesia capacity in Madagascar shows that halothane is the only available inhalational anesthetic [8]. Due to lack of modern inhalational anesthetics, general anesthesia in LMICs are often ketamine based, which is an intravenous anesthetic agent [73, p. 360]. The reason why halothane and ether is still used in many LMICs is the low cost [46, p. 27].

4.2 Trained staff

Maera et al. [45] state that "Human resources are the backbone of health-care delivery systems". Many countries lack adequate numbers of health-care personnel, as well as trained anesthesia workforce [14]. According to Maera et al. [45] "44% of the world's population lives in countries with a specialist surgical workforce density lower than 20 per 100 000 population, and only 28% lives in countries with a specialist surgical workforce density higher than 40 per 100 000 population". The shortage of surgical care and anesthesia providers is highest in LMICs, and especially in remote and rural areas [14]. In a bulletin on the WHO website, Cherian et al. [14] provide examples of the low density of physician anesthesiologists in some LMICs: In Afghanistan, with a population of 32 million, there are only 9 physician anesthesiologist, and in Uganda, with a population of 27 million, there are only 13.

The result of the low numbers of physician anesthesiologist is that anesthesia is being provided by non-physician anesthesiologists. This can be one of the factors related to the high mortality rate from anesthesia procedures in LMICs compared to a much lower rate in the United Kingdom [14].

There are different reasons to why the numbers of anesthesiologists is much lower in LMICs than in more resourced countries. Cherian, M. et al. [14] state that “The lack of anaesthesia training in nursing and medical school, minimal training incentives and limited availability of jobs dissuade many from entering this speciality”. Another problem is migration of trained staff to more resourced countries. According to Boggs [9] "one in eight physicians trained in Sub-Saharan Africa is lost to medical migration".

4.3 Infrastructure

The availability and reliability of clean, running water, electricity and sources of oxygen is essential factors for a hospital to be able to offer safe surgical procedures and hence, safe delivery of anesthesia [45]. In many LMICs these factors are limited and sometimes unavailable.

A lot of medical equipment and procedures require electric power to function. Therefore, a reliable and continuous supply of electricity is often necessary for providing safe surgical care and anesthesia. Examples are operating room lightning, anesthesia machines, pulse oximeters and ventilators. Kushner et al. [42], investigated essential surgical and anesthesia capacity at 132 facilities in 8 LMICs, and found that only 36% of the facilities had electricity always available, while 64% had sometimes or never electricity available. Vo et al. [79], surveyed 590 facilities in 22 LMICs about their anesthesia-related capacity, and found that 41% of the facilities had an interrupted or no available supply of electricity. In hospitals where electricity is not available a generator can be the primary source for electricity [2]. The use of a generator is not optimal since they can malfunction and require fuel to operate.

Kushner et al. [42] surveyed 132 facilities in 8 LMICs, and found that oxygen was always

available only at 21% of the facilities, and never available to 46%. Where oxygen is available, sources are mainly cylinders or oxygen concentrators. Some hospitals have oxygen concentrators that stay unused due to a lack of personnel able to repair defect machines, or because of insufficient electricity to run the machine [9] [35]. Availability of a reliable cylinder supply is a problem in countries that lack access to reliable public infrastructure [9]. If the cylinders have to be refilled, there must be adequate roads for transport of cylinders.

Adequate road infrastructure and available transportation is important for the transportation of patients to and between hospitals. Sometimes the closest hospital can not provide the appropriate surgical procedure, and the patient must be transported to a hospital with a higher level of care. In these situations, poor roads and non-functional ambulances can be limited factors [51].

Another problem hospitals in LMICs face, is the lack of functional operating rooms. Based on analysis of profiles, Funk et al. [29] estimated that "high-income subregions all averaged more than 14 per 100 000 people, whereas all low-income subregions, representing 2.2 billion people, had fewer than two theatres per 100 000" [29]. In Sierra Leone in 2011, there were 17 functional operating rooms scattered over 10 hospitals. Some hospitals had more operating rooms, but with limited resources and supplies such as anesthesia machines, oxygen and electricity [31], [41].

Lack of operating rooms [9], together with other factors such as unreliable infrastructure [45], a lack of adequate equipment [9] and a lack of trained personnel [45] are related to the large unmet surgical need and anesthesia care in LMICs.

4.4 Equipment

According to Hodges et al. [35], there is a shortage of equipment in LMICs. Vo et al. [79] estimates that 46,6% of the facilities surveyed did not have reliable access to a functioning anesthesia machine, and that 47% did not have continuous access to pulse oximetry. Perry and Malkin [60] examined 112040 pieces of equipment in LMICs, and found that an average

of 38.3% of equipment in LMICs is out of service. For anesthesia machines they found an average of 32% were out of service. Perry and Malking [60] propose three main causes for the high numbers; lack of training, health technology management, and infrastructure.

There is a lack of personnel that know how to repair anesthesia equipment, which often breaks down or malfunctions in LMICs [60]. According to Hodges et al. [35] "only 36% of anaesthetists worked in a setting where there were individuals trained to repair equipment". In the majority of the cases where equipment could not be repaired locally, components were sent to regional centres for repair. Perry and Malkin [60] also found that "at least 50% of [both operator and service manuals were] not found in the surveyed health systems". The result is that even if there is anesthesia equipment present at a hospital, much of it is unusable [55] [27]. Perry and Malkin [60] found that "lack of spare parts, lack of disposables and lack of required accessories" were common reasons for why equipment was out of service.

Another important aspect of equipment use in LMICs is that cost should be kept low. Often the initial cost of the device is of less importance compared to the cost of consumables, spare parts, and service - the cost of ownership [80]. This can easily get overlooked when designing equipment for LMICs. It is therefore very important that equipment made for LMICs is durable, has a long life span, is easy to service, and has a low cost over time.

4.4.1 Vaporizers

Because of the poor medical situation and infrastructure in many LMICs, not all vaporizers are suitable for use. ISO has, by request from The World Health Organization (WHO), made a standard for “Anaesthetic systems for use in areas with limited logistical supplies of electricity and anaesthetic gases”. ISO present four minimum criteria for anesthetic equipment designed for these countries [37].

1. ability to function in the absence of a regular supply of compressed medical gases
2. ability to continue to function safely when the supply of medical gases fails
3. ability to function if mains electrical supplies are interrupted, or are subject to unpre-

dictable increases or decreases in voltage

4. ability to function in a challenging environment, including high temperatures, humidity, shocks, vibration, and dust

Additionally, based on our convensations with Dr. Fenton and Dr. Lonnee, we propose that a vaporizer made for LMICs also needs to be:

5. Easy to operate and understand
6. Easy to repair for local technicians
7. Cheap

Lack of pressurized gas and unreliable electricity in many hospitals in LMICs limit the use of any vaporizer that depends on pressurized gas. This means that all plenum vaporizers are unusable in all areas in LMICs. Although measured flow vaporizers are not intrinsically dependant on electricity, modern models rely on both electricity and pressurized gas to function. This is because the administration of anesthetic vapour in measured flow vaporizers is achieved most often by heating the agent which requires electricity. Modern measured flow vaporizers are therefore not suited for use in LMICs. Additionally, because of cost and the need for measured flow vaporizers desflurane is rarely used in LMICs [46, p. 27].

Dr. Herman Lonnee[1] says is is *possible*, but not practical, to use the method of direct injection into the breathing system in LMICs. This includes the AnaConDa. The method of direct injection usually relies on electricity or battery. Direct injection of anesthetic depends on a syringe pump, which uses plastic syringes. Dr. Fenton has informed us[2] that, in his experience the use of these syringes is problematic in LMICs. They are hard to fill and get lost or broken. He also added that the syringe pump drivers are not well understood, which is a problem in emergency situations. The problem has therefore more to do with the consumables of the technology, rather than with the technological solution itself.

[1] Email correspondence 2017-11-20
[2] Email correspondence 2017-11-16

Draw-Over

The draw-over vaporizer is currently used in many LMICs because of its ability to function without pressurized gas or electricity [82]. They are robust, portable, and simple to use and understand [53]. Some models can be used both with pressurized gas or with room air, making them very versatile. Draw-over vaporizers like the UAM vaporizer [72] and the Diamedica Vaporiser [20] are made specifically for use LMICs.

Although draw-over vaporizers are commonly used in LMICS there are some limitations to their usefulness in LMICs. In general, draw-over vaporizers are less accurate than plenum vaporizers and have a higher variability in ouput concentration when used in high temperature settings. Some limitations have more to do with the general problems with anesthesia in LMICs, like the lack of technical support which affects all equipment including draw-over vaporizers. Even though draw-over vaporizers are less complex compared to plenum vaporizers, they still malfunction and break down. Hodges et. al [35] asked anesthesiologists in Uganda about equipment at their hospital. List 4.4.1 shows the responses specifically about vaporizers.

1. "... one vaporiser is stuck so the other is moved from room to room"
2. "The draw over apparatus is lying unrepaired for the last 10 years"
3. "The EMO[3] vaporiser has not been serviced for 20 years"

A substance called thymol is included in halothane as a stabilizing agent. In older draw-over vaporizers this could clog up the wicks which would reduce the efficiency of the vaporizer. In newer models the wicks are made of a synthetic material which does not absorb thymol [18, p. 48].

4.4.2 Anesthesia Machines Made for LMICs

High-end anesthesia machines are complex, expensive, utilize advanced electronics, and are dependent of pressurized gas. They are not usable where sources of oxygen and other medical

[3] An old draw-over vaporizer commonly used in LMICs

gases or electricity are unreliable or unavailable. There are a few anesthesia machines made specifically for use in LMICs that can use room air as carrier gas. Among them is the CE-marked UAM and the Diamedica Glostavent.

Due to limited resources in LMICs the UAM differs from the high-end machines common in HICs. What distinguishes the UAM most from the high-end machines is that, because the vaporizer is a draw-over type, it can function without a continuous supply of high pressurized gases. It can be used with pressurized gas if it is available, but if it is not or if the supply-flow fails, the machine will switch to using room air as carrier gas. When the machine is used like this the flow can be drawn through the system by use of a bellows, a self-inflating bag or by respiratory efforts of the patient.

4.5 Donations and Problems with Sales in LMICs

sAs previously mentioned, plenum vaporizers are not usable in areas where pressurized gas is sparse and electricity is not reliable. Even so, there are many plenum vaporizers in hospitals in LMICs. According to Angela Enright [25], the fact that high-end anesthesia machines are unusable in these areas, "is either unknown to, or ignored by, well-meaning donors or even purchasing agents in hospitals or ministries of health". This means that there are many hospitals in low-resource areas with high-end anesthesia equipment that is unusable because of the poor medical situation in LMICs. The term *anesthesia graveyard* and *equipment graveyard* is used to describe this situation, where perfectly fine equipment is stowed away because it is unusable for the hospital it is donated to or bought for. Figure 4.1 taken by Dr. Fenton, shows an EMO vaporizer used as a doorstop.

Dzwonczyk and Riha [22] found that 86% of the equipment examined in seven hospitals in Haiti were donated, with only 28% of all equipment working properly. They go on to say that "A poorly conceived donation may not only be useless, but may, in fact, evoke a new unwanted financial and/or environmental burden on the recipient". This echoes statements made by Perry and Malkin [60], who state that equipment may not be usable in LMICs due to inadequate infrastructure, like a lack of pressurized gas and stable electricity. Donations are

Figure 4.1: An EMO vaporizer used as a doorstop

also often made without a service contract, which means that if the equipment malfunctions or breaks down, hospitals are often left with an unusable piece of equipment [60]. The problem of disposal of the device is then left to the hospital. According to Meara [45], "Hospitals often feel obligated to accept donations even when the equipment or supplies are not useful". Figure 4.2 shows medical equipment which has been thrown out by a hospital in Malawi.

Dr. Fenton [27, p. 24-25] references a news correspondence in Anaesthesia News, and states that "electronic compressed gas supply-dependent circle system machines are still being sent to rural hospitals with no oxygen cylinders or soda lime[4], fluctuating electric power with surges and anesthetists with limited training, where even the crude existing drawover equipment is not maintained".

Jon Anner, the president of East Meets West[5], states that "Front-end aesthetics [of medical devices] are in fact important" [80]. Anner goes on to say that "Devices need to look modern, so that hospitals are proud to use them and patients feel that they are receiving the proper treatment".

[4] CO_2 absorber

[5] a non-governmental organization focusing among other things on health and medicine in Asia and Africa

Figure 4.2: Medical equipment thrown out from a hospital in Malawi [71]

According to Dr. Fenton[6], anesthesiologists he worked with in LMICs were wondering why their draw-over vaporizers, which are not CE marked, were different than the ones that were used in HICs. The anesthesiologists viewed it as "a poor solution for a poor country, or that they were used as guinea pigs" [27]. He goes on to say "In fact, any machine designated 'especially for the third world' is doomed to fail, even if works: the 'third world' may need it but it doesn't want it. Technology credentials must be internationally acceptable" [27]. This proposes a very different problem with equipment in LMICs to those discussed previously. Not only does equipment made for use in LMICs have to be usable in LMICs, but it also has to be usable in HICs.

[6]Conversation in Oxford

Chapter 5

Concept by Dr. Fenton

In this chapter a concept device developed by Dr. Paul Fenton will be presented. It will be evaluated to see if:

- It is possible to make the device
- It is possible to use it in LMICs

5.1 Identifying Problems and Needs

When developing a new product it is important to keep in mind what the needs for the product are. The users of medical devices are the medical personnel handling the device, and the patient using it. The anesthetic vaporizer that Dr. Fenton conceptualized should be usable in both LMICs and HIC, mainly because anesthesiologists in LMICs do not want equipment specially made for them as discussed in Section 4.5. This means that the device should meet the needs for users in both LMICs as well as HICs. The main problems in LMICs with regards to vaporizers are:

1. There is a lack of pressurized gas and unreliable electricity
2. Draw-over vaporizers are not very accurate
3. Modern vaporizers can be hard to use in LMICs (e.g. fill with anesthetic)

4. Modern vaporizers are hard to service without technical expertise
5. Modern vaporizers are expensive
6. In LMICs, vaporizers are handled roughly and are used in unforgiving environments

For use in HIC the device should be usable with a circle system and with low-flow anesthesia. It should also be safe, accurate, and easy to operate.

Based on the list of problems in LMICs, the demands from HICs, and the ISO standard mentioned in Section 4.4.1 a preliminary user demand specification matrix has been constructed. This matrix should be used to assess if the concept device is usable in LMICs. As is seen, the category "should have" is empty. It is thought that more user needs will check this category when user needs in HICs are considered. It is therefore left in the matrix.

Table 5.1: User demand specification matrix

User demand	**Must have**	**Performance Value**	**Should have**
Usable without electricity and compressed medical gases	x		
Deliver specified concentration of anesthetic agent, within ±0.2% of target concentration	x		
Clearly display the % of anesthetic agent in the gas going to the patient breathing system	x		
Easy to service by locally trained technicians	x		
Robust construction to withstand rough handling	x		
Resist corrosion in humid environments	x		
Accurate at temperatures from 5-40 °C	x		
Quick, easy, and simple to use	x		
Easy to fill, with no keyed filling	x		
Usable with low flow down to 0.2 l/min	x		
Usable with a circle breathing system	x		
Battery life		$>$ 5h	
Weight		$<$ 5kg	

5.2 Presentation of the Concept

Dr. Fentons concept device is a battery powered, electronically controlled, target-controlled, direct injection type delivery system. It uses a closed-loop feedback system with sensor measurements. A flow schematic is shown in Figure 5.1. What follows is a presentation of the concept device as Dr. Fenton presented it. No components were specified further.

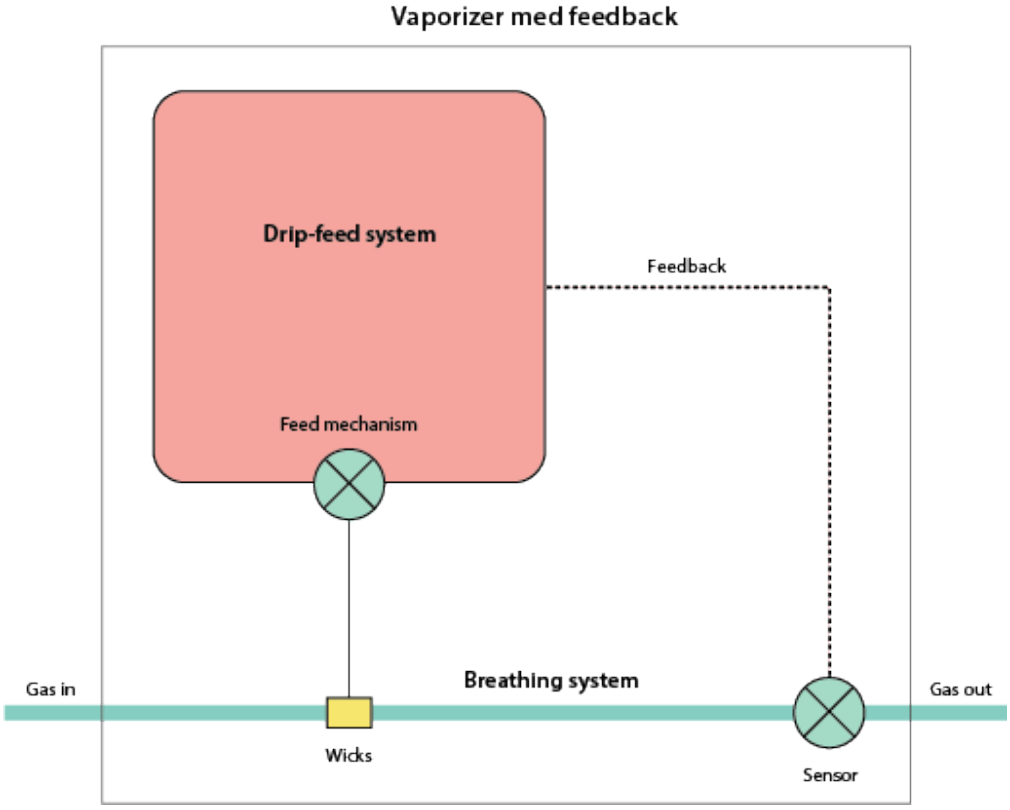


Figure 5.1: Dr. Fentons concept

The device consists of an anesthetic agent reservoir with an electronically controlled feed mechanism, wicks, a gas analyzer, and a microcontroller. Anesthetic agent will be released into the gas stream directed to the patient, where it lands on wicks and instantly evaporates. The gas containing anesthetic agent will flow past a gas analyzing sensor which measures the anesthetic agent concentration. Based on the sensor measurements the electronically controlled feed mechanism will self regulate. The idea is that the operator can set the concentration at e.g. 2%, and the device will self regulate the administration rate so that this target concentration will always be met. The device will be connected to a breathing

circuit directing gas to the patient.

In the original concept the feed rate of the feed mechanism was initially meant to only regulate it self based on the feedback from the gas analyzer. It is uncertain if this will give adequate control. If it does not, it is possible to use a TCI model with feedback from the gas analyzer to reach the target concentration.

The evaluation of the concept design is performed for two reasons. Firstly we want to see if it is at all possible to make the concept device, and secondly we want to see if it is usable in LMICs. Evaluation will begin with a discussion of the physical considerations that have to be taken when designing such a device. The second part is an evaluation of the different components. This will be achieved by first stating what the purpose of the component is, and second explaining how the mechanism can be set up. If there is any ambiguity in how the component can be set up a few different mechanisms will be evaluated.

5.2.1 Physical Considerations of the Device

Because the vaporizer has to be usable both with and without pressurized gas the internal resistance has to be low. The only components in the concept device that create any resistance to flow is the wicks and the gas sensor. In theory, the liquid anesthetic should evaporate immediately when injected into the fresh gas flow line [69]. Therefore, it may not be necessary to include wicks. If the agent does not evaporate on its own, another way to increase the vaporization is to spray the anesthetic agent as a fine mist into the fresh gas flow. This will ensure full vaporization and mixture in the fresh gas flow and will not increase the resistance.

As explained in Subsection 3.4.2 direct injection devices can achieve a rapid increase in concentration output, but a decrease has to be controlled by high flow rates. According to Dr. Fenton [1] this should not be a problem, even during controlled ventilation. To flush a demand flow system you simply move the self-inflating bag or bellow vigorously to get rid of the anesthetic vapour, with the patient not connected.

The gas sensor should measure the agent concentration in the gas directed to the patient.

[1] Email correspondence 2017-11-16

Based on the measure the injection rate can be regulated. If the feedback system and sensor are responsive enough the system can be very accurate. For safely reasons, the gas analysis should take place as close to the patient as possible. A small test tube can run from the device to the breathing circuit close to the patient. There will be a certain time delay between the sensor measurements, and to when the newly administered agent will reach the patient. As an example lets say the target concentration is 2%. If the gas close to the patient is measured at 1.9% the feed mechanism will administer more anesthetic agent into the breathing circuit. The system does not explicitly take into consideration what the concentration in the gas between the patient and the device is. If the concentration here is 2% the newly administered agent will increase the concentration to above 2%, which is not what was specified. This will have to be tested rigorously to find a system that works safely.

The concept makes use of a microcontroller and a motor which necessitates electric power. If the power usage of the device can be kept low a battery should be sufficient. Since the concept is based on feeding small amounts of anesthetic agent the energy loss and temperature decrease will probably be small at the injection site and no temperature compensation should be needed. If temperature compensation is needed, heat from the microcontroller and battery can be directed to injection site. The Datex-Ohmeda ADU anesthesia workstation has a similar mechanism [18, p. 56].

Dr. Fenton has not yet given thought to any specific way to conserve anesthetic use. If the system is used in a circle circuit breathing system the anesthetic use should be low. If it is not, a carbon fiber layer like that in AnaConDa could be employed. The set up of the device would then probably have to be changed compared to what Dr. Fenton had in mind when designing it. If this is seriously considered at a later stage, a patent search should be performed to ensure that no intellectual properties are breached.

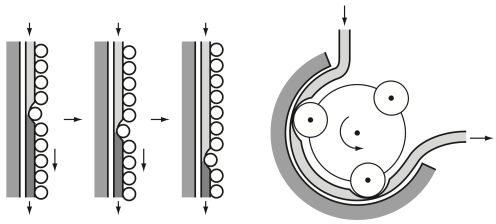
5.2.2 Feed mechanism

To administer a precise amount of liquid agent, Dr. Fenton propose that an electronically controlled feed mechanism has to be included. The feed mechanism has to be very precise

to be able to precisely control the amounts administered. Two different feed mechanisms are discussed to see if it is possible to use such a mechanism: a syringe pump, or a radial pump.

The function of a syringe pump was discussed in Section 3.4.2. To cut cost and dependence on other equipment the syringe pump should be custom made for the concept device. As opposed to the syringe pump used with for example the AnaConDa the pump used for this concept should be an internal part of the concept device. This will increase simplicity and decrease the problems with syringe pumps that were explained in Section 4.4.1.

(a) The Graseby: a small, battery driven syringe pump [18, p. 404]



(b) Peristaltic mechanisms [18, p. 403]

Figure 5.2

A syringe pump can be made with a motor driving for example a screw-threaded rod, with the rod connected to the plunger of a syringe [18, p. 404]. Again, this syringe should not be a loose plastic or glass syringe but an internal piece of the device. The distance the internal syringe pump is pushed down will correspond to a specific amount of agent administered. Since the internal pump is controlled by the microcontroller it can be programmed to deliver anesthetic agent at a specific rate. Depending on the motor a syringe pump can deliver liquids at very low flow rates. Examples of syringe pumps with low flow rates are the ones supplied by Cole Parmer [57]. It is therefore important that a precise motor is used, to ensure adequately low flow rates. A small battery driven syringe pump is shown in Figure 5.2a.

The radial pump is the original concept idea by Dr. Fenton. It is a tube of elastic material, like that of a balloon. A motor rotates and squeezes the liquid forward in the tube. This can be used to administer a certain amount of anesthetic agent. This system, which can also be designed with a linear tube, is often used in infusion pumps. The mechanism, shown in

Figure 5.2b, is called a peristaltic mechanisms. Infusion systems often include ultrasonic or optics based air-detection to ensure no air is being pumped into the patient [18, p. 403].

The distance traveled by the motor may have to be measured by a distance sensor as a safety mechanism to prevent inadequate administration. One possible solution for a distance sensor is the Hall effect sensor which can be set up to measure how many revolutions the motor shaft has taken. It is then easy to calculate the linear distance traveled. There are an abundance of different distance sensors many of which are cheap and small, and its inclusion should not impose any problems.

One problem with the feed mechanism is the filling method. It should be easy and safe to fill the system, both before and during an operation. Of course, it is impossible to fill the syringe and radial balloon pump when they are fully compressed. Therefore, they have to be reset before filling. This could be a problem if anesthetic agent has to be topped up during an operation. One proposed solution for the internal syringe pump is to include two syringes. This way, when one syringe is empty, the motor can simply pull back and begin administration with the second syringe. The medical operator then has time to fill the empty syringe if need be.

5.2.3 Microcontroller and Sensors

A microcontroller will have to be used to drive the feed mechanism. To measure physical properties it is possible to use sensors that can measure analog, physical properties and send analog or digital signals to a microcontroller. The microcontroller will then use these measurements to change the feed rate. It should also be able to give some visual messages to the user. This can be printing of important messages onto a screen, or flashing a light in case of an emergency. All sensors and electronic components need to be small, accurate, cheap, and to have a fast response time.

Microcontroller

The microcontroller is needed to read sensor data and adjust the feed rate accordingly. The minimum necessary requirements are listed below in List 5.2.3. It should also hook up to a monitor to visually indicate the oxygen and anesthetic gas concentration, as well as other measurements that medical staff might need. Safety measures like blinking lights, alarms, and complete shut off of feed can also be included. There may be a need for more than one microcontroller or microchips. There are several microcontroller available that meet the requirements.

1. Fast response time
2. Inputs for sensor connections
3. Outputs for motor and screen connections
4. Battery driven and low power consumption
5. Small and light

Gas analyzer

For the concept device, a continuous and accurate reading of the amount of anesthetic agent in the gas going to the patient is needed. The concentration measurement will be used as feedback to control the feed mechanism.

The common way to analyze gas for anesthetic use is with a gas analyzer. Depending on the model it can measure the presence or quantities of one or multiple gases. It may be necessary to include two gas analyzers - one at the inlet to the patient, and one at the outlet from the patient, to analyze how much anesthetic agent is taken up by the patient. If the device is used with a circle system the anesthetic agent circulating in the system should be measured accurately.

There are several common ways to analyze an anesthetic agent [30]. The physical principles behind these analyzers will not be presented in this text but some commonly used gas

analyzers are based on: infrared spectroscopy, Raman scattering, and mass spectrometry [30].

The topic of gas analyzers is comprehensive with a multitude of different types that use different physical phenomenons to analyze the gas. Depending on accuracy they can often be expensive, as well as power hungry. Some types of gas analyzers also need special equipment. For example, a Raman scattering gas analyzer may use a laser and a cooling system [30]. If the concept is going to be evaluated further great care should be taken when selecting a proper gas analyzing mechanism.

While gas analyzers for anesthesia can be very precise and have fast response times, they are often expensive and complex. The SomnoSuit, discussed in Subsection 3.4.2, uses the ideal gas law to calculate the anesthetic agent concentration in the gas. This solution uses a simple pressure sensor, which can be very small and cheap.

5.2.4 Modular System

An electrical system with several sensors is of course inherently complex. One problems that was still present in the concept when Dr. Fenton presented it was the complexity of the system. This includes both the complexities of handling the unit and the complexities of repair and troubleshooting.

An ideated solution was pitched to and approved by Dr. Fenton [2]. The solution is a module based system. This system is based on the idea that five separate units are built into their own casing. The units can then easily be changed out with spare units. If one unit has to be opened, it can be done without tempering with other parts that may be unknown to the person opening it. It is very important that the units are built to withstand rough use and harsh environments. There are several examples of enclosed electronic equipment built for this, like laptops and hard drives for offshore use. All modules should have electronic connection points, so that they can communicate between each other. Five modules have been thought of, and listed in List 5.2.4.

[2]Email correspondence 2017-11-13

1. Tray and control panel
2. Feed
3. Microcontroller / CPU
4. Gas analyzer
5. Battery

The tray should be a box with empty spaces for the other modules. In an enclosed part of the tray there should be an inlet, an outlet, and the breathing tube connecting these, where the carrier gas flows through. These will not be removable. Two different control panels have been considered: a touch screen, or a manual control panel with knobs, buttons, and a small screen. The control panel could act as a lid covering the tray which contains the other modules. By having the control panel act as a lid it should be harder to loose any of the modules. The feed module will contain everything needed for the injection. This includes the feed mechanism and a filling port.

The microcontroller unit should contain everything that is used to control the system. Any electronic component or part that does not need to be close to the sensor or feed should be kept here. The gas analyzer should be kept in its own separate units. It is then easy to replace if it malfunctions or for some other reason has to be replaced. The battery should also be kept in its own module so that it is easily removed for charging or replacement. More than one battery module could be supplied so that the unit is usable even when the other module is charging.

This modular system proposes some problems. It comprises of several loose parts, which means that they can be lost, or misplaced when taken out of the device. This could possibly be prevented if the modules have to be fastened in some way, e.g. with a screw. This system is only a suggested solution to a problem. There may be other ways to solve this problem, which should be evaluated if the concept is developed further.

5.3 Comparisons

To see if a new concept device is marketable we compare it to currently used devices on the market. As discussed in Subsection 4.4.1 not all vaporizers can be used in LMICs. Of currently available vaporizers the only one that is usable in most areas in LMICs is the draw-over.

Modern plenum and measured flow vaporizers demand pressurized gas and electricity. It is therefore pointless to compare the Dr. Fenton device to these types since they are made for different uses. Direct injection systems like the AnaConDa are not dependant on pressurized gas or mains electricity, but are dependant on a battery to drive the syringe pump and a gas analyzer for safe administration. As mentioned in Subsection 4.4.1, Dr. Lonnee informed us that the AnaConDa is in theory usable in LMICs, but not in practice. With modifications, the AnaConDa may be a suitable alternative to the draw-over vaporizer in LMICs. The device concept will therefore be compared with a generic draw-over vaporizer and the AnaConDa.

The comparison will be based on the factors in List 5.3. These factors are taken from the user needs matrix shown in Table 5.1, and are taken to be the most important factors for use of a vaporizer in LMICs. We pay no regard to the fact that the vaporizer has to be used without electricity and pressurized gas, because all vaporizers that depend on this have been excluded from the comparison.

Other user needs like the need for the device to be easily serviced can not be accurately assessed for the concept device before the device is developed further. Of course, any further development should be performed with *all* user needs in mind. Other factors like the need to display the % of anesthetic agent in the gas going to the patient should be easy to include in an electric system. It could still be too expensive, or complex to include - but it is very *possible* to include it.

The comparison is therefore based on the most important factors for use of a vaporizer in LMICs, and are the ones we can *actually* asses. If these factors are met, further development should be performed to ensure that the other user needs are met as well.

1. Accuracy of output concentration
2. Stability of output concentration
3. Safety
4. Low cost
5. Marketability

With regards to accuracy, the concept device has the potential to perform far better than a draw-over vaporizer and on par with the AnaConDa. Since the device is electronically controlled with a feedback mechanism it has the ability to self-adjust so that the target concentration is always reached.

The output concentration of a draw-over vaporizer is dependant on temperature and fresh gas flow rate. Depending on the use, a draw-over vaporizer can be relatively unstable, often with concentrations larger than $\pm 0.5\%$ of the target concentration, and sometimes concentration deviations of over $\pm 1\%$ [24]. The output concentration for both the concept device and the AnaConDa is independent on temperature. Because of the inclusion of TCI with feedback from the gas analyzer measuring the concentration of anesthetic agent the concept device should be stable.

The safety of anesthesia often depends on other factors besides the vaporizer choice. Draw-over vaporizers are relatively safe, depending on set-up and use. The AnaConDa has to be used with a gas analyzer which greatly increases the safety. If there is no gas analyzer present the safety of delivery with the AnaConDa is drastically reduced. If the syringe is set-up improperly or malfunctions, over- or underdosing could occur. The AnaConDa depends on plastic syringes which can be lost and troublesome to refill, which reduces the safe use. Since the concept device can not be used without the built-in gas analyzer the safety is greatly increased.

Because of the poor financial resources of LMICs, cost is an important aspect of equipment made for LMICs. As mentioned in Section 4.4, it is important to remember that the variable cost is often more important than the initial cost. Since the draw-over vaporizer is most often

used with high fresh gas flow rates it uses a lot of anesthetic agent which increases the cost of anesthetic agent. The AnaConDa consumes little anesthetic due to the inclusion of the active carbon filter, but since it meant to be disposed after use, the cost is entirely variable. Since the concept device uses TCI with feedback from the gas analyzer, it may be possible to use little anesthetic. Other inhalational anesthesia machines using TCI have a very low usage of anesthetic as well as medical gases. The device has the potential to have a low operational cost. The cost of the concept device has not been investigated further but is expected to be relatively high, especially because of the inclusion of the gas analyzer. Although it may be possible to use low-flow anesthesia or have a low consumption of anesthetic Dr. Fenton advises us[3] that the anaesthetic consumption is not a main problem, and should be handled thereafter.

One problem with selling a medical device to LMICs is that there is little desire for equipment made specifically for LMICs. Aesthetics is therefore important when designing the device. The draw-over is often disliked because it is seen as, like Dr. Fenton put it, "poor equipment for poor people". It is not known how the AnaConDa would do sales wise in LMICs since it has not been tried. Care should be taken with further development of the concept device to ensure saleability.

Table 5.2 shows how the different vaporizers score with a score from one to five, with five as the top score. This table is based entirely on the comparison, and is simply made to visualize the discussion.

Table 5.2: Comparison

Specification	**Concept device**	**Draw-over**	**AnaConDa**
Accuracy of output concentration	●●●●●	●●●	●●●●●
Stability of output concentration	●●●●●	●●	●●●●●
Safety	●●●●●	●●●	●●●●
Low cost	●●	●●●●	●●●
Marketability	Unknown	●●	Unknown

[3]Email correspondence 2017-12-10

5.4 Concept Evaluation

Since the concept presented was quite broad it first had to be narrowed down. We tried to focus on *what* the components of the device should do, and not on the components them selves. Therefore, no specific component or part of the concept were evaluated. Rather, the concept device is evaluated as a whole.

It seems possible to make the device. All the parts that the device is made of are readily available. This allows for further development where different compositions of the device parts can be examined. There has been no evaluation of the cost of the concept device, since no specific components has been specified. With further development a preliminary cost assessment can and should be performed.

The performance of the device can, as of now, not be evaluated further than in theory. Other TCI systems, using the method of direct injection are proven to be accurate. Since the concept device is such a type there is little reason to believe the device will perform any worse. The actual performance has to be considered during development. Prototypes have to be made to find the optimal construction of the device.

In terms of technical solutions the device is usable in LMICs. It should be usable with a battery and does, in theory, not depend on pressurized gases. The accuracy can also in theory surpass the draw-over vaporizer. In practical terms, it is very dependant on cost and marketability. The marketability of a product is extremely hard to assess at the concept stage, and should really be evaluated by people with backgrounds in marketing that know the medical market in LMICs. It may be needed to get the device CE-marked or certified by a standard to be bought in LMICs. The marketability should be kept in mind with further development.

Some of the user needs for LMICs are hard to assess before the concept is more specified. These are for example the need for the concept device to be easy to use and easy to clean. It is also impossible to specify the size or weight of the unit as per now.

5.4.1 Limitations of the Concept

There are some limitations of the concept that should be considered. Small electronic components can break and a failure in the electronic part of the device will have to be repaired by technically skilled workers. The introduction of electronic parts also necessities a battery, which can cause problems of its own. As mentioned, since the modules in the modular system are standalone units they may be lost or misplaced.

5.4.2 Patent Search

If the concept presented in this report is going to be manufactured for sale it should not infringe on any existing patents. To find out if the concept infringes on any patent, Eivind Andersen, Head of projects at NTNU Technology Transfer AS (TTO) was contacted. TTO helps employees at NTNU develop their ideas and projects into marketable products [74]. According to Andersen, a patent search would be very expensive. He advised us to contact Patentstyret, the Norwegian patent offices, to see if they could help. Patentstyret has a price list on their website. The cost of an initial patent search is more than 1180 NOK per hour, with an additional 250 NOK for every relevant journal they discover [59].

A preliminary patent search using search engines like Google Patents, ORIA, and Patentstyret gave no results when searching for any device similar to the concept. According to Baum, injection of volatile agent directly into the breathing circuit was first tried in 1981 [7]. This means that the idea or concept has been around for over 35 years. Patents are often limited to 20 years [58], which indicates that the principle of direct injection is not patented, and if it were, the patent has probably expired. Further patent investigation will have to be performed if the device is going to be produced for sale.

Chapter 6

Summary

6.1 Summary and Conclusions

In this project, two topics have been thoroughly researched. In Chapter 3 different anesthetic vaporizers were researched. Both vaporizers commonly used in HICs and LMICs was examined, as well as alternative devices that see less use. In Chapter 4 the situation with anesthesia care in LMICs was examined. The general situation of medical care was presented, and the problems with vaporizers and equipment in LMICs was examined. Based on the research a concept device by Dr. Paul Fenton has been evaluated. The concept was presented in this text as Dr. Fenton presented it to us. The different components mentioned were specified by us and evaluated only to see if it is possible to make the concept device. The problem statement for the project has therefore been met.

The evaluation was performed to examine two aspects. Firstly, an evaluation to see if it is possible to build and use the device, and secondly an evaluation to see if the device is usable in LMICs. The evaluation was performed based on the whole concept device, and not the components it comprises of. A user demand specification matrix was constructed to specify the most important factors for use of vaporizers in LMICs. One of the factors is that LMICs often buy equipment used in HICs even if this equipment is unusable. The user needs of HICs was therefore also added to the user demand specification. These user needs have not

been clearly assessed, since the main goal of the evaluation was to see if the concept device was usable in LMICs.

We conclude that as the concept stands now it is *possible* to build it and in theory it is possible to use it in LMICs. We draw no conclusion as to the performance or the cost of the device, or to the actual usability in LMICs.

6.2 Discussion

For the research, we examined commonly used vaporizers. Some of the vaporizers examined were not directly used in the evaluation or comparison of the concept device. They were included because they give an overview of the limitations with vaporizer use in LMICs, as well as a technical understanding of how inhalational vaporizers function. It is also important to examine currently used products that are used for the same purpose as the device that is being developed.

We researched the situation of anesthesia care in LMICs. This situation is constantly changing, and the category of LMICs contain several vastly different countries with different problems and needs. Some of the literature we used is older than others and some of the articles examined the situation in specific countries. We still used these since they give an overview of the situation. The concept device should be usable in all LMICs, and any country-specific situation should therefore also be evaluated.

The evaluation of the concept is a preliminary one. Since there was no evaluation of the cost of the device or the practical performance, it is hard to say if the device will be used in LMICs even if it reaches the market. It may for example be too expensive or perform too poorly.

The evaluation of the device was harder than anticipated. Since the area of anesthesia was foreign to us before this project the research phase took longer time than expected. There was little time to specify or evaluate the individual parts that the concept comprises of. The result is that the evaluation is based on the concept as a whole. It would be beneficial to

evaluate the different parts to see if there are other possible ways to solve the problems they propose. This should be performed during further development.

6.3 Recommendations for Further Work

The work done in this project is preliminary and requires further development. List 6.3 presents our recommendations for further work.

1. Establishing a comprehensive target specifications list based on the user needs
2. Establishing target specifications for each component
3. Establishing a morphology matrix based on different solutions for different components
4. Choosing one solution to the concept and prototyping it

The user demands presented in this text should be developed further before making the target specification list. It is important to remember that the product design methodology is an iterative process. This means that all tasks that are performed should be revisited and evaluated, to see if the results they gave were the best possible given the new information at hand. Some new user needs may thought of after further design on the concept. The user needs of anesthesiologists in HICs should also be further investigated.

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Appendix A

Acronyms

LMIC Low and middle income countries

HIC High income countries

SVP Saturated vapour pressure

Appendix B

Additional Information

B.1 Literature Search

ORIA was used extensively in the literature search. In ORIA, it is possible to view how many of the results are found in other databases. Databases that yield high results are often field-specific databases. As an example, searches on anaesthesia often had a high number of results from Scopus (Elsevier[1]) and MEDLINE/PubMed, databases related to the field of medicine. Often, the database with the highest number of results was chosen to search the topic more specifically, since the high number of results was seen as an indication of the area of expertise of the research publisher. All examples below will be shown with results from ORIA and Elsevier. To clearly specify our searches, we used Boolean operators AND and OR in our searches. A good search should be specific enough so that only relevant information is included, but broad enough so that no relevant information is excluded.

There were two specific words that were important when searching. Since both vaporizers and anaesthesia is written differently between American and British English it was important to include all spellings when searching. An example of how different results you can get with different spellings is given in Table B.1. Using multiple spellings yield a much higher search

[1] One of the largest publisher of scientific, technical, and medical information

Table B.1: Search with different spelling variations

	# of results	
Search phrase	**ORIA**	**Elsevier**
vaporizer AND anaesthesia	4324	1314
vaporiser AND anaesthesia	745	1314
vapouriser AND anaesthesia	69	8
(vaporizer OR vaporiser OR vapouriser) AND (anaesthesia)	4888	1321
(vaporizer OR vaporiser OR vapouriser) AND (anaesthe* OR anesthe*)	5967	1583

Table B.2: Search with increasing specificity

	# of results	
Search phrase	**ORIA**	**Elsevier**
(vaporizers OR vaporisers OR vapourisers OR vapourizers) AND (anaesthesia OR anesthesia) AND (temperature)	138	581
(anaesthesia OR anesthesia) AND (vaporiser OR vaporizer OR vapouriser) AND temperature AND (compensation OR compensating OR compensator)	7	178
(anaesthesia OR anesthesia) AND (vaporiser OR vaporizer OR vapouriser) AND ("temperature compensation")	5	27

result. Elsevier automatically searches for alternative spelling variants, which is why we get the same amount of results with different spellings[2]. We used the Boolean operators AND and OR extensively to specify our searches. The last row in Table B.1 uses the truncating operator (anaesthe*), which searches for all words staring with anaesthe. The proximity operator was also used for searching. This operator is used to search for two words separated by a specified number (or less) of random words. E.g. anaesthe* w/2 vaporizer, will search for anaesthesia or anaesthetics and vaporizer seperated by two words or less.

Table B.2 below show the results from a search on temperature compensating devices that are found in vaporizers. The three searches get increasingly more specific which is mirrored in the number of results. The highest number of results in Table B.2 was 138 and 581 for Elsevier and ORIA respectively, which means that these are the only papers in these databases that mention both temperature and anesthetic vaporizers.

[2]It seems like Elsevier does not recognize vapouriser as a proper spelling

B.2 Nitrous Oxide as Carrier Gas

The use of nitrous oxide as carrier gas has been questioned in many articles, and there is ambiguity whether use of the gas should be limited. An article about the use of nitrous oxide in Scandinavian countries shows that usage is decreasing [36]. According to Jahn U. R. et al. "Nitrous oxide is simply outdated" [39]. Moreover, nitrous oxide is a greenhouse gas, and according to Ravishankara et al. "reductions in N2O emissions would benefit both the ozone layer and the climate" [62].

B.3 Hazards and Safety Features

The use of vaporizers is associated with some risks. The book Clinical Anesthesia [11, p. 573-574] presents a list of hazards associated with vaporizers, which is recreated in List B.3. The last point is not included in the book, but by a separate list by Charavarti [12].

1. **Misfilling**
2. **Tipping**
3. **Vaporizers in parallel**
4. **Overfilling**.
5. **Underfilling**.
6. **Leaks**.
7. **Electronic failure**.

To combat these risks, modern vaporizers are made with a number of safety features. Some vaporizers are agent specific, and have keyed fillers that only allow filling from agent specific containers [11, p. 573], which minimize risk of misfilling [12]. Misfilling can be detected, and prevented, if a gas analyzer is used [12]. In addition, all anesthetic agents and agent specific vaporizers are color coded [82], which should prevent the wrong anesthetic agent from being used in agent specific vaporizers.

Overfilling can be caused by a faulty sight glass, or by incorrect filling [11, p. 573]. By locating the filler port on the side of the unit, the risk of overfilling is reduced [12]. If underfilling occurs, the output concentration can be inadequate [11, p. 573]. Especially in the event of a combination of high flow rate and a low fill state ($<$ 25% full). As mentioned in Section 2.2, some manifold systems include a vapour-interlock system, which prevents multiple vaporizers from being used at once [11, p. 573].

Leaks can result in patient awareness [11, p. 573-574]. Some common sources of leaks are a loose filler cap, or a damaged or misfit O-ring [3]. Automatic leak checks can be carried out by some modern anesthesia machines. If not, a medical worker should perform one.

The risk of tipping is highest during transportation, or when attaching and removing the vaporizer from the backbar. Tipping or tilting will cause anesthetic agent left in the vaporizer to leak into the bypass chamber. The next time the vaporizer is used, it will output a concentration far higher than what the user specified. Modern models also include "anti-spill protection designs" [11, p. 573], which decreases the risk of tipping. One example of this is in the Dräger Vapor 2000, where the vaporizing chamber can be isolated completely during transport of the unit [11, p. 573].

Vaporizers are commonly placed securely on the backbar on the anesthesia machine, which secures them from tipping. Figure B.1 shows the OMV supplied with the Triservice apparatus, used by the British military [18, p. 488]. This vaporizer has been modified with feet, which reduces the risk of tipping. Some vaporizers like the Diamedica are bottom heavy, which also prevents tipping [24].

Any vaporizer that is electronically controlled can malfunction if an electronic failure occurs [12].

[3] O-rings are used in vaporizers to seal the connection between two components

Figure B.1: OMV with stand

Jacob Søgnen Jensen, Tuva Kristine Østby

Development of a New Anaesthetic Vaporizer Concept

NTNU
Norwegian University of
Science and Technology

ENGINEERS WITHOUT BORDERS