

Portable, Neonatal, Continuous Positive Airway Pressure Device for Low-Resource Settings

Evaluation of Feasibility through Simulation and Prototyping

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By

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Preface

My interest in neonatal CPAP for low- and middle-income countries was sparked during an internship at Diamedica, a small company in Barnstaple UK that makes anaesthesia and intensive care equipment for low-resource settings, owned and operated by Robert Neighbour. In July 2017, Robert and I travelled to Mbale, Uganda to meet with Dr. Kathy Burgoine and spend time in her neonatal intensive care unit (NICU). In just 3 years, Dr. Burgoine's commitment to saving lives of vulnerable infants has resulted in a reduction in neonatal mortality from 52% to 11% in the NICU at Mbale Regional Referral Hospital. Dr. Burgoine attributed a significant portion of this success to the use of continuous positive airway pressure (CPAP). I witnessed this impact first-hand when I met a 3-month-old baby (pictured below with her mother) who was born weighing 600 g, given CPAP treatment, and survived against all odds. Dr. Burgoine told me that preterm neonates in particular respond very well to CPAP, and she has optimistic views on the efficacy of prophylactic application of CPAP for preterms. I completed a systematic literature review on this topic, and indeed, prophylactic CPAP for preterms in low- and middle-income countries has the potential to further reduce neonatal mortality. Dr. Burgoine formulated an idea to develop a low-cost portable CPAP device for hospitals and health centres in sub-Saharan Africa, designed to encourage clinicians to provide treatment in the delivery room. I was inspired by this idea and the incredible impact it could have. Robert and Dr. Burgoine were supportive of me taking the first steps to investigate the potential of this new device, and thus it became my master's thesis. I have thoroughly enjoyed working on this project and hope to continue working in this field for the rest of my career.

*Kate Loe
Delft, July 2018*



Abstract

An estimated 9 million infants are born prematurely each year in south Asia and sub-Saharan Africa, and the leading cause of death in preterms is respiratory distress syndrome (RDS). Continuous positive airway pressure (CPAP) is a popular treatment for RDS and has been proven to be safe, feasible, and effective for use in low- and middle-income countries (LMICs). The well-documented success of supportive CPAP in LMICs and prophylactic CPAP in developed countries indicates that delivery room CPAP has the potential to be implemented successfully in LMICs. The aim of this thesis is to explore the feasibility of a simple, low-cost, portable neonatal CPAP device for use in the delivery room in LMICs. A portable CPAP device was modelled in Simulink to predict the pressure and flowrate at any point in the CPAP circuit. A prototype composed of a centrifugal fan, silicone tubing, nasal cannula, and a PEEP valve was constructed. The prototype was tested using a Dräger Infant Test Lung to simulate a breathing neonate. The model predicted that neonates with higher peak inspiratory flows risked rebreathing exhaled gas. When compared to the experimental data, it was determined that the model underestimated resistance in the circuit and overestimated the mean pressure delivered to the patient. The prototype effectively delivered a positive pressure to the simulated patient; however, the pressure was not consistent across all experimental conditions. Cannula type, amount of leak, and breathing pattern all impacted the treatment delivered. The Simulink model can be used as a tool to aid in design decisions, but is not highly accurate, and thus does not eliminate the need for practical experimentation. The prototype was a good proof-of-concept and should be investigated further in consultation with clinicians.

Acknowledgements

Thank you to my supervisor Jenny Dankelman for introducing me to the field of medical device design for low- and middle-income countries. Next, I am appreciative of Robert Neighbour, director of Diamedica UK Ltd. Thank you for mentoring me through my internship in the UK, including trips to Uganda and Rwanda, for sending me to the Annual Conference of the Society for Tropical Paediatrics and International Child Health, and for your continued support from abroad during this thesis. I would also like to thank Dr. Kathy Burgoine, head of neonatology at Mbale Regional Referral Hospital in Eastern Uganda, who proposed the idea for this project.

To my PhD student supervisors, Roos Oosting and Tom Goos, thank you for your encouragement and guidance. Thank you to Roos for your involvement with my literature study and colloquia presentation, and for sharing your expertise on healthcare in African countries to inform my design criteria for the portable CPAP. Tom, I could not have done this project without your technical knowledge about CPAP, neonatal resuscitation, and fluid mechanics. Thank you for your patience and dedication in helping me navigate Simulink, LabVIEW, and practical experimentation. Additionally, a huge thanks to Jos van Driel from the TU Delft Meetshop for your invaluable help with LabVIEW.

I could not have done this project without the support of everyone in the department of Medical Technology of the Erasmus Medical Centre, Sophia Children's Hospital in Rotterdam. Special thanks to Arie Koedood for making me feel welcome, and to Frank Sterke for spending an afternoon troubleshooting an electronics problem for me. An additional thank you Arjan van Dijke for your support in the Misit Lab.

To my friends, thank you Lauren Safai and Arjen Jongschaap for talking through ideas with me, and a huge thank you to my parents for unwavering support and encouragement throughout this degree. Finally, I would like to thank Marshall Quinn, for always being there to come up with new ideas, help me problem solve, and provide emotional support.

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1 Introduction

In this chapter, continuous positive airway pressure (CPAP) is introduced and its mechanism of treatment is explained. Providing CPAP for the patient group of interest, preterm neonates in low- and middle-income countries (LMICs), is discussed, then the aim of the thesis is stated. Commercial and clinical affiliations that guided the direction of the thesis are also stated. Finally, the report structure is summarized.

1.1 Continuous Positive Airway Pressure (CPAP)

Continuous Positive Airway Pressure (CPAP) refers to a non-invasive respiratory support device that applies a positive pressure to the lungs. As shown in Figure 1, a CPAP device delivers a humidified flow of blended air and oxygen to the patient through a non-invasive interface such as nasal prongs or a face mask. A positive pressure is maintained in the CPAP circuit using end-expiratory pressure control. The “type” of CPAP is characterized by the method of pressure control, the two most popular types being ventilator-driven CPAP and bubble CPAP [1]. The schematic in Figure 1 depicts a bubble CPAP, where the pressure control takes the form of a tube submerged in water.

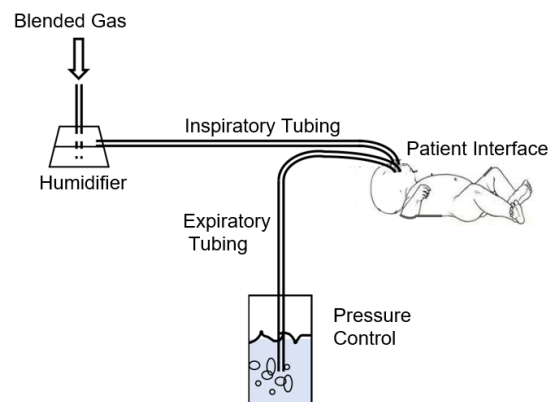


Figure 1: Schematic of a Continuous Positive Airway Pressure Device.

Normal breathing is caused by changes in volume of the thoracic cavity. When the volume increases, the result is a negative alveolar pressure of approximately -1 mmHg (-1.4 cmH₂O) which initiates an inhale. A decreased volume and subsequent $+1$ mmHg ($+1.4$ cmH₂O) pressure change initiates an exhale. Between breaths, alveolar pressure returns to atmospheric pressure. This process is illustrated in Figure 2 [2, p. 16]. The application of CPAP shifts the illustrated waveform up by the desired amount, indicated by the CPAP pressure setting.

Increased pressure during exhalation is called positive end expiratory pressure (PEEP). Exhaling against PEEP increases functional residual capacity of the lung, the volume of gas that is maintained inside the lungs after an exhale, during normal breathing [3][4]. This increases the surface area available for gas exchange by recruiting areas of the lung that would otherwise not be utilized, thus improving oxygenation [5][6]. Between breaths, the continuous positive pressure keeps the alveoli from collapsing, meaning less inspiratory effort is required to inflate them. The increased pressure during inhalation helps the lungs to fill, therefore reducing the work of breathing [7].

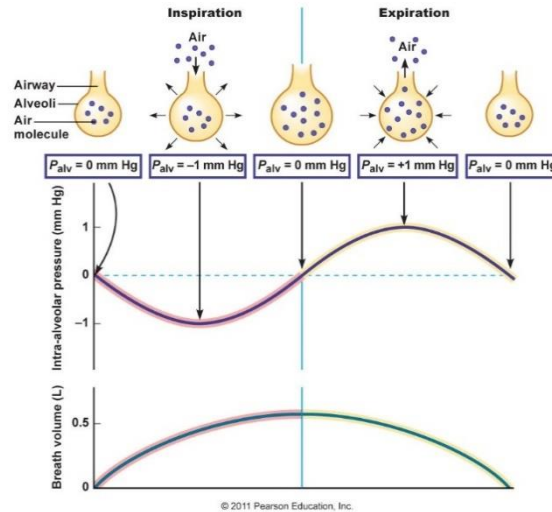


Figure 2: Alveolar pressures during breathing cycle [2, p. 16].

CPAP can be useful for children and adults, but this thesis will focus only on neonatal CPAP, that is CPAP given to infants within the first 28 days of life. When neonates are born prematurely, defined as <37 weeks gestational age (GA), complications with breathing, metabolism, and temperature control are probable [8]. Respiratory distress syndrome (RDS) is the leading cause of death in preterm infants, with the incidence increasing with decreasing gestational age [9]. Preterms have immature lungs that are deficient in surfactant, thus the lungs tend to collapse, which leads to laboured breathing and hypoxia [6]. CPAP is a simple and popular form of respiratory support to treat RDS.

Given the high prevalence of RDS in preterms, some clinicians apply CPAP to preterms in the delivery room, before symptoms of RDS have emerged. A 2016 systematic review and meta-analysis by Subramaniam *et al.* found strong evidence that prophylactic CPAP is superior to supportive care, with moderate evidence supporting the idea that prophylactic CPAP within the first 15 minutes of life reduces the incidence of bronchopulmonary dysplasia and the need for assisted ventilation and surfactant [6].

1.2 CPAP in Low- and Middle-Income Countries (LMICs)

Prematurity is a leading cause of death in neonates, and an estimated 15 million infants are born prematurely each year, with more than 60% of these births occurring in south Asia and sub-Saharan Africa [10]. The UN has committed to reducing neonatal mortality to 12 deaths per 1000 live births by 2030 (Goal 3, Target 3.2 of [11]). The regional neonatal mortality rate for Africa, where most of the world's low- and middle-income countries (LMICs) are located, is 27 deaths per 1000 live births [12]. Strategies to achieve this goal must therefore be tailored to LMICs to see a large improvement. Published research from several LMICs (India [13], Armenia [14], Rwanda [15], Malawi [16], Kenya [17], Nicaragua [18], Uganda [19], South Africa [20], Brazil [21], Iran [22], and China [23]) has indicated that CPAP is a safe, feasible, and effective treatment for preterms in low-resource settings. It is an inexpensive option [15] that has been shown to decrease mortality and decrease the number of infants referred to a higher level of care [17][20]. Despite increasing usage in developed countries, few studies have documented use of CPAP for preterms in the delivery room in LMICs. However, the well-documented success of supportive CPAP in LMICs and prophylactic CPAP in developed countries indicates that delivery room CPAP has the potential to be implemented successfully in LMICs.

1.3 Aim

Following a systematic literature review of the topic, it was determined that there is a need for a CPAP device designed specifically to encourage prophylactic use of CPAP on preterm infants in LMICs, immediately following birth. The aim of this thesis is to explore the feasibility of a simple, low-cost, portable neonatal CPAP device. This will be accomplished through modelling of the device in Simulink R2017b, then constructing and testing a portable CPAP prototype.

1.4 Commercial and Clinical Affiliations

Dr. Kathy Burgoine is the head of the neonatal intensive care unit (NICU) at Mbale Regional Referral Hospital in Eastern Uganda [24]. Through personal experience with neonatal CPAP, she believes that all preterms born in the hospital could benefit from receiving this treatment in the delivery room, before admission to the NICU. Mbale Regional Referral Hospital has 10,000 births per year [24], and 5-18% of babies are born prematurely [25]; this could mean a CPAP device is needed in the delivery room up to 5 times per day. Dr. Burgoine formulated the idea for a portable CPAP device, designed specifically for delivery room use in low-resource settings, such as Mbale, Uganda. The (non-portable) CPAP machines currently being used in the NICU are made by Diamedica UK Ltd.

Diamedica UK Ltd. is a company that designs, manufactures, and sells anaesthesia machines and intensive care equipment specifically created for low-resource settings [26]. The company has a range of anaesthesia machines including the DPA: Diamedica Portable Anaesthesia series. They have had success thus far with the Diamedica Baby CPAP, and now hope to add a portable CPAP to their line of products.

This thesis project was completed considering Diamedica UK Ltd. as the future commercial manufacturer of the portable CPAP device, and clinicians at Mbale Regional Referral Hospital as end users. Past experiences of Dr. Burgoine and Diamedica's managing director Robert Neighbour guided some design choices, as did consideration of feasibility of manufacturing within the framework of Diamedica.

1.5 Report Structure

This document details the design of a portable neonatal CPAP device for low-resource settings. The design criteria for the device is outlined (2 Design Criteria), followed by the theoretical principles applicable to the device (3 Theory). The device was first simulated using a model created in Simulink R2017b (4 Simulink Model), then a prototype was constructed and tested (5 Prototype). The Simulink model is compared to test data of the prototype (6 Model/Prototype Comparison). Finally, results of the model and prototype are discussed and measured against the design criteria, and recommendations for future work are made (7 Discussion).

2 Design Criteria

The portable CPAP prototype is intended for transient use, to help preterm neonates breathe during the time between birth and admission to a NICU. To keep cost and complexity low, the device will differ from most other commercial CPAP devices in 3 ways:

1. It will have only one setting of pressure and flowrate
2. It will provide a flow of air, with no option for supplemental oxygen
3. It will not heat or humidify the gas delivered to the patient

The portable CPAP prototype will only have one possible flowrate and pressure setting to ensure quick and easy application to the infant after birth. During in-person interviews with clinicians in the NICU at Mbale Regional Referral Hospital, it was determined that all infants admitted to the unit are started on CPAP at the same setting: 5 L/min of air, 5 L/min of oxygen, and a pressure of 5 cmH₂O. Pressure and flow are later adjusted according to periodic assessments of the infant. The portable CPAP prototype will provide the initial settings, then pressure and flow can be titrated once the infant is transferred to a more complex CPAP device in the NICU. This procedure of using one initial setting is supported in literature. A 2015 crossover study determined that a fixed flow was more effective at delivering pressure during CPAP than a titrated flow [27]. With regards to the pressure setting, six studies of delivery room CPAP reported using a single initial setting of 5 cmH₂O on all studied preterms [3], [28]–[32]. It is therefore expected that a portable CPAP prototype with a single setting will effectively provide respiratory support until a more complex CPAP device is available.

The decision to exclude supplemental oxygen from the prototype allows it to be very lightweight and portable. This is unconventional for a CPAP device but does not greatly compromise the efficacy when used for a short period of time. Neonatal resuscitation is defined as a set of interventions that help a newborn to breathe immediately following birth [33]. Delivery room CPAP can therefore be considered a resuscitation strategy, used as a short-term tool to help neonates breathe until longer-term care can be initiated. Current clinical best practice is to resuscitate neonates using air (21% oxygen). This is supported by a 2004 Cochrane meta-analysis by Davis *et al.* [34] and the 2013 European Consensus Guidelines on the Management of Neonatal Respiratory Distress Syndrome in Preterm Infants [35]. Additionally, CPAP increases functional residual capacity in the lung, thereby increasing the surface area available for gas exchange [36]. Thus, the pressure alone works to improve oxygenation, even without an increased fraction of oxygen in the inspired gas.

The portable CPAP prototype will not heat or humidify air delivered to the patient, to minimize cost and complexity. To avoid mucosal injury, gases delivered during CPAP are typically heated and humidified [37]. This is mainly required to compensate for the dryness of medical gases from a wall or cylinder. In a recent study, Dawson *et al.* found the relative humidity of piped air in a New Zealand hospital to be 5.4±0.7%, and piped oxygen to be 2.1±1.1% [38]. When using the portable CPAP prototype, the infant will be breathing filtered room air, which naturally has a higher relative humidity. For example, the average annual relative humidity in Kampala, Uganda is 77% [39]. It is expected that the humidity in ambient air will be sufficiently safe and comfortable for preterms, at least for short-term use.

Providing initial respiratory support with heated gas helps with thermoregulation of the patient and has been shown to increase the incidence of normothermia (36.5-37.5°C) upon admission to a NICU [40]. Air from the portable CPAP prototype will not be heated and will be delivered to the patient at room temperature. Room temperature in the NICU at Mbale Regional Referral Hospital ranges from 25°C to 35°C, and thermoregulation of patients is sufficiently maintained using Kangaroo Mother Care (skin-to-skin) [24]. It is therefore assumed that providing CPAP with room temperature air will not negatively impact core body temperature in preterms over a short period of time.

Using literature and expert opinions, a set of quantifiable design criteria was determined in order to guide the design process and evaluate iterations of the simulation and subsequent prototype.

At the most general level, the device should:

1. Provide the basic functionality of a CPAP device
2. Be suitable for low-resource settings (LRS)
3. Be safe for the patient
4. Be user-friendly

Each of these criteria was broken down into sub-criteria, which were then broken down further into one or more metrics. The device will be evaluated for each metric, receiving a score of *Fail*, *Borderline*, or *Excellent*. All quantifiable design criteria are listed in Table 2, and the rationale is detailed in Appendix A.

All quantifiable design criteria in Table 2 are all important to creating a safe and effective device, however, it is not feasible to evaluate all criteria for every design iteration. Therefore, five metrics that evaluate the basic functionality of a CPAP device were selected for a preliminary evaluation scheme, shown in Table 1. These 5 metrics are key to the success of the device and can be easily evaluated for a simulation or prototype iteration.

Table 1: Portable CPAP preliminary evaluation scheme. Within the scope of this project, simulations and prototype iterations will be evaluated for these five metrics only.

<i>Metric</i>	<i>Fail</i>	<i>Borderline</i>	<i>Excellent</i>
Mean pressure delivered to the patient	Outside 2-9 cmH ₂ O	Within 2-9 cmH ₂ O	4-6 cmH ₂ O
Pressure fluctuations on inhale and exhale	Outside 0-10 cmH ₂ O	Within 0-10 cmH ₂ O	Within 2-8 cmH ₂ O
Bias flow delivered to the patient	Outside 2-12 L/min	2-5 or 10-12 L/min	5-10 L/min
Likelihood of rebreathing	Negative flow in exp limb	Zero flow in exp limb	Positive flow in exp limb
Range of neonate sizes	Unsafe for 500-2500 g	500-2500 g	500-3500 g

Iterations of the Simulink model and prototype will be compared against the preliminary evaluation scheme (Table 1). Table 2 is shown below to completely specify the device, however, only Table 1 will be used within the context of this thesis.

Table 2: Quantifiable design criteria for portable neonatal CPAP device. Metrics marked with an asterisk (*) are included in the preliminary evaluation scheme.

The device should...	Sub-criteria	Metric	Fail	Borderline	Excellent
Provide the basic functionality of a CPAP device	Apply a safe positive pressure to the lungs	Mean pressure*	Outside 2-9 cmH ₂ O	Within 2-9 cmH ₂ O	4-6 cmH ₂ O or adjustable
		Fluctuations due to inhale and exhale*	Outside 0-10 cmH ₂ O	Within 0-10 cmH ₂ O	Within 2-8 cmH ₂ O
		Pressure throughout battery discharge cycle	Drops >1.5 cmH ₂ O	Drops 0.5-1.5 cmH ₂ O	Drops <0.5 cmH ₂ O
	Provide a safe and effective flowrate	Bias flow*	Outside 2-12 L/min	2-5 or 10-12 L/min	5-10 L/min
		Rebreathing*	Negative flow in exp limb	Zero flow in exp limb	Positive flow in exp limb
	Be battery powered	Lifetime	<1 year	1-5 years	>5 years
		Recharging time	>2 hours	0.5-2 hours	<0.5 hours
		Use time between charges	<1 hour	1-5 hours	>5 hours
	Fit all sizes of neonate	Neonate weight*	Unsafe for 500-2500 g	500-2500 g	500-4000 g
Be suitable for LRS	Be low-cost	Price	>1000 EUR	600-1000 EUR	<600 EUR
	Use minimal consumables	Number of consumables	Any single use	Any <20 uses	All >20 uses
	Be robust and built-to-last	Dust	IP 1st number 0-1	IP 1st number 2-4	IP 1st number 5-6
		Liquids	IP 2nd number 0-1	IP 2nd number 2-4	IP 2nd number 5-8
		Mechanical impact	IP 3rd number 0-2	IP 3rd number 3-4	IP 3rd number 5-6
		Extreme temperatures	Malfunctions in 15-35°C	Functions in 10-35°C	Functions in 10-45°C
	Be easy to clean and maintain	Cleaning time: per patient use	>15 minutes	7-15 minutes	<7 minutes
		Cleaning time: additional per month	>3 hours	0.5-3 hours	<30 minutes
		Maintenance time	>40 hours/year	5-40 hours/year	<5 hours/year
Be safe for the patient	Provide clean gas	Filtration	No filtration	Only dust	Bacteria, viruses, and dust
	Produce safe noise levels	Sound level	L _{eq} >55 dB	L _{eq} =50-55 dB	L _{eq} <50 dB
	Provide safe levels of humidification	Relative humidity	<40% RH	40-80% RH	>80% RH
	Provide gas at a safe temperature	Gas temperature	<26 or >38°C	26-31°C	32-38°C
Be user-friendly	Be portable	Weight	>9 kg	3-9 kg	<3 kg
		Orientation	Malfunctions at <40° tilt	Functional at 40-90° tilt	Functional at >90° tilt
	Be easy to use	Training time	>5 hours	1-5 hours	<1 hour
	Be fast to set up	Set up time	>3 minutes	1-3 minutes	<1 minute

3 Theory

A CPAP device in general is composed of three main components: air source, conduit (including patient interface), and pressure control. The portable CPAP prototype described in this thesis used a centrifugal fan as the air source, silicone tubing as the conduit, a nasal cannula as the patient interface, and a positive-end expiratory pressure (PEEP) valve to control the pressure. Each of these components can be described using theoretical principles.

3.1 Air Source

A centrifugal fan is a type of pump that uses rotating blades, also called an impeller, which create an increase in kinetic energy in the fluid. The volute casing, as shown in Figure 3, reduces the velocity of the gas as it exits the pump, which is accompanied by a raise in pressure [41]. This gives the fluid a uniform velocity profile. The flow through the pump is complex, unsteady, and three-dimensional, thus the average one-dimensional flow between inlet and outlet will be studied here.

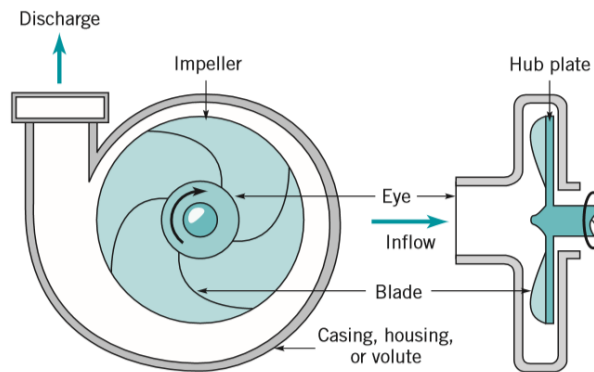


Figure 3: Components of a centrifugal pump [41].

Centrifugal pumps are characterized by a pump curve, as shown in Figure 4. A pump curve allows the pump outlet pressure to be determined for any given flowrate, and is empirically determined for a particular pump geometry and operating speed. The system curve classifies total pressure drop in the system at a given flowrate. The system curve is determined by system parameters including change in elevation, pipe sizes and lengths, friction factors, and minor losses. Frictional losses are proportional to flowrate if the flow is laminar and to flowrate squared if the flow is turbulent [41].

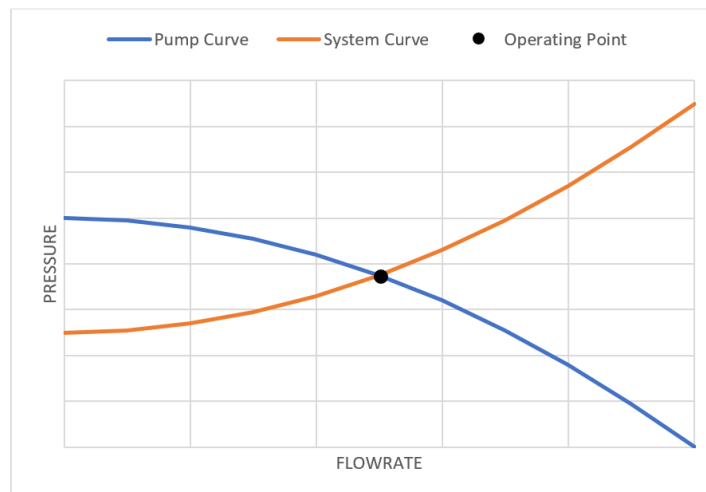


Figure 4: Sample pump curve and system curve. The operating point determines actual pump outlet pressure and flow during use.

The operating point describes the actual pump outlet pressure and flow during use and is located at the intersection of the pump curve and system curve. If either the pump or system curve are changed, the operating point changes. For the portable CPAP prototype, it is imperative that the operating point occur at a safe and effective flowrate and pressure for neonates.

3.2 Conduit

The conduit for the portable CPAP prototype is composed of three components: the inspiratory limb, nasal cannula, and expiratory limb. The inspiratory and expiratory tubing are identical, flexible, silicone tubes of approximately 1 cm diameter and 1.2 m length. The nasal cannula is the patient interface, which lies between the inspiratory and expiratory limbs. Two types of nasal cannula were analyzed for use in the portable CPAP prototype. The Hudson cannula, a popular cannula CE marked for CPAP, is shown connected to a doll in Figure 5. The inspiratory limb leads to the blue side of the cannula, and the expiratory limb is connected to the clear side of the cannula. The RAM cannula (Figure 6) is designed for use with low-flow oxygen and is not intended for CPAP. It is under consideration for the prototype because it is more user friendly than the Hudson, and is thus commonly used for CPAP in LMICs. Even if the prototype is designed for the Hudson cannula, clinicians in LMICs may substitute the RAM cannula. When used for CPAP, the inspiratory and expiratory limbs are connected to the cannula using a Y-piece (Figure 6, right).

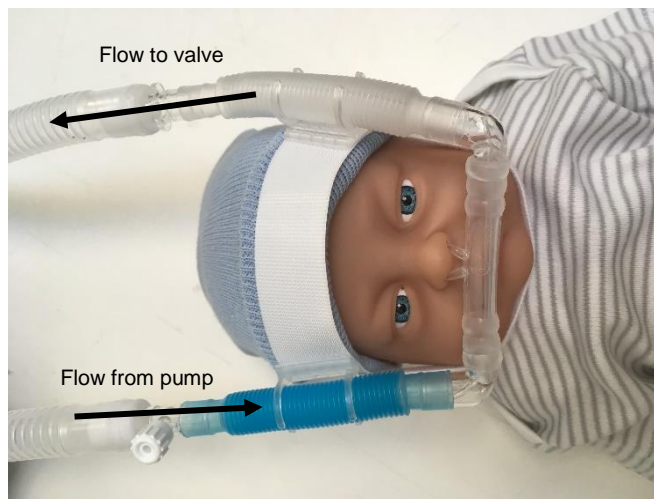


Figure 5: Doll connected to CPAP circuit using the Hudson cannula.



Figure 6: Doll connected to CPAP circuit using the RAM cannula with Y-piece.

In the portable CPAP prototype, the air flows from the pump outlet, through the inspiratory limb, nasal cannula, and expiratory limb, then finally reaches the valve. The purpose of the CPAP device is to deliver a constant, positive pressure to the patient, and there will inevitably be a pressure drop in each section of tubing from the pump to the valve. The magnitude of pressure losses can be calculated using Poiseuille's Law, which allows a prediction of the pressure delivered to the patient.

Poiseuille's Law, also called the Hagen-Poiseuille equation, is most simply described by Equation 1, where ΔP is the pressure drop [Pa], Q is the flowrate through the tube [m^3/s], and R represents resistance, which is calculated as per Equation 2. Resistance is dependent on tubing geometry (length L [m], radius r [m]) and fluid viscosity [kg/ms] and is thus a constant property of the system. It is important to note that the radius of the tubing is raised to the power of 4, thus, radius has a strong influence on pressure drop.

$$\Delta P = QR \quad (1)$$

$$R = \frac{8\mu L}{\pi r^4} \quad (2)$$

Poiseuille's Law (Equation 1) can only be used for steady, laminar, incompressible, viscous flow of a Newtonian fluid in a rigid cylindrical tube of constant cross-sectional area. Thus, the following assumptions about the flow behavior are required (pg 22 of [42]):

1. Steady flow
2. Constant viscosity
3. Incompressible flow
4. Fully developed flow
5. Laminar flow
6. No-slip at the wall

Each assumption must be confirmed. First, Assumption 1 of steady flow means the flowrate does not change over time. The flowrate will change over time as the patient breathes into the CPAP circuit, however, calculations of pressure drop are done in Simulink R2017b using a timestep of 0.001 s. It is assumed that this step size is sufficiently small that the flowrate is not changing within the iteration.

Air is a Newtonian fluid, and it is assumed that the temperature is constant within a small range of fluctuations; therefore, Assumption 2 of constant viscosity will hold true [43]. The pump that will be used in the portable CPAP is a centrifugal fan, and the change in gas density through a fan is usually less than 7% (about 1 psi when the fluid is air). This value is negligible and allows density to be treated as constant, therefore the flow is incompressible and Assumption 3 holds true [41]. This means that conservation of mass (Equation 3) also applies to the system, where Q is flowrate, A is cross-sectional area, and V is velocity.

$$Q = AV = \text{constant} \quad (3)$$

Assumption 4 indicates that the Hagen-Poiseuille equation is only valid in the fully developed region of flow, and not in the hydrodynamic entrance region, illustrated in Figure 7. The length of the hydrodynamic entrance region, or "entrance length," can be calculated for laminar flow. The ratio of entrance length to tube diameter is approximately equal to 0.06 divided by the Reynolds number (pg 19, [42]). There is no exact maximum entrance length to assume fully developed flow for the whole conduit, however, the entrance length should be much smaller than the length of the conduit itself. It is assumed this is true for the portable CPAP prototype, because the inspiratory and expiratory limbs are long and narrow. The pressure gradient along the length of the tube is assumed to be constant in the region of fully developed flow.

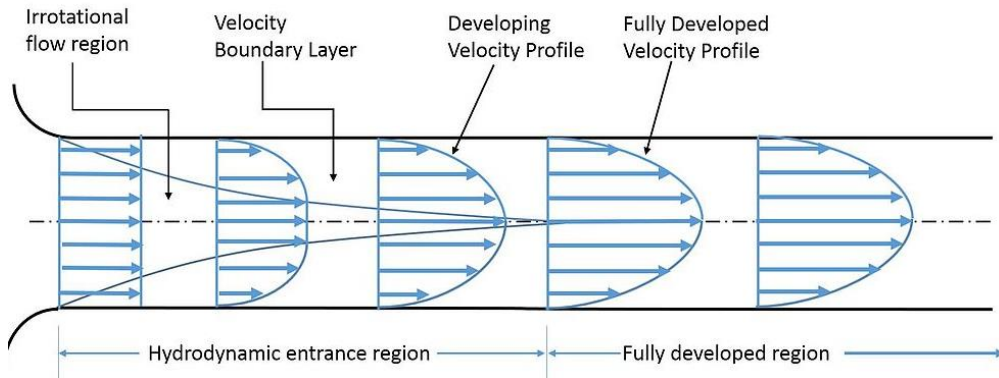


Figure 7: Entrance region and fully developed region of pipe flow, between which the velocity profile transitions from linear to parabolic [44].

The validity of Assumption 5 (laminar flow) is determined by the Reynolds number, a dimensionless constant used to describe fluid flow. It is the ratio of inertial forces to viscous forces, calculated using Equation 4, where ρ is fluid density [kg/m³], V is average velocity [m/s], D is tube diameter [m] and μ is dynamic viscosity [kg/ms]. The Reynolds number (Re) uses the average velocity ($V_{avg} = V_{max}/2$), which should not be confused with the maximum velocity, found at the centre of the tube. When $Re < 2000$, the flow is laminar, from 2000-4000 is transitional, and $Re > 4000$ indicates turbulent flow (pg 18 of [42]). These numbers are a guideline, and will also vary depending on roughness of the entrance length, vibration of the tubing, and other factors (pg 386, [41]). The Reynolds number must be less than 2000 in all sections of tubing for Assumption 5 to hold true, and this will be checked during simulation of the portable CPAP in Simulink.

$$Re = \frac{\rho V D}{\mu} \quad (4)$$

Assumption 6, the no-slip condition, means that velocity at the wall is 0, and the maximum velocity occurs at the centre. This is true for all fluids, because the molecules of fluid adhere to the conduit walls (pg 8, [42]).

There are other features in the CPAP circuit that can cause a change in pressure. The pressure change from tubing of one diameter to another can be calculated using Bernoulli's equation for incompressible, inviscid flow along a streamline (pg 116 of [41]). Ignoring the effects of gravity, the pressure drop across a sudden diameter change is calculated using Equation 5, where P is pressure [Pa], ρ is density [kg/m³], g is the gravitational constant 9.81 m/s², and V is velocity [m/s].

$$P_2 - P_1 = \frac{1}{2} \rho \left(\frac{Q}{A_1} \right)^2 - \frac{1}{2} \rho \left(\frac{Q}{A_2} \right)^2 \quad (5)$$

Finally, there are minor losses in the system due to areas where the flow must go around a corner, which can be calculated using Equation 6 (pg 422 of [41]). The pressure drop ΔP depends on velocity V , the gravitational constant g , and the minor loss coefficient K_L . Minor loss coefficients can be found in lookup tables. For example, the minor loss coefficient for a regular, 90°, threaded elbow is 1.5, which is relevant for the elbows in the Hudson cannula (pg 422 of [41]).

$$\Delta P = K_L \frac{V^2}{2g} \quad (6)$$

Using these equations to calculate pressure losses in the system, it is possible to determine the pressure at any point of interest, including at the patient and at the valve.

3.3 Pressure Control

The pressure in the portable CPAP prototype circuit is controlled using a positive end expiratory pressure (PEEP) valve attached to the end of the expiratory limb. A PEEP valve uses a small disk on a spring to control the pressure, as shown in Figure 8.

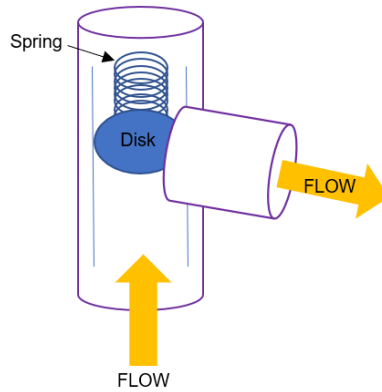


Figure 8: Diagram of a PEEP Valve.

The pressure delivered by a PEEP valve is set by the manufacturer, and for this project, PEEP valves with a pressure setting of 5 cmH₂O will be used. Adjustable PEEP valves can also be used, such as the Ambu PEEP [45], which allows the user to change the spring constant by tightening or loosening the end cap. An ideal PEEP valve would give the specified pressure at any flowrate. In reality, they cannot achieve this at high and low flowrates, thus the relationship between pressure and flow must be empirically determined for each valve.

4 Simulink Model

The first step in creating the portable CPAP was to make a Simulink model. The purpose of the model was to simulate the flow through the portable CPAP device for a variety of conditions. The model allowed input parameters to be varied and outputs of interest to be measured, which subsequently aided in design decision making. Screenshots of all subsystems of the model are found in Appendix B.

4.1 Model Methods

A model was created using MATLAB and Simulink R2017b to make predictions about the behavior of the portable CPAP prototype. The model calculates the system curve, and thus determines the operating point for any given pump curve. The model also examines how a patient breathing into the CPAP circuit impacts the behavior of the device. By modelling the portable CPAP prototype in this way, pressure and flow at any point in the circuit can be determined, thus providing a robust understanding of how such a device would function.

The methods of calculating pressure and flow in the circuit are explained in section 4.1.1. Then, three key inputs to the model are discussed in detail: the pump curve, the valve curve, and the patient breathing model. The pump curve and valve curve are empirically determined equations relating pressure and flow. Given the pump outlet pressure, the pump curve outputs the pump flow. The valve curve outputs the pressure applied by the PEEP valve, given a flowrate. The patient breathing model simulates the flowrate generated by the patient breathing at the nasal cannula. Patient flow was modelled in two ways: a sine wave model and a custom model that aimed to replicate a waveform seen on a ventilator.

4.1.1 Pressure Drop

By definition, a CPAP circuit has a continuous positive pressure within it. However, the pressure is not constant at all points in the circuit. As outlined in section 3.2, flow through a long tube will experience a pressure drop that is dependent on flowrate and tube geometry. Pressure drop in each limb of tubing of the portable CPAP prototype can be calculated using Equations 1, 5, and 6. Summed with the pressure applied by the PEEP valve, this defines the pressure the pump must work against. Additionally, it is important to calculate pressure drop in each limb of tubing individually to determine the pressure delivered to the patient.

There are two flowrate inputs to the system: pump flow (Q_{pump}) and cannula flow (Q_{cannula}), where cannula flow is the flowrate entering or leaving the CPAP circuit due to the patient breathing. The flowrate in any given limb of tubing can be described in terms of Q_{pump} and Q_{cannula} . For example, flow in the inspiratory limb is equal to Q_{pump} , and in the expiratory limb is equal to $Q_{\text{pump}} - Q_{\text{cannula}}$. Flow through the nasal cannula is more complex; Figure 9 shows diagrams of both cannula types with arrows illustrating the flowrate through each section.

Pressure drop in the inspiratory and expiratory limbs is calculated using Poiseuille's Law (Equation 1). Poiseuille's Law was also used to calculate pressure drop in the nasal cannula, in addition to some other pressure losses, shown in grey in Figure 9. Minor losses in the elbows of the Hudson cannula, minor losses in the turn of the Y-piece, and the sudden diameter change where the Y-piece meets the RAM cannula were included in the calculations. Pressure delivered to the patient is calculated as the sum of the valve pressure, pressure drop in the expiratory limb, and pressure drop in the second half of the nasal cannula. The Simulink model uses a variant subsystem to test both types of cannula.

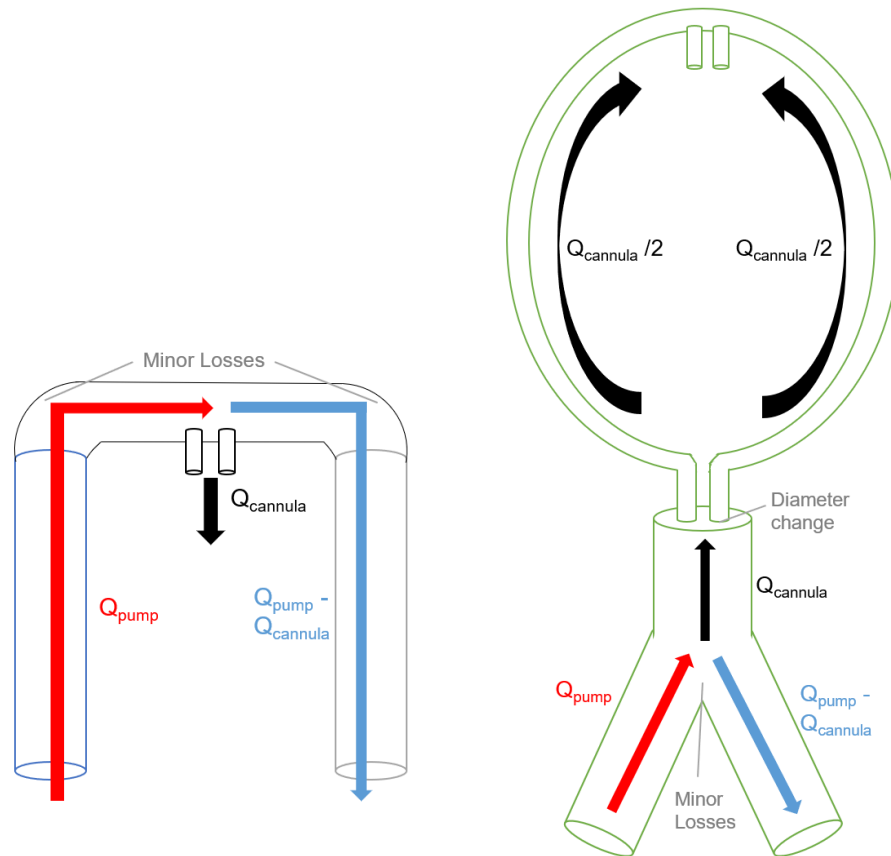


Figure 9: Flowrate in different sections of the Hudson cannula (left) and RAM cannula (right). Pressure drop in each section is calculated according to Poiseuille's law, and additional pressure losses (shown in grey) are due to a sudden diameter change (Bernoulli's law) and minor losses in sharp turns of the tubing.

4.1.2 Pump Curve

A pump curve defines a relationship between pressure and flowrate that is unique to a particular pump and input voltage. The pump curve is often provided by the manufacturer when purchasing a pump, however, gathering empirical data is beneficial to provide insight into use in a particular application. Two pumps were considered for the portable CPAP prototype and pump curves were empirically determined for both. Both pumps are made by Micronel UK [46] due to their relationship with Diamedica UK Ltd. The U51DL and U71HL radial blowers, shown in Figure 10, both include integrated electronics that control RPM.

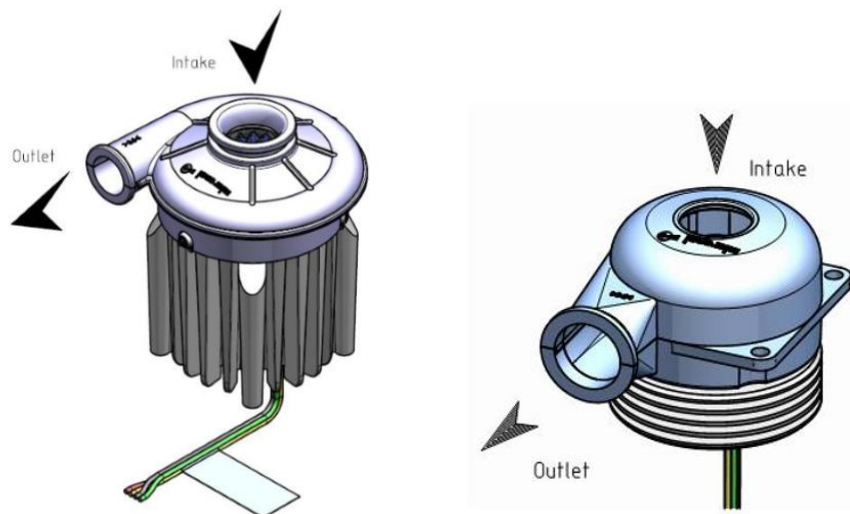


Figure 10: U71HL-024KM-4 (left) and U51DL-024KK-4 (right) radial blowers with integrated electronics [46].

The pumps were tested at a variety of RPM settings to determine a series of empirical pump curves. The U51DL required a 9V input to achieve this range of RPMs, and the U71HL required a 12V input. Each pump was directly connected to a flowmeter (FlowAnalyser PF-300 [47]) with an adjustable PEEP valve at the flowmeter exit. The FlowLab software was initiated to collect paired readings of pressure and flow at a sample rate of 200Hz for 60 seconds. During that time, the PEEP valve was slowly adjusted between fully closed and fully open. This was repeated three times for each RPM setting. The raw data from these tests are presented in Figure 11 (U51DL) and Figure 12 (U71HL). The RPM settings are abbreviated such that k represents 1000, i.e. 17k = 17000 RPM. It should be noted that there is increased noise around 2-8 L/min of flow for both pumps, and for all RPM settings. It is assumed that this is an artefact of the adjustable PEEP valve and not a characteristic of the pump. This will be discussed further in Chapter 7 (Discussion).

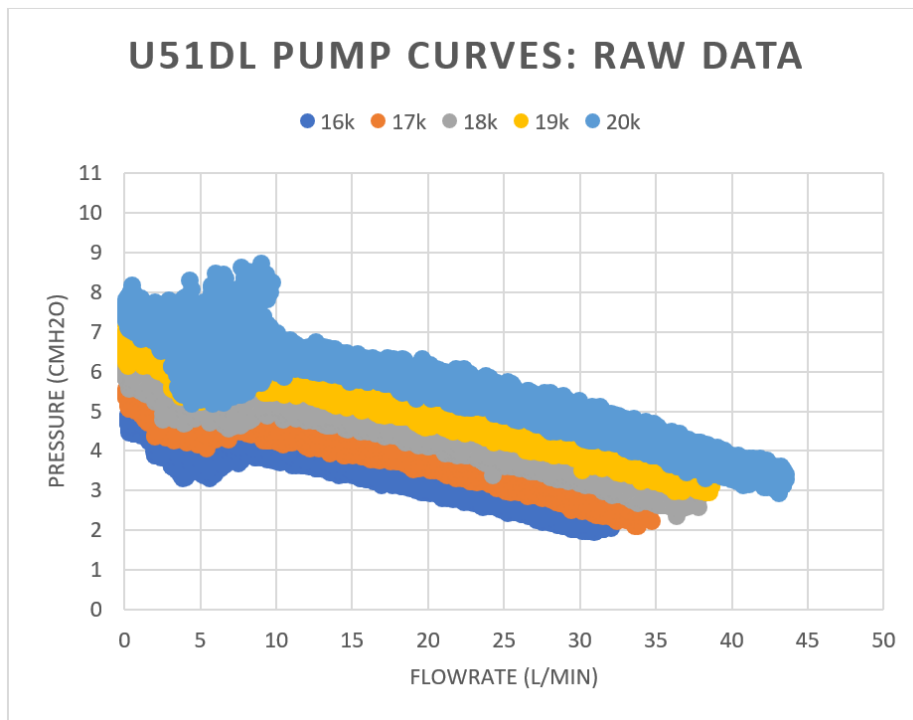


Figure 11: Empirical testing raw data for U51DL pump.

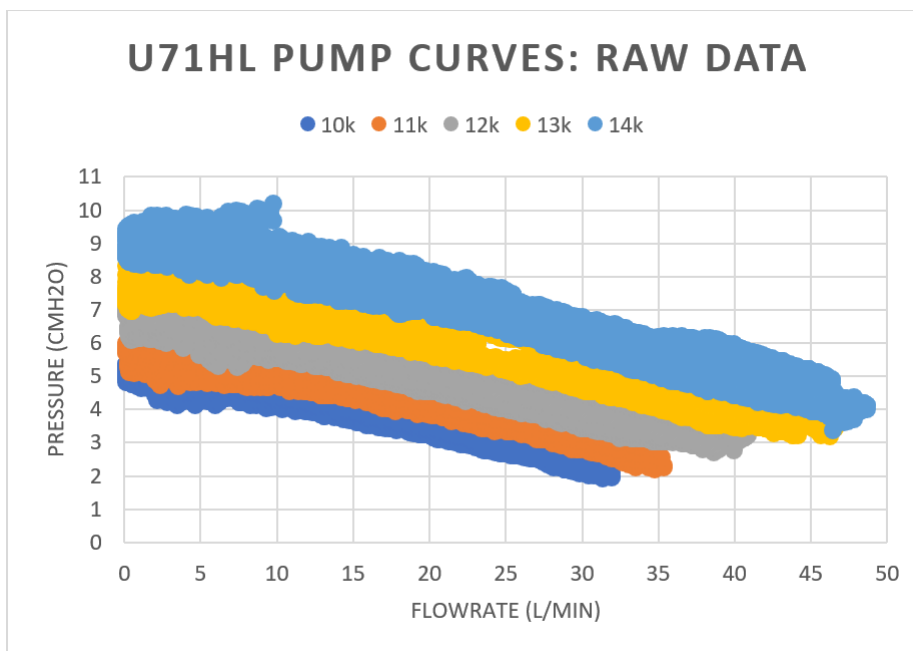


Figure 12: Empirical testing raw data for U71HL pump.

Using Excel 2016, the line of best fit was determined from the raw data, for each RPM. All R^2 values were greater than 0.9, indicating that a linear fit is a good estimate. The line of best fit will be hereafter referred to as the pump curve. Pump curves at each tested RPM are displayed for the U51DL in Figure 13 and the U71HL in Figure 14. The operating point boundary forms a rectangle from 5-10 L/min and from 4-6 cmH₂O. Shown in both figures, this represents the desired pressure and flowrate as defined in the preliminary evaluation scheme (Table 1). A pump curve defines pressure at the pump outlet, but the pressure delivered to the patient will likely be somewhat lower. Therefore, a pump outlet pressure of slightly higher than 6 cmH₂O is not necessarily a problem. The exact upper limit will depend on the characteristics of the patient and CPAP circuit.

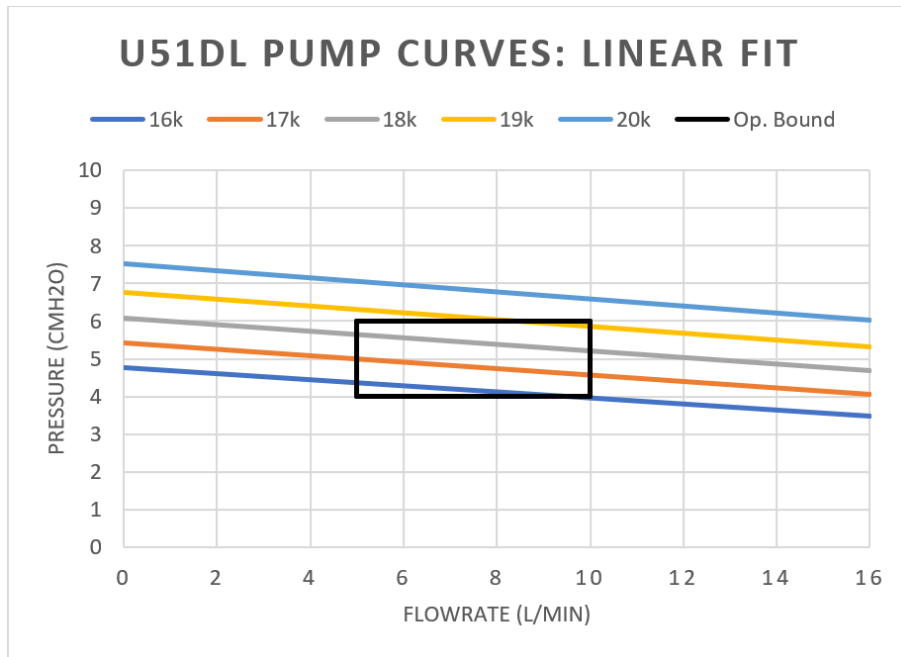


Figure 13: Pump curves for various RPMs for U51DL pump.

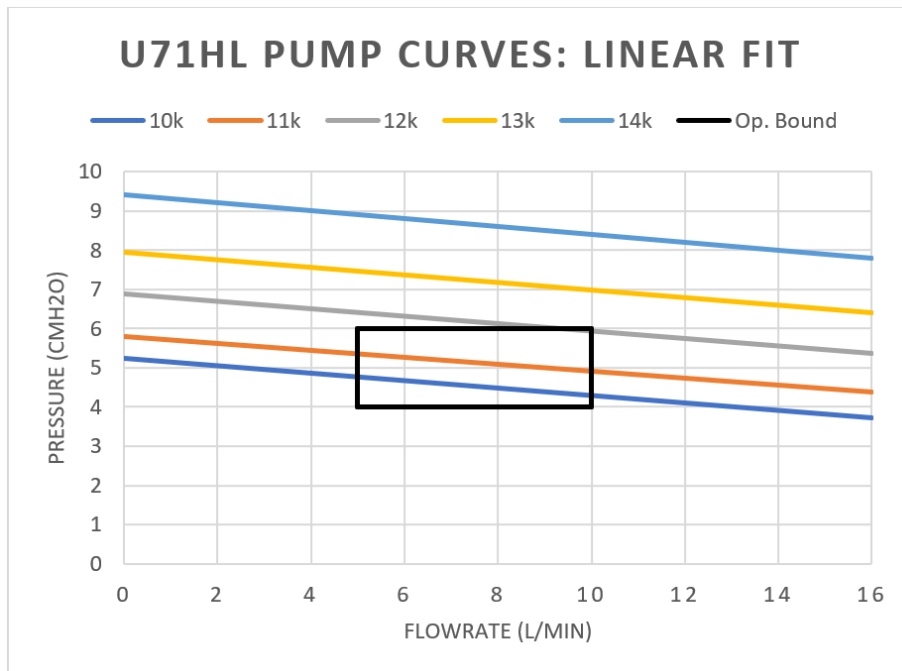


Figure 14: Pump curves for various RPMs for U71HL pump.

The pump curve equations are shown in Table 3 in terms of pump flow Q (L/min) and pump outlet pressure P (cmH₂O). The empirical input to the Simulink model is the slope and y-intercept of the selected pump curve equation.

Table 3: Pump curve equations in terms of pressure in cmH₂O (P) and flowrate in L/min (Q) at five RPM settings per pump.

Pump	RPM	Equation	R ²
U51DL	16k	$P = -0.0802Q + 4.7667$	0.9792
	17k	$P = -0.0857Q + 5.4365$	0.9831
	18k	$P = -0.0865Q + 6.0709$	0.9807
	19k	$P = -0.09Q + 6.7588$	0.9838
	20k	$P = -0.093Q + 7.5264$	0.9755
U71HL	10k	$P = -0.0955Q + 5.2504$	0.9865
	11k	$P = -0.0883Q + 5.7996$	0.964
	12k	$P = -0.0949Q + 6.8899$	0.9568
	13k	$P = -0.0969Q + 7.9565$	0.9521
	14k	$P = -0.1023Q + 9.428$	0.9453

Suitable RPM settings for each pump are 16-19k for the U51DL pump and 10-12k for the U71HL pump because these pump curves pass through the operating point boundary. Either pump should be appropriate for generation of a proof-of-concept prototype, however, moving forward, the U51DL was exclusively used. The U51DL had inlet and outlet fittings that were already compatible with the rest of the CPAP circuit and relevant test equipment. Additionally, the U51DL responded faster when a change was made to the RPM setting, without overshoot or oscillations. Therefore, the U51DL was used for convenience of testing. It is assumed that the U71HL pump would function similarly and could respond well to RPM control given better PID tuning.

4.1.3 Valve Curve

The pressure generated by the PEEP valve is flow dependent in a certain range of flowrates, a relationship that is not often provided by the manufacturer. The 5 cmH₂O Clariti PEEP valve from Armstrong Medical [48] was selected for the portable CPAP prototype due to availability at the Diamedica UK Ltd. workshop. The valve was tested using the FlowAnalyser PF-300 [47] to generate a series of paired points of flowrate and pressure. Flow was varied in increments of 0.5 L/min from 0 to 15 L/min using wall air in the department of Medical Technology of the Erasmus Medical Centre, Sophia Children’s Hospital in Rotterdam, the Netherlands. The valve was attached to the outlet of the flowmeter, and pressure was measured for each flowrate.

The paired points of pressure and flow were plotted (Figure 15), then piecewise curve fitting was completed in Excel 2016. The valve curve took the form of a second order polynomial combined with a linear function, transitioning from parabola to line at a flowrate assigned the variable *u*. The value of *u* was determined by looking at the curve; for the 5 cmH₂O Clariti PEEP valve, *u* = 6 L/min.

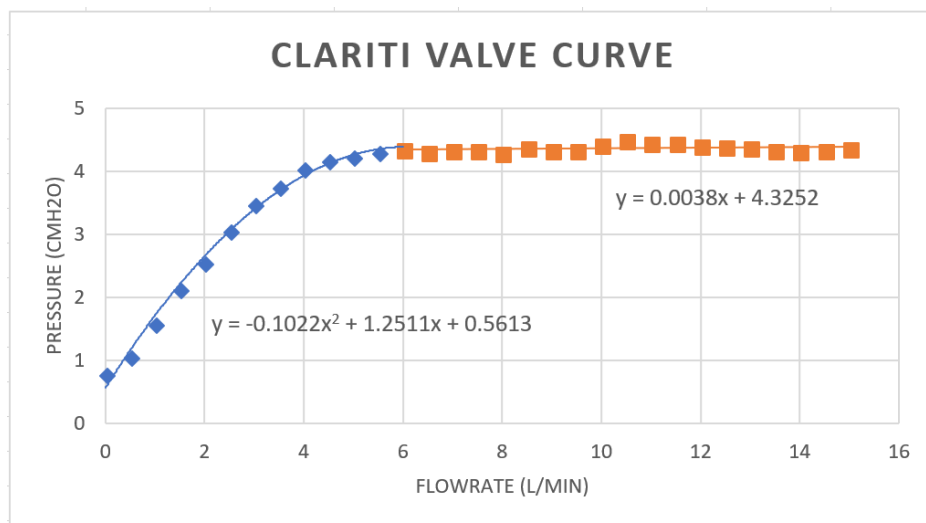


Figure 15: Raw data relating pressure and flowrate for the Clariti 5 cmH₂O PEEP valve.

For the Simulink model, the curve had to be slightly modified to ensure there was no discontinuity where flowrate = u. For flowrates less than u, pressure was calculated as per the equation of the parabola in Figure 15, with coefficients a, b, and c (Equation 7). For all flowrates higher than u, the curve is approximated as a flat line with a slope of 0 (Equation 8). The y-intercept is found by letting Q=u in Equation 7. The two functions are equal for Q=u, thus ensuring a continuous function, plotted in Figure 16.

$$P = aQ^2 + bQ + c \text{ for } Q \leq u \tag{7}$$

$$P = au^2 + bu + c \text{ for } Q \geq u \tag{8}$$

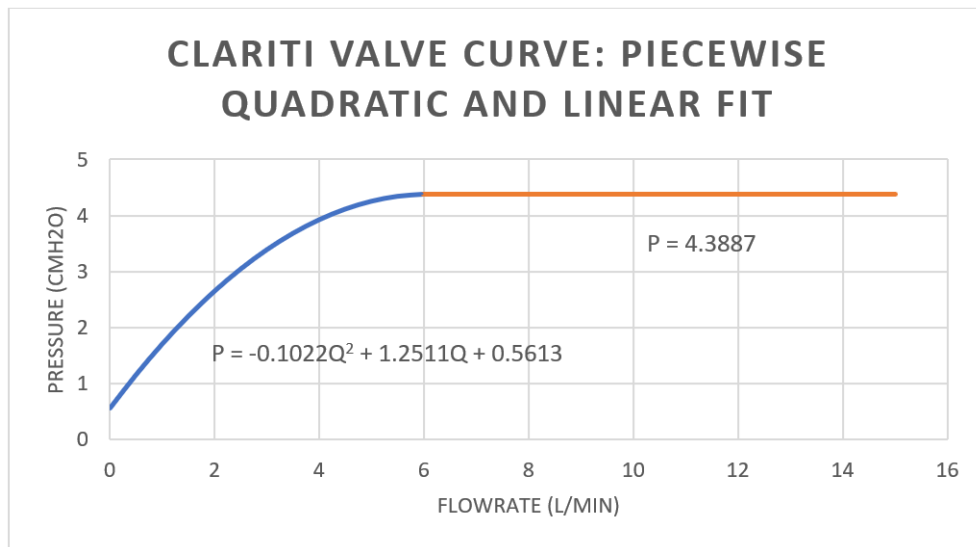


Figure 16: Valve curve represented as a continuous function for the Clariti 5 cmH₂O PEEP valve. Parabolic function is exactly as determined from curve fitting, linear function has been modified to remove discontinuity at Q = 6 L/min.

Future valves under consideration should be empirically tested, then curve fitting should be performed in the same way. The value of u and equation of the parabola will vary across different PEEP valves. Additionally, the linear portion will not go on infinitely, and a slope of 0 may not be a good approximation for all valves. It should be confirmed that linear portion of the valve curve is valid for all relevant flowrates.

4.1.4 Patient Breathing

The flowrate into and out of the patient’s lungs must be considered when analyzing flow in the CPAP device. This flowrate is calculated as the derivative of volume in the patient’s lungs over time. If a model of lung volume can be created, the waveform of flowrate simply follows.

The two most important parameters to characterize a patient breathing are tidal volume and breathing rate. Tidal volume (V_T) is the volume of gas that moves in or out of the patient’s lungs in each breath, during normal breathing. Tidal volume is proportional to patient mass and can be approximated at 7 mL/kg [4]. Breathing rate is usually described in terms of breaths per minute (BPM). Newborns typically breathe at a rate of 30-60 BPM, however, the portable CPAP prototype is intended for preterm neonates with respiratory distress syndrome, which is characterized by a BPM greater than 60 (called tachypnea) [49]. Transient tachypnea of the newborn develops in the first few hours of life, and is characterized by a breathing rate that fluctuates between 80-120 BPM [50, p. 28].

Patient breathing can be modelled as a volume waveform over time, written in terms of V_T and BPM. Two ways to model patient breathing are presented below: a simple sine wave model, and a custom model designed to mimic the volume waveform seen on a ventilator.

4.1.4.1 Sine Wave Breathing Model

A sine wave is a simple periodic function that cycles smoothly between a low value and a high value at a set frequency. It is therefore a good starting point to model the volume in a neonate's lungs. The general equation of a sine wave is shown in Equation 9, where A is the peak deviation from the mean and f is the number of cycles per second. Phase shift is not considered, because during breathing, time zero is arbitrary.

$$y(t) = A\sin(2\pi ft) \quad (9)$$

This equation can be rewritten in terms of V_T [L] and BPM to solve for volume in the lungs as a function of time (Equation 10). The amplitude of this sine wave is half the tidal volume and the frequency is the number of breaths per second. The sine wave is shifted up by half the tidal volume, so the minimum value of the sine wave is zero.

$$V(t) = \frac{V_T}{2} + \frac{V_T}{2} \sin\left(\frac{2\pi BPM}{60} t\right) \quad (10)$$

Flowrate [L/s] is calculated as the derivative of volume [L] vs. time [s]. By differentiating Equation 10 then multiplying by 60, the equation for flowrate in L/min is calculated (Equation 11). Equation 11 has a mean of zero; a positive value for Q means flow is entering the lungs (inhalation) and a negative flow means flow is leaving the lungs (exhalation).

$$Q(t) = V_T \pi BPM * \cos\left(\frac{2\pi BPM}{60} t\right) \quad (11)$$

The amplitude of Equation 11 is the peak inspiratory/expiratory flow. This is the flowrate that the portable CPAP prototype must accommodate for. When the patient inhales, the flowrate in the expiratory limb decreases by the peak inspiratory flow. It is imperative that peak inspiratory flow not exceed the flowrate from the pump, which would result in rebreathing. When the patient exhales, the flowrate in the expiratory limb increases by the peak expiratory flow. The flowrate from the pump summed with the peak expiratory flow should not overwhelm the valve resulting in overpressure.

4.1.4.2 Custom Breathing Model

Patient flowrate is a key input to the Simulink model; thus, it was important to create a volume vs time waveform that had an accurate shape. The custom patient breathing model was created to achieve a higher level of fidelity than a simple sine wave. A neonatal ventilator was connected to a test lung at the department of Medical Technology of the Erasmus Medical Centre, Sophia Children's Hospital in Rotterdam, the Netherlands and a photograph was taken of the volume waveform (Figure 17). The photo was analyzed using WebPlotDigitizer [51] and using piecewise curve fitting in Excel 2016, it was verified to take the shape of two second order polynomial functions, with R^2 values of 0.9994 and 0.9975 on the inhale and exhale respectively. Knowing this general shape, it was possible to calculate a piecewise equation for volume vs. time in terms of variables that allow the patient characteristics to be modified. For purposes of the simulation, it was assumed that the patient first inhales, takes a pause with full lungs, exhales, then takes a pause with empty lungs of equal duration to the first pause.

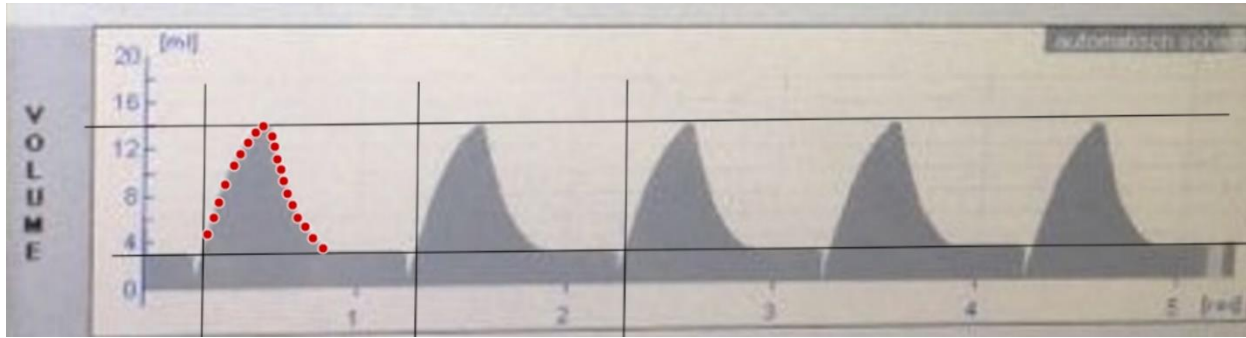


Figure 17: A photo of the screen of a neonatal ventilator was imported into WebPlotDigitizer [51] and piecewise curve fitting was done in Excel 2016.

The custom breathing model takes an additional parameter into account: inhale to exhale ratio. The sine wave model can only represent a ratio of 1:1, where equal time is spent inhaling as is spent exhaling. In reality, the inhale to exhale (I:E) ratio can vary. An adult breathes normally with a ratio of approximately 1:2, meaning exhalation takes approximately twice the time of inhalation [52]. This ratio can be as high as 1:4 in patients with asthma, and an inverse ratio (2:1) can be used to ventilate non-compliant lungs [52]. An I:E setting of 1:1 is recommended for mechanical ventilation of infants [53].

A MATLAB script was written to characterize the volume vs. time waveform using a set of variables, summarized in Table 4. Tidal volume in litres (V_T), breathing rate in breaths/minute (BPM), and the inhale/exhale/pause ratio can be set manually by the user in MATLAB, where i_ratio is the numerator and e_ratio is the denominator of the I:E ratio. The variable p_frac is the fraction of time in the breath where no air is entering or leaving the lungs. For example, if p_frac is set to 0.3, then 30% of the total breath period is a pause; thus 15% of the breath period is a pause with full lungs and 15% of the breath period is a pause with empty lungs. These values are used to calculate the duration of inhalation and exhalation in seconds (t_i and t_e , respectively), and the duration of one pause in seconds (t_p), where both pauses are of equal duration (for a total pause duration of $2*t_p$).

Table 4: Summary of variables used to describe characteristics of the patient's breathing pattern.

Variable	Definition	Value
V_T	Tidal volume (litres)	Set by the user
BPM	Breathing rate (breaths/minute)	Set by the user
i_ratio	Numerator of the I/E ratio	Set by the user
e_ratio	Denominator of the I/E ratio	Set by the user
p_frac	Fraction of the breath time that is pause	Set by the user
T	Duration of one breath (seconds)	60/BPM
t_i	Duration of inhale (seconds)	$(T - T*p_frac)*(i_ratio/(i_ratio + e_ratio))$
t_e	Duration of exhale (seconds)	$(T - T*p_frac)*(e_ratio/(i_ratio + e_ratio))$
t_p	Duration of one pause (seconds)	$T*p_frac/2$

These variables are used to define the volume vs. time waveform, which is made up of 4 functions, listed below in Table 5 and illustrated in Figure 18.

Table 5: List of functions that comprise the custom breathing model.

Part of breath cycle	Function	Interval
Inhale	$f(x)$	$[0 : t_i]$
Pause (full lungs)	$h_1(x)$	$[t_i : t_i+t_p]$
Exhale	$g(x)$	$[t_i+t_p : t_i+t_p+t_e]$
Pause (empty lungs)	$h_2(x)$	$[t_i+t_p+t_e : T]$

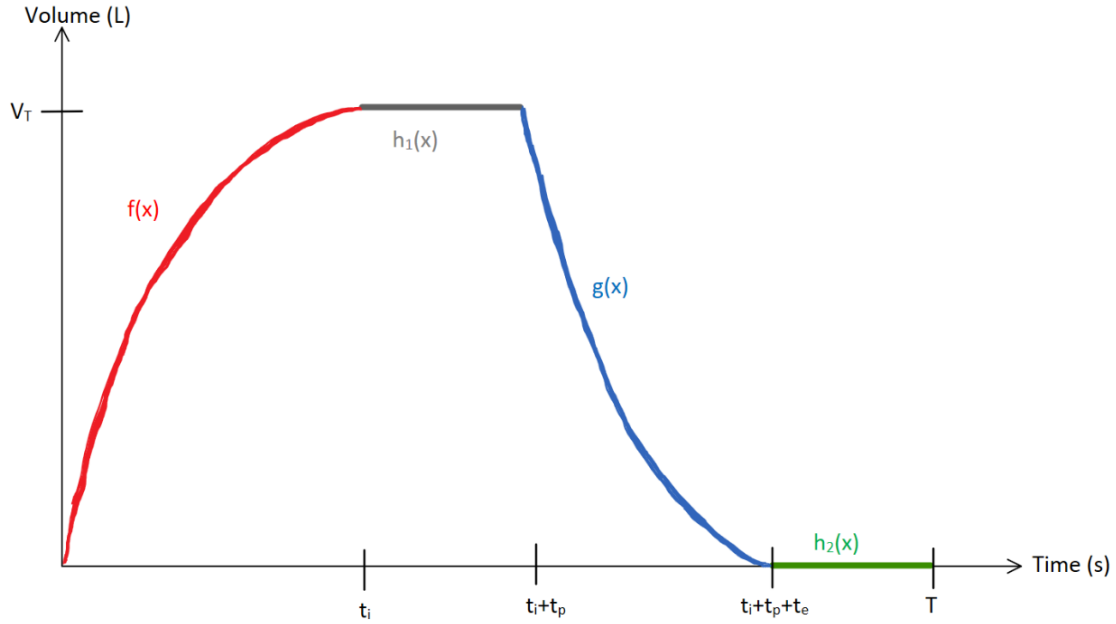


Figure 18: Custom model of volume in the patient's lungs for one breath. The waveform is composed of 4 functions for the time intervals shown on the graph. The total time for one breath T can also be written as $t_i+2t_p+t_e$.

The functions are described as per the set of Equations 12-15. The derivation is detailed in Appendix C.

$$f(x) = \frac{-V_T}{t_i^2} x^2 + \frac{2V_T}{t_i} x \quad (12)$$

$$h_1(x) = V_T \quad (13)$$

$$g(x) = \frac{V_T}{t_e^2} x^2 + \left(\frac{-2V_T(t_i+t_e+t_p)}{t_e^2} \right) x + \left(\frac{V_T t_p^2}{t_e^2} + \frac{2V_T t_p(t_i+t_e)}{t_e^2} + \frac{V_T(t_i+t_e)^2}{t_e^2} \right) \quad (14)$$

$$h_2(x) = 0 \quad (15)$$

The volume function must repeat every T seconds to simulate the system for multiple breaths. To achieve this, the simulation time (t) was passed through a sawtooth function (Equation 16). This generates a signal that rises linearly from 0 to T , then starts again from 0. That signal was then used as the input time for the volume function, allowing it to repeat. A discrete FIR filter was applied to prepare the volume signal for numerical differentiation.

$$input\ time = \frac{T}{2} \left(1 + \text{sawtooth} \left(\frac{2\pi t}{T} \right) \right) \quad (16)$$

The final consideration for simulation of breathing is leak. During inhalation, it is assumed that the patient draws their full breath from the CPAP device through the nasal cannula. When exhaling however, some percentage of the exhaled gas will leak out of the circuit at the cannula, because a perfect seal to the patient's nose is unlikely. The simulation takes this into account, and the % leak can be set manually in MATLAB. It does not consider leak at other locations in the circuit. Leak was applied in this way to both the sine wave model and the custom model.

In summary, these theoretical principles can be used to predict the behavior of a portable CPAP device. Given empirical data from a selected pump and valve, the dimensions of a selected cannula and tubing set, and a set of patient parameters, the pressure and flow at any location in the circuit can be calculated throughout the breathing cycle.

4.2 Model Results

The Simulink model was first run as an open loop model to generate a system curve. The open loop model was tested by inputting flowrates directly, without the use of a pump curve and without a feedback loop. The open loop model results describe the portable CPAP system curve and explain how various parameters impact it. The closed loop model introduces the pump into the system thereby adding feedback. These results characterize the operating point and how it changes during use.

4.2.1 Open Loop Model

As introduced in Figure 4, the system curve is calculated by summing all pressure losses in the system at any given flowrate, and thus, the system curve indicates the required pump outlet pressure at each flowrate. The inclusion of a patient breathing disturbs the flow in the CPAP, therefore patient parameters have an important impact on the system curve. The custom breathing model was used to test this impact. Realistic boundary conditions for tidal volume, breathing rate, I:E ratio and leak are summarized in Table 6. All patient parameters affect the cannula flow, and thus are sorted by whether they contribute to raising or lowering the cannula flow. Tidal volumes correspond to a neonate of 500 g (lower flow) and 3500 g (higher flow) at 7 mL/kg [54], [55]. A BPM of 30 is the low range of healthy, and 120 BPM is possible in severe tachypnea [50].

Table 6: Possible values for patient parameters, categorized by whether they contribute to raising or lowering patient flow.

Parameter	Lower Flow	Medium Flow	Higher Flow
Tidal Volume (V_T)	3.5 mL	15 mL	24.5 mL
Breathing Rate (BPM)	30/minute	60/minute	120/minute
I:E Ratio	1:1	1:2	1:4
Leak	50%	20%	0%

As a representative test for how these parameters impact the CPAP system curve, tidal volume was varied while all other parameters were held constant. There are two curves for each tidal volume plotted in Figure 19: the higher represents the system curve during exhalation and the lower represents the system curve during inhalation. A pump curve (U51DL, 17k) is plotted for reference. The variation in system curve from inhale to exhale means the operating point will shift during use. During inhalation, pump pressure decreases and pump flow increases, and vice versa for exhalation. This effect is more pronounced in larger patients.

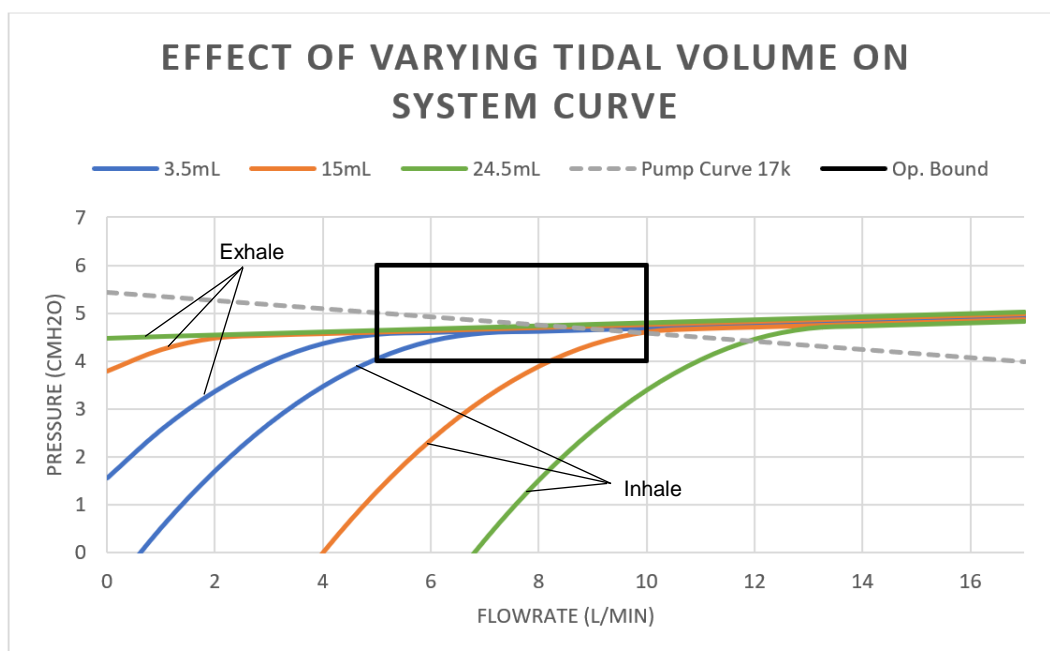


Figure 19: System curve variation as predicted by the Simulink model. Tidal volume was varied to simulate a small (3.5 mL), medium (15 mL), and large (24.5 mL) patient. Selected pump curve is U51DL pump set to 17k RPM. Constant settings: BPM = 60, I:E ratio = 1:1, 20% pause time and 20% leak.

The system curves shown in Figure 19 all take a similar shape to the valve curve. The linear portion is nearly identical for all patient types, but the flowrate at which the system curve transitions from non-linear to linear varies for each patient type. For the largest patient ($V_T = 24.5$ mL), the inhalation system curve becomes linear at 13 L/min, and for the smallest patient ($V_T = 3.5$ mL) the linear portion begins at 7 L/min. This is due to the variation in peak inspiratory flow. Recall that for the 5 cmH₂O Clariti PEEP valve, the valve curve is linear only at flows greater than 6 L/min. When a patient produces a large peak inspiratory flowrate due to a larger tidal volume, faster BPM, or shorter inhale time, this may cause the expiratory limb flow to drop below 6 L/min, where the valve curve is nonlinear.

Peak inspiratory flow is the minimum flowrate that a patient requires from the CPAP to ensure that the patient is not rebreathing gas from the expiratory limb. The peak inspiratory flow produced by each type of patient in Figure 19 is indicated by the flowrate at which the inhale system curve crosses the x-axis (1 L/min for 3.5 mL, 4 L/min for 15 mL, and 7 L/min for 24.5 mL).

Examining the intersection of the system curves with the pump curve, it is clear that this system is less suitable for the largest patient, as the operating point lies outside of the operating point boundary during inhalation. These results indicate that a different PEEP valve may be required to design a prototype that is suitable for patients with larger peak inspiratory flowrates. The valve curve should transition from non-linear to linear at the lowest possible flowrate. Other pump curves can be considered in combination with a variety of valves to reach the optimal solution.

The system curve characterizes pump outlet pressure and pump flowrate, but it is also important to analyze the patient pressure at each possible pump flowrate. Though the cannula type does not affect the pump pressure curve, it does affect the patient pressure curve. The pressure delivered to a patient with a large tidal volume (24.5 mL) during inhalation and exhalation are plotted in Figure 20 for the RAM and Hudson cannulas. As seen in Figure 20, the inhale and exhale pressure curves are closer together for the Hudson cannula than for the RAM. The RAM cannula has larger fluctuations in pressure, experiencing a >1 cmH₂O difference between inhale and exhale pressure in the linear portion of the curve. These results indicate that the RAM cannula is a more challenging design choice due to the pressure fluctuations, however, it is still possible to design a CPAP that is safe for use with the RAM cannula, as this magnitude of fluctuations still receives an excellent score in the preliminary evaluation scheme (Table 1).

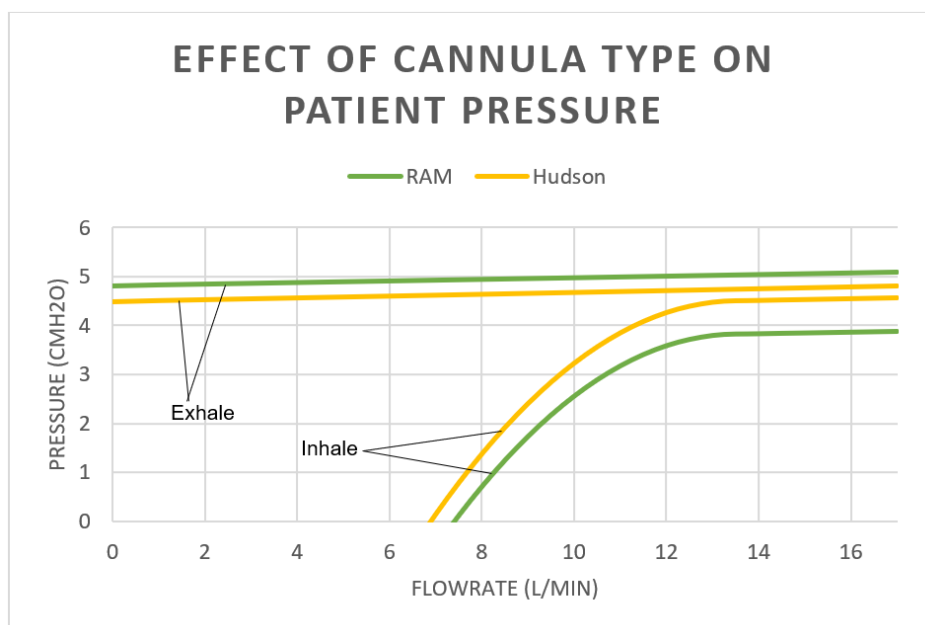


Figure 20: For a patient with 24.5 mL tidal volume, patient pressure curve for RAM and Hudson cannulas. Simulation for patient with BPM of 60, I/E ratio of 1:1, 20% pause time and 20% leak.

In summary, the results suggest that a patient with a large inspiratory flowrate risks experiencing a larger flowrate and lower pressure during inhalation. Using the RAM cannula resulted in larger fluctuations in patient

pressure. The model also suggests that a valve with a higher pressure at low flowrates and slightly higher pressure overall may improve device robustness for larger patients.

4.2.2 Closed Loop Model

The closed loop model combines the pump and system curves in a feedback loop, thus determining the actual operating point. The model was run first for a *no patient* condition. With no patient breathing, pump flow and pressure were approximately 8.8 L/min and 4.7 cmH₂O for the 17k RPM setting and 13.7 L/min and 4.9 cmH₂O for the 18k RPM setting. As illustrated in Figure 21, setting the pump to 17k RPM produced an operating point closest to the centre of the operating point boundary.

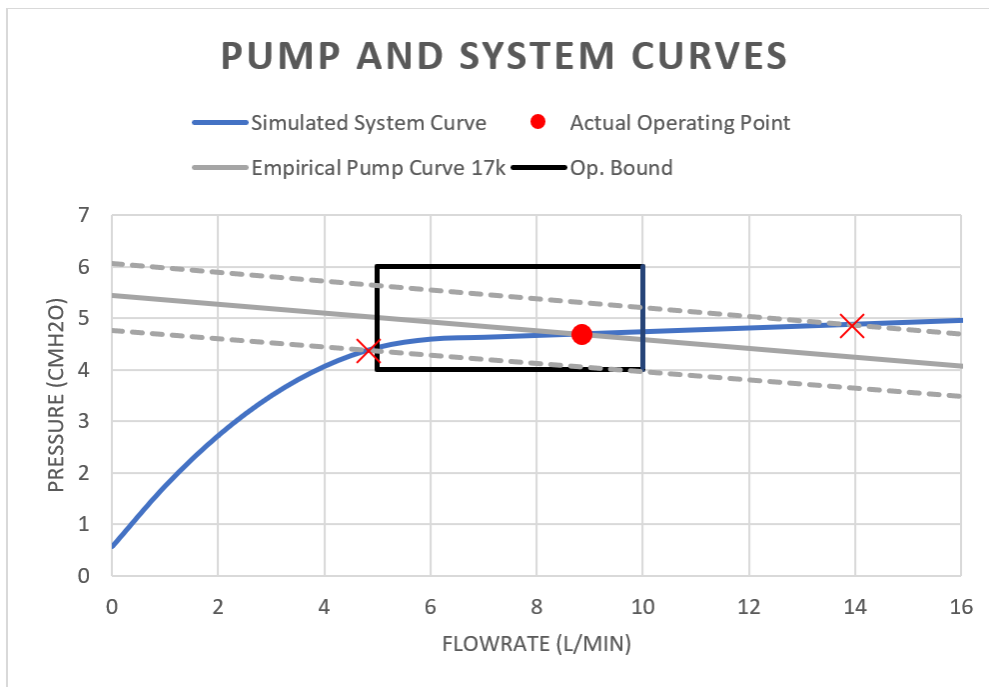


Figure 21: System curve (no patient, 5 cmH₂O Clariti PEEP valve, Hudson cannula) and pump curve for U51DL pump at 16k (dotted, low), 17k (solid), and 18k (dotted, high) RPM. Actual operating point (the intersection of pump and system curves) is inside the desired operating point boundaries for 17k.

Then, the custom breathing model was used to simulate flow disturbances from a patient. The low, medium and high flow conditions (as described in Table 6) were simulated. First, the 17k RPM setting was used. The low flow condition resulted in very small fluctuations in pump flow and pressure and a fairly constant patient pressure of 4.5 cmH₂O. The medium and high flow conditions, however, caused model instability.

High cannula flow resulting in model instability can be caused by increasing V_T , BPM, or exhale time. The instability is thought to be due to programmatic implementation, rather than fundamental physical issues. To explain this instability, pump pressure is displayed in Figure 22 for three breathing rates: 87 BPM (blue), 88 BPM (orange), and 89 BPM (purple), for an RPM setting of 18k. The fluctuations increase in amplitude as BPM increases. The system becomes unstable at 90 BPM (Figure 23). Fluctuations take the same shape for pump flow, and when the flow fluctuations have a large enough amplitude that patient pressure and expiratory limb flow become negative, the model displays an error and stops running. This result therefore indicates an upper bound in cannula flow for that combination of pump and valve. A negative expiratory limb flow is an unacceptable design result, as it indicates rebreathing of exhaled air, thus instability in the system will be interpreted as an unacceptable combination of parameters. However, the fluctuations are not indicative of the true behavior of the prototype and it is recommended that this issue be remedied in future work. The point at which the system becomes unstable will vary depending on the RPM setting.

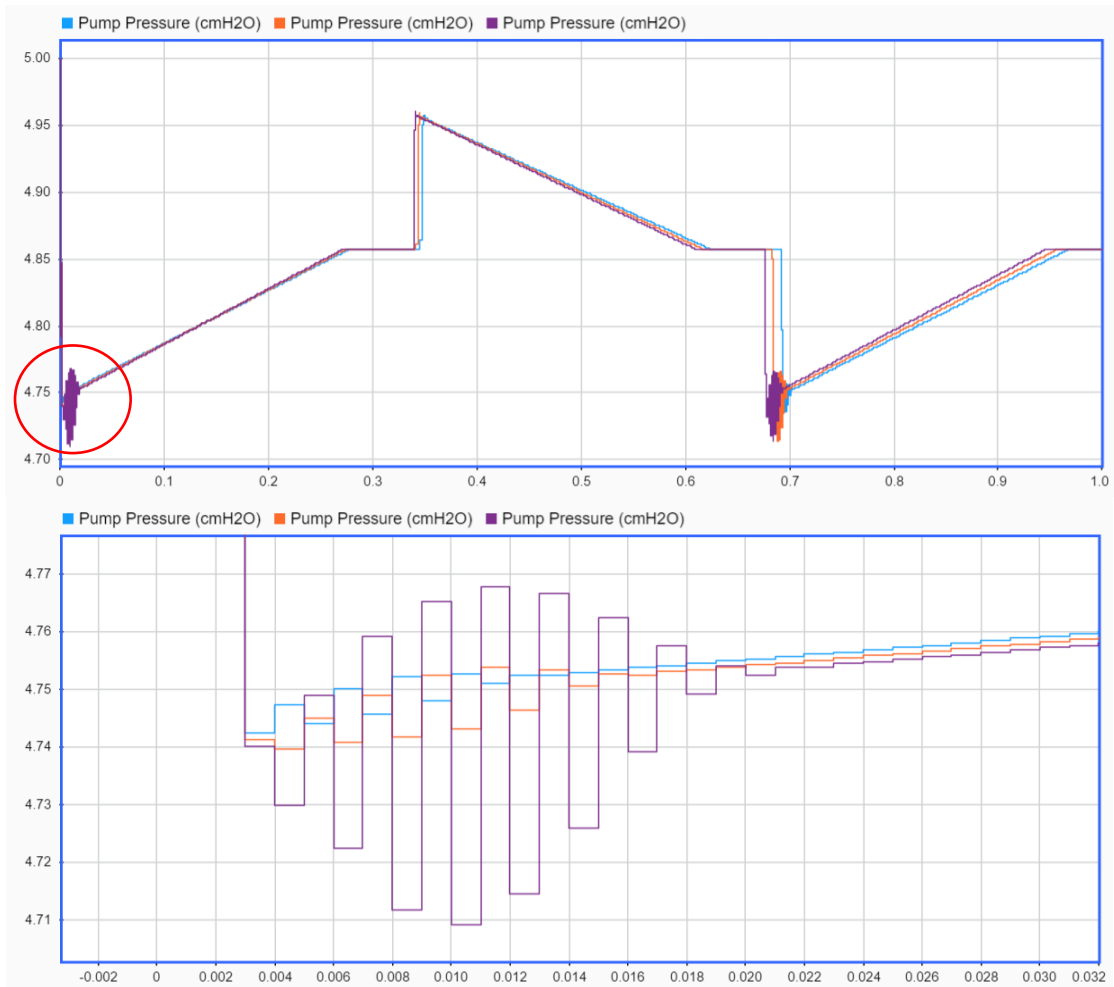


Figure 22: Pressure fluctuations at the beginning of the inhale increase in amplitude as cannula flow increases. Breathing rates are 87 (blue), 88 (orange), and 89 (purple).

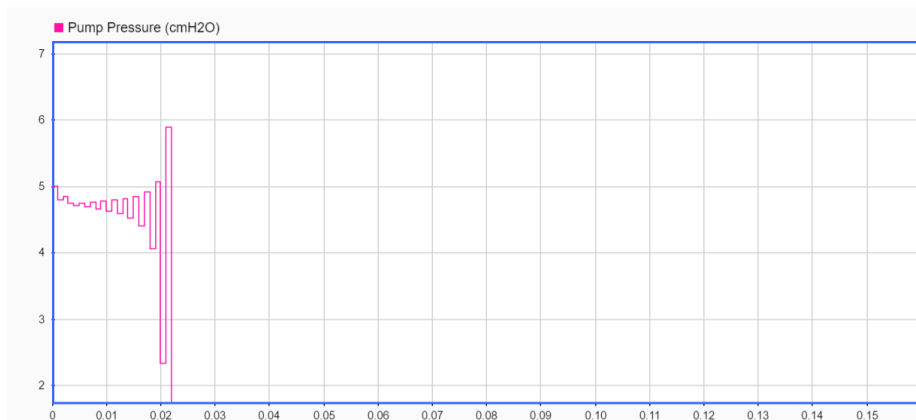


Figure 23: Closed loop model becomes unstable at the start of the first inhale at 90BPM.

The low, medium and high flow conditions were simulated again for 18k RPM, where the pump flow is 13.7 L/min. This time, the medium flow condition did not result in instability, and delivered a patient pressure of approximately 4.7 cmH₂O on exhalation and 4.5 cmH₂O on inhalation. The high flow condition still resulted in instability. This result indicates a possible barrier to a one-size-fits-all CPAP: the maximum recommended flowrate of 10 L/min may be insufficient for a patient breathing with high peak flows, particularly during inhalation. The model results indicate that 18k RPM is advisable for small to medium patients, pending approval from a neonatologist to provide a flowrate greater than 10 L/min. Finally, after simulating the portable CPAP under a variety of conditions, the maximum Reynolds number was never above 200, indicating a safely laminar flow throughout the CPAP circuit.

5 Prototype

A portable CPAP prototype was constructed by connecting the components introduced in previous sections of this report. The results of the Simulink model indicated that the U51DL pump and 5 cmH₂O Clariti PEEP Valve may be suitable as the air source and pressure control respectively, and thus the prototype used those components. All subsequent references to “the pump” and “the valve” refer to these components in particular. Inspiratory and expiratory limbs were made from silicone tubing. Two versions of the prototype were constructed: one using the RAM cannula (Figure 24, left) and one using the Hudson cannula (Figure 24, right). A heat and moisture exchanger (HME) filter was connected to the pump inlet. A heat and moisture exchanger (HME) filter was connected to the pump inlet.

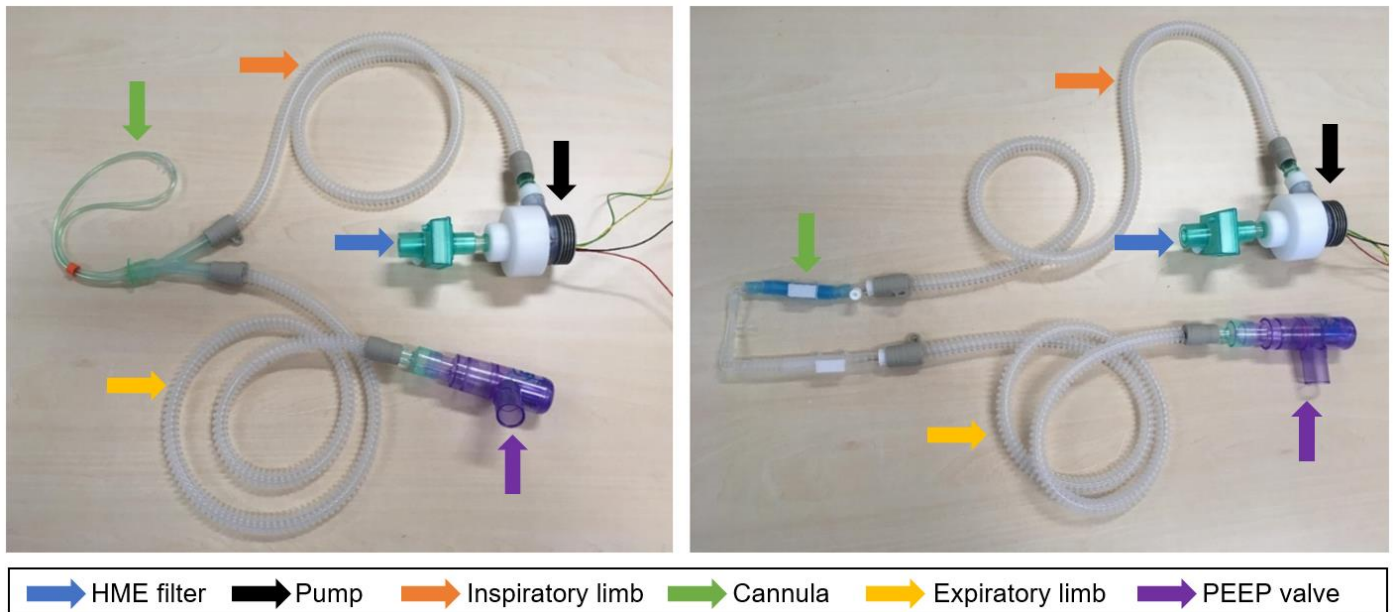


Figure 24: Prototype with RAM cannula (left) and prototype with Hudson cannula (right).

The pump was connected to a power supply and data acquisition driver (NI-DAQ) to control the RPM using LabVIEW. Integrated electronics in the pump allow RPM to be measured using the frequency signal connection (yellow wire), where the frequency signal multiplied by 20 is equal to the pump RPM. The set speed connection (green wire) uses a duty cycle between 0 and 5V to control the RPM. The power supply and RPM control are not portable; this would need to be modified to complete the prototype (further details are found in the discussion).

5.1 Experimentation Methods

The dependent variables of interest were pressure (cmH₂O) and flowrate (L/min). All experimentation was conducted at the department of Medical Technology of the Erasmus Medical Centre, Sophia Children’s Hospital in Rotterdam, the Netherlands, where both measurements were taken using the FlowAnalyser PF-300 [47]. Data was sampled at 200 Hz and recorded using FlowLab for FlowAnalyser Software. Flowrate was reported to one decimal place, and pressure to two. Data was collected for one minute, the minimum time allowed by the software. The software output paired points of pressure and flow over time.

Pressure and flow were measured at three locations in the circuit: at the patient (Pat), pump outlet (Pum) and immediately upstream of the valve (Val), shown in Figure 25.

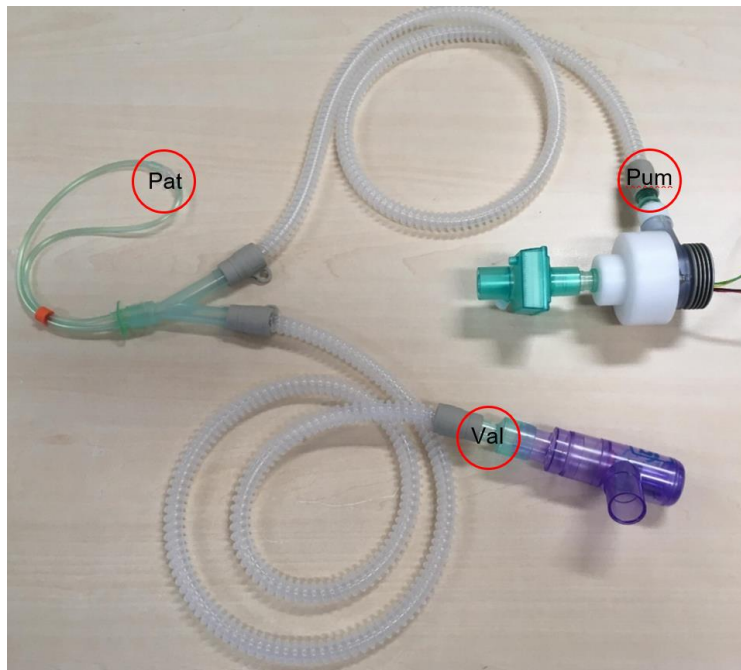


Figure 25: Locations in the circuit where pressure and flow can be measured.

First, the device was tested with no patient connected. The nasal prongs were sealed, and pressure and flow were recorded at the pump and valve only. The pump was tested at 16k, 17k, 18k, 19k, and 20k RPM, with and without the HME filter, to select an appropriate RPM setting to use moving forward. Valve orientation was also examined; pressure and flow at the pump outlet were compared for the valve oriented up, sideways, and down, where up and down are defined by the writing on the valve.

Next, a breathing patient was simulated using a Dräger Infant Test Lung. The lung was actuated manually to the beat of a 60-beats-per-minute song to simulate breaths. The 60 second data collection was broken into three segments to compare three breathing patterns. From 10-20 seconds, the lung was pushed and released, representing a sharp exhale. From 25-35 seconds, the lung was pulled and released, representing a sharp inhale. Finally, from 40-50 seconds, the lung was pushed and pulled evenly without pausing, representing even breaths. Other methods of simulating a patient breathing were considered, and are detailed in Appendix D.

This procedure was performed first with the lung only, to establish a *no CPAP* baseline for patient pressure and flow. Then the CPAP prototype was connected by tightly attaching the cannula to the Dräger Infant Test Lung using electrical tape (Figure 26). To simulate a *sealed* condition (Figure 26, left) this pressure fitting was connected directly to the test lung. To simulate an *intentional leak* condition (Figure 26, right) an additional fitting with a tube open to the atmosphere was connected between the pressure fitting and the lung. The procedure was repeated for both types of cannula.

Figure 27 displays a schematic of the test conditions that were chosen to analyze the CPAP prototype and simulated patient together. Every combination of cannula type, presence of leak, and breathing pattern was tested, generating 12 experimental conditions. Subsequent references to experimental condition use the letter codes introduced in Figure 27. For example, an experimental setup using the RAM cannula, with intentional leak, actuated with a sharp exhale is referred to as R/IL/SE.

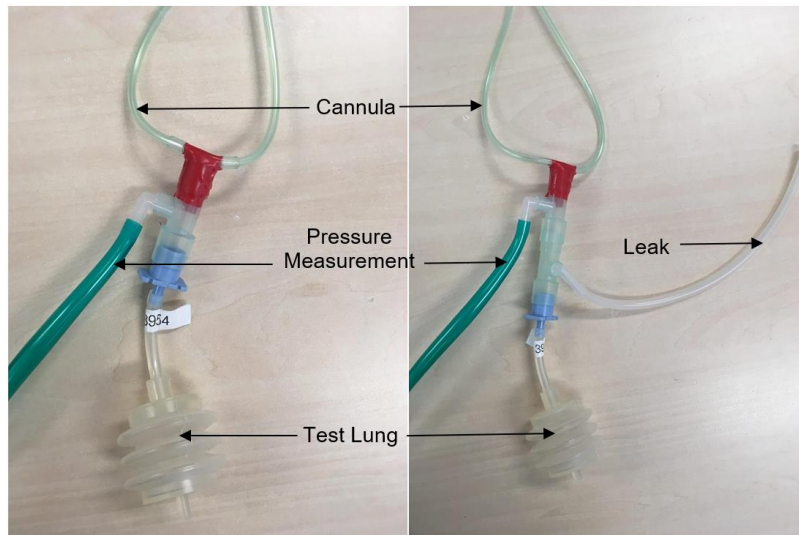


Figure 26: RAM Cannula connected to Dräger Infant Test Lung, sealed (left) and with intentional leak (right).

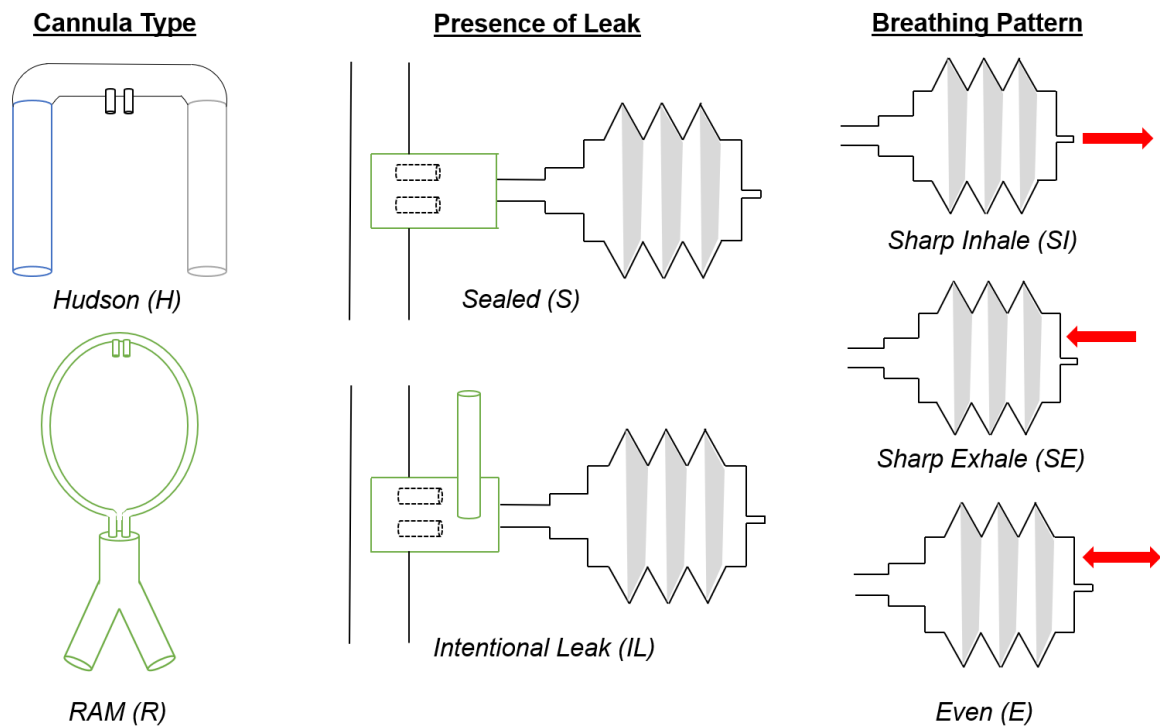


Figure 27: Schematic of experimental conditions for testing CPAP and simulated patient together. The letters in parentheses indicate the condition, for example, H/S/SI refers to an experimental setup using the Hudson cannula, sealed to the test lung, breathing with a sharp inhale.

Pressure and flow can only be recorded at one location for each data collection, so the procedure was repeated five times for each experimental condition, as per Table 7. Measurements A, B, and C provide repeat measurements for pressure, and C, D, and E provide repeat measurements for flow. The redundancies allow the phase of measurements A, B, D, and E to be matched to the phase of measurement C during data processing, therefore allowing the pressure and flow at each location in the circuit to be compared at the same point in the breath.

Table 7: Pressure and flow measurements for simulated patient with CPAP.

Label	A	B	C	D	E
Flow	Pat	Val	Pum	Pum	Pum
Pressure	Pat	Pat	Pat	Val	Pum

Patient pressure and pump flow were selected to assist in phase shifting because pilot experimentation showed the clearest fluctuations in those two measurements. Redundant measurements (C, D, E flowrate; A, B, C pressure) were used for phase matching, then the median signal was chosen for analysis and the other measurements were discarded. Ten breaths were recorded, and three representative breaths (three seconds of data) from each dataset were selected to include in this document.

5.2 Experimentation Results

5.2.1 No Patient Results

The first step in testing the prototype was to determine an appropriate RPM setting. Five settings were tested (16k – 20k RPM) and pressure and flowrate were measured at the pump outlet. This was repeated with and without the HME filter connected to the pump inlet. The actual operating point for each RPM is shown in Figure 28, i.e. the intersection of the pump and system curves. The closest actual operating point to the centre of the operating point boundaries was at a setting of 19k RPM. All subsequent tests of the prototype were done with a setting of 19k RPM and include the HME filter at pump inlet.

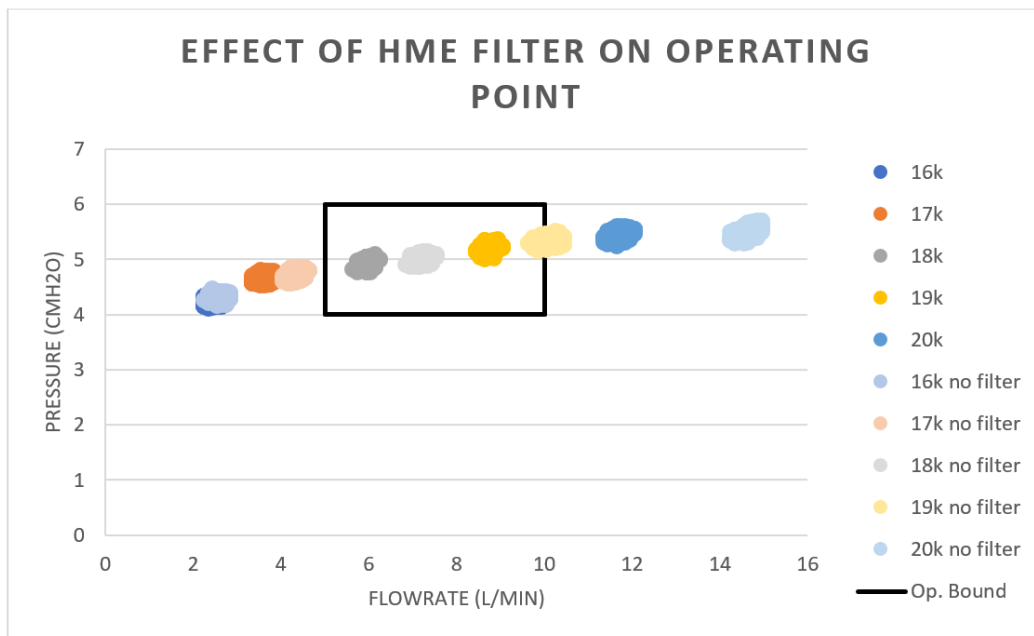


Figure 28: Actual operating points for various RPMs, with and without the HME filter at pump inlet (U51DL). Pressure and flow were measured at the pump outlet.

The effect of valve orientation on pump pressure and flow (actual operating point) was tested, and the results are shown in Figure 29. A measured effect was observed.

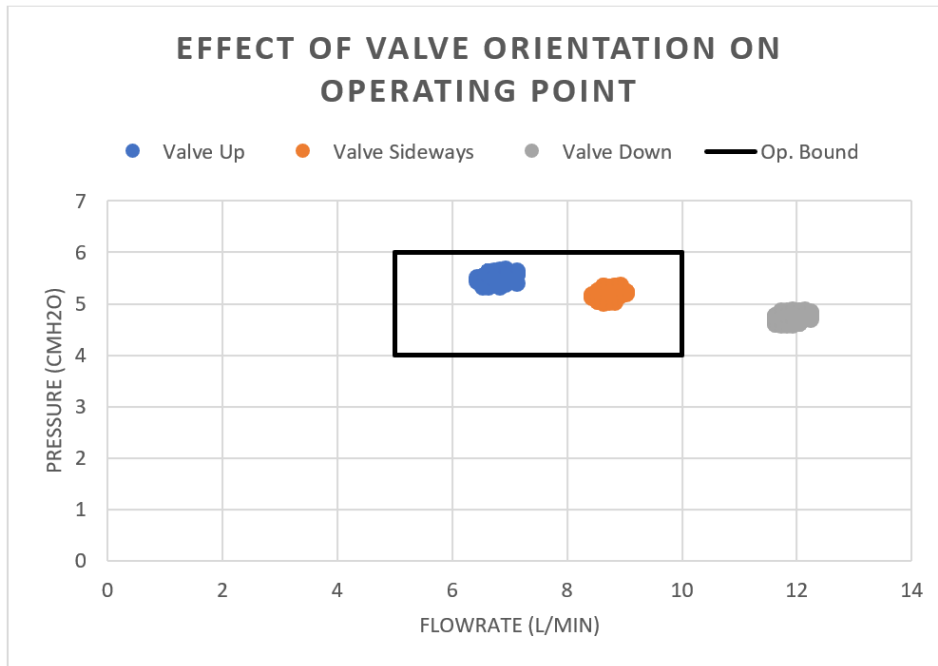


Figure 29: Effect of valve orientation on pump pressure and flow for 5 cmH₂O Clariti PEEP valve, U51DL pump.

Testing the portable CPAP prototype with no patient indicated that the addition of a filter and the valve orientation can affect the actual operating point of the pump. The valve orientation can be set in the final design of the prototype, though ideally the prototype will be safe for all orientations. The actual operating point falls within the operating boundary for the U51DL pump set to 19k RPM, with the PEEP valve oriented sideways, thus these conditions were selected to test the prototype with a simulated patient.

5.2.2 Simulated Patient Results

A patient was simulated by manually actuating a Dräger Infant Test Lung, and the portable CPAP prototype was set to 19k RPM, with the PEEP valve oriented sideways. In the data presented in this section and in Appendix E, positive patient flow indicates an inhale, negative patient flow indicates an exhale, and zero patient flow indicates a pause.

First, the CPAP was compared to a *No CPAP* baseline condition, to demonstrate the effect of the device. Three representative breaths were selected from the *No CPAP* condition and matched to three similar breaths from a CPAP condition; patient flow and pressure are plotted over time in Figure 30. The near-identical flowrate waveform indicates the breaths are comparable between the two conditions. Without CPAP, the patient pressure stayed at 0 cmH₂O in the pauses between breaths and fluctuated slightly above and slightly below during exhalation and inhalation respectively. When CPAP was applied to the patient, the pressure increased during all parts of the breath, particularly so during the exhale phase.

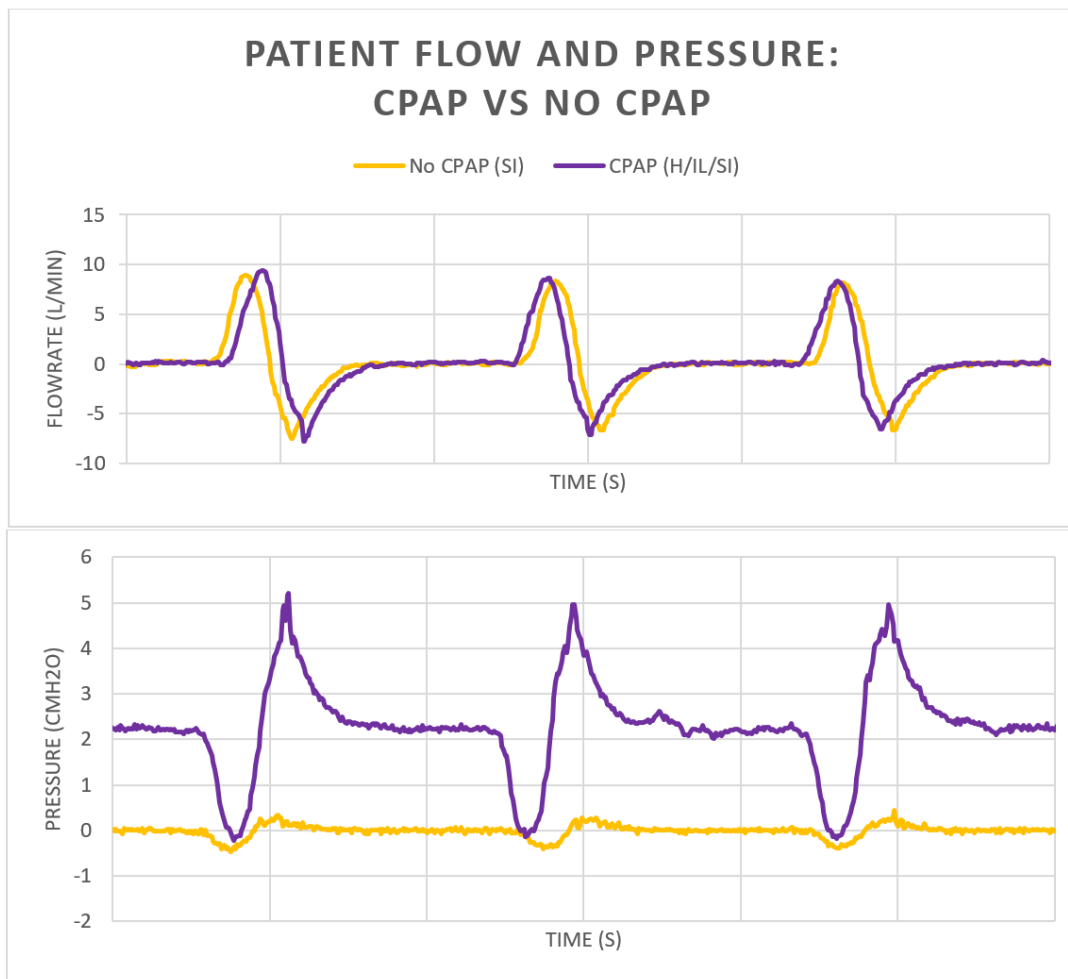


Figure 30: Experimental data of CPAP vs. No CPAP for three representative breaths. The portable CPAP prototype used the Hudson cannula with intentional leak. The test lung was actuated with a sharp inhale for both CPAP and No CPAP.

Flowrate and pressure measured during CPAP at the patient, pump outlet, and valve are shown for all conditions in Appendix E. In general, these graphs show that greater patient flowrates correspond to greater patient pressures. In comparing breathing patterns, a *Sharp Inhale* generated a larger pressure drop, and a *Sharp Exhale* generated a larger pressure spike. Comparing *Intentional Leak* and *Sealed* conditions, it appeared that introducing an intentional leak resulted in higher pump flow. Additionally, the conditions with *Intentional Leak* displayed lower patient pressures during the pauses between breaths. A difference was also observed when comparing the cannula types; patient pressure spikes during exhale were higher when using the RAM cannula, especially in the *Sealed, Sharp Exhale* condition.

The most important parameter to analyze is patient pressure, because it is the main purpose of the treatment. To understand how each variable affects patient pressure, the full 10 second data collection was analyzed. As shown in Figure 31, data labels were manually added to each breath, labelling each local maximum (exhale), local minimum (inhale) and a representative point in each flat section (pause). This was repeated for all 12 CPAP conditions. Figure 32 shows the mean patient pressure for the exhale, pause, and inhale for each condition, with standard deviation shown as error bars.

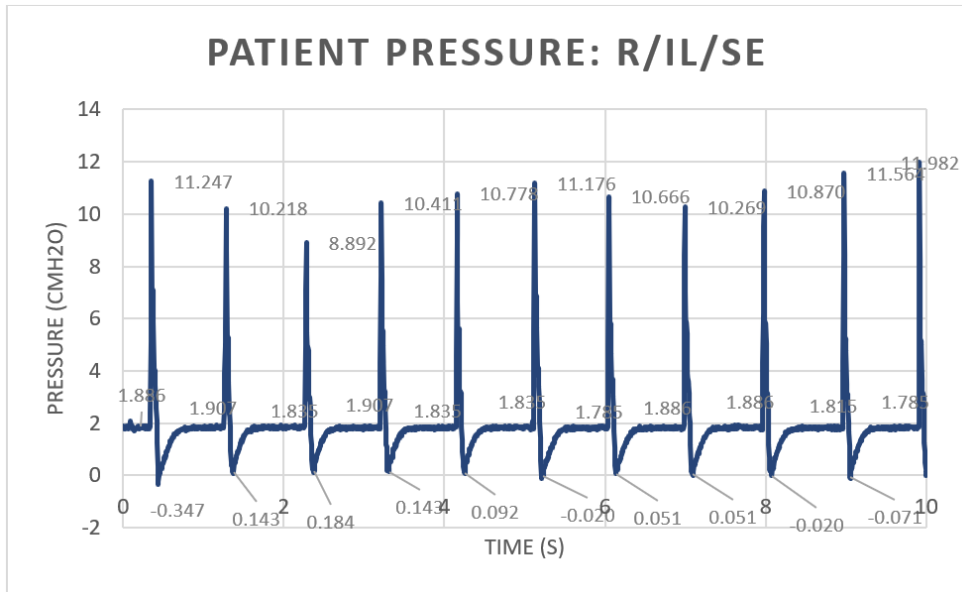


Figure 31: Data collection of patient pressure for R/IL/SE condition. Data labels were manually selected to locate all local maxima (exhale), local minima (inhale), and a representative point in each flat section (pause).

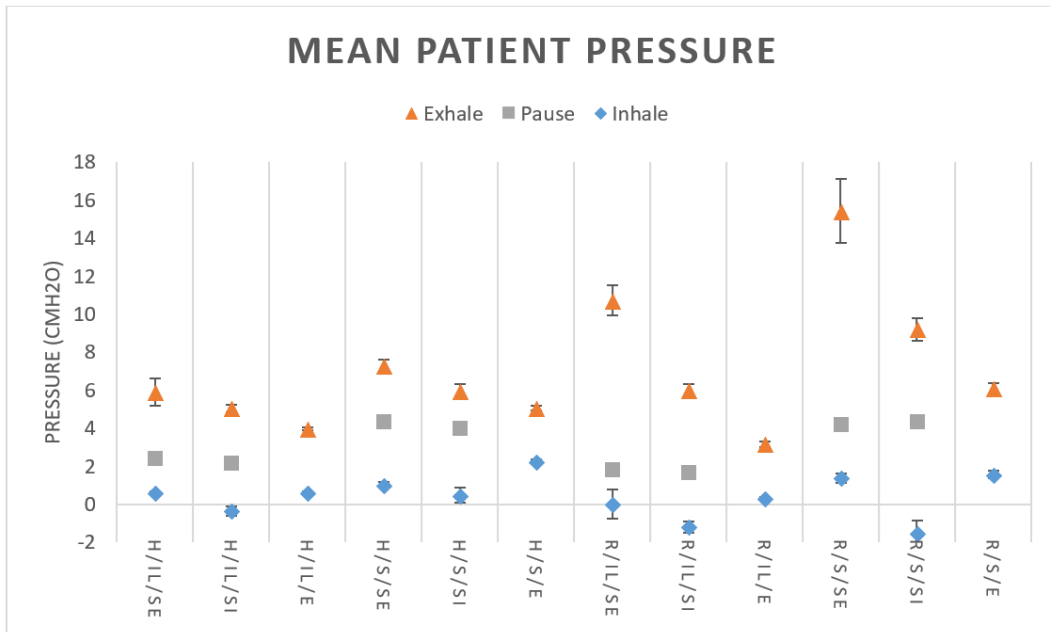


Figure 32: Mean patient pressure delivered during exhale, pause, and inhale for 12 CPAP conditions: Hudson (H) or RAM (R) cannula; Intentional Leak (IL) or Sealed (S); and Sharp Exhale (SE), Sharp Inhale (SI), or Even (E) breathing pattern.

A two-sided Wilcoxon rank sum test was performed to test for statistical significance between conditions. Most of the results were significantly different ($p < 0.05$), with only a few exceptions. Breathing pattern did not impact patient pressure during the Pause phase, nor did the choice of cannula. Additionally, *Sharp Exhale* and *Even Breathing* did not result in different pressures during the inhale phase. All other conditions impacted patient pressure significantly.

6 Model/Prototype Comparison

Results from the Simulink model were compared to experimental prototype data. Tidal volume, breathing rate, and leak were determined from the prototype data, then were input to the Simulink model. Output from the model was compared to the prototype data, and differences were noted (6.2 First Model Iteration). Then, adjustments were made to the model in attempt to generate output that more closely matched the prototype data (6.3 Second Model Iteration).

6.1 Model Input

To examine the similarities and differences between the Simulink model and prototype, the input to the model had to be precisely matched to the prototype data. For this reason, the model and prototype were only compared for the *Even Breathing* experimental conditions, because this breathing pattern can be replicated using a sine wave. Sample data from the prototype and its corresponding sine wave are shown in Figure 33. The prototype data is much less smooth, but Figure 33 visually indicates that a sine wave may be a good estimate to make predictions in Simulink.

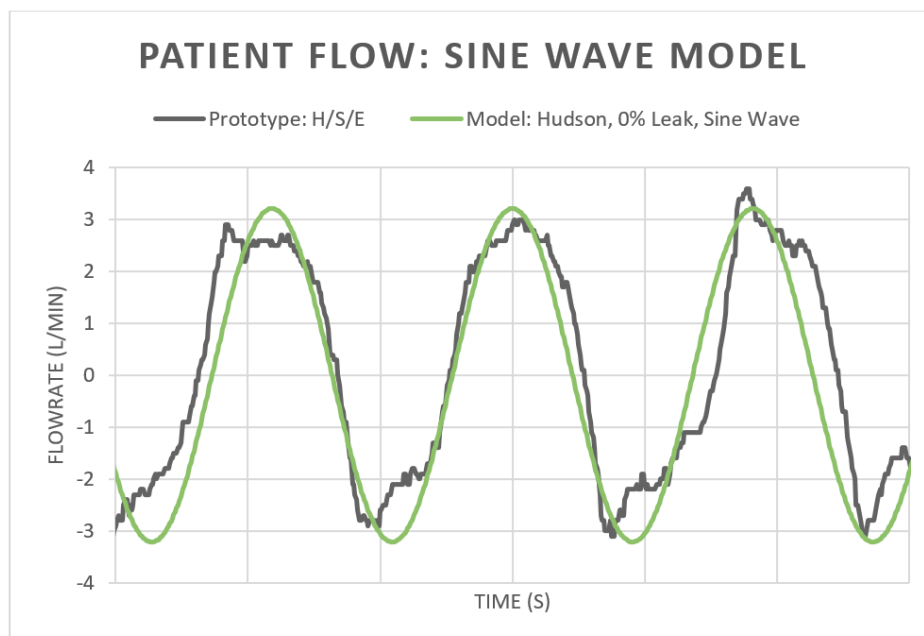


Figure 33: Experimental data for patient flow compared against the sine wave breathing model for the Hudson, Sealed, Even breathing condition.

To generate a patient flow waveform in Simulink for each experimental condition, tidal volume, breathing rate, and leak were calculated from the patient flow measurements. Breathing rate was determined by counting the number of full breaths during the 10 second data collection, dividing by 10 to get breaths per second, then multiplying by 60 to give breaths per minute. Approximately 11 breaths were seen for all experimental conditions, so the breathing rate was set to 66.

Tidal volume was determined by integrating patient flow to obtain the area under the curve of each individual inhale or exhale. The Riemann sum integration method was used. There were 10 full inhales and 10 full exhales, meaning each condition had a dataset of 20 tidal volumes. The average and standard deviation of these volumes is reported in Table 8. The experimenter attempted to produce identical tidal volumes for all data collections when actuating the test lung, however, the average tidal volume generated during the *Hudson, Intentional Leak* condition was much larger. This does not affect comparison between model and prototype, but should be considered when comparing prototype data across conditions.

Leak was calculated as per Equation 17, and the error in leak was calculated as per Equations 18 and 19 [56]. The variables Q_{max} and Q_{min} are the peak flowrates during exhalation and inhalation respectively, averaged over 10 breaths. The symbol δ indicates the error in a value, and δ_{max} and δ_{min} are standard deviations of the set of peak flowrates.

$$Leak = 100 \times \frac{Q_{max} - |Q_{min}|}{Q_{max}} \quad (17)$$

$$\delta_{max-min} = \sqrt{\delta_{max}^2 + \delta_{min}^2} \quad (18)$$

$$\frac{\delta_{Leak}}{Leak} = \sqrt{\left(\frac{\delta_{max-min}}{Q_{max} - |Q_{min}|}\right)^2 + \left(\frac{\delta_{max}}{Q_{max}}\right)^2} \quad (19)$$

The average values for tidal volume and leak, summarized in Table 8, were input to the model. The patient flow waveform was calculated using the sine wave model (Equation 11 from section 4.1.4).

Table 8: Tidal volumes and % leak for each condition, as calculated from experimental data of the prototype. Breathing rate was estimated to be approximately 66 BPM for all conditions (11 breaths over 10 seconds).

	V_T (mL)	Leak (%)
Hudson / Intentional Leak	25.8 ± 1.8	18.6 ± 9.5
Hudson / Sealed	15.5 ± 2.0	14.4 ± 26.0
RAM / Intentional Leak	14.3 ± 1.2	22.3 ± 8.3
RAM / Sealed	15.6 ± 1.4	14.4 ± 12.4

All four even breathing experimental CPAP conditions listed in Table 8 were then simulated using the Simulink model.

6.2 First Model Iteration

The prototype data was compared to the output of the first model iteration, which uses only theoretical principles. A model/prototype comparison for the *Hudson, Intentional Leak* and *RAM, Sealed* conditions are shown in Figure 34 and Figure 35 respectively. The figures display flow and pressure at the patient, pump, and valve. All four experimental conditions were simulated, but only two are shown here, for conciseness. The additional graphs are found in Appendix F.

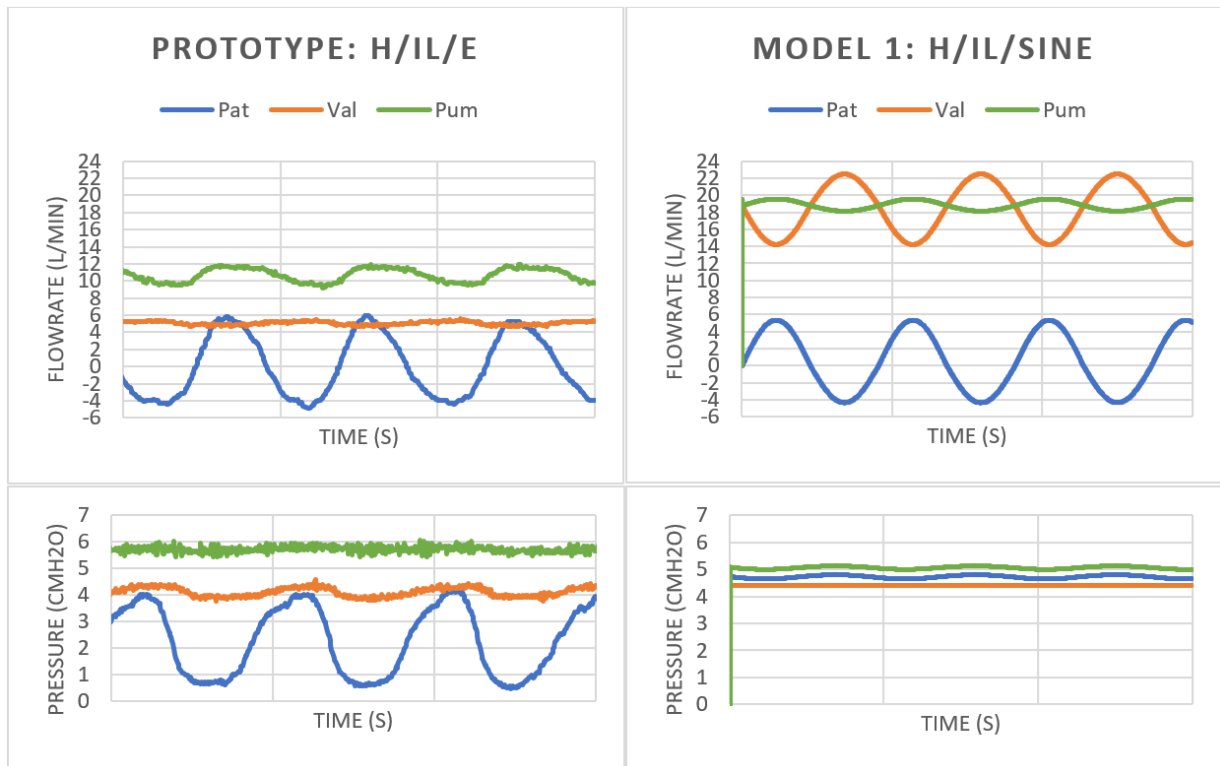


Figure 34: Comparison of prototype data (left) and model output (right) for flow (top) and pressure (bottom) measured at the patient (Pat), valve (Val), and pump outlet (Pum), for the Hudson, Intentional Leak experimental condition.

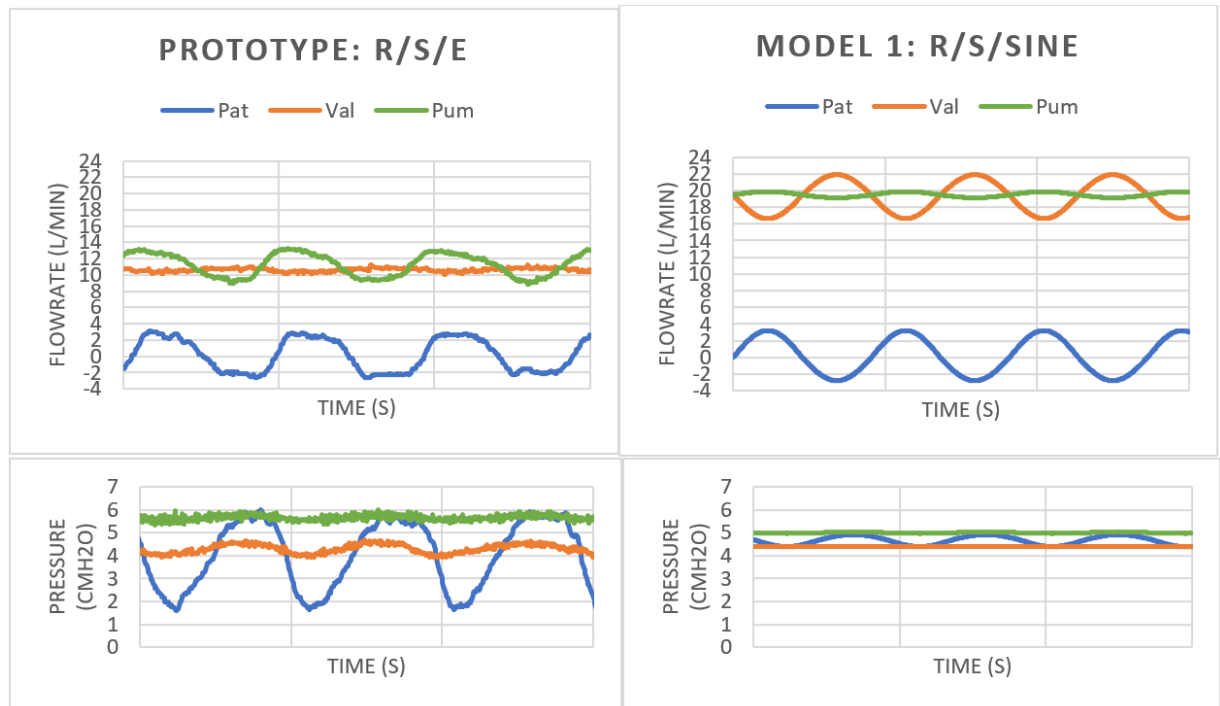


Figure 35: Comparison of prototype data (left) and model output (right) for flow (top) and pressure (bottom) measured at the patient (Pat), valve (Val), and pump outlet (Pum), for the RAM, Sealed experimental condition.

Including the *Hudson, Sealed* and *RAM, Intentional Leak* conditions shown in Appendix F, some systematic differences common to all conditions were noted. As compared to the model, the prototype data showed a consistently lower pump flow and higher pump pressure. During peak inspiratory flow for the prototype, patient pressure was the lowest measured pressure across all conditions, whereas in the model, valve pressure was always lowest. Additionally, patient pressure fluctuations were always much greater in the prototype data than in the Simulink model. An attempt was made to explain these systematic differences and correct for them in a second iteration of the Simulink model.

6.3 Second Model Iteration

Adjustments were made to the model to match its output more closely to the prototype data. The prototype data compared is compared to the second model iteration in Figure 36 (H/IL) and Figure 37 (R/S). Graphs for other two patient conditions (H/S and R/IL) are shown in Appendix F.

The prototype data indicated a consistently lower pump flow and higher pump pressure as compared to the first iteration of the model. Therefore, the operating point output by the model needed to be shifted, which was achieved by adjusting the system curve. Recall that pump pressure was calculated by summing the pressure losses in the system. Therefore, the underestimated pump pressure in the model was a result of underestimated pressure losses. To increase the total pressure losses in the model, tubing resistance in the inspiratory and expiratory limbs was multiplied by a constant (2.5) determined by trial and error. Additionally, the pump pressure initial condition was changed from 5 to 5.5 cmH₂O to improve stability at start up. As shown in Figure 36 and Figure 37, pump pressure and flow more closely resembled the prototype data after this adjustment was made.

The patient pressure waveform can be characterized by its amplitude and signal mean. In the first model iteration, neither amplitude nor mean resembled the prototype data, and therefore both were adjusted in the second model iteration. Continuous, positive patient pressure is the intended effect of CPAP, therefore all other changes to the model were focused on patient pressure only. Through trial and error, it was determined that patient pressure could be more accurately matched to that of the prototype data by making adjustments outside of the feedback loop. The patient pressure that was included in the feedback loop was unadjusted, i.e. calculated in the same way as the first iteration of the model. All subsequently described changes were made only to the model output data and did not impact any other calculations within the model.

The approximate signal mean of patient pressure in the first iteration of the model was 5 cmH₂O, and thus could be represented by Equation 20, where A represents amplitude.

$$P = A\sin(t) + 5 \quad (20)$$

The prototype data showed an average patient pressure amplitude of 1.7±0.4 cmH₂O. The amplitude as predicted by the first model iteration was approximately 0.25 cmH₂O for all conditions, approximately six times smaller. The amplitude of the patient pressure waveform was therefore increased by a factor of 6 in the second iteration of the model. The signal was multiplied by 6 (Equation 21), then 25 was subtracted from the signal (Equation 22) to allow for an increased amplitude without an increased mean. The equation is simplified in Equation 23.

$$P = 6(A\sin(t) + 5) \quad (21)$$

$$P = 6A\sin(t) + 6 \times 5 - 25 \quad (22)$$

$$P = 6A\sin(t) + 5 \quad (23)$$

The prototype data resulted in patient pressure signal means of approximately 2.3 cmH₂O (H/IL/E), 3.7 cmH₂O (H/S/E), 1.7 cmH₂O (R/IL/E), and 3.8 cmH₂O (R/S/E). All experimental means were lower than the first iteration of the model predicted. Leak has been shown to impact pressure delivery in neonatal ventilation [57], so this may be the cause of the difference. After the adjustment to amplitude was made, a constant value was subtracted from the patient pressure waveform to lower it by a value proportional to leak. Assuming the signal initially had a mean of 5 cmH₂O, a value of 5*Leak (where Leak is expressed as a number between 0 and 1) was subtracted to drop the mean pressure by the same percentage. Using trial and error, it was estimated that twice this value was required to match the model and prototype signals. Thus, the final equation for patient pressure is shown in Equation 24.

$$P = 6A\sin(t) + 5 - 10 \times Leak \quad (24)$$

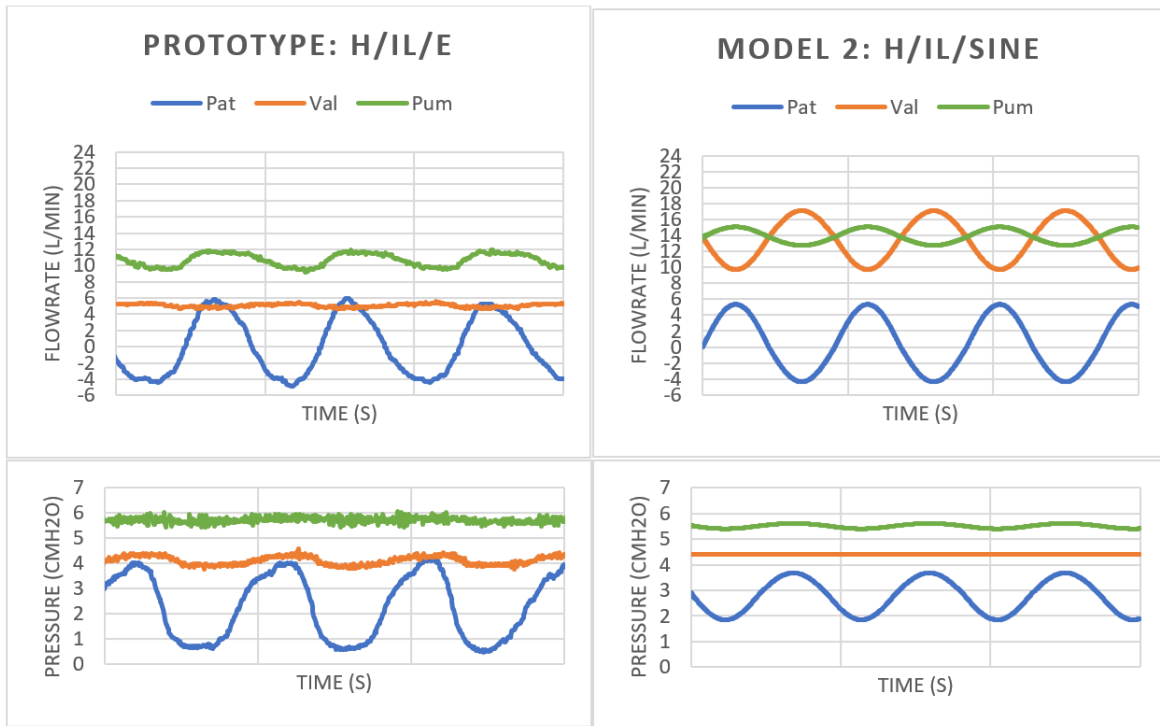


Figure 36: Comparison of prototype data (left) and second iteration model output (right) for flow (top) and pressure (bottom) measured at the patient (Pat), valve (Val), and pump outlet (Pum), for the Hudson, Intentional Leak experimental condition.

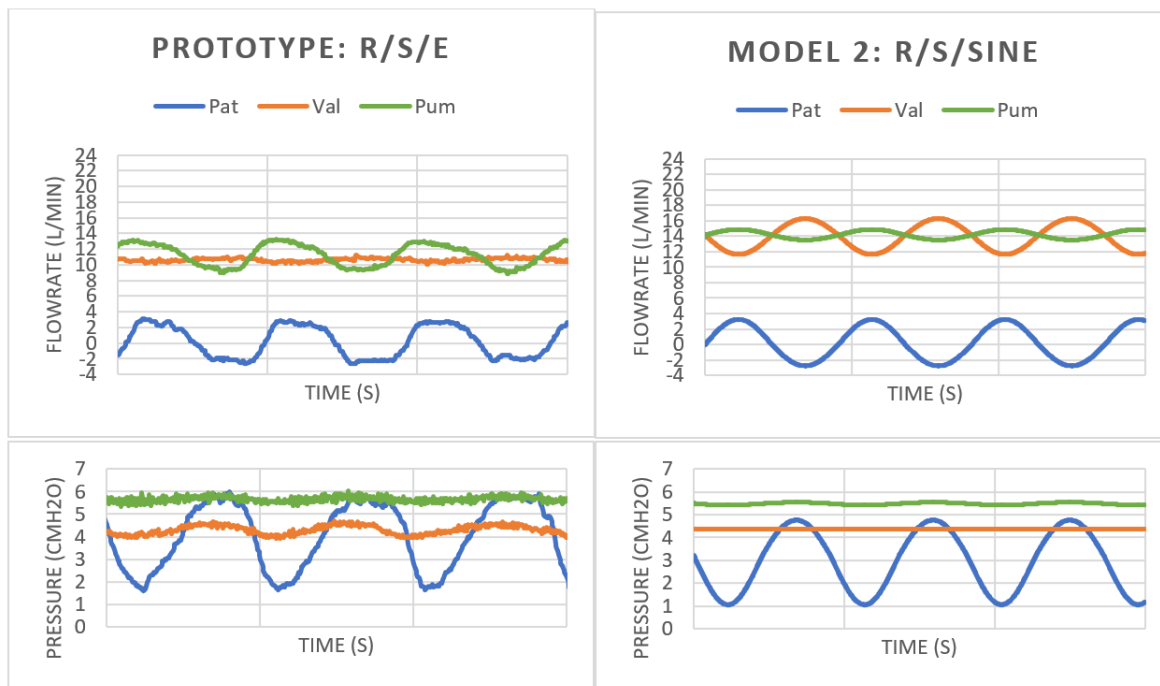


Figure 37: Comparison of prototype data (left) and second iteration model output (right) for flow (top) and pressure (bottom) measured at the patient (Pat), valve (Val), and pump outlet (Pum), for the RAM, Sealed experimental condition.

The second iteration of the model showed an improved resemblance to the prototype data. However, it still underestimated fluctuations in patient pressure for Hudson cannula conditions, and slightly overestimated pump flow. Other differences and possible explanations will be discussed in the following section.

7 Discussion

The aim of this thesis was to explore the feasibility of a simple, low-cost, portable CPAP device that would encourage delivery room treatment of preterms in LMICs. The device was first modelled in Simulink, then a prototype was built and tested. In this chapter, the usefulness of the model as a design tool is assessed, including possible explanations for differences observed between the model and prototype test data. The prototype is evaluated against the five design criteria selected for the preliminary evaluation scheme, and suggestions for future work on the model and prototype are made.

7.1 Model

The first iteration of the Simulink model used theoretical principles to calculate the pressure and flow at any point in the CPAP circuit. After analyzing data collected from tests of the prototype, a second iteration of the model was completed in order to match the model to the prototype data. Both iterations of the model are tools that can be used as a first step in designing a portable CPAP device.

The first iteration of the model considerably underestimated the resistance in the circuit. This resulted in the model predicting a higher pump flow and lower pump pressure than was seen experimentally. The resistance was approximately 2.5 times greater in tests of the prototype. Resistance was calculated using the Hagen-Poiseuille equation for steady, laminar flow, and the discrepancy could be explained by a variety of factors. First, the inspiratory and expiratory limbs were coiled during testing which could have disrupted the flow within them. Surface roughness was not taken into account when calculating the resistance, nor were any of the fittings required to connect the circuit. There was likely some added resistance from the inclusion of the flowmeter in the circuit. Finally, flow in the Y-piece of the RAM cannula may have been turbulent. During one experimental data collection with no simulated patient breathing, flow measurements were taken in 3 places: at the pump outlet, between the Y-piece and expiratory limb, and at the valve. Pump flow was 8.8 ± 0.1 L/min, Y-piece flow was 7.5 ± 0.1 L/min, and valve flow was 8.5 ± 0.1 L/min. The Y-piece is upstream of the valve; it is not possible for more air to enter the circuit after that point. It is assumed that turbulent flow in the Y-piece caused the flowrate to be underestimated. Frictional losses are proportional to flowrate if the flow is laminar and to flowrate squared if the flow is turbulent [41], so this would add a considerable pressure drop, and may explain the discrepancy between model and prototype.

Even after increasing the resistance 2.5 times, the second iteration of the model still slightly overestimated pump flow. Pump flow may be a difficult parameter to accurately predict, because the pump curve has a relatively flat slope. This means that a very small error in pressure calculations will result in a much larger error in the predicted flowrate. The relationship between pressure and flow is different for every pump, and in using the model as a design tool, this relationship should be well understood by the user, in order to interpret model results effectively. Another reason why the second iteration of the model overestimated pump flow is due to the choice to multiply the resistance by 2.5, rather than a higher value. The resistance factor of 2.5 could not be increased any higher, or the model would become unstable. Model instability occurred when resistance against the pump was too high or too low, or when flow in the expiratory limb became negative. The instability does not accurately represent what happens in such a scenario, and therefore an important recommendation for future iterations of the model is to eliminate model instability.

Fluctuations in valve pressure were observed in prototype testing that were not predicted by the model. This can be explained by valve stickiness. The valve tends to stick in its past position, so when the flow raises a small amount, the pressure will increase. Similarly, if the flowrate decreases slightly, the pressure will drop. This could also be explained as a delay in response from the spring. Large, rapid changes in flowrate would likely not show this effect, however, the flow fluctuations within the portable CPAP prototype are small enough that pressure fluctuations are experienced at the valve. Future iterations of the model should attempt to include this effect.

Patient pressure was not well predicted by the first iteration of the model. This is likely because the model did not take into account the pressures generated by the patient, it only calculated pressure caused by the CPAP device. Testing of the prototype indicated that during peak inspiratory flow, patient pressure was the lowest pressure in the circuit for all test conditions. This is logical; the patient must generate a pressure lower than their environment in order to draw air into the lungs. Similarly, the patient must generate a pressure greater than the valve pressure in order to exhale into it. These intrathoracic pressure differences were not included in the first iteration of the model. This explains why the patient pressure fluctuations were greater experimentally than in the first iteration of the model. The second iteration of the model increased the amplitude of the patient pressure six fold, which improved similarity to test data. However, the pressure amplitudes were still underestimated in the Hudson cannula conditions. It was unclear how amplitude was related to the input parameters. The pressures generated as a result of synergy between CPAP and lung should be examined in detail and included in future iterations of the model.

The mean of the patient pressure signal was overestimated by the model. This is likely because the first iteration of the model did not include the impact of leak on pressure. As shown by De Paoli *et al.* in a 2005 study, leak has a considerable impact on mean pressure delivered to the patient during CPAP [58]. During testing of the prototype, there was up to 40% leak in the system. The effect of leak on pressure was subsequently included in the second iteration of the model, which improved similarity between model and prototype data. The effect of leak should be examined through more rigorous benchtop tests, and should be incorporated into future iterations of the model in a more robust way.

Adjustments to patient pressure in the second iteration of the model were made outside of the feedback loop. This was done because in the prototype test data, patient pressure fluctuations did not impact behavior of the pump to the extent that was expected theoretically. It was initially assumed that the large pressure drop at the cannula during inhale would cause a decrease in resistance, resulting in a huge increase in pump flow, and the opposite effect would be seen during exhale. In testing of the prototype, the pump flow and pressure remained fairly constant despite large fluctuations in patient pressure. This is good news for the feasibility of the portable CPAP, however, it is unclear why this occurred. Possible explanations could be a slow response of the pump to changes in resistance, or pressure relief due to leak at the cannula. Future experiments should be conducted to examine why patient pressure did not impact the pump to the expected extent.

Overall, the first iteration of the model can function as a guideline to select a pump, RPM setting, and PEEP valve. In the case of the U51DL pump, the open loop model results indicated that a setting of 17k RPM would be appropriate, but the closed loop model indicated that 17k would not be sufficient for medium to large patients, and 18k would be a better choice. In testing the prototype, 19k was most suitable, likely due to higher resistance in the CPAP circuit. The model therefore served as a useful starting point, but was not precise enough to eliminate the need to test the prototype. Adjustments made in the second iteration of the model were all specific to a particular set of experimental data and may not be accurate for other portable CPAP designs or simulated patients. The model should be mathematically examined and validated using a high-fidelity patient simulator and a variety of CPAP devices in order to improve accuracy and robustness. In summary, the model has provided insight into how to model a CPAP device and can be used as a tool to guide designs of future CPAP devices.

7.2 Prototype

A portable CPAP prototype was designed with the aid of the Simulink model. The prototype was composed of a centrifugal fan, silicone tubing, a nasal cannula (Hudson or RAM cannula), and a PEEP valve. The silicone tubing and two types of nasal cannula were selected because they are industry standards. They are readily available in the Diamedica workshop, and well understood by clinicians. Similarly, the Clariti 5 cmH₂O PEEP valve was selected due to availability from Diamedica. The Simulink model confirmed that the Clariti valve would be suitable, so no other valves were investigated. In further development of the prototype, protocols for cleaning this PEEP valve should be studied, and other valves should be considered if necessary.

Two pumps were investigated as potential air sources for the portable CPAP prototype: the U51DL and U71HL radial blowers, both made by Micronel UK. The U51DL blower requires 9V of input voltage, a standard

and affordable battery requirement. The U71HL needs at least 10V to start, thus a 12V battery would be required. The U71HL is cheaper but heavier (96.48 GBP, 358 g), and the U51DL is lighter but more expensive (156.40 GBP, 120 g). The U51DL was selected for this prototype due to testing convenience, but either pump could be used in the device. Further testing of both pumps within the context of the prototype will be required to choose between them.

The prototype was tested by manually actuating a Dräger Infant Test Lung. To determine if this test apparatus was realistic, the flow output was compared to a 2009 study of breathing patterns at birth in term and preterm infants [59]. The study found that preterms produce peak inspiratory flows of 6.2 ± 3.9 L/min and peak expiratory flows of 3.8 ± 2.4 L/min. Peak flow is the key patient parameter that impacts the performance of the CPAP, and the testing methods replicated these flowrates well. The study also found that patient flow patterns were quite irregular. This supports the testing method that was chosen, as inconsistencies between breaths are representative of true patient behavior.

Based on the experimental test data, the prototype was evaluated against the preliminary evaluation scheme (Table 1), copied here for reference:

<i>Metric</i>	<i>Fail</i>	<i>Borderline</i>	<i>Excellent</i>
Mean pressure delivered to the patient	Outside 2-9 cmH ₂ O	Within 2-9 cmH ₂ O	4-6 cmH ₂ O
Pressure fluctuations on inhale and exhale	Outside 0-10 cmH ₂ O	Within 0-10 cmH ₂ O	Within 2-8 cmH ₂ O
Bias flow delivered to the patient	Outside 2-12 L/min	2-5 or 10-12 L/min	5-10 L/min
Likelihood of rebreathing	Negative flow in exp limb	Zero flow in exp limb	Positive flow in exp limb
Range of neonate sizes	Unsafe for 500-2500 g	500-2500 g	500-3500 g

Mean pressure delivered to the patient was *Excellent* for the Sealed conditions (4.2 ± 0.2 cmH₂O for Hudson and 4.3 ± 0.1 cmH₂O for RAM). When Intentional Leak was introduced into the system, mean pressure dropped to 2.3 ± 0.1 cmH₂O for Hudson and 1.8 ± 0.1 cmH₂O for RAM, which receive a score of *Borderline* and *Fail*, respectively. Interestingly, the Sealed experimental conditions had a mean leak of 14.4%, not 0.0%, as was attempted. It is assumed that leak plays an important role in determining mean pressure delivered to the patient [58], however, leak was not controlled precisely enough to draw any conclusions.

Pressure fluctuations on inhale and exhale were mainly within the *Borderline* range, though the RAM cannula conditions displayed larger fluctuations in pressure than the Hudson cannula conditions. The sharp exhale caused a very high spike in pressure in the RAM cannula (10.7 ± 0.8 cmH₂O for Intentional Leak condition, 15.4 ± 1.7 cmH₂O for Sealed condition), but much less in the Hudson (5.9 ± 0.7 cmH₂O for Intentional Leak condition, 7.3 ± 0.3 cmH₂O for Sealed condition). Similarly, in the Hudson, Sealed condition and in both RAM conditions, a sharp inhale caused pressure to drop below zero. Technically, the device receives a *Fail* for delivering patient pressures below zero in some conditions, however, this criterion should be revisited with a clinician, as it may not truly indicate an unsafe device. A PEEP valve with a higher pressure setting should be explored as a solution to negative pressures, and the reason for the high pressure spikes during sharp exhales should be examined further using a high-fidelity patient simulator.

Bias flow delivered to the patient, likelihood of rebreathing, and range of neonate sizes are closely related metrics. Results from the Simulink model, experimental data, and literature indicate that it may not be possible to create a one-size-fits-all CPAP device. Essentially, the *Excellent* scoring levels for bias flow and likelihood of rebreathing may be mutually exclusive for larger neonates. Literature indicates a recommended flowrate of 5-10 L/min for CPAP [27], however, a 2009 study of infant breathing patterns stated that preterms can have a peak inspiratory flow of 6.2 ± 3.9 L/min [59]. Greater flowrates may be required to eliminate the possibility of rebreathing for larger neonates, or neonates with severe tachypnea. In testing of the prototype, pump flow exceeded 10 L/min for the Hudson cannula and exceeded 12 L/min for the RAM cannula, which receive scores of *Borderline* and *Fail* respectively. However, this criterion should be discussed with a clinician regarding tradeoffs between providing insufficient flow and providing flow that is too high. Likelihood of

rebreathing received an *Excellent* score. It was not possible to accurately generate various tidal volumes in the manually actuated test lung, so the success for a range of neonate sizes is inconclusive.

The portable CPAP prototype was a good proof-of-concept and the idea should be pursued further. The next step should be to consult a clinician to discuss tradeoffs in the preliminary evaluation scheme. In particular, the literature was inconclusive regarding acceptable patient pressure fluctuations during inhalation and exhalation. To investigate this, pressures and flows delivered by the portable CPAP prototype during simulated breathing should be compared to a commercially available CPAP device. If the measured patient pressure is not statistically different between the two devices, it could be reasonably assumed that the portable CPAP prototype is providing safe pressures.

The comprehensive design criteria listed in Table 2 can be used to further develop the prototype once the preliminary evaluation scheme has been passed. To make the device portable, the power supply should be switched to a battery. The RPM control can be made portable using a microcontroller or a variable resistor. Input voltage stability should also be considered, and a battery that does not decrease in voltage as it discharges should be selected. If a one-size-fits-all portable CPAP proves to be unsafe, a microcontroller could be implemented to provide two or more RPM settings, allowing the user to adjust the pump flow to an appropriate level for the neonate's size.

8 Conclusion

This master's thesis indicates that 1) a CPAP device can be modelled in Simulink and 2) a portable CPAP device for use in low-resource settings is a feasible concept. The Simulink model provided valuable insight into how a portable CPAP device would function. The model was used as a tool to aid in design decisions, but was not highly accurate, and thus did not eliminate the need for practical experimentation. Guided by the model, a portable CPAP prototype was constructed and tested. The device did not meet all design criteria in the preliminary evaluation scheme, however, it was a good proof-of-concept, and should be explored further with input from clinicians. A low-cost, portable CPAP device for low-resource settings is an idea worth pursuing and may have the potential to become a commercial product used by neonates worldwide.

9 References

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A Design Criteria Rationale

Rationale for all design criteria in Table 2 are detailed below. Much of the information in this section was derived from professional experiences of Robert Neighbour, managing director of Diamedica UK Ltd., who frequently visits hospitals in LMICs worldwide.

A.1 Provide the basic functionality of a CPAP device

1a. Apply a safe positive pressure to the lungs

The purpose of a CPAP device is to provide positive pressure to the lungs of the neonate via a non-invasive interface. A systematic review of 42 peer-reviewed journal articles reported 4-8 cmH₂O as a starting pressure for preterm CPAP, with 5 cmH₂O being the most common choice. Most CPAP devices including the Diamedica Baby CPAP offer an adjustable range from 1-10 cmH₂O. The pressure in the nasal cannula will likely rise and fall when the patient inhales or exhales, thus, fluctuations must be evaluated and classified. The fluctuations should not be much larger than they would be in normal breathing, because this would indicate an increased work of breathing. Finally, the pressure should be maintained as long as the device is switched on, regardless of the battery discharge level.

1b. Provide a safe and effective flowrate

A flowrate is required to apply the desired pressure to the lungs and to clear exhaled gas from the nasal cannula. There should be no possibility of rebreathing exhaled gas, but the flowrate should not be so high as to risk pneumothorax or nasal trauma [36]. Recommended flowrates for neonatal CPAP are 5-10 L/min [28].

1c. Be battery powered

The device should function for at least 1 hour without being plugged into the wall and should be recharged in a timely manner so that frequent use is possible. The battery lifetime should be considered because it contributes to device lifetime. Safety is important for the user and patient, and impact on the environment at end-of-life is important for long term sustainability and the effect of widespread use of the device. The device must have a battery indicator to warn when the battery charge is running low.

1d. Function for all sizes of neonate

The device is intended for preterm neonates, however, respiratory distress at birth is also possible in term neonates. The device should ideally be safe for all sizes of neonate, as indicated by Figure 38. The device should effectively treat neonates from 500 g to 3500 g.

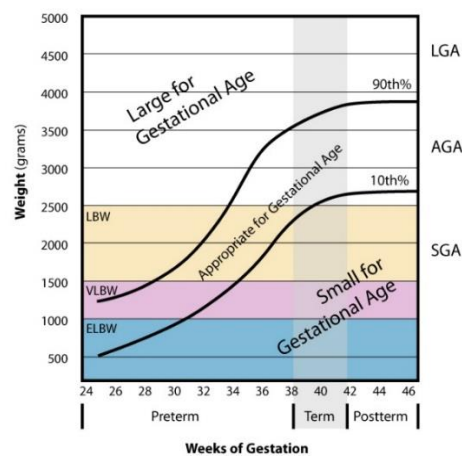


Figure 38: Birth weight vs. gestational age in weeks [55]

A.2 *Be suitable for low-resource settings*

2a. *Be low-cost*

A low cost is imperative when designing medical equipment for low-resource settings. Typical customers are either an NGO, relying largely on donations to purchase the device, or a public hospital, which may be underfunded and may struggle with corruption. To justify a purchase, the value for money must be high and extra features should be kept to a minimum. Additionally, hospitals may be less organized or less secure in low-resource settings, so the risk of medical devices being stolen or damaged is higher. Lastly, a low cost would allow hospitals to have many devices on hand, which increases the probability that a CPAP is available for every preterm birth that occurs. Mbale Regional Referral Hospital has 10,000 births per year [25], and 5-18% of babies are born preterm [26]; this could mean a portable CPAP is needed up to 5 times per day. Given the time required to clean and recharge a device, a referral hospital like Mbale should have at least 5 devices. The two main CPAP devices on the market for use in LMICs are the Pumani bCPAP (800USD = 640EUR) and the Diamedica Baby CPAP (2000GBP = 2260EUR) (prices informed by Robert Neighbour). The portable CPAP will have fewer features and therefore should be less expensive than both existing devices.

2b. *Use minimal consumables*

Low-resource hospitals and health centres will likely have a poor supply chain for restocking consumables, and thus there may be a considerable waiting period until more can be delivered. Staff will inevitably be forced to use single use components multiple times or think of creative ways to use the device without the consumable. The device should account for this challenge and function with no single use parts.

2c. *Be robust and built-to-last*

Low-resource settings are a harsh environment for a medical device. The device will be used more frequently and for longer periods of time without rest than it would in a high-resource hospital. Temperatures can be high, and the air may be dusty. The device will need to withstand being dropped. It should be resistant to water damage in the event it is used in the rain or gets improperly cleaned. These metrics can be evaluated as per the Ingress Protection Rating (Figure 39) to classify the degree of protection against dust, water, and mechanical impact. The neonatal unit at Mbale Regional Referral Hospital in Eastern Uganda reported temperatures from 25-35°C [25] and low-resource hospitals in cooler climates should also be considered, thus the device must function in 10-35°C. Finally, the battery charger should be resistant to power fluctuations, as these are common in low-income countries.

IP First number - Protection against solid objects

0	No special protection
1	Protected against solid objects over 50 mm, e.g. accidental touch by persons hands
2	Protected against solid objects over 12 mm, e.g. persons fingers
3	Protected against solid objects over 2.5 mm (tools and wires)
4	Protected against solid objects over 1 mm (tools, wires, and small wires)
5	Protected against dust limited ingress (no harmful deposit)
6	Totally protected against dust

IP Second number - Protection against liquids

0	No protection
1	Protection against vertically falling drops of water e.g. condensation
2	Protection against direct sprays of water up to 15° from the vertical
3	Protected against direct sprays of water up to 60° from the vertical
4	Protection against water sprayed from all directions - limited ingress permitted
5	Protected against low pressure jets of water from all directions - limited ingress
6	Protected against temporary flooding of water, e.g. for use on ship decks - limited ingress permitted
7	Protected against the effect of immersion between 15 cm and 1 m
8	Protects against long periods of immersion under pressure

IP Third number - Protection against mechanical impacts (commonly omitted, the third number is not a part of IEC 60529)

0	No protection
1	Protects against impact of 0.225 joule (e.g. 150 g weight falling from 15 cm height)
2	Protected against impact of 0.375 joule (e.g. 250 g weight falling from 15 cm height)
3	Protected against impact of 0.5 joule (e.g. 250 g weight falling from 20 cm height)
4	Protected against impact of 2.0 joule (e.g. 500 g weight falling from 40 cm height)
5	Protected against impact of 6.0 joule (e.g. 1.5 kg weight falling from 40 cm height)
6	Protected against impact of 20.0 joule (e.g. 5 kg weight falling from 40 cm height)

Figure 39: Ingress Protection Rating tables [60]

2d. Be easy to clean and maintain

Low-resource hospitals may have no designated maintenance department, or a poorly equipped one with few tools and few spare parts. For cleaning, there may be no central sterilization department. There may not be a reliable autoclave or consistent access to clean water. An additional challenge is that the portable CPAP device is intended for use by two departments: delivery and neonatal intensive care. Communication may be difficult between departments, and responsibility for cleaning and maintenance of the portable CPAP could be forgotten. It is assumed that the device will need to be cleaned in some way after each patient, with additional cleaning weekly or monthly. It should be easy to troubleshoot issues without taking the entire device apart, therefore, specific failure detection should be built into the device so problems can be fixed before harm can be done to the patient or the device. The device should always provide a flow of gas to the patient, and thus an audible alarm should sound if the pump inlet or outlet is blocked, or if the patient tubing is kinked, obstructing flow.

A.3 Be safe for the patient

3a. Provide clean gas

The gas delivered to the patient should be free from bacteria, viruses and dust because preterm infants are particularly vulnerable to infections [9].

3b. Produce safe and comfortable noise levels

The entire device will be in close proximity to a preterm neonate, thus the noise emitted from the motor, pump, valve, or other components must be limited to safe and comfortable levels. Elevated sound levels can lead to cochlear damage, weakening of blood vessel walls, and poorer vital signs and oxygen saturation [61]. Safe sound limits can be described by L_{eq} , which is defined as the “equivalent steady noise level that would contain

the same noise energy as a time-varying noise level across the same sampling period.” For preterm infants, the hourly L_{eq} should not exceed 50 dB [61].

3c. Provide gas at a safe and comfortable humidity

Delivery of under-humidified gas can cause impaired ciliary function, reduced clearance of secretions, damage to the airway mucosa, and reduced compliance and functional residual capacity [62]. These effects are even more pronounced in a preterm neonate, due to their immature lungs. Ventilating preterms with cold, dry gas for five minutes has been shown to result in increased airway resistance and work of breathing [40]. Ambient air has a relative humidity (RH) of 30-40%, thus providing a reference point for the minimum allowable humidity [63].

3d. Provide gas at a safe and comfortable temperature

Gas should be provided at a safe and comfortable temperature, which generally means it needs to be heated. Giving respiratory support with cold gas in the delivery room may lead to increased admission hypothermia [40]. Normothermia is defined as 36.5-37.5°C [62], so it is assumed that the gas should be delivered at a temperature close 37°C [37].

3e. Be comfortable for the patient

There should be a minimal risk of nasal trauma due to geometry and positioning of the patient interface. No pressure points should be seen on the patient’s head, and the device should not vibrate or make jerky movements near the patient.

A.4 Be user-friendly

4a. Be portable

The device must be portable so the neonate can continue treatment while in transport from the delivery room to the NICU. A portable device should be lightweight, comfortable to carry or wear, and function in different orientations. A 2004 literature review found that a safe weight for a backpack is 10-15% of the user’s body weight [64], and the average adult weight in Africa is around 60kg [65]. A mass of 9kg will therefore represent the maximum allowable weight for the device. The device needs to be comfortable for the user to encourage use. The user should comfortably carry the device for the duration of the battery charge and have both hands free to hold and attend to the infant. The device should be compatible with kangaroo mother care (KMC) and with an incubator. As indicated by the IEC standards for neonatal transport incubators [66], the device should be stable when tilted 10° in normal use and 20° in transport, and the lateral force to tip it over should be greater than 100N.

4b. Be easy to use

Hospitals and health centres in low-income countries may be understaffed. There may be inconsistent or inadequate training of clinicians, and high staff turnover. The device will be transferred between the delivery ward and the neonatal intensive care unit while still in use, and therefore must be very easy to use to prevent confusion and errors.

4c. Be fast to set up

The device is intended for delivery room use, and preterms should be given CPAP as soon as possible after birth. Assuming the device is already clean and charged, it should take no more than a few minutes to set up and start using on the patient, to keep the lungs from collapsing and losing functional residual capacity.

B Simulink Model Screenshots

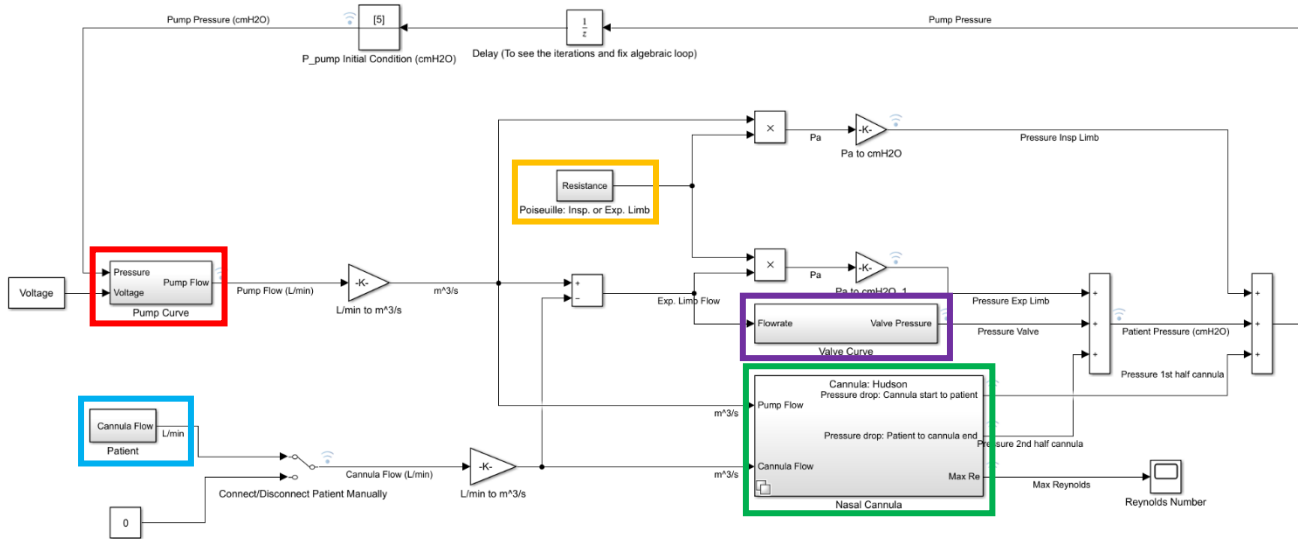


Figure 40: Top level model

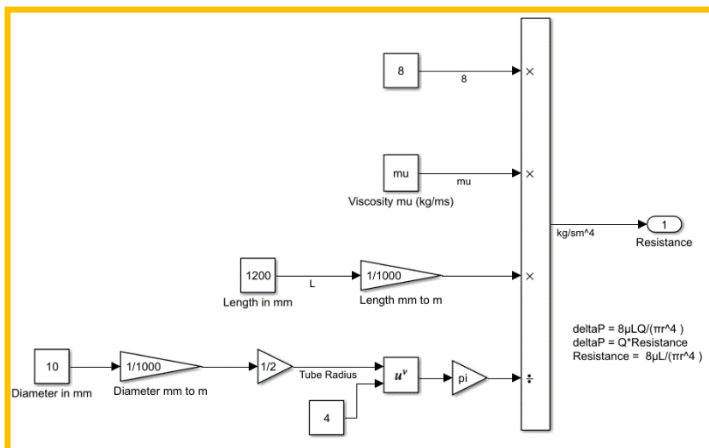


Figure 41: Resistance block (inspiratory and expiratory limb)

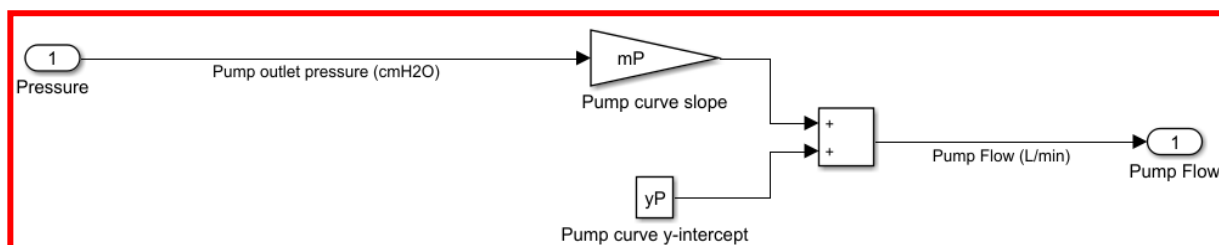


Figure 42: Pump curve

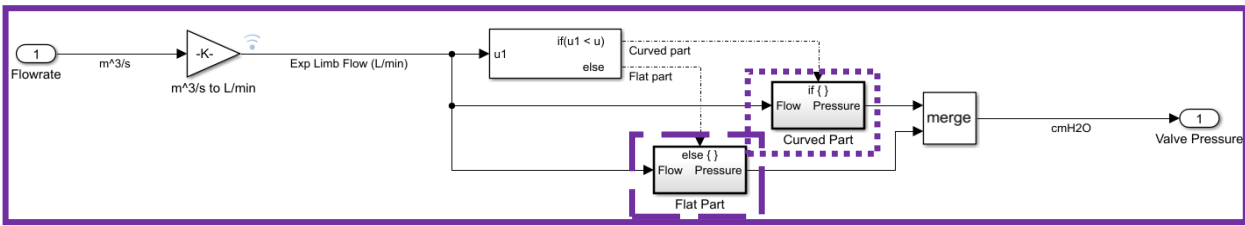


Figure 43: Valve curve

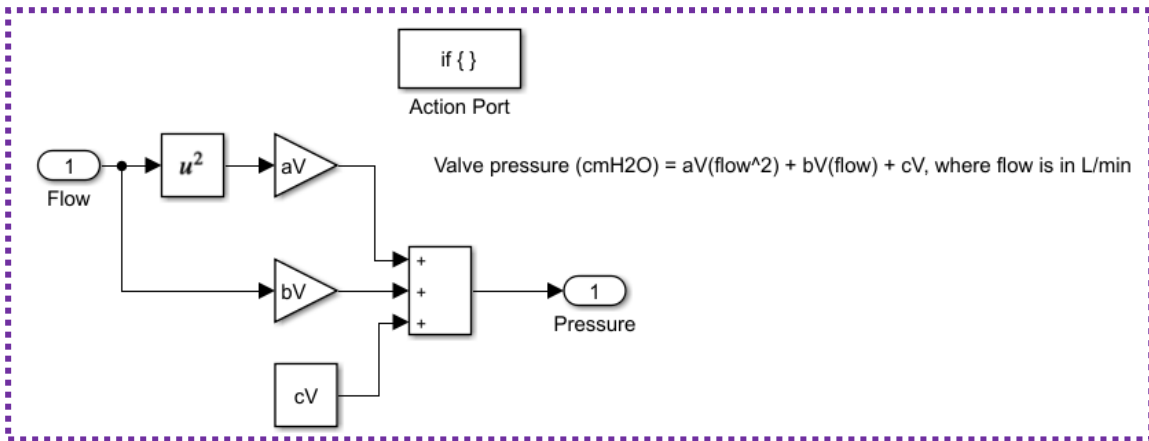


Figure 44: Valve curve: curved (non-linear) part

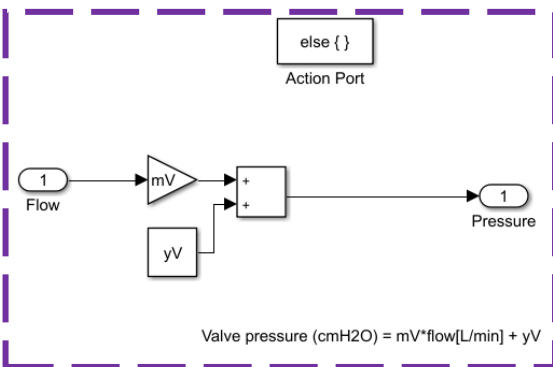


Figure 45: Valve curve: flat (linear) part

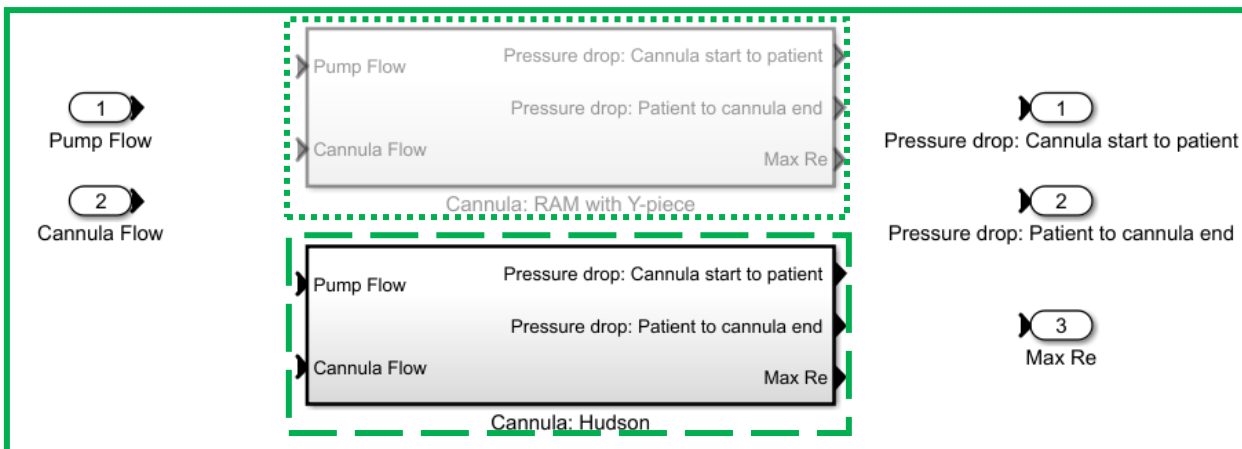


Figure 46: Cannula variant subsystem

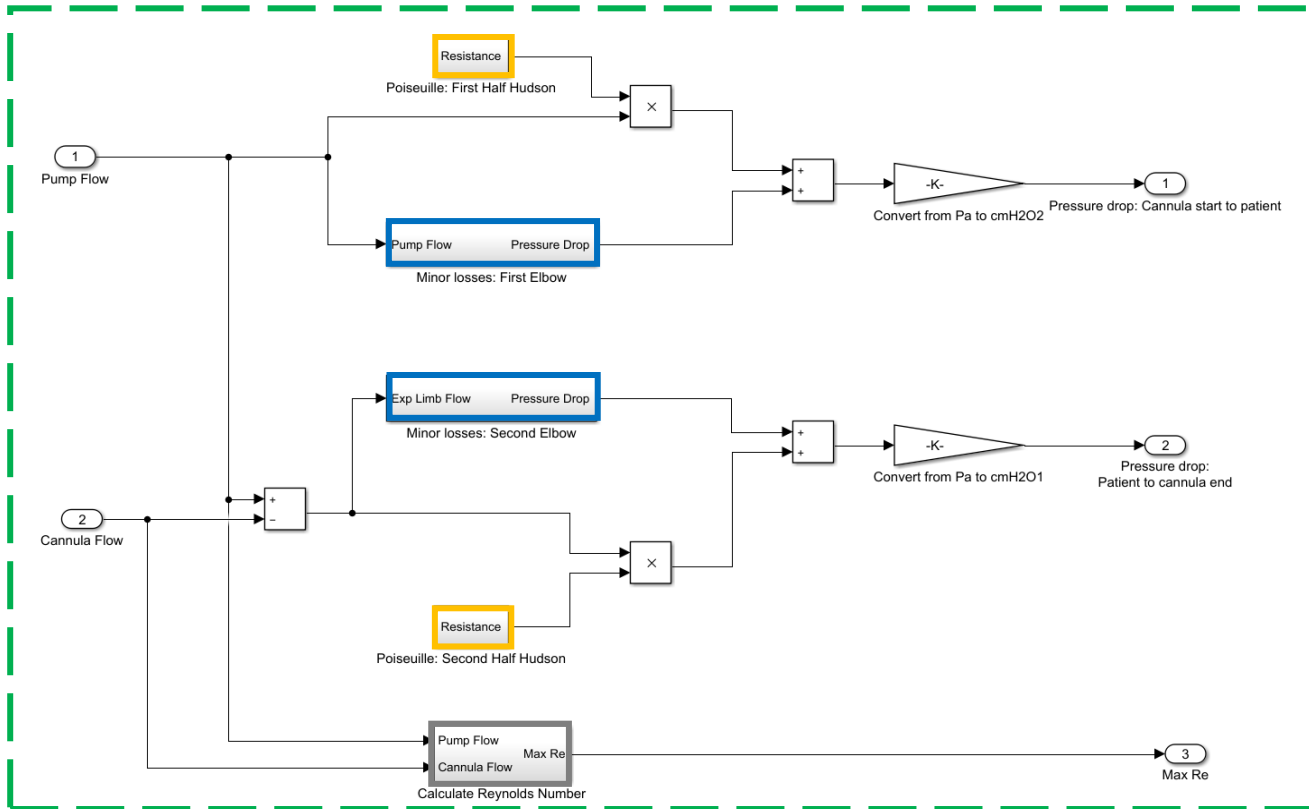


Figure 47: Hudson cannula block

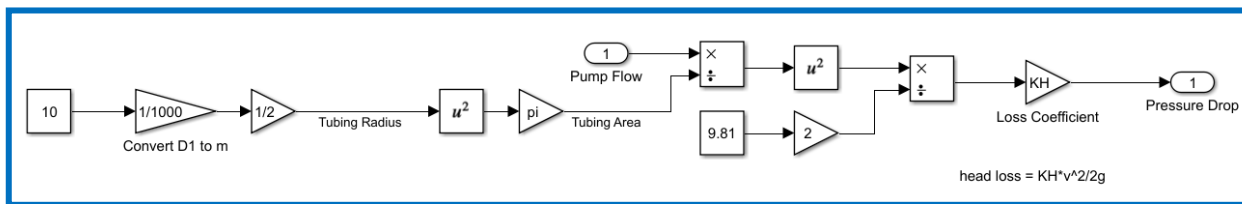


Figure 48: Minor losses: First Elbow

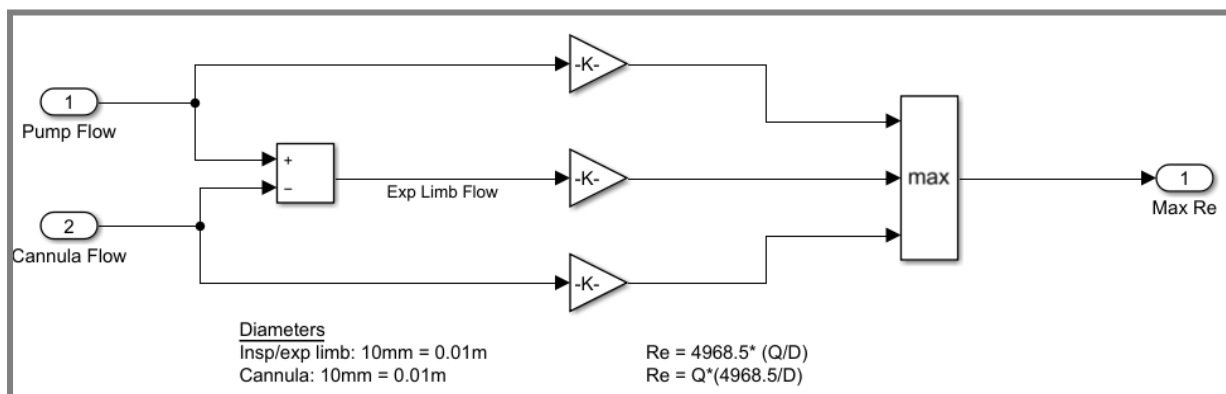


Figure 49: Calculate Reynolds Number

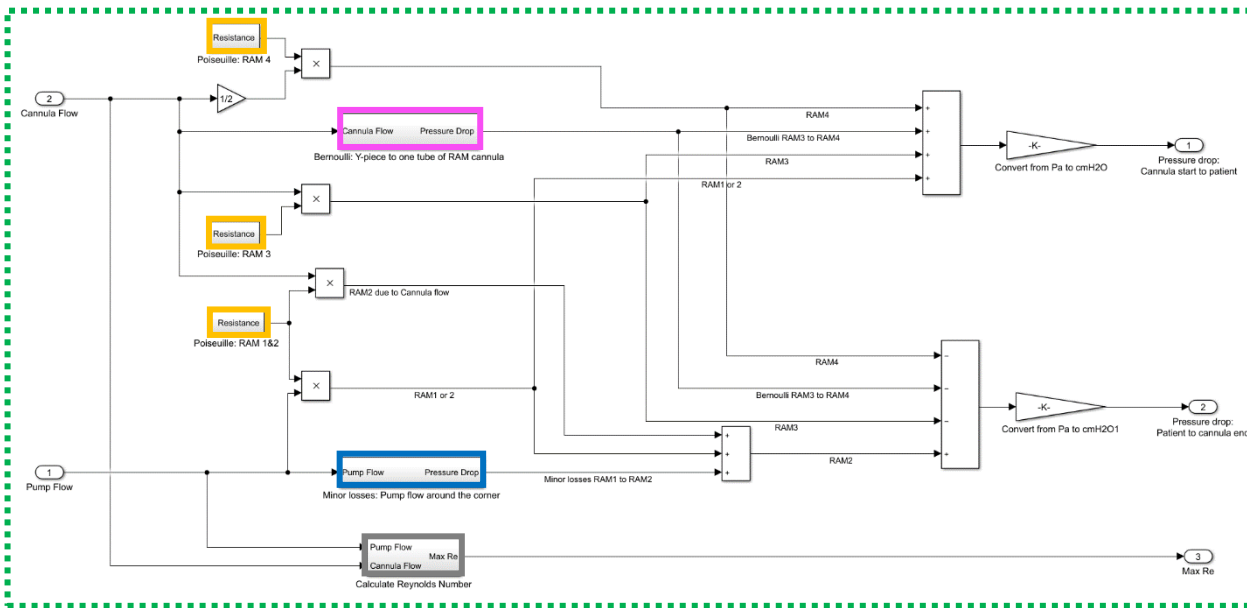


Figure 50: RAM Cannula with Y-piece

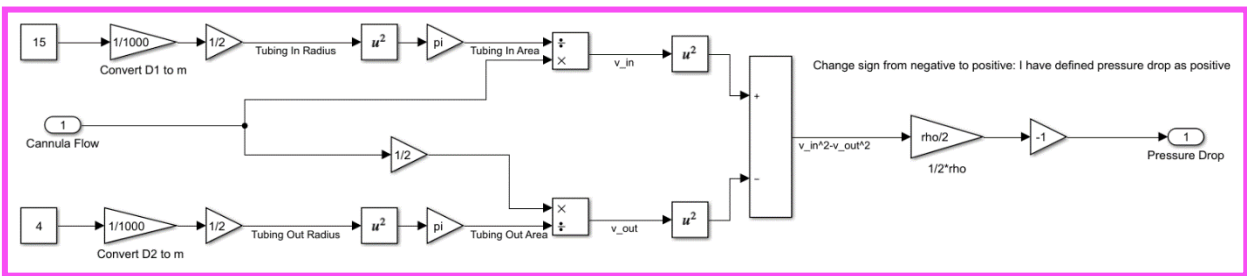


Figure 51: Bernoulli: Y-piece to one tube of RAM cannula

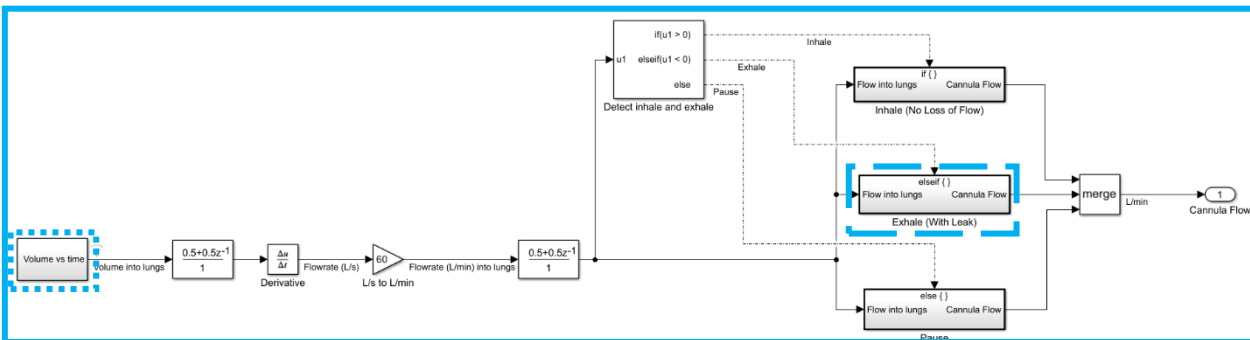


Figure 52: Cannula Flow Block

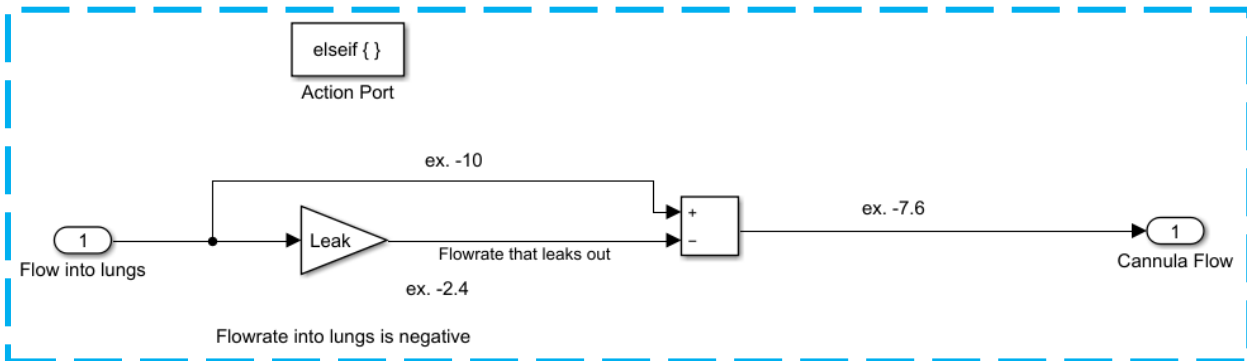


Figure 53: Cannula flow during exhale

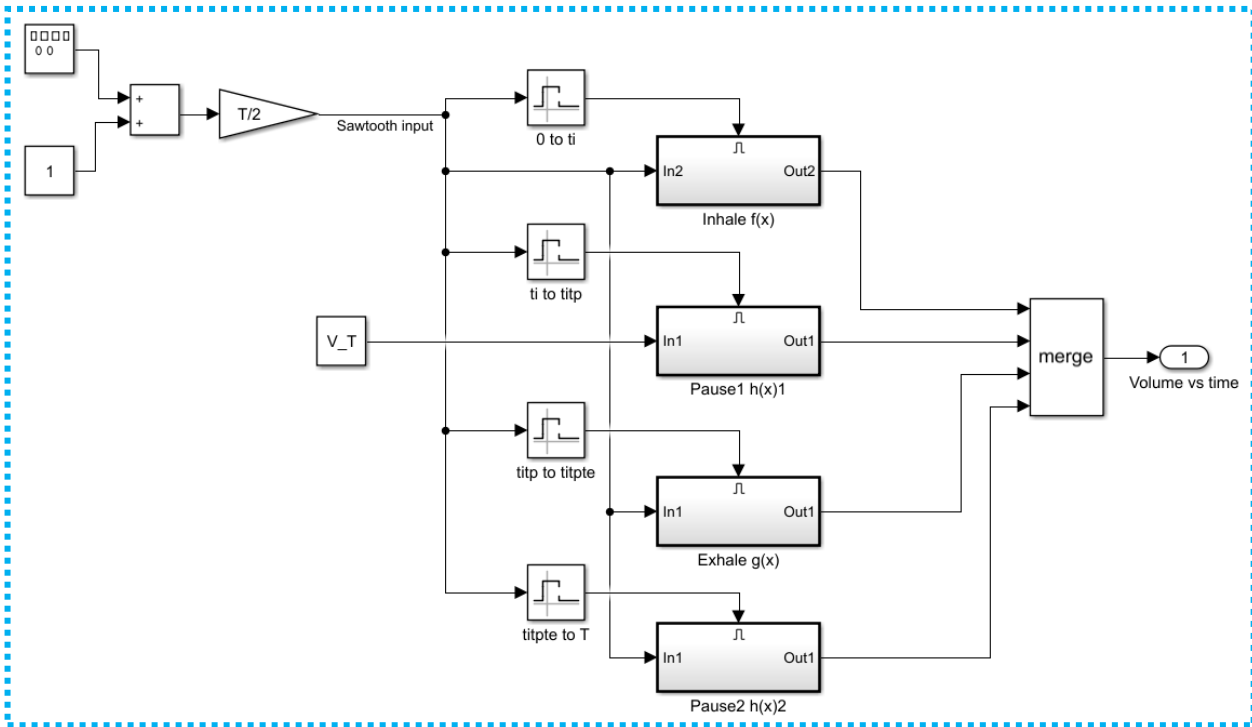


Figure 54: Volume vs. time: custom model

C Custom Breathing Model Derivation

The custom breathing model describing volume in the patient's lungs over time is composed of four separate functions, with each expressed in terms of the variables V_T , t_i , t_e , and t_p . The function $h_1(x)$ describes a pause with full lungs, so the function is constant at Volume = V_T . Similarly, $h_2(x)$ describes a pause with empty lungs and is constant at Volume = 0. The derivations for the inhale function $f(x)$ and exhale function $g(x)$ are more complex and are detailed below.

C.1 Derivation of Inhale $f(x)$

The general equation of a parabola is:

$$f(x) = ax^2 + bx + c \quad (1)$$

Three equations are required to solve for the three unknowns a , b , and c . These equations can be created by selecting three known points on the parabola and substituting them into Equation 1. From Figure 18, 3 known points are $(0,0)$, (t_i, V_T) , and $(2t_i, 0)$. This gives the three equations:

$$0 = a(0)^2 + b(0) + c \quad (2)$$

$$V_T = at_i^2 + bt_i + c \quad (3)$$

$$0 = a(2t_i)^2 + b(2t_i) + c \quad (4)$$

From Equation 2, $c = 0$. Using Equations 3 and 4, the coefficients a and b can be determined, and thus the equation for $f(x)$ is:

$$f(x) = \frac{-V_T}{t_i^2} x^2 + \frac{2V_T}{t_i} x \quad (5)$$

C.2 Derivation of Exhale $g(x)$

The equation for $g(x)$ is easiest to solve for by starting with the function $g_0(x)$ (Figure 55), then shifting it to the right by t_p to account for the pause with full lungs.

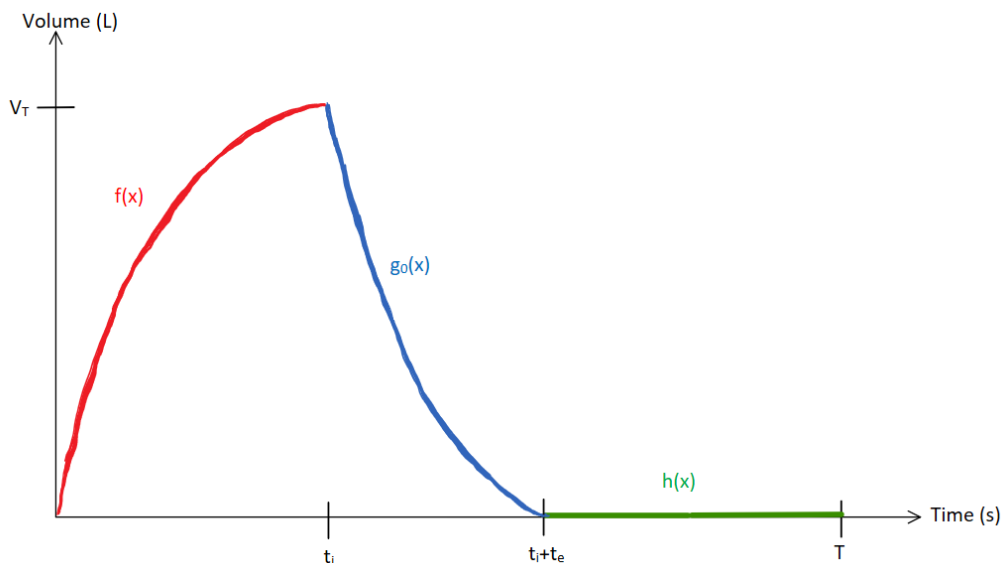


Figure 55: Volume vs. time plot with function $g_0(x)$.

The general equation of a parabola is

$$g_0(x) = a_0x^2 + b_0x + c_0 \quad (1)$$

Three equations are required to solve for the three unknowns a_0 , b_0 , and c_0 . These equations can be created by selecting three known points on the parabola and substituting them into Equation 1. From Figure 55, three known points are (t_i, V_T) , $(t_i+t_e, 0)$, and (t_i+2t_e, V_T) . This gives the three equations:

$$V_T = a_0t_i^2 + b_0t_i + c_0 \quad (2)$$

$$0 = a_0(t_i + t_e)^2 + b_0(t_i + t_e) + c_0 \quad (3)$$

$$V_T = a_0(t_i + 2t_e)^2 + b_0(t_i + 2t_e) + c_0 \quad (4)$$

Using substitution, the coefficients are calculated to be:

$$a_0 = \frac{V_T}{t_e^2} \quad (5)$$

$$b_0 = \frac{-2V_T(t_i+t_e)}{t_e^2} \quad (6)$$

$$c_0 = \frac{V_T(t_i+t_e)^2}{t_e^2} \quad (7)$$

Then to calculate $g(x)$, $g_0(x)$ must be shifted to the right by t_p . This is done by subtracting t_p from each instance of x in the equation:

$$g(x) = a_0(x - t_p)^2 + b_0(x - t_p) + c_0 \quad (8)$$

Collecting like terms results in:

$$g(x) = a_0x^2 + (-2a_0t_p + b_0)x + (t_p^2 - b_0t_p + c_0) \quad (9)$$

Subbing in Equations 5-7 gives the equation for $g(x)$ in terms of V_T , t_i , t_e , and t_p :

$$g(x) = \frac{V_T}{t_e^2}x^2 + \left(\frac{-2V_T(t_i+t_e+t_p)}{t_e^2}\right)x + \left(\frac{V_Tt_p^2}{t_e^2} + \frac{2V_Tt_p(t_i+t_e)}{t_e^2} + \frac{V_T(t_i+t_e)^2}{t_e^2}\right) \quad (10)$$

D Automated Simulated Patient

Experimentation of the portable CPAP prototype was done by manually actuating a Dräger Infant Test Lung to simulate a patient breathing. Before finalizing this test procedure, alternate ways to simulate a breathing neonate were explored.

First, the Diamedica Helix Portable Pediatric Ventilator was investigated for use as a simulated patient. This is a pneumatically driven ventilator designed for use in low-resource settings, and thus can be more easily modified than the expensive ventilators used in Erasmus Medical Centre. The ventilator was directly connected to the nasal cannula, allowing it to draw air in from the CPAP and exhale into it. The tidal volume is imprecisely adjustable, and it proved difficult to adjust tidal volume to below 30 mL, which is above the maximum volume of interest. The pressures measured at the cannula were extremely high, greater than 30 cmH₂O during exhalation and less than -30 cmH₂O during inhalation. It was assumed that the pressures were a result of the ventilator and not of the CPAP, so this idea was abandoned.

Pilot testing of the Dräger Infant Test Lung was promising. Ideas were then explored to actuate the lung with the same tidal volume consistently, so that comparison across conditions would be more conclusive. Therefore, some ideas to automate the actuation of the lung were explored. The most feasible way to do this seemed to be by translating rotational motion into linear motion using either a slider and crank mechanism or a cam. A slider and crank device was designed in SolidWorks and 3D printed in polycarbonate, shown in Figure 56. The mechanism was quite unstable. The wheel tended to jump off its axel, and the slider tended to jump out of the guides. The wheel was turned manually, but it appeared necessary to apply a motor to turn the wheel in order to generate identical simulated breaths each time. This idea was considered, but there was not enough time to explore iterative design of a simulated patient, especially because there was no guarantee that it would result in a higher fidelity simulation than manual actuation.



Figure 56: Slider and crank mechanism was 3D printed in polycarbonate to automatically actuate the test lung.

E Simulated Patient Results

Pressure and flow data from experiments involving the Dräger Infant Test Lung are presented below for all experimental conditions. The *No CPAP* condition presents flowrate and pressure measured at the patient only. The tests including the portable CPAP prototype show flowrate and pressure measured at the patient, pump outlet, and PEEP valve.

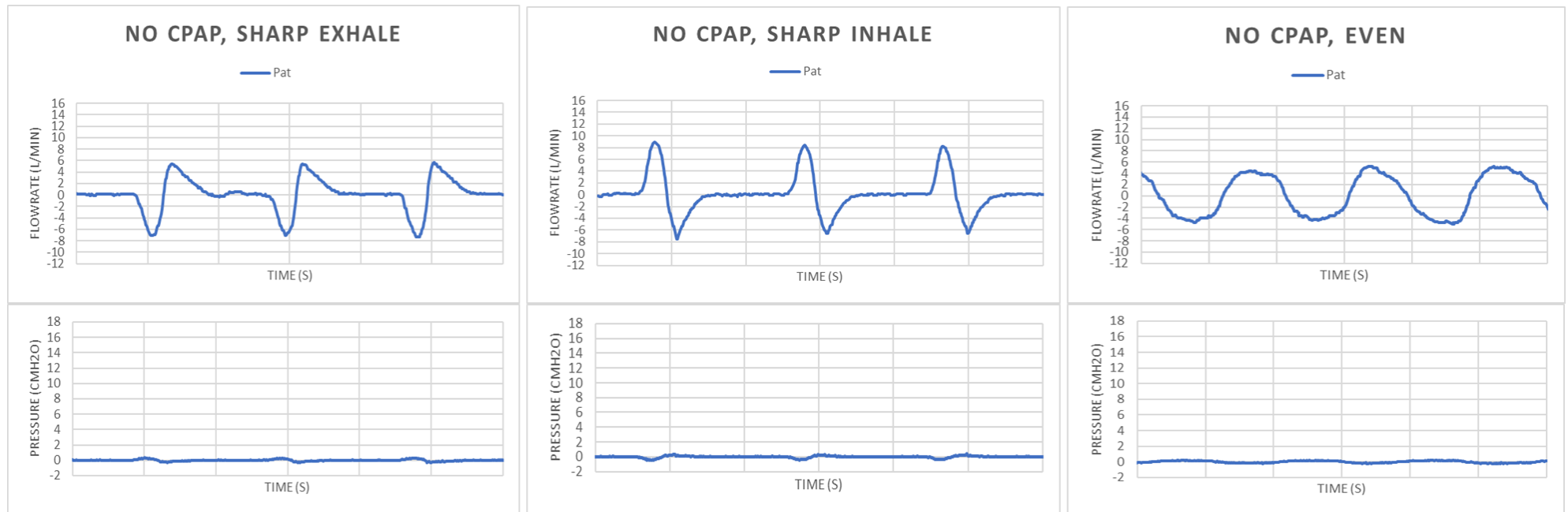


Figure 57: No CPAP - experimental patient flow and pressure, testing performed with Dräger test lung.

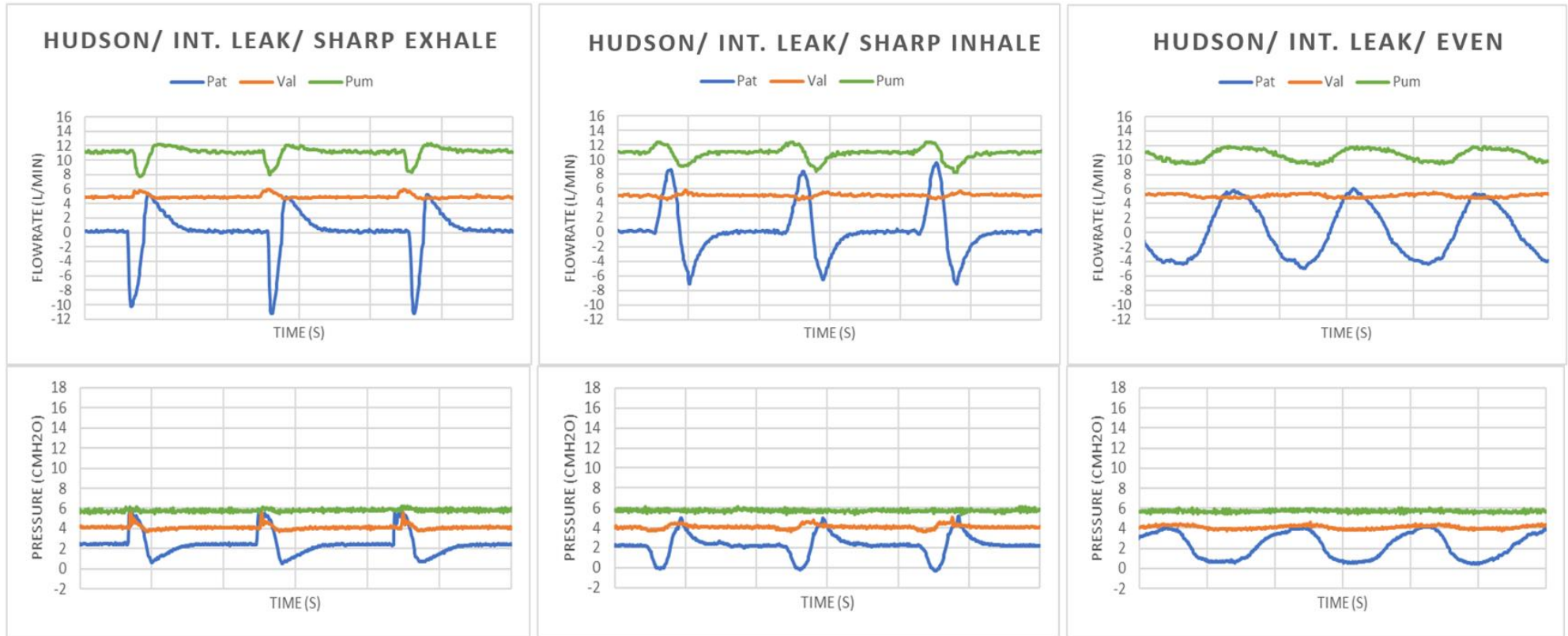


Figure 58: Hudson cannula, Intentional Leak - experimental flows and pressures from testing of CPAP prototype with Dräger test lung.

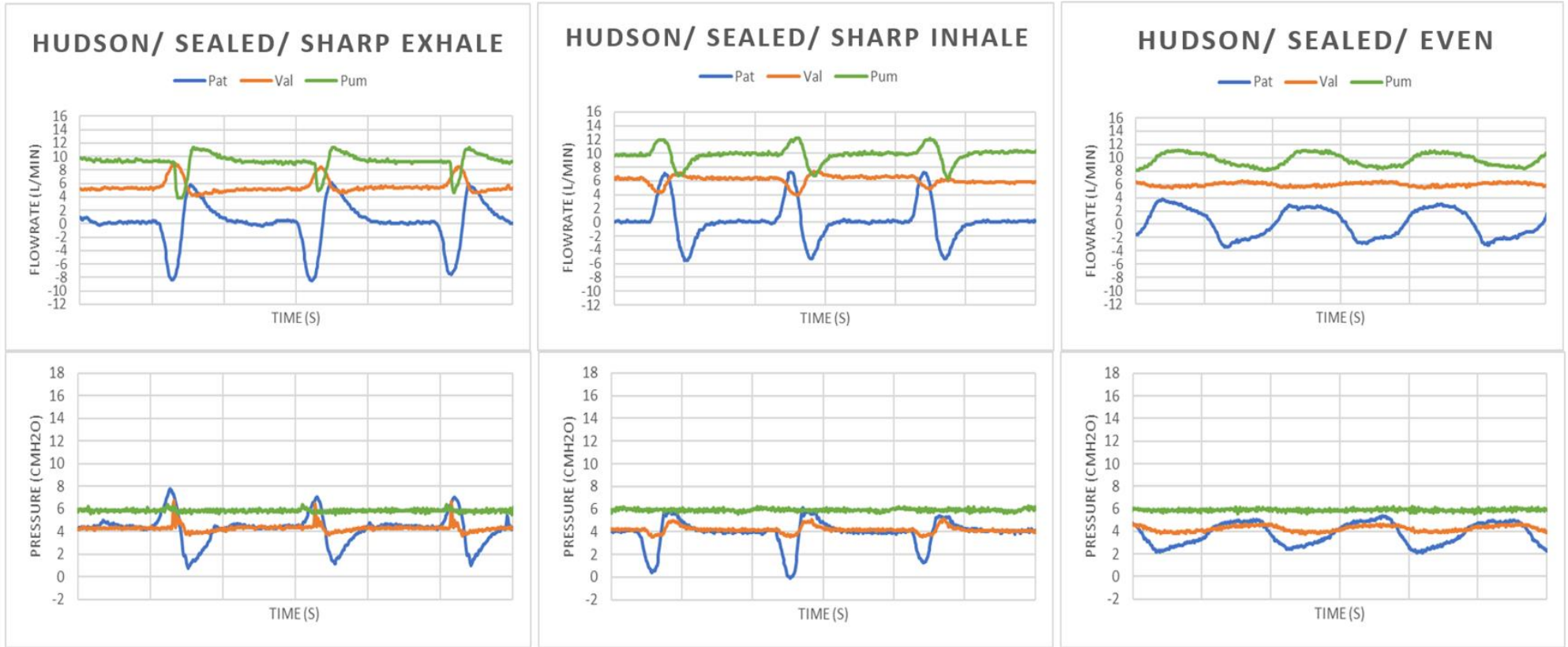


Figure 59: Hudson cannula, Sealed - experimental flows and pressures from testing of CPAP prototype with Dräger test lung.

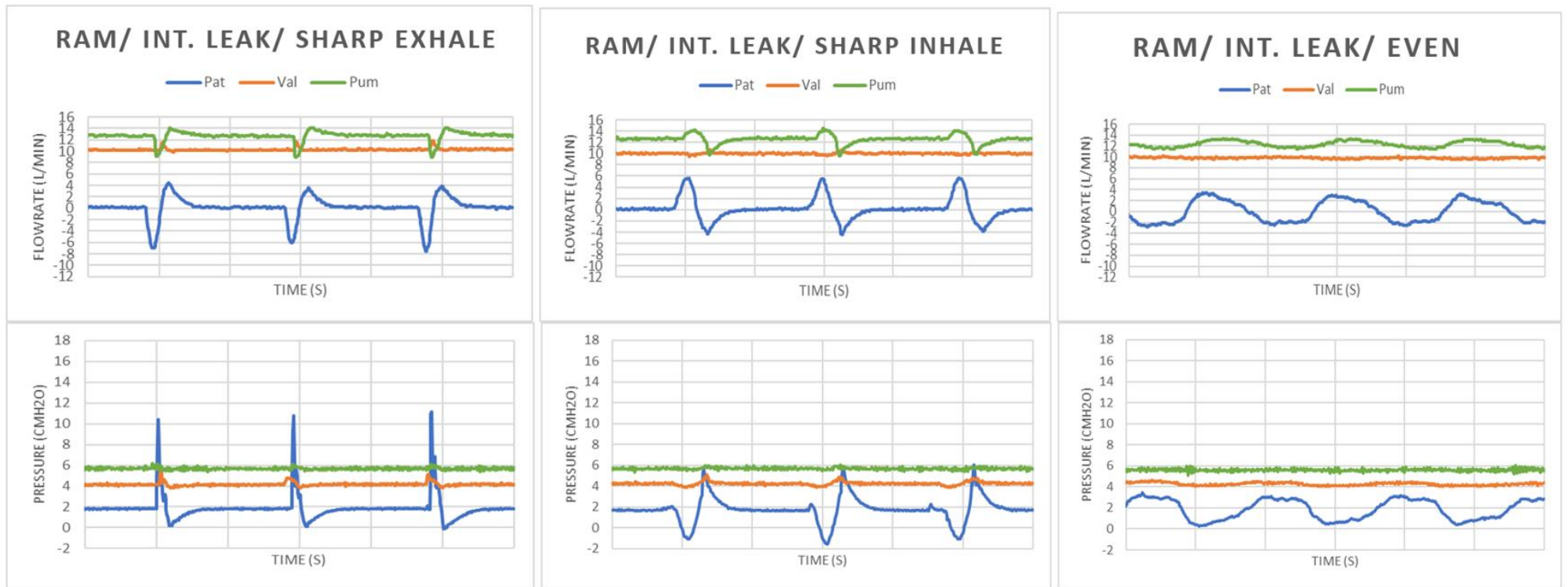


Figure 60: RAM cannula, Intentional Leak - experimental flows and pressures from testing of CPAP prototype with Dräger test lung.

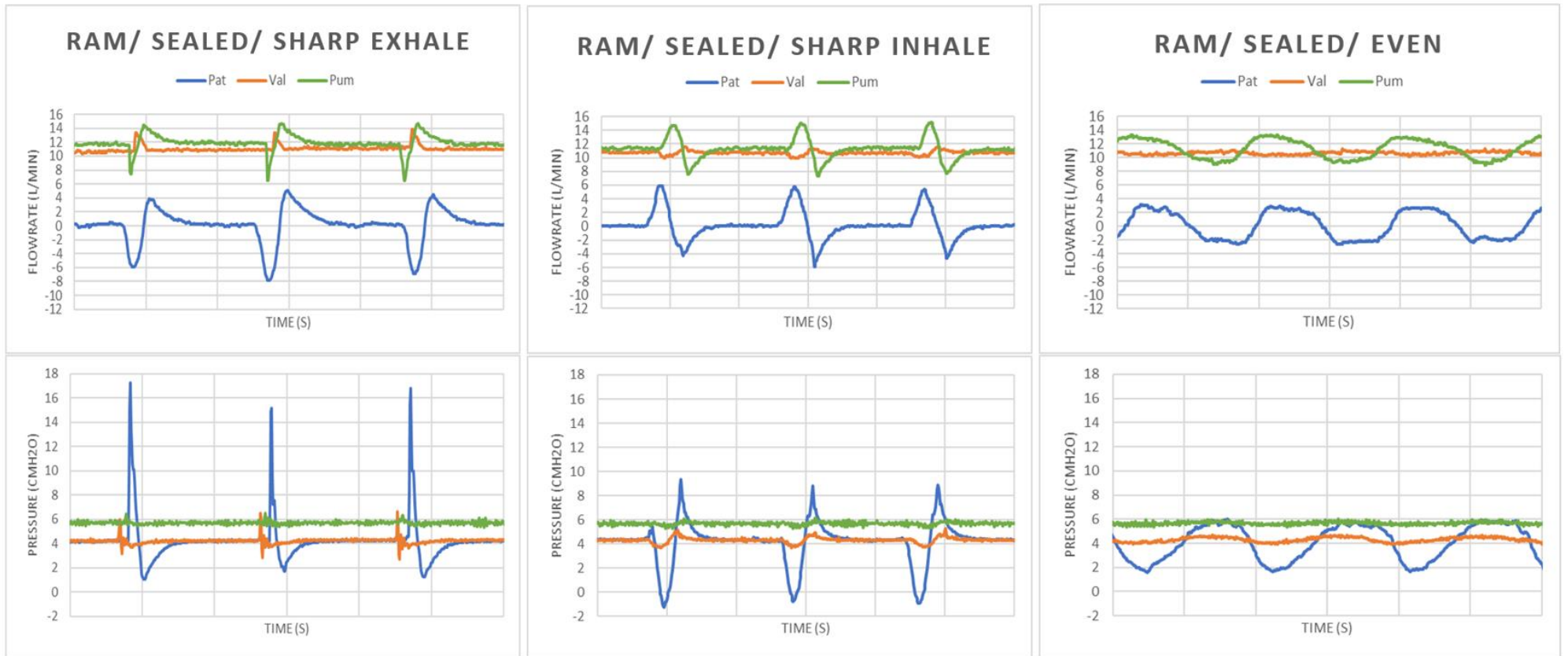


Figure 61: RAM cannula, Sealed - experimental flows and pressures from testing of CPAP prototype with Dräger test lung.

F Model/Prototype Comparison Graphs

The additional model/prototype comparison graphs not included in sections 6.2 and 6.3 are shown below.

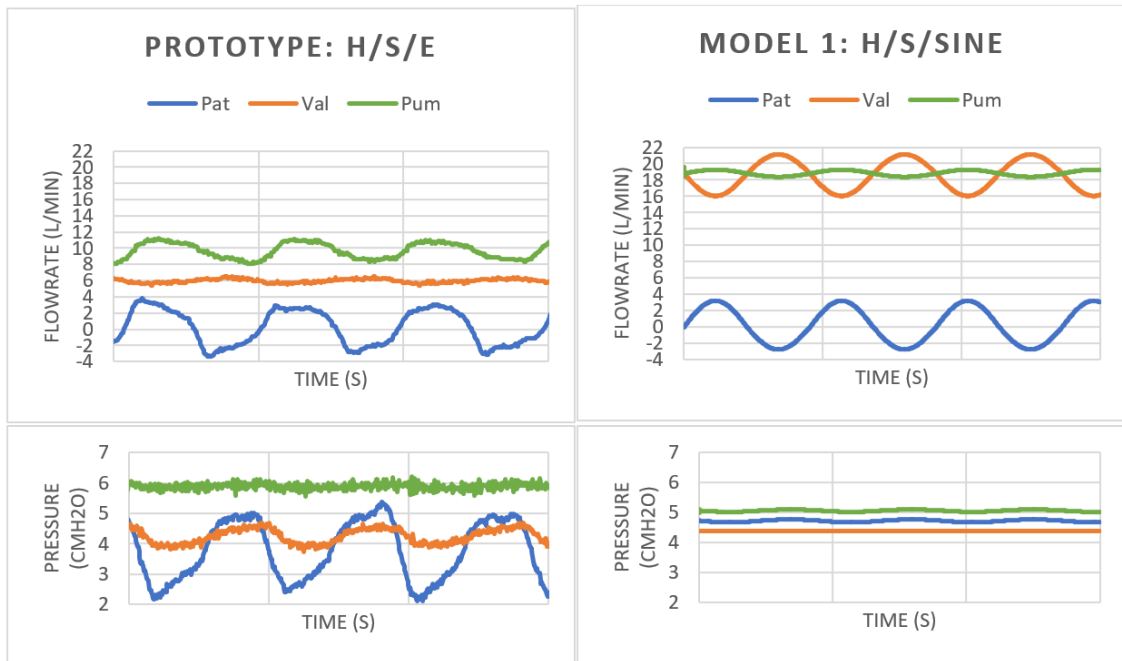


Figure 62: First Model Iteration: Hudson, Sealed

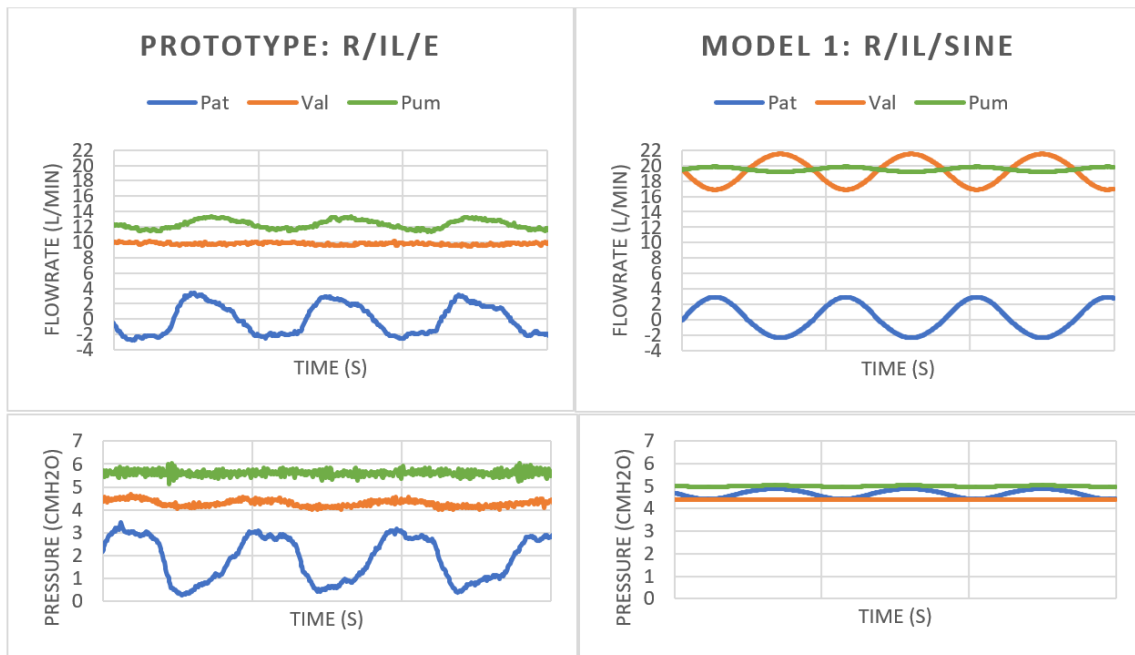


Figure 63: First Model Iteration: RAM, Intentional Leak

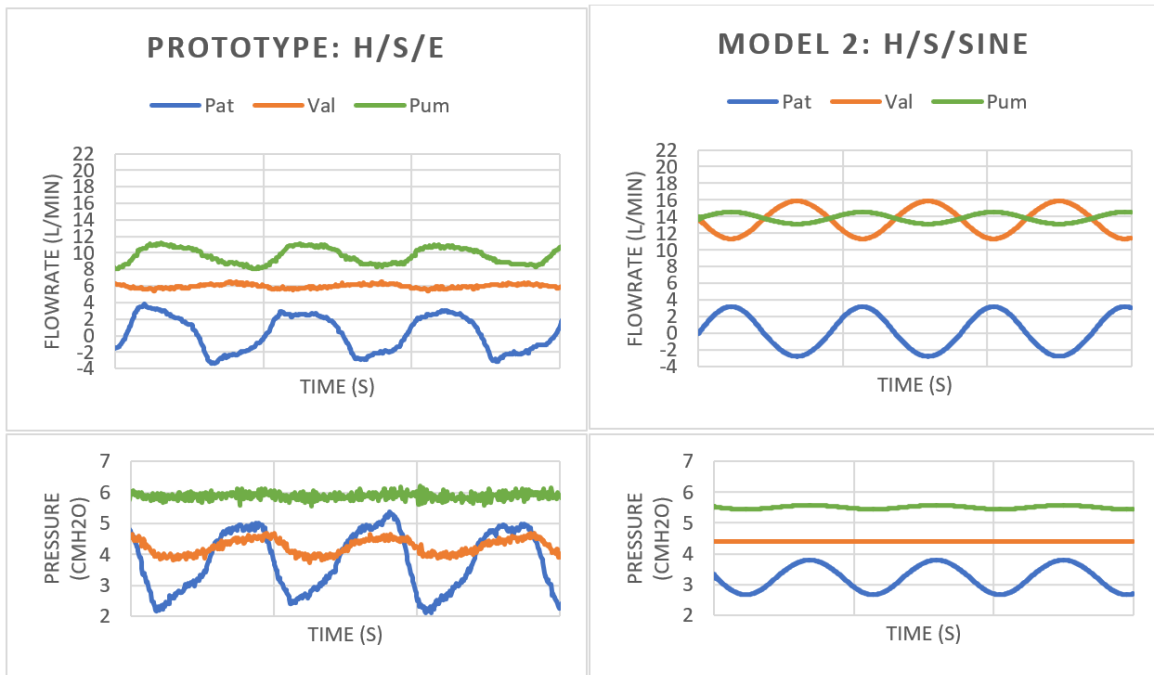


Figure 64: Second Model Iteration: Hudson, Sealed

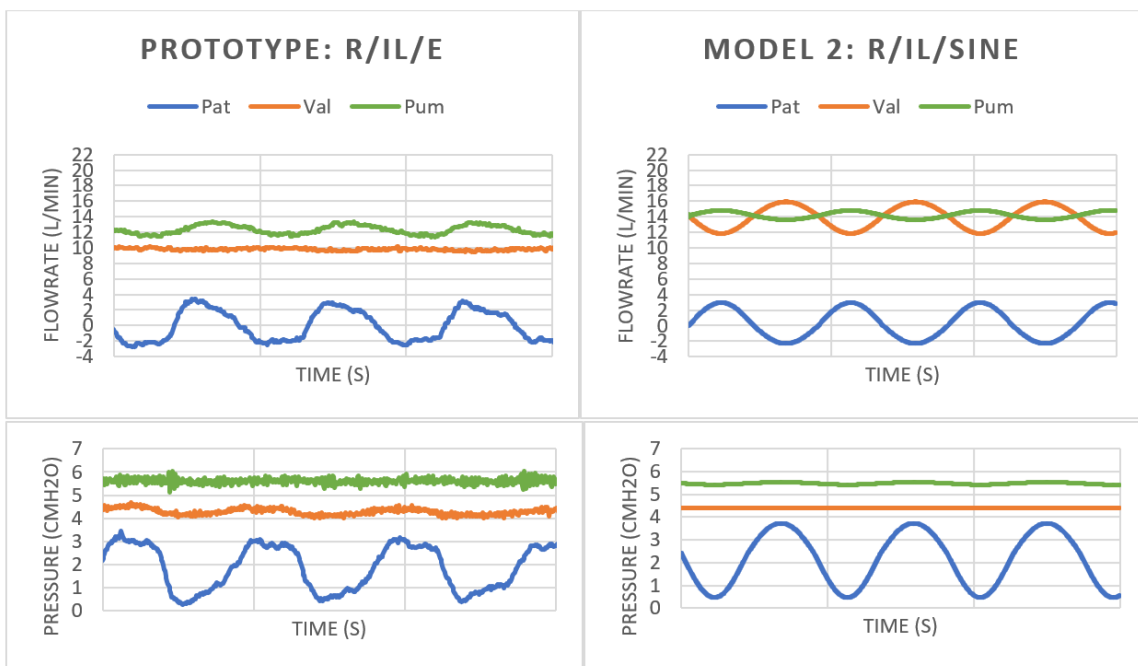


Figure 65: Second Model Iteration: RAM, Intentional Leak