CZECH TECHNICAL UNIVERSITY IN PRAGUE

FACULTY OF BIOMEDICAL ENGINEERING

Department of Biomedical Technology

Model tool – Bubble CPAP

Bachelor Thesis

Study program: Biomedical and Clinical Technology
Study branch: Biomedical Technician

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Kladno 2022

BACHELOR'S THESIS ASSIGNMENT

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II. BACHELOR'S THESIS DETAILS

Bachelor's thesis title in English:

Model tool - Bubble CPAP

Bachelor's thesis title in Czech:

Modelová pomůcka - Bubble CPAP

Guidelines:

Design and implement a tool for teaching and laboratory measurements, based on the principle of the Bubble CPAP. The proposed solution must allow the measurement of min. 1 pressure in the ventilation circuit and must allow flow control in the range 0-12 L / min with a step of 1 L / min or continuous control. Control and display the measured pressure using the Simulink software.

Bibliography / sources:

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DECLARATION

I hereby declare that I have completed this thesis having the topic "Model tool – Bubble CPAP" independently, and that I have attached an exhaustive list of citations of the employed sources.

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ACKNOWLEDGEMENTS

I would like to thank my supervisor doc. Ing. Petr Kudrna, Ph.D. for all the valuable advices and unwavering guidance I received throughout the work on the project. I am very glad I have a chance to work with such a great mind.

ABSTRACT

Title of the Thesis: Model tool – Bubble CPAP

Newborn respiratory distress syndrome (NRDS) is one of the most common cause in neonatal deaths. The widely used method to solve NRDS is ventilation. Ventilation method can be 2 types: invasive and non-invasive. Invasive method is effective, however very expensive and requires trained personnel to use and maintain it. Bubble CPAP is non-invasive, simple, effective, and low-cost device. This bachelor thesis aims to develop the teaching tool bubble CPAP for demonstration in study purposes and future modification. Designed bubble CPAP is able to control the flow from flow mass controller and read the pressure oscillations. Control of flow and reading of the pressure values are performed with help of Simulink software. The work also compared the influence of the flow and depth of immersion of expiratory tube on the pressure oscillations created by bubbles in water column. Due to limitations in hardware, the designed bubble CPAP is not able correctly interpret the high-frequency pressure oscillations. Even though, the designed project is able to demonstrate main principles and patterns of the bubble CPAP.

Key words

Bubble CPAP, Newborn respiratory distress syndrome, Arduino, Simulink, CPAP

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List of symbols and abbreviations

List of symbols

Symbol	Unit	Importance
Vref	Volts	Reference voltage
V	Volts	Voltage
$\bar{x}$		Arithmetic average
S^2		Standard deviation
n		Number of measurements
ΔD		Difference between Agilent Digital Multimeter voltage and Arduino Input voltage
P_{aw}	cmH_2O	Airway pressure

List of abbreviations

Abbreviation	Importance
CPAP	Continuous positive airway pressure
bCPAP	Bubble continuous positive airway pressure
MAP	Mean airway pressure
NRDS	Newborn respiratory distress syndrome
ARDS	Acute respiratory distress syndrome
$PaCO_2$	Partial pressure of carbon dioxide
P_{aw}	Airway pressure
PEEP	Positive end-expiratory pressure
HFNC	High-flow nasal cavity
MFC	Mass flow controller
PWM	Pulse width modulation

1 Introduction

The leading contributor for the newborn's deaths is a newborn respiratory syndrome (NRDS). The respiratory failure can result from sepsis, diarrhea, prematurity, pneumonia, and etc. Overall, NRDS account for almost 80% of neonatal deaths globally. [1]

One of the method of management respiratory distress is assisted ventilation. Exist two types of ventilation assistance: invasive and non-invasive.

Invasive ventilation traditionally associated with conventional mechanical ventilation. Normally, the breathing is facilitated by creating a negative pressure in the chest using diaphragm. On the other hand, the mechanical ventilation delivers positive pressure to the trachea which facilitates the blow of air in the lungs. It causes the lungs to increase in volume and then recoil naturally [2]. However, lungs and especially lungs of premature infants are not designed to tolerate forced positive pressure. High-frequency oscillatory ventilation is used as lung protective strategy. It expected to result in less injury since it reduces fluctuations of high frequency tidal volume. In developed countries for treatment of respiratory distress high-frequency ventilators are used with success. The high-frequency ventilators are usually implemented during severe respiratory failure. [3] It helps to maintain lung volume during expiration, provides comfortable breathing, and delivery of oxygen. It has reduced the neonatal mortality significantly. However, such devices are expensive which makes them unavailable for the developing countries. Moreover, the usage of named devices requires to have highly trained personnel in order to operate and maintain it.

As a common non-invasive ventilation technique, bubble CPAP is used. It provides continuous positive airway pressure to the newborn infants with lung diseases. Most frequent application of CPAP is in premature infants with respiratory distress syndrome. [4] During last few decades till today the bubble CPAP is quite popular since it is safe, simple in use and inexpensive. Bubble CPAP was created as an alternative to the traditional CPAP. It transmits small-amplitude, high-frequency pressure oscillations around MAP.

Bubble CPAP, unlike traditional CPAP provided by mechanical ventilation, maintain the pressure by submerging the end of expiratory tube to the water. [5] Pressure depends on the depth on which the tube is submerged in water. The exhalation against the column of water generates the bubbles, which creates noisy pressure oscillations. It promotes the alveolar recruitment helping oxygenation. [6]

As was mentioned earlier, bubble CPAP is widely used tool which significant in its effectiveness and simplicity. For future biomedical technicians it is a very important to know how this device works and how to use it.

2 Overview of the current state of the art

Respiration system is a system of organs responsible for breathing, where exchange of oxygen and carbon dioxide occurs. The main organ of respiratory systems are lungs located in thorax and protected by thoracic cage, composed of bones and muscles. Through system of pipes, namely, conducting airway, the air is pumped in and out. Exist upper and lower airways. Upper airway system includes nose, sinuses, the pharynx. The lower airway system comprises larynx, the trachea, stem bronchi, intrapulmonary bronchi, the bronchioles, and alveolar ducts. [7]

To enchase a movement of the air it is required to create a pressure gradient. Pressure gradient occurs if in one area the pressure is high, whereas in other – low. The air moves from high pressure area to the low pressure area. During normal breathing the suction of the air in the lungs occurs due to movement of intercostal muscles and diaphragmatic muscles. During breathing in, the intercostal muscles move up and out, whereas diaphragmic muscles move out and down which creates a negative atmospheric pressure. Meanwhile, during breathing in, the air pressure in alveoli is lower than atmospheric pressure. During breathing out, the intercostal and diaphragmic muscles relax. When intrathoracic pressure become greater than outside pressure and the pressure in the alveoli is being higher than atmospheric pressure, it facilitates the air to move out from the lungs. [8]

This concept is applied to the normal breathing and to the negative pressure ventilation, namely, iron lungs. The negative pressure ventilation was used in early stages of lung ventilation and was actively used in 1950 on polio patients. The core principle in iron lungs is to generate a negative pressure around the body of a patient. It lowered the pressure inside the lungs and pulled the rib cage outward, which resulted in movement of air inside the lungs. Such ventilation is designed in way that it replicates the normal breathing. However, when the iron lungs are used, it creates plethora of practical problems. For example, they are too huge, and it is very complicated to perform medical manipulations on patient. [9]

The positive pressure ventilation was described in 1952 in Copenhagen. [10] The principle of positive pressure ventilation is to create a higher pressure outside of the patient. It is done by blowing the air into the patient's lung. Once the breath is delivered, the lungs of the patient relax. It facilitates the movement of air from the lungs to the outside.

Positive pressure ventilation can be delivered invasively and non-invasively. Invasive method uses ventilators, whereas non-invasive through special face mask.

Most often the positive pressure ventilation is used in acute settings. This type of ventilation made an assistant ventilation much easier. For the neonates the endotracheal (ET) tube is usually used. However, the way the positive pressure ventilation works is unnatural for the human lungs. Human, and especially newborn's, lungs are not designed to tolerate such high positive pressure. The problem in ventilation in newborns and premature infants is that their lungs are not fully formed yet. Their lungs lack the surfactant. The surfactant enables alveoli to expand with very little pressure gradient. In order to ventilate the newborns, considerate amount of pressure must be applied. However, such approach, which is used in conventional ventilators, causes complications. For example, airways of infants get distended, alveoli are raptured, inflammatory sensors are triggered. Overall, it might lead to chronic disease. A big portion of premature infants outgrow the chronic lung disease. However, others suffer from lung problems in their first years of life. Newborn respiratory distress syndrome (NRDS) and acute respiratory distress syndrome (ARDS) are main problems of mechanical ventilation in infants and adults. [11]

Continuous positive airway pressure (CPAP) is one of types of positive pressure ventilation, which is used to maintain constantly open airways in patient with spontaneous breathing. It is done by applying a flow of air into the airways. CPAP can deliver positive end-expiratory pressure (PEEP) and maintains the set pressure during respiration. PEEP is a pressure in alveoli in the end of the expiration. [12]

Continuous positive airway pressure is widely used in the world. The device greatly decreased the neonatal mortality. By the delivering continuous positive pressure to the airways, it prevents alveolar and lung collapse, improving oxygenation, ventilation, and reducing respiratory fatigue as well. [13]

2.1 Methods of delivering CPAP

CPAP can be delivered by several ways, namely via mechanical ventilators, commercial pressure drivers, high-flow nasal cavity (HFNC), and bubble CPAP.

With a ventilator the generation of CPAP occurs by patient's exhalation against a mechanical one-way valve located on the expiratory limb of the circuit of ventilator. Nevertheless, the ventilators are considered to be a complex and expensive devices. In addition, they require much higher level of training and larger amount of oxygen or medical air to run. The unproper use of delivery of CPAP via ventilator might lead to a profound consequences such as complications from anesthesia, under- and over-sedation, ventilator associated pneumonia, accidental extubating, trauma to the lungs from high pressures or large tidal volumes, or lung injury from exposure to excessive oxygen.

Pressure drivers can deliver CPAP as well. Pressure drivers require a tight fit of a nasal prongs or a CPAP face mask. The main drawback of such method is that if the air leakage occurs, the effect of CPAP will dissipate. [14]

In addition, such ways of delivering of pressure is only available on high-resource countries. On the other hand, the alternative might be the delivery of CPAP via HFNC therapy and bubble CPAP.

HFNC and bCPAP can be used in resource-limited settings. Both HFNC and bubble CPAP have proven their efficiency. [15] Observational and controlled clinical studies illustrated that providing respiratory support with HFNC is effective therapy for low-weight premature newborns. The bCPAP has significant advantage over the HFNC. It is difficult to identify the pressure delivered via HFNS. Whereas in the bCPAP, the delivered pressure is indicated by the end of the expiratory tube which is immersed to a depth of water in centimeters.

Bubble CPAP was used successfully as well. Numerous clinical researches were conducted to study the bubble CPAP's effectiveness and safety. For example, an observational study of the introduction of a new technique for ventilatory support for neonates with respiratory distress was conducted in NICU hospital in May 2003. The neonates admitted to the NICU 18 months prior and 18 months after the introduction of bubble CPAP were studied. The results are following. In this study no difference in mortality between neonates with respiratory distress who received intubation and mechanical ventilation and neonates managed with bubble CPAP was detected. In addition, the use of bubble CPAP reduced the need for mechanical ventilation to fifty percent. [16] The systematic review for time interval from 1956 to 2014 studied the patients who initially received bubble CPAP and patients received oxygen therapy, followed mechanical ventilation if needed. The results in three studies showed that the initial use of bubble CPAP reduced need in mechanical ventilation by 30-50 %. In another trials, the comparison of bubble CPAP and ventilator CPAP showed similar mortality and complication rate. [17]

Also, exists a study which compares effectiveness and safety of bubble CPAP and CPAP on preterm lambs. The methods in the study are following: first group of preterm lambs received bubble CPAP with flow 8 *L/min*, whereas the second group received CPAP at flow 8 *L/min* as well. The third group received bCPAP with flow 12 *L/min*. The findings of the study says that the flow (8 and 12 *L/min*) did not influence the outcomes in bubble CPAP. On the other hand, bubble CPAP technique compared to CPAP, showed a higher pH, $Pa(O_2)$, oxygen uptake, decreased ventilation inhomogeneity. Concluded, that bubble CPAP offer higher protection of the lung against injury in preterm lambs. [18]

2.2 Components of bubble CPAP

Basic device circuit of bubble CPAP is composed of following elements: continuous flow source with humidifier (A), inspiratory limb (B), expiratory limb (C), a patient interface which includes nasal mask (D), pressure generator which is water column (E). [19]

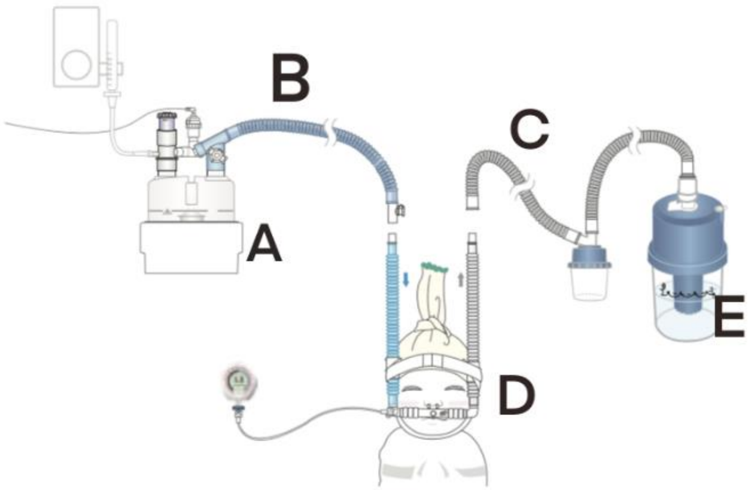


Figure 2.1 Bubble CPAP circuit's components. Author: [20]

2.2.1 General description of components

Oxygenation source can also be represented as a flow generator. It usually humidifies and warms up the inhaled gases. Flow from flow generator is maintained with help of flowmeter. The optimal flow rate is considered as 5 to 12 liters per minute. [21] From the flow generator, the inhaled gases go to the patient interface via inspiratory limb. The patient interface can be of four types which will be described later. The expiratory tube heading from patient interface to the pressure generator contains exhaled gases. The bubble CPAP produces a positive airway pressure by placing the distal part of expiratory tube into the water. The depth on what tube is emerged regulates the pressure. As the gases leaves the expiratory tube, it creates bubbles in the water. Continuous bubbling and pressure oscillation is created when the pressure is delivered to the patient without a leakage.

2.2.2 Source of continuous gas flow

A continuous flow is usually obtained from the oxygen source. O_2 cylinders and O_2 concentrators are the most commonly used O_2 sources for bubble CPAP. O_2 concentrators are electrically powered devices. They draw in an ambient air and extract nitrogen, leaving 90-95% of a pure O_2. Meanwhile, O_2 cylinders contain liquid O_2 distilled at high pressures and low temperatures in a special facility. The major drawback is that the cylinder needed to be refilled regularly. [22]

2.2.3 Flow control

The pressure delivered to the patient depends on the flow rates in bubble CPAP. Flow of the oxygen can be controlled by two ways: either by controlling the amount of oxygen from oxygen source or at the point of blending air and oxygen. [23]

The flow inside the bubble CPAP can be influenced by several parameters, such as circuit's diameter, length, and integrate. The approximate flow can be assessed by observing the rate of bubbling.

The flow of gas in bubble CPAP can be fixed and titrated. The study which compared the clinical effect of fixed and titrated flow on preterm infants was conducted in a Level III neonatal intensive care unit. In the study, the set of data for different CPAP pressures (4, 5, and 6 cm H2O) with a fixed and titrated flow was collected. As a fixed flow they used 5 *L/min*, whereas the titrated flow is a flow just enough to ensure bubbling. It was found out that in preterm infants the fixed flow was more effective than titrated to ensure adequate visible bubbling. The benefits of using a fixed flow are better oxygenation and ventilation and higher delivered pressure as well. [24]

The experiment performed by Tsyr-Yuh Ho on effects of flow rate on delivery of bubble CPAP in an in vitro model was studying the relationship between intra-tubing pressure changes and flow rates. In the experiment the system composed of glass bottle filled with sterile water to a depth 10cm. Distal connecting tube was immersed under water seal to a depth of 5cm. A flowmeter was used, setting sixteen different flow rates, ranging from 2 *l/min* to 20 *l/min*. The results of the studies showed strong correlation between flow rate and intra-tubing pressure generated by the bubble CPAP system. The intra-tubing pressure changed and eventually increased as the flow rate was increased. [25]

The influence of bias flow rate is also crucial. For example, in the study "High Bias Gas Flows Increase Lung Injury in the Ventilated Preterm Lamb" [26] the preterm lambs were ventilated for 2 hours by different bias flows, namely, 4 *L/min*, 8 *L/min*, 18 *L/min*, and 28 *L/min*. The results show that the high bias gas flow increase the lung injury. Higher ventilation pressure, and decreased ventilator efficiency was observed. Worth to mention that rise rate of inspiratory flow is lower at 28 *L/min*, than in 18 *L/min*. Most likely because of creation of turbulent flow.

2.2.4 Patient interface

The patient interface has four types: nasal prongs/cannulas, nasal catheters, nasopharyngeal (NP) catheters and nasal/face mask. [27] The most commonly used patient interface is nasal prongs. Such patient interface is the easiest to use, causing the least amount of complications. [28] Nasal cannula consists of flexible tube which placed under the nose. Inside the nostrils non-invasively inserted two nasal prongs. The mask covers nose and mouth.

Nasal and NP catheters might be used as well. However, they require more nursing intervention. In addition, nasal and NP catheters application can lead to more complications. [29]

At low-flow O_2 to achieve the same partial pressure, nasal cannulas demand more oxygen flow compared to the NP catheters. NP catheters produce the higher PEEP than the nasal prongs at lower oxygen flow. However, it is only the case of the NP catheter with larger size. It was found out that NP catheter of size 8 FR produce PEEP, whereas smaller size does not produce PEEP. [30]

2.2.5 Expiratory limb

The expiratory tube of bCPAP system is made of non-collapsible plastic. It connects the patient interface with the pressure generator. In pressure generator the expiratory limb is immersed to the water to create the bubbling.

Clinicians prescribe the level of airway pressure desired for the infant. As an estimate of delivered pressure the depth of the expiratory tube in water is most frequently used. Many institutions develop homemade bubble CPAP systems, and they frequently lack safety alarms and high-pressure relief valves. [31] The bias flow circulating in the bubble CPAP system might cause unwanted pressure to raise. [32] Which means that the pressure indicated by emerged expiratory tube in water might differ from the delivered to the patient pressure. Tiffany M Youngquist in the study "Effects of Condensate in the Exhalation Limb of Neonatal Circuits on Airway Pressure During Bubble CPAP" investigated if the increase level of condensate within the bubble CPAP circuit result in a greater pressure than in a dry circuit.

Results of this study showed that condensate in the exhalation limb of the patient circuit during bubble CPAP significantly increase the pressure delivered to the patient. For example, at a flow of 6 L/min a dry circuit delivers a peak pressure of 7.5 cm H2O (mean P at expiratory tube immersed to the water 4.9 cm H2O) while a wet circuit containing 10 mL of condensate delivers a peak pressure of 10.4 cm H2O (mean P at expiratory tube immersed to the water 5.8 cm H2O), which is twice the set CPAP level. [33] Higher delivered pressure to the patient than those intended can result in severe consequences, such as air leaks, gastric distention, overdistention, increased $PaCO_2$, compromised cardiac output. [34]

The expiratory limb is influenced by the diameter of the tube as well. The different diameters of the expiratory tube were compared. The larger the diameter of expiratory rube, the greater the oscillations in pressure and volume, especially in preterm infants with low lung compliance. [35]

2.2.6 Pressure generator

The pressure generator is usually water bottle in which the expiratory tube is immersed. The depth in centimeters of expiratory limb immersion equals to the CPAP pressure. Usually, the delivered pressure is set between 5 and 8 cm H_2O. [36]

The pressure generator can be home-made and or commercially produced. Home-made versions are proven to be effective enough for their costs. [37] Commercial models differ from each other in regards of control mechanisms of the pressure generated by the water column. Three main manufactures of bCPAP Fisher and Paykel's, Babi Plus, and WaterPAP. Fisher and Paykel's bCPAP uses a rigid tube which fits inside the reservoir and generates the pressure. Babi Plus' pressure generator includes an expiratory limb with rotation mechanism that changes the depth and controls pressure. WaterPAP has a water bottle with corrugated tube with a plastic lid that holds the tubing at one place.

2.2.7 Original design and deviation of the design

First CPAP system was introduced in 1971 by Gregory et al. The resistor clamp was forming the distending pressure. This version of the device had a water submersion pop-off pressure valve and for that reason was often mistaken for a bCPAP. [38]

The original bubble CPAP replaced resistor clamp with wide-bore expiratory tube which was immersed in water, and the interface was composed of short binasal prongs. These were connected to the tubing. The original design of the bubble CPAP had no dead space. [39]

The simplicity of the bubble CPAP design lead to wide use in low-income countries with various deviation. New devices with alterations from the original design. The most three common alterations within the design are increased dead space, high resistance interface and varying diameter of the expiratory tube. The new designs raised the concerns: 'Increasing use of CPAP without regulation is a concern. Many devices are in the "homemade" category; several low-cost bCPAP devices are being developed specifically for low-income countries but need to be evaluated for durability, reliability, and safety.' [40]

One of the study assessed the effect of different interface resistances, diameters of expiratory tubing, and the modified dead space on artificial lungs. While evaluating the resistance interface, three resistance interface were used, where two represented traditional interface with short nasal prongs, and the other was modified nasal oxygen cannulas as an example of high-resistance interface. The resistance of expiatory tubing increases as its diameter decreases. Therefore, for testing different expiratory limb's resistances, different diameters of tube were used. The results indicated that the higher interface resistance might lead to an unintentionally high resistance to breathing. The smaller diameter of the expiratory tubing leads to unwanted increase of pressure in the CPAP generated by the submersion depth. The increased resistance of expiratory limb leads to higher resistance on breathing as well. The exceedingly high CPAP pressure with narrow diameter of expiratory limb leads to the leakage of gas at the nose, through the mouth or to the gut. Neglection of the dead space and risk of rebreathing while modifying the original bCPAP design can lead to the rebreathing and respiratory failure due to large dead space. [41]

Another possible modification of bubble CPAP is changing the angle of the expiratory tube. In the study "High amplitude bubble continuous positive airway pressure decreases lung injury in rats with ventilator-induced lung injury" [42] the rats with ventilator-induced lung injury were treated by a) conventional bubble CPAP (expiratory limb at the angle 0°), b) high-amplitude bubble CPAP (expiratory limb at angle 135°) or c) spontaneous breathing. The injury of a lung was artificially induced by applying on rats mechanical ventilation during 90 minutes. The parameters which were evaluated are gas exchange, lung volume, and pulmonary inflammation severity.

According to the study "Life-support system benefits from noise" [43] which says that if applied driving pressure is imposed to the noise, the alveoli recruitment might benefit from it. It is related to the principle of stochastic resonance which suggests that the most favorable amplification can be achieved by optimized frequency and amplitude of superimposed noise. The factors which influence on the size and frequency of the pressure noise, or oscillations, are the depth of submergence of the expiratory tube, the bias flow, and the expiratory tube angle. In the study "Noninvasive respiratory support of juvenile rabbits by high-amplitude bubble continuous positive airway pressure" [44] was found out that bubble CPAP is able to produce high amplitude with an expiratory tube at angle 135°.

The results of "High amplitude bubble continuous positive airway pressure decreases lung injury in rats with ventilator-induced lung injury" showed that high amplitude bubble CPAP (expiratory tube at angle 135°) reduces lung inflammation and distension of alveolar. Therefore, the high-amplitude bubble CPAP might provide more protective effect than bubble CPAP with expiratory tube at 0°.

2.2.8 Adverse effect of oscillating pressure

In bubble CPAP the mean pressure which the patient's airways receives is not constant. The airway pressure is fluctuating approximately 4 cm H_2O around the mean pressure. [45] For example, if the expiratory tube is immerged to the pressure generator at the level 5 cm H_2O, the applied pressure will be oscillating in interval from 3 to 7 cm H_2O. The pressure swings are created by pressure amplitude caused by the bubbling in water bottle, and it reflects back through the expiratory limb of the circuit. The pressure swings are also referred as 'noise.' Studies suggested that the pressure amplitudes contributed to the alveolar recruitment and maintenance of airway patency. The positive effect is most pronounced in preterm newborn with lung low compliance.

However, in some cases it is possible to observe the unwanted raise of the pressure swings. In the report from Youngquist, they examined the effect of condensate in the expiratory tube on bCPAP system. As the amount of condensate increased, the pressure oscillations increased as well. [33] In practice, the neonatal receiving 8 cm H_2O with 20 mL of condensate in the expiratory tube in fact will receive pressure oscillation fluctuating around 3 and 13 cm H_2O at the airway. In case of the newborns with a low lung compliance, great amount of pressure will be transmitted to the alveoli. The small among of pressure oscillation is helpful, however larger amount of oscillation can be harmful. [46] It rises the problem that many bubble CPAP lacking safety features and alarms which are present in ventilator-derived CPAP systems.

3 Aims

Although bubble CPAP was first introduced and used in 1971 [38], possible adverse effects of bubbles were not studied enough. Therefore, there are a lot of space for the future research in the area of bubble CPAP. In order to provide students the possibility to work with bubble CPAP, the teaching tool is required. This bachelor thesis aims to design and implement a tool based on bubble CPAP designated for teaching purposes and laboratory measurements. The tool must allow control the flow in range of 0-12 L/min with a step of 1 L/min or continuous control and read the pressure in the ventilation circuit. Control of flow and display of the pressure must be done by the Simulink software.

The aim can be divided into following steps:

1. Software part – bubble CPAP model in Simulink software which allows reading of the pressure and controlling the flow in the bubble CPAP circuit.
2. Hardware part – connection of microcontroller board with flowmeter and pressure sensor.
3. Validation of correct work of the device

4 Methods

The project is dedicated to design the bubble CPAP for its further modification and improvement. To accomplish the goal of the project the bubble CPAP needs to fulfill some predetermined parameters. The assignment of the project requires bubble CPAP to have adjustable flow rate for flowmeter and be able to display the pressure measured by pressure transducer.

In this chapter the model in Simulink Software which controls the flow and reads the pressure, the design of bubble CPAP and its components will be described.

4.1 General description of the methods

A bubble CPAP system designed in this project is aiming to allow to control the flow in range of 0-12 *L/min* by changing the value of voltage delivered to flow mass controller. The reading of pressure values from pressure transducer is required as well.

The bubble CPAP system in this project is composed of following components:

- Controlling interface in Simulink Software which allows 1. To control a voltage in range of 0-5 *V* which transmitted to the flow mass controller and 2. To display the voltage received from pressure transducer in range of 0-5 *V*. Further, the controlling interface in Simulink Software will be referred as Simulink Model.
- Microcontroller board which transmits voltage from Simulink Model to flow mass controller and from pressure transducer to Simulink Model.
- Mass flow controller or flowmeter which automatically controls the flow in a certain range.
- Pressure transducer which transforms physical quantity to a voltage. The voltage can be read by microcontroller board and displayed by Simulink Model

The figure 4.1 represents the relationship between Simulink Model, microcontroller board, flowmeter, and pressure sensor. As it can be seen, the main parts of Simulink Model are flow controller, which is responsible for setting the voltage delivered to microcontroller board. Simulink Model also consists of pressure display which displays the readings of voltage delivered from microcontroller board. The microcontroller board is receiving this voltage from pressure transducer. The voltage which is from flow controller in Simulink Model will be further referred as a Pulse Width Modulation (PWM) signal, and voltage displayed on Pressure Display – Input Analog Signal. The Pulse Width Modulation (PWM) signal delivered to microcontroller board after which it is converted to the Output Analog Signal and sent to the flow mass controller. The voltage allows to set the desired flow rate. On the other hand, the pressure sensor sends Input

Analog Signal to microcontroller board to display it in and Simulink Model at pressure display.

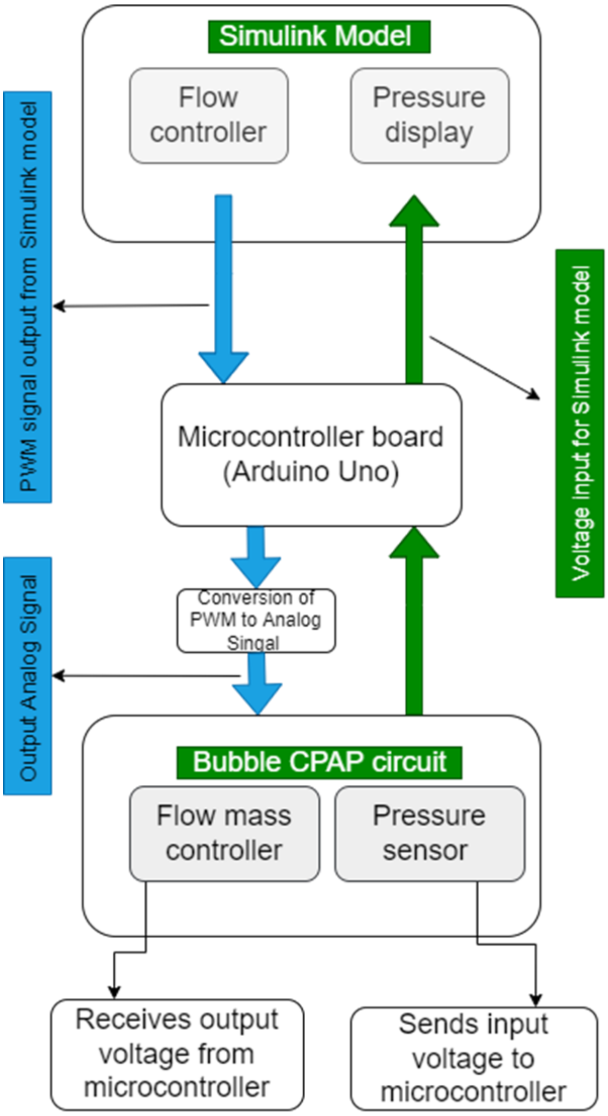


Figure 4.1 Relationship between Simulink Model, microcontroller board, flowmeter, and pressure sensor

The Figure 4.2 represents the flowchart in the further work, where the beginning of the work is a controlling interface in a Simulink software, and the ending point are measurements of pressure oscillations at different levels of immersion of expiratory tube which will influence the PEEP and at different flow rate.

The first step is to create a Simulink Model which will be able to produce adjustable voltage. The signal should be transmitted to a flow mass controller. Simultaneously, the Simulink Model must be able to read input voltage received from the pressure sensor.

The flow mass controller requires a supply of constant, not alternating analog signal, in other words, the mass flow controller requires DC signal. The limitation of microcontroller board Arduino Uno is an obstacle to produce DC signal. Therefore, next step is to convert PWM to DC signal. The reason why PWM was chosen will be described later.

Meanwhile, the microcontroller needs to be connected to the mass flow controller. According to the manual of used flow mass controller, such connection can be performed through 15-pin «D» connector. It is important to identify which pins are needed to be connected.

When the control of flow by changing the Output Voltage is achieved, it is important to identify what value of voltage corresponds to flow rate. Therefore, the calibration curve for voltage and flow rate is required.

On the other hand, the pressure sensor is working on a principle of converting a physical quantity to the analog electrical signal. Therefore, the value which will be displayed in Simulink Model, will be the voltage value which corresponds to some pressure. The calibration curve of voltage and pressure in cmH_2O is required as well. The procedure will be described in further subchapters.

The final step of the project is measurements of pressure oscillations at different levels of expiratory tube immersion and at different values of flow rate. The changes in flow rate influence the bubbling in the bubble CPAP. Bubbling in our case is equivalent to pressure oscillations. Therefore, the greater the flow rate, the greater the amount of oscillations of the pressure.

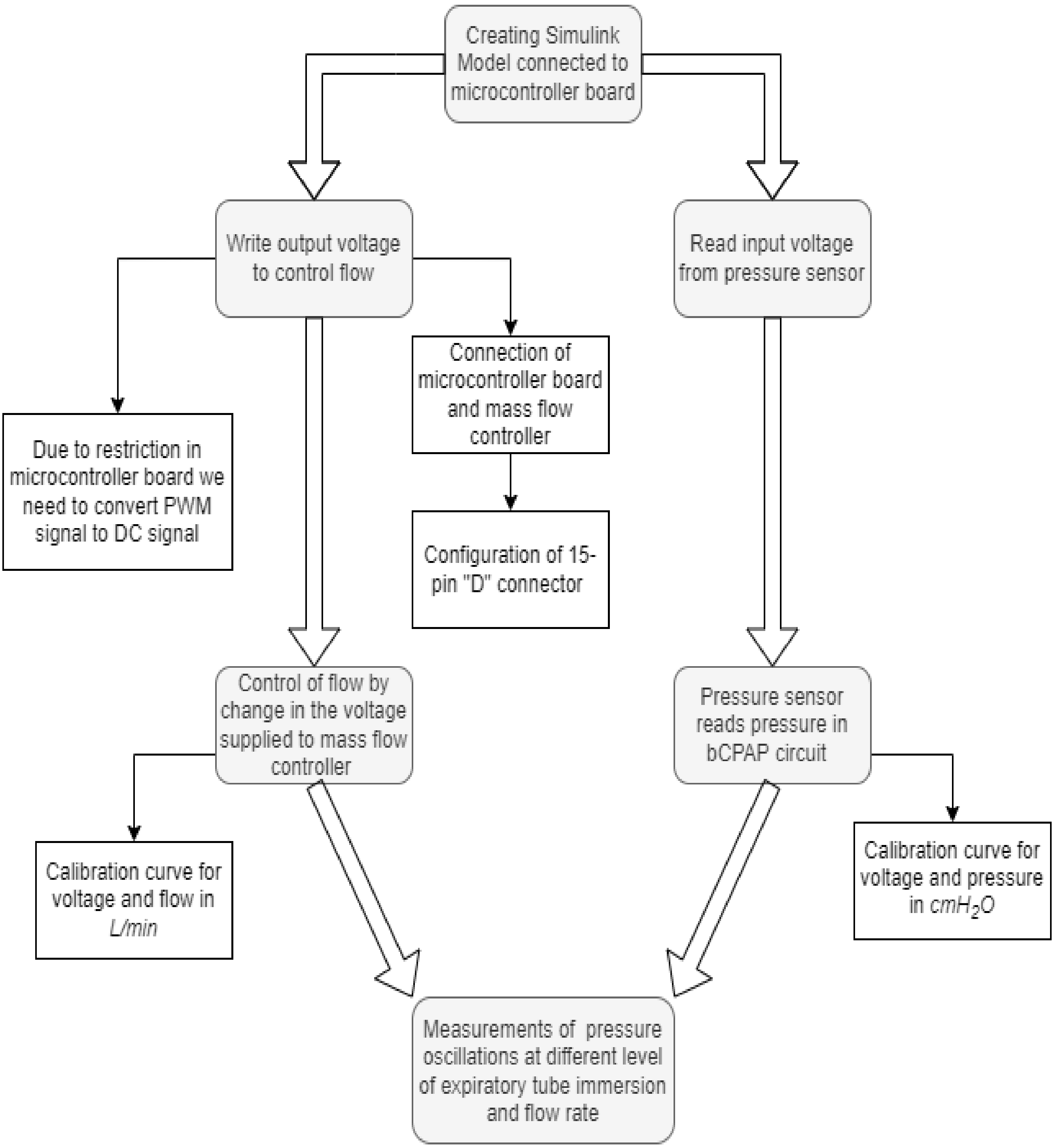


Figure 4.2 Flowchart of the project bubble CPAP

4.2 Simulink model

The figure 4.3 represents the main components of the Simulink Model – Arduino output and Arduino Input. As was mentioned earlier, Arduino Output sends the signal to the microcontroller in order to control flow in flow mass controller. Arduino Input reads the voltage values from pressure transducer.

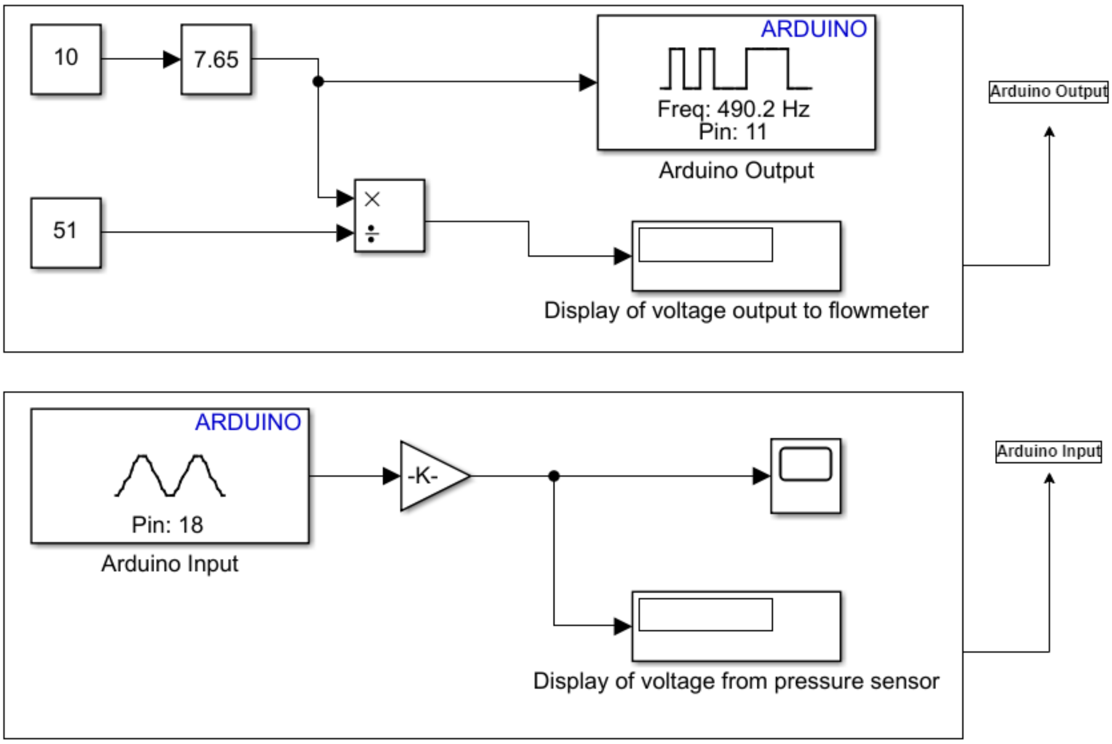


Figure 4.3 Simulink Model, main components: Arduino Output and Input

The Arduino Output is consisting of following parts:

- Constant and slider gain
- PWM signal generator – Arduino Output
- Display of voltage output to flowmeter

For writing the output for microcontroller board, the PWM signal generator at frequency 490.2 *Hz* was chosen. PWM block in Simulink Software accepts values in range of 0 to 255. For achieving such values in this range, the constant value of 10 and slider gain in range of 0 to 25.5 were used.

The question why PWM was used while flow mass controller requires the DC signal is arises. The reason is in limitation of microcontroller board Arduino Uno. Arduino Uno does not support the analog output, although in Simulink Software the block Analog Output for Arduino exists.

PWM, or Pulse Width Modulation, is a technique which allows to deliver a specific amount of average power to the device. The common types of signals are digital and analog. Digital signal has only two states: on and off. It can be interpreted as 1 or 0. If digital signal is used to control the device, only two states are available: a state of maximum power and the state off. Therefore, it is not possible to control the delivered power to the device. On the other hand, analog signal is a continuous in time signal. In electronics, analog and digital signal are very different, however they often used together. For example, analog signal (pressure or temperature) is being read by microcontroller which can only perceive the digital signal.

PWM helps to control or drive devices which requires analog input. PWM can output. PWM can be used for controlling the speed-variable motors. The main advantage of PWM over a digital signal output, is that PWM allows to control delivered power to the device. However, the PWM is not true analog signal. It only simulates analog signal by applying the power in pulses. For example, control of the fan. In PWM signal, the voltage is being applied and then removed in some time interval. However, the movement of the fan does not stop due to inertia. According to the duration of applying the voltage, the voltage delivered to the device is defined. Voltage delivered to the device is an average voltage of “on” and “off state”. If the duration of “on” state is increasing, the duration of “off” state is decreasing respectively and average voltage is increased.

The parameter describing PWM is a duty cycle in units of precents. Duty cycle is a proportion of “on” time to the period of time. The duty cycle of 0 % corresponds to the no power, and infinitely great state “0”. On the other hand, the duty cycle 100 % expresses infinite state “1”. The figure 4.4 illustrates the PWM at different duty cycles. Let’s assume, that the highest voltage level is 5 *V*, and the lowest 0 *V*. At duty cycle 50%, only half of the highest voltage will be delivered which is 2.5 *V*. Respectively, at duty cycle 75 and 25 %, the average voltage will 75 and 25 % from the highest voltage.

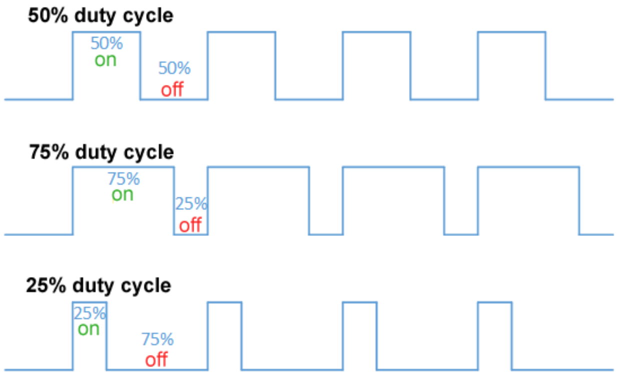


Figure 4.4 PWM signal at different duty cycles

As I mentioned earlier, it is not possible to use just PWM signal to control flow of flow mass controller. The patient must receive the constant, not time varying flow. PWM, on the other hand, sends pulsating signals which is not suitable.

For reading the analog input the block Arduino Analog Input was used. The block measures the voltage of an analog input pin in Arduino Uno board. For all boards, except of Arduino Due, Arduino MKR1000, Arduino MKR WiFi 1010, Arduino MKRZero, and Arduino Nano 33 IoT, the voltage is measured as a 10-bit value ranging between 0 and 1023. An output of 0 indicates that the voltage at the specified pin equals to the ground voltage, an output of 1023 indicates that the voltage at the specified pin equals the analog reference voltage. In order to create user-friendly interface, the program show the values on scope and display as a voltage. In order to do so, I added the gain block using following equation:

$$V = \frac{V_{ref}}{1023} \tag{4.1}$$

4.3 Microcontroller board – Arduino uno

In this project as the microcontroller the Arduino Uno was used. Arduino Uni is a sophisticated, simple, and comparing to the other boards cheaper choice. The microcontroller is equipped with n ATmega328P and the ATMega 16U2 Processor. Its flash memory is 32 *KB*, and SRAM is 2 *KB*. The operating voltage of microcontroller is 5 *V*. Arduino Uno contains 14 digital input/output pins, 6 of them can be used for PWM, and 6 analog inputs.

As can be seen on Figure 4.5, the PWM signal is directed to pin 11, which further can go to the flowmeter. However, we know that it is required to convert PWM signal to DC signal which will be further discussed. The voltage from pressure sensor goes to the pin A4 (or 18) and displayed in Simulink Model.

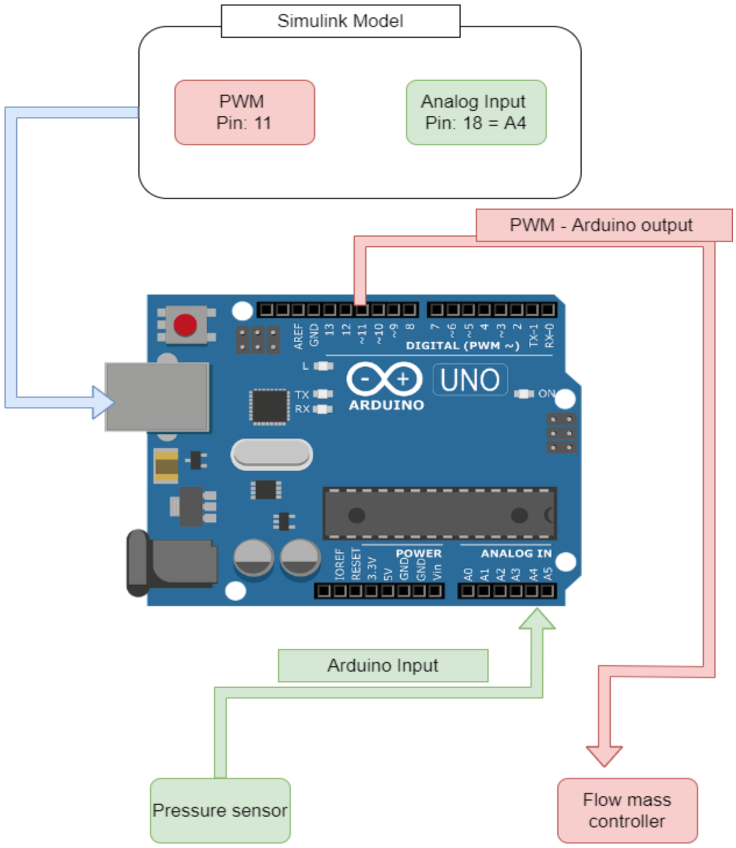


Figure 4.5 Simulink Model and Arduino Uno connection

The verification of the correct output PWM signal from microcontroller board and correct readings of Input Voltage by microcontroller board is necessary.

For verification of correct writing of PWM of the output from microcontroller board, the Arduino Uno’s pin 11 and ground was connected to oscilloscope. Then, I measured the pulse width “0” and “1” in *ms*. Simultaneously, I was measuring the voltage by digital multimeter. The final step of the verification of correct PWM output is to calculate duty cycle:

$$Duty\ cycle = \frac{T_1}{T_1 + T_0} \tag{4.2}$$

Where:

T_1 – time period in state on

T_0 – time period in state off

The verification of the Analog Input is performed with help of voltage source. On the voltage source known values of voltage are set and displayed on the Simulink Model.

The verification of Analog input was performed by connecting the power supply and setting the voltage across the range from 0 *V* to 5 *V* with step 0.5 *V*. The pin to which was connected the wires from power supply is A4. Then, the voltage was read on Pressure Display in Simulink Model.

4.4 Conversion of PWM to Analog Digital Output

Flow mass controller must be controlled my analog signal. The alternating signal cannot be used. Alternating signal implies swings in signal, which is not acceptable for controlling the flow. The flow mass controller requires steady continuous signal which can be adjusted with some step. We know, that the PWM can control the power delivered to the device. A device which is driven by the PWM signal receives the voltage in pulses. However, such method is unacceptable for driving the mass flow controller. If the signal is in pulses, the flow produced by mass flow controller will be pulsating as well. The patient on which the bubble CPAP is used requires constant and stable flow. DC signal is a signal which is steady, continuous and can be controlled. However, the microcontroller board does not allow to produce analog signal. Therefore, for adjustment of voltage level the PWM signal can be used, and then converted to the DC analog signal.

The simplest method how to convert PWM signal to the DC signal, is using RC circuit or low-pass filter. The main component is the capacitor that shunts the pulsating voltage to ground, which produces a DC voltage. The RC filter which is shown by Figure 4.6 was used.

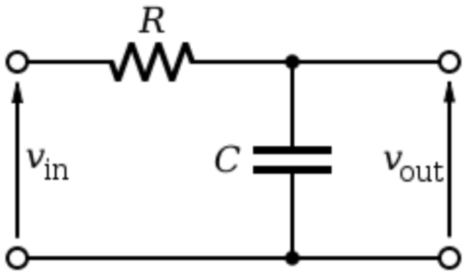


Figure 4.6 RC circuit

The input voltage is defined by the Flow Controller in Simulink Model, which allows to set values of voltage. The output voltage is measured between the node between capacitor and resistor and ground. For this circuit I needed to identify two variables: resistance and capacitance. In order to determine sophisticated values for resistance in units of Ohms and capacitance in Farads, I needed to consider the PWM's response time. Response time is a "time-delay" between input and output of a continuous signal. Response time can also be referred as Time Constant. It is denotated by Greek letter τ (tau) in units of seconds. It can be found by following formula:

$$\tau = \mathrm{R} \cdot \mathrm{C} \tag{4.3}$$

Where

R – resistance in Ω

C – capacitance in *F*

τ – time constant in seconds

The optimal values of the resistance and capacitance of the RC filter strongly correlates with the frequency of PWM. As was mentioned in subchapter Simulink Model (4.2), the frequency of PWM is 490.2 *Hz*. The formula by which it is connected to resistance and capacitance is following:

$$fpwm = \frac{1}{2\pi RC} \tag{4.4}$$

Where R is resistance in Ohms, capacitance in Farads, and fpwm in Hertz. The equation can be rearranged in the way that it will pe possible to find values of resistance and capacitance with known frequency. However, it leaves us with two degrees of freedom. For simplicity, I chose the common value of resistance of 1 $k\Omega$. Therefore, the capacitance can be found as:

$$C = \frac{1}{2\pi Rfpwm} \tag{4.5}$$

The resulting value of capacitance is 159 μF. I used approximate value of capacitance of 100 μF. I analyzed the time response for both values and no significant difference was detected. The Figure 4.7 and Figure 4.8 shows the response time is around 0.1-0.2 seconds, therefore, the response is less than in 0.5 seconds which is quite quick response. The simulation was done in OKAWA Electronic Design [47].

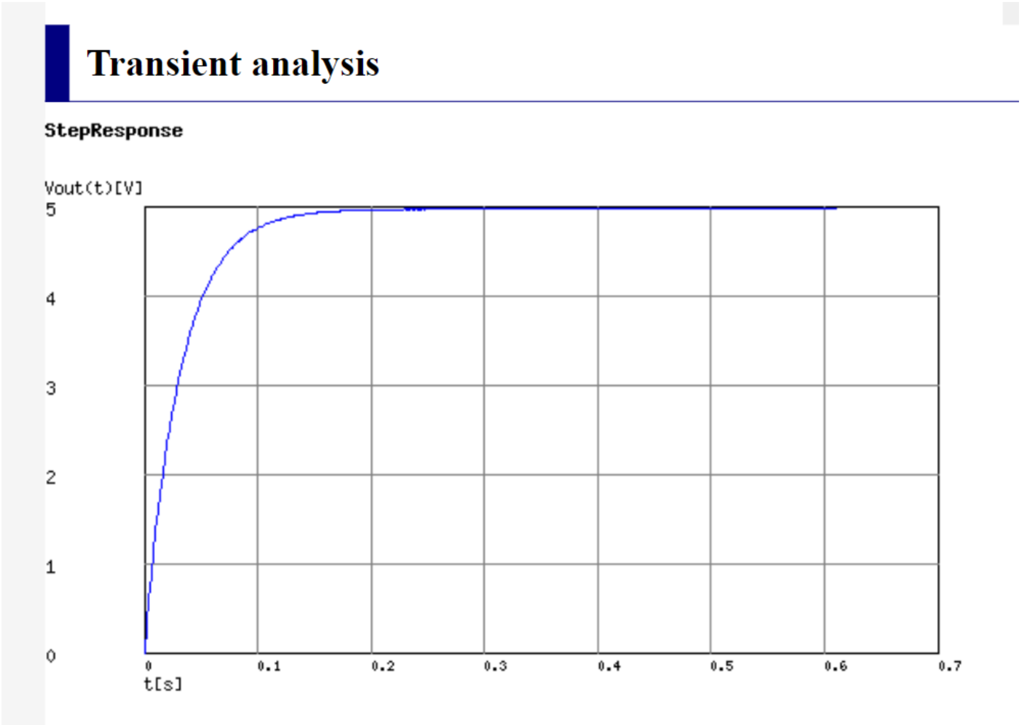


Figure 4.8 Response time for C=159 μF

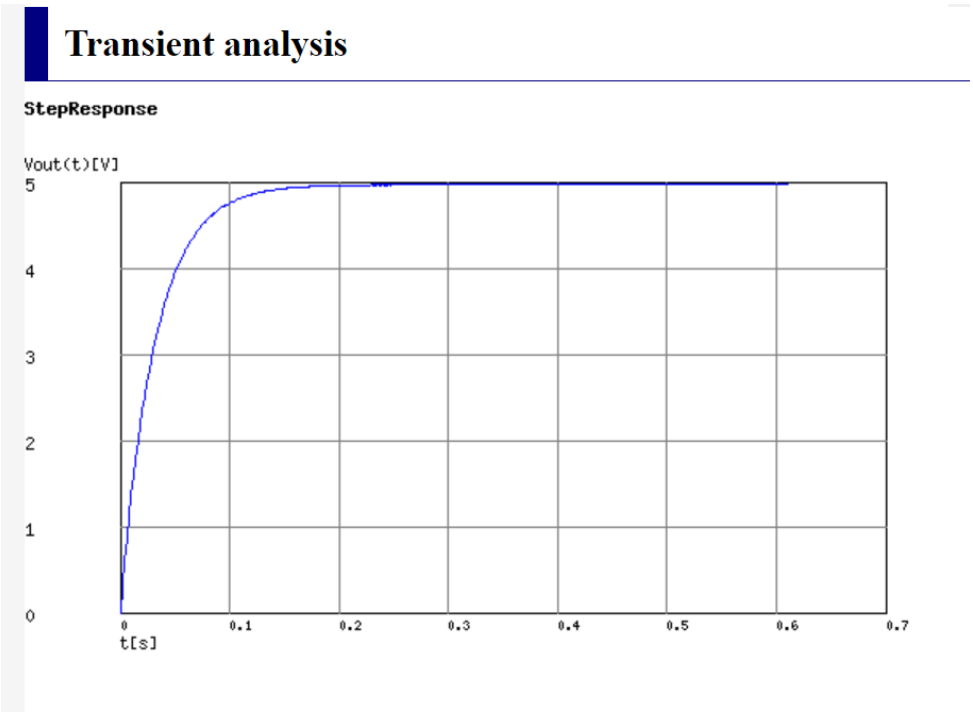


Figure 4.7 Response time for C=100 µF

As can be seen in the Figure 4.6, the pin 11 is connected to one end of the resistor of 1 $K\Omega$, whereas the other end of resistor is connected to the positive leg of the capacitor of 100 µF. The ground from the pin GND in Arduino Uno is connected to the negative leg of the capacitor.

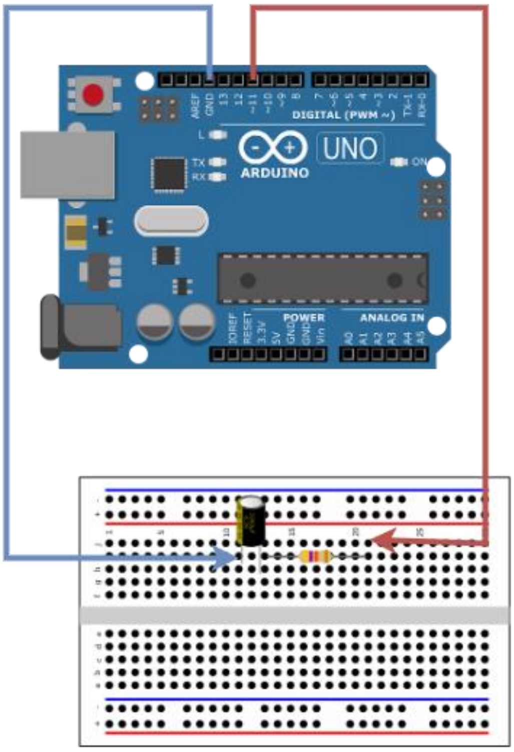


Figure 4.9 Conversion of PWM to DC, schematic of RC circuit and Arduino Uno

After converting the PWM to DC signal I verified the DC signal from the low-pass filter. For that purpose, I compared the set value of voltage in Simulink Model in block Output Voltage and the voltage after RC circuit measured by multimeter. I performed such measurements 10 times after which I calculated type A uncertainty.

Type A uncertainty of measured voltage is the standard derivation of the mean obtained experimentally and calculated by:

$$U_A(x) = \sqrt{\frac{1}{n(n-1)} \cdot \sum_{i=1}^{n} (x_i - \bar{x})^2} \tag{4.6}$$

Where

$U_A(x)$ – type A uncertainty

n – number of values

x_i – each of the value of the data

$\bar{x}$ – arithmetical average. Formula of arithmetical average:

$$\bar{x} = \frac{\sum x_i}{n-1} \tag{4.7}$$

I also calculated the standard deviation within samples to evaluate how each set of samples differ one from another. Standard deviation denotated by “s” was calculated by formula:

$$s = \sqrt{\frac{\Sigma(x_i - \bar{x})}{n-1}}$$

(4.8)

Where

n – number of values

x_i – each of the value of the data

$\bar{x}$ – arithmetical average.

4.5 Mass flow controller

Mass flow controller (MFC) is used whenever accurate measurement and control of mass flow of gas is required regardless the change in pressure and temperature within specified range. As can be seen in Figure 4.2 Schematic of MFC [48], a MFC is composed of following parts: a bypass, a sensor, an electronics board, and a regulating valve. [49] The flow is divided between capillary tube and flow restrictor. In capillary tube the mass flow is measured, whereas in flow resistor or bypass, the majority of flow passes. Sensor in MFC can only measure small flow, the design of bypass allows a flow through the sensor and bypass to be proportional to the flow for which the MFC is actually built. The purpose of electronics board is to amplify and linearize the sensor signal. The signal which is proportional to the total flow which circulates in the device is the output of the electronics board.

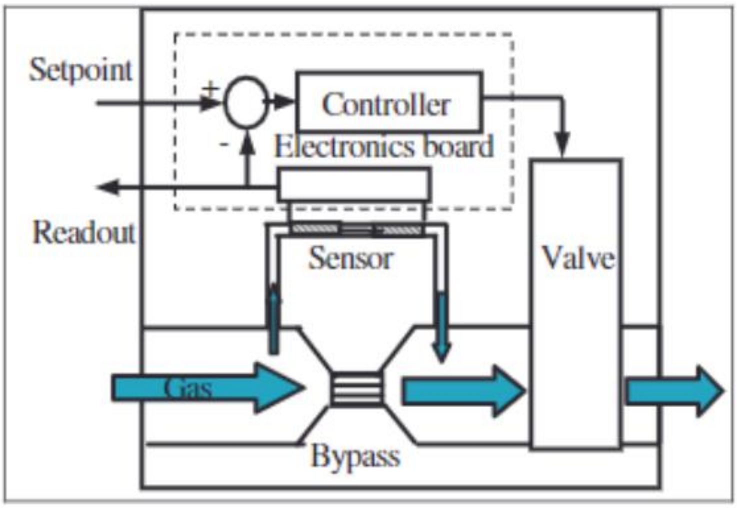


Figure 4.10 Schematic of MFC [48]

4.5.1 Flowmeter Omega FMA 5455

In the following subchapter I will present the specifications of Omega FMA 5455 as specified in the datasheet for flow controller. [50] The Omega FMA 5455 is a classical representatives of the mass flow controller described above at the subchapter 4.3 Mass flow controller.

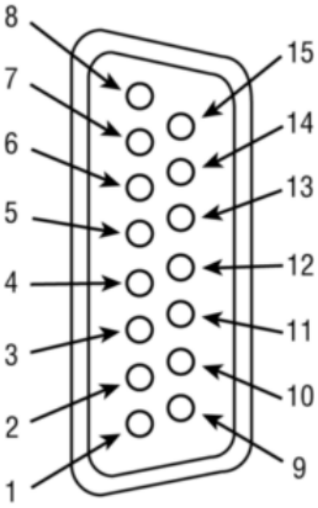
- *Speed:* 0-100 L/min (range indicates min-max value of the speed)
- *Accuracy:* ±1.5% FS from 20 to 100% of range; ±3% FS from 0 to 20% of range.
- *Repeatability:* ±0.5% of full scale
- *Temp Coefficient:* 0.15% FS/°C

- *Pressure Coefficient:* 0.01% FS per psi (0.07 bar)
- *Maximum Pressure Drop:* 50 psid
- *Response Time;* approximately 2 seconds to within ±2% of set flow rate for 25% to 100% of full scale flow.
- Maximum gas pressure: 1000 psig (69 bars)
- *Gas and Ambient Temperature:* 5 to 50°C
- *Leak Integrity:* 1 x 10^{-7} cc/sec of He max to outside environment
- *Materials in Fluid Contact:*
  Aluminum Models: 316 SS, brass and FKM O-rings
  Stainless Steel Models: 316 SS and FKM O-rings
- *Output Signal:*
  Linear 0 to 5 Vdc: 1000 Ω minimum load
  4 to 20 mA: 50 to 500 Ω loop resistance, ±20 mV max noise
- *Transducer Power:* 12 to 15 Vdc power at 800 mA maximum

4.5.2 "D" connector's pins

It is important to connect the wires to appropriate pins. Following table and figures represent pins which were used in 15-pin "D" connector.

PIN	FUNCTION
1	0 to 5 VDC Flow Signal Common
2	0 to 5 VDC Flow Signal Output
3	Common
4	Open (Purge)
5	Common, Power Supply
6	(unassigned)
7	+12 VDC (+24 VDC*) Power Supply
8	Remote Setpoint Input
9	4 to 20 mA (-) Flow Signal Return (use with 14)
10	Remote Setpoint Common (use with 8)
11	+5VDC Reference Output for Remote Setpoint
12	Valve Off Control
13	Auxiliary +12 VDC (+24 VDC*) Power Output (For Loads <100 mA)
14	4 to 20 mA (+) Flow Signal Output
15	Chassis Ground



1 & 2	0-5 VDC OUTPUT	5 & 7	+12 VDC (+24 VDC*) POWER SUPPLY
3 & 4	PURGE	8 & 10	0-5 VDC OR 4-20 mA REMOTE SETPOINT
3 & 12	VALVE OFF CONTROL	9 & 14	4-20 mA OUTPUT
5 & 13	AUXILIARY +12 VDC (+24 VDC*) POWER OUTPUT (FOR LOADS <100 mA)	10 & 11	+5 VDC CONTROL SOURCE

Figure 4.11 FMA 5455 15-pin "D" connector configuration [50].

Table 4.1 Pins used in 15-pin "D" connector

Pin	Function of the pin	Note	Color
8	Remote Setpoint Input	Connected to output pin in	Orange
10	Common ground for Remote Setpoint Input	Connected to pin GND in Arduino Uno	Orange and white
5	Common Ground for power supply	Connected to external power supply	Blue and white
7	Power supply +12VDC	Connected to external power supply	Blue

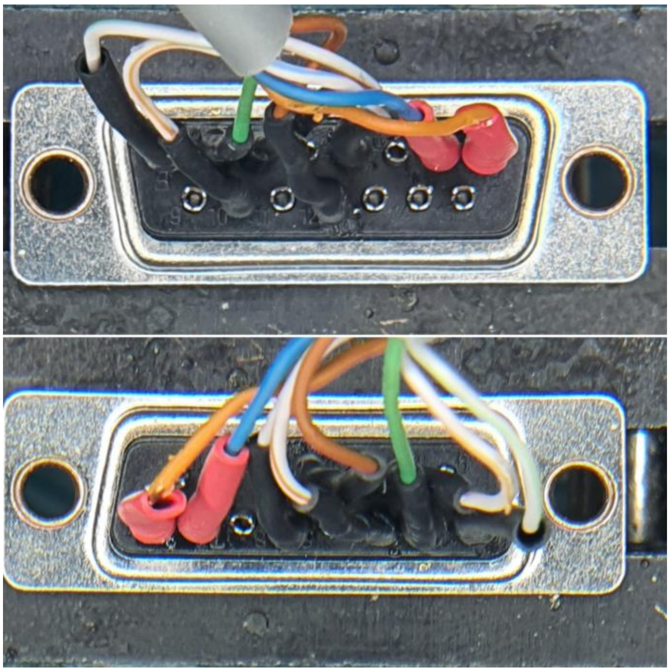


Figure 4.12 Soldering of the 15-pin "D" connector

Setpoints can be controlled locally or remotely. For fulfilling the aims of the project, it is necessary use remote control of setpoints. Setpoints input responds to the analog signal from 0 to 5 *V*. Voltage is linear representation of 0 to 100% of the full scale mass flow rate. For remote control, an analog signal can be applied directly to the setpoint and common ground connections of the FMA 5455 transducer.

The flow signal output can be viewed in Simulink Software as well. It is done in order to verify that desired signal delivered from the microcontroller board Arduino Uno to the flowmeter.

The valve off control pins allow to turn on and off the flow regardless the flow which was set before.

4.6 F&P bubble CPAP system

Exists various system for bubble CPAP in this project F&P bubble CPAP system was used. The following table represents the F&P bubble CPAP system characteristics:

Table 4.2 Parameters and characteristics of F&P bubble CPAP system

Parameter	Characteristics
Input flow range	4–15 *L/min*
Recommended Input Flow	6–8 *L/min*
Set CPAP Pressure Range	3–10 cmH_2O
Length of inspiratory tube	1.1 *m*
Length of expiratory tube	1.2 *m*

Figure 4.13 shows the components which were used from F&P bubble CPAP system: bubble CPAP generator (or column filled with water) and bubble CPAP circuit (or expiratory and inspiratory tube) was used.

Figure 4.13 Column filled with water and expiratory & inspiratory tubes (from left to right)

4.7 Calibration curve for flow mass controller: flow and voltage

Calibration curve is a graph where instrumental response changes when the known quantity is changed. In case of flow mass controller, the known quantity is voltage. The voltage is set in Simulink Model, whereas the response of the flow mass controller is detected by the Neonatal Respiration Monitoring by Florian. The response of the flow mass controller on the supplied voltage is a flow with some flow rate measured in *L/min*.

The set up for calibration curve is following: the microcontroller board and power supply are connected to the flow mass controller. The inspiratory tube from flow mass controller is connected to the Neonatal Respiration Monitoring by Florian.

I changed the voltage with step 0.05 *V* and observed the flow rate displayed by monitoring system changing with change of the voltage. The voltage was increased until alarm system prohibited increase of the flow. Normally, bubble CPAP for neonates is supplied with 5-10 *L/min*. Applying much higher bias flow is irrelevant and dangerous.

I measured the change of the flow depending on the voltage 10 times. Then, calculated arithmetical average and standard deviation by formulas (4.7) and (4.8). Then, I constructed the calibration curve based on arithmetical average of 10 measurements and respective voltage.

4.8 Calibration curve for pressure transducer: pressure and voltage

In case of pressure transducer's calibration curve, the known quantity is pressure, and the response the known quantity is voltage. Voltage is displayed by Simulink Model or digital multimeter.

The set up for calibration of pressure transducer is shown by Figure 4.14 and composed of following elements:

(A) – plastic water filled with water which serves as a source of measured pressure.
(B) – pressure cuff which will inflated to raise the pressure and then deflated to reduce the pressure.
(C) – pressure balloon. By compressing the pump, we inflate the cuff.
(D) – strain sphygmomanometers which will allow us to read the pressure values.
(E) – Edwards pressure transducer which converts pressure to readable by Simulink Model voltage.
(F) – power supply; pressure transducer connected to power supply of ±10 *V*.
(G) – digital multimeter which reads the values of voltage.

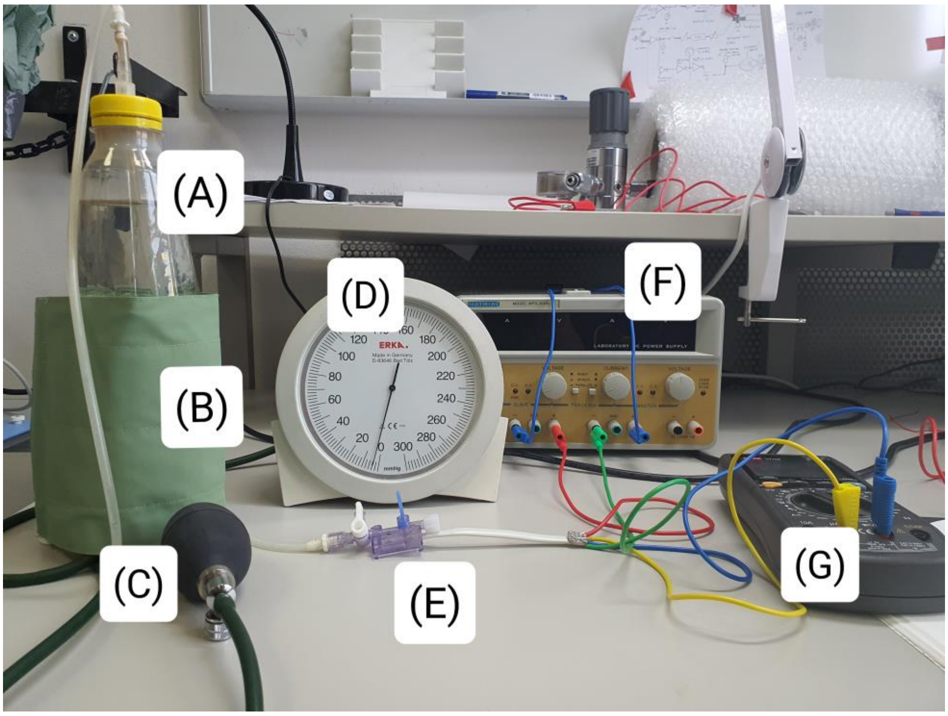


Figure 4.14 Set up for calibration the pressure transducer

Note, that the connection of power supply is incorrect. The correct version of connection can be found in Appendix. It is important to perform zeroing – at atmospheric pressure the voltage supposed to be zero. The three-way valve in pressure transducer must be in open position as shown in Figure 4.15.

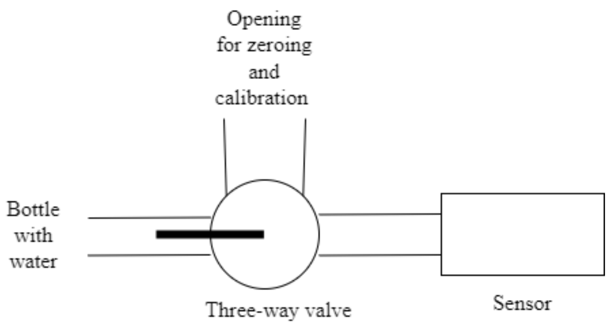


Figure 4.15 Position of three-way valve for zeroing

Then, after zeroing, I turned valve into position for measuring as shown in Figure 4.16 Using balloon, I increased a pressure at pressure cuff to 200 *mmHg* and then observed a voltage change as the pressure decreased. The measurements performed in mmHg, however bubble CPAP operating a pressure in cmH_2O. The conversion of *mmHg* to cmH_2O is done by formula:

$$1\ cmH2O = 1\ mmHg \cdot 1.359547 \tag{4.9}$$

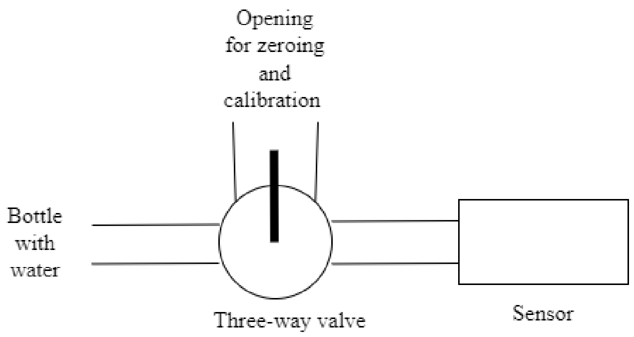


Figure 4.16 Position of three-way valve for measurements

4.9 Final arrangement and verification of correct work of teaching tool – bubble CPAP

There are a few variable which can be controlled in designed bubble CPAP in this project. First of all, it is flow rate from the flow mass controller which can be regulated in Simulink Model by flow controller part. On the other hand, the expiratory tube which is submerged into the container filled with water, can be immersed to the different depth or level in water. The depth of immersion controls the pressure delivered to the patient airways. Both variables can potentially influence the bubbling in the container with water. Due to the bubbling, the mean pressure applied to the neonatal is not constant, and rather the actual pressure is fluctuating around the mean. According to the study of J Jane Pillow & Javeed N Travadi in study “Bubble CPAP: Is the Noise Important? An In Vitro Study” [51], the increase of flow rate facilitates the increase of mean pressure and magnitude of oscillations.

For the verification of the correct work of the system the following experiment will be conducted: the pressure oscillations and its mean were evaluated across the range of the different levels of expiratory tube immersion (3, 5, 7, 10 cmH_2O) at each of four flow rates 5, 8, 10 ,15 *l/min*.

The Figure 4.18 shows the arrangement for this experiment. Simulink Model controls the flow from flow mass controller. Also, it is supplied by the 12 *V* from the power supply. The flow goes to the patient interface via inspiratory tube. From the patient interface the expiratory tube goes to the column with water. The expiratory tube can be immersed at some defined level. Pressure transducer is placed in the area near to patient interface, where it measures the pressure oscillations, and then displays in Simulink Model on Pressure Display.

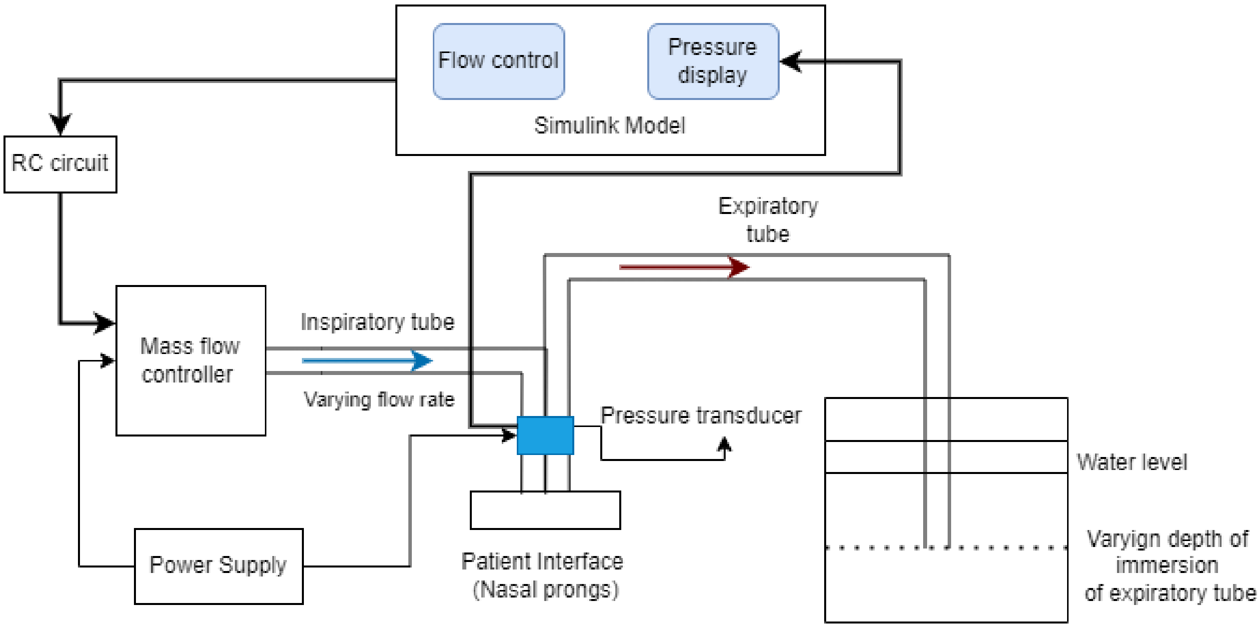


Figure 4.18 Arrangement for measurements of pressure oscillations at different level of expiratory tube immersion and different flow rate

The Figure 4.17 illustrates the depths of expiratory tube immersion (3, 5, 7, 10 cmH_2O).

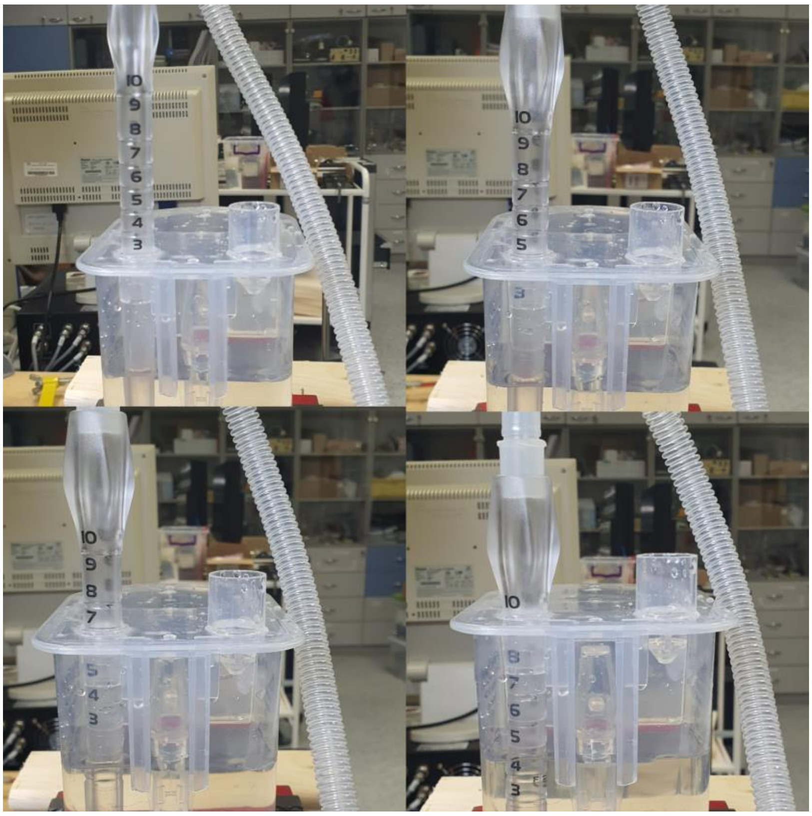


Figure 4.17 Expiratory tube immersion levels

After obtaining data at different levels of immersion of tube and flow rates, the data which was in unit of *mV* was converted to the cmH_2O according to the calibration curve for pressure between 2.7 to 13.5 cmH_2O.

Then, the data was evaluated by two-way Anova. The test was chosen, because we have two factors which influencing the values of pressure: flow and immersions of expiratory tube. The test will evaluate how the mean of pressure will change affected by two independent variables. A p value of < 0.05 is considered to be significant. There are 3 hypothesis of effect of flow and immersion depth.

H_0: Bias flow has no effect on the mean pressure of pressure oscillations.

H_a: Bias flow has effect on the mean pressure of pressure oscillations.

$H_{0:}$ Depth of immersion of expiratory tube has no effect on the mean pressure of pressure oscillations

$H_{a:}$ Depth of immersion of expiratory tube has effect on the mean pressure of pressure oscillations

$H_{0:}$ Bias flow and depth of immersion of expiratory tube has no effect on the mean pressure of pressure oscillations

$H_{a:}$ Bias flow and depth of immersion of expiratory tube has effect on the mean pressure of pressure oscillations

5 Results

This chapter represents the results of the findings described in the Methods.

The first subchapter of the Results is dedicated to show the results of the measurements of the PWM signal. The PWM signal is an initial signal from the Simulink Model which will be further transferred to the DC signal. The subchapter in Methods describing the process of obtaining results is 4.3. The procedure of next subchapter Arduino Input signal verification was described in subchapter Methods 4.3. Verification of DC signal was described in Methods subchapter 4.4. The calibration curve for flow mass controller: flow and voltage was described in subchapter 4.7 and calibration curve for pressure transducer: pressure and voltage in 4.8. Subchapter 5.6 represents the results the verification process of the whole bubble CPAP system, changing the flow and immersion depth of expiratory tube.

5.1 PWM block verification

This subchapter of the Results consists of Table 5.1 which shows the results of verification of the PWM signal created by Simulink Model. It is important to verify the signal in order to later convert it to the DC signal. The first column of a table represents the input voltage which was set in a Simulink Model, the Output Voltage is a voltage measured on digital multimeter. Also, the pulse width at state “0” and “1” was measured by oscilloscope. The most important column is Duty cycle expressed in precents, which calculation were described in methods. Duty cycle allows us to understand the ration between pulse width at state “1” and the whole period of a pulse.

Table 5.1 PWM signal verification by oscilloscope Arduino Input reading verification

Input Voltage (*V*)	Output Voltage (*V*)	Pulse width PWM “0” (*ms*)	Pulse width PWM “1” (*ms*)	Duty cycle (*%*)
0.00	0.00	Infinity	0.00	0.00
0.50	0.49	1.82	0.22	10.78
1.00	1.00	1.62	0.42	20.58
1.50	1.49	1.42	0.62	30.39
2.00	2.00	1.20	0.80	39.21
2.50	2.49	1.02	1.02	50.00
3.00	3.01	0.82	1.22	59.80
3.50	3.50	0.62	1.42	69.60
4.00	4.01	0.40	1.64	80.39
4.50	4.51	0.22	1.82	89.21
5.00	5.02	0.00	2.04	100.00

5.2 Arduino Input signal verification.

The verification of Arduino Input signal consists of a Table 5.2 which shows the values of a set voltage on power supple and Arduino Input from the Pressure Display in Simulink Model.

Table 5.2 Arduino Input signal verification with set values on voltage source

Set Voltage (*V*)	Arduino input (*V*)
0.00	0.004
0.50	0.557
1.00	1.051
1.50	1.564
2.00	2.087
2.50	2.586
3.00	3.113
3.50	3.568
4.00	4.091
4.50	4.604
5.00	5.000

5.3 Verification of DC signal

After the PWM signal was converted to DC signal, it was required to verify the DC signal. The Verification of DC signal is composed of three tables. Table 5.3 and Table 5.4 consist of the columns with the set voltage in Simulink Model and measurements of the output voltage measured at multimeter. The Table 5.5 shows the set voltage in Simulink Model and the arithmetical average, standard deviation, and type A uncertainty of the 10 measurements of the output voltage.

Table 5.3 Verification of DC signal, set voltage versus measured voltage on digital multimeter, measurements 1-5

Set Voltage (*V*)	1 Measurement (*V*)	2 Measurement (*V*)	3 Measurement (*V*)	4 Measurement (*V*)	5 Measurement (*V*)
0.00	0.00	0.00	0.00	0.00	0.00
0.50	0.47	0.48	0.48	0.48	0.48
1.00	0.98	0.99	0.99	0.99	1.01
1.50	1.47	1.49	1.48	1.48	1.50
2.00	1.98	1.97	1.98	1.98	1.99
2.50	2.48	2.49	2.48	2.48	2.49
3.00	2.98	2.97	2.99	2.99	2.98
3.50	3.46	3.47	3.49	3.49	3.50
4.00	3.99	3.97	3.99	3.99	3.98
4.50	4.47	4.47	4.47	4.47	4.47
5.00	4.99	4.99	4.99	4.99	4.99

Table 5.4 Verification of DC signal, set voltage versus measured voltage on digital multimeter, measurements 6-10

Set Voltage (*V*)	6 Measurement (*V*)	7 Measurement (*V*)	8 Measurement (*V*)	9 Measurement (*V*)	10 Measurement (*V*)
0.00	0.00	0.00	0.00	0.00	0.00
0.50	0.48	0.48	0.49	0.48	0.48
1.00	0.98	0.99	1.00	1.00	1.02
1.50	1.48	1.51	1.49	1.50	1.49
2.00	1.98	1.99	1.98	2.01	2.00
2.50	2.49	2.49	2.50	2.48	2.47
3.00	2.98	3.00	3.00	2.99	2.98
3.50	3.49	3.48	3.49	3.48	3.49
4.00	4.00	3.98	3.99	3.99	3.98
4.50	4.47	4.50	4.47	4.47	4.48
5.00	4.99	5.00	4.99	4.98	4.99

Table 5.5 Arithmetical average, standard deviation and type A uncertainty of 10 measurements of voltage

Set voltage	Arithmetical average (*V*)	Standard deviation	Type A uncertainty
0.00	0.000	0.000000	0.000000
0.50	0.480	0.408656	0.001414
1.00	0.995	0.258844	0.003808
1.50	1.489	0.09083	0.003592
2.00	1.986	0.204939	0.003521
2.50	2.485	0.130384	0.002550
3.00	2.986	0.134164	0.002898
3.50	3.484	0.100000	0.003521
4.00	3.986	0.054772	0.002530
4.50	4.474	0.114018	0.002898
5.00	4.990	0.151658	0.001414

5.4 Calibration curve for flow mass controller: flow and voltage

The subchapter is dedicated to illustrate the calibration curve for the mass flow controller between voltage and flow. The voltage set in Simulink Model corresponds to some flow in *L/min*, and this relation must be established to further controlling of the flow. The subchapter is composed of two tables and one graph. The Table 5.6 shows the set voltage in Simulink Model supplied to the flow mass controller, and the response of the flow monitoring system which was connected to the tubes from flow mass controller. The measurements of the flow corresponding to certain voltage was done 5 times. Then, the arithmetical average and standard deviation of 5 measurements of the flow was calculated. Based on the arithmetical average of the flow and respective to the flow voltage, the calibration curve was constructed, which is shown by Figure 5.1

The equation for relation between flow and voltage is following:

$$Flow = 24.602 \cdot V + 0.767 \tag{5.1}$$

Where V is a voltage measured in Volts.

The photos of flow measured by flow monitoring system can be find in an attachment zip file.

Table 5.6 Verification of the flow, set voltage in Simulink Model versus flow

Set Voltage (*V*)	Set value	1 Measurement (*L/min*)	2 Measurement (*L/min*)	3 Measurement (*L/min*)	4 Measurement (*L/min*)	5 Measurement (*L/min*)
0.00	0.000	0.00	0.00	0.00	0.00	0.00
0.05	0.255	2.00	2.20	1.95	1.50	1.20
0.10	0.510	4.00	4.20	3.90	3.80	3.50
0.15	0.765	5.00	5.10	4.95	5.00	4.85
0.20	1.020	5.50	5.80	5.90	5.90	5.50
0.25	1.275	6.80	7.10	7.00	6.95	6.80
0.30	1.530	8.00	8.30	8.00	8.00	8.00
0.35	1.785	10.00	10.00	9.80	9.90	9.80
0.40	2.040	10.10	10.10	10.10	10.00	10.00
0.45	2.295	11.50	11.30	11.40	11.20	11.30
0.50	2.550	14.00	13.70	13.80	14.00	13.70
0.55	2.805	14.60	14.30	14.50	14.60	14.40
0.60	3.060	15.00	14.90	15.00	15.00	14.90

Table 5.7 Arithmetical Average of the flow and its standard deviation

Set Voltage (*V*)	Arithmetical average of the flow (*L/min*)	Standard deviation of the flow
0.00	0.00	0.000000
0.05	1.77	0.365513
0.10	3.88	0.231517
0.15	4.98	0.081240
0.20	5.72	0.183303
0.25	6.93	0.116619
0.30	8.06	0.120000
0.35	9.90	0.089443
0.40	10.06	0.048990
0.45	11.34	0.101980
0.50	13.84	0.135647
0.55	14.48	0.116619
0.60	14.96	0.048990

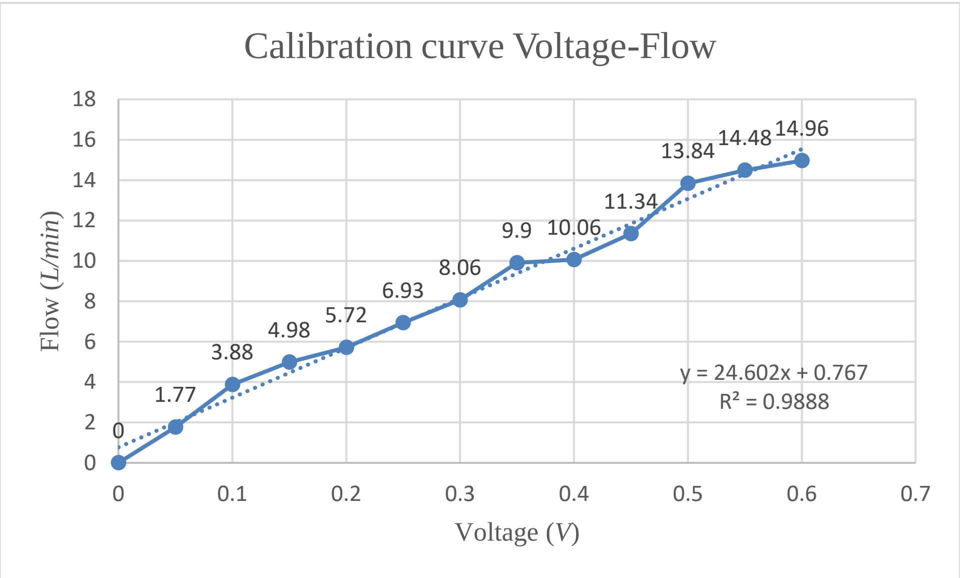


Figure 5.1 Calibration curve for flow mass controller

5.5 Calibration curve for pressure transducer: pressure and voltage

The following subchapter represent the calibration of pressure and voltage. The subchapter consists of one table and two graphs. Table represents the pressure in *mmHg*, the second column is a converted pressure in *mmHg* to pressure in cmH_2O and the last column is a respective voltage in *mV*.

Figure 3.1 represents the calibration curve of pressure and voltage in range of 2.7 to 271.9 cmH_2O. However, it is too big range of the values. The further measurements will be performed in range of 3-10 cmH_2O. The figure 5.3 represents the calibration curve between pressure and voltage in range of 2.7 to 13.5 cmH_2O. The equation will be further used for conversion of voltage to pressure in cmH_2O.

$$Pressure = 25.895 \cdot V - 13.595 \tag{5.2}$$

Table 5.8 Calibration of pressure transducer, set voltage in Simulink Model versus measured pressure

Pressure (*mmHg*)	Pressure (cmH_2O)	Voltage (*mV*)
200	271.902	3.00
160	217.522	2.50
120	163.410	2.10
100	135.951	1.90
80	108.761	1.80
60	81.5706	1.60
40	54.3804	1.50
15	20.3926	1.40
10	13.5951	0.91
5	6.79755	0.85
3	4.07853	0.81
2	2.71902	0.58

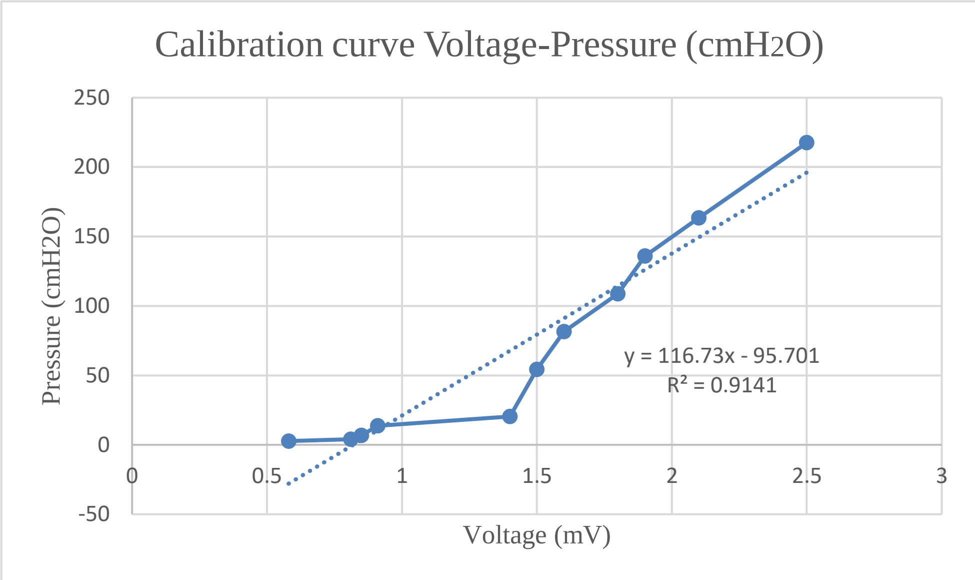


Figure 5.2 Calibration curve for pressure transducer

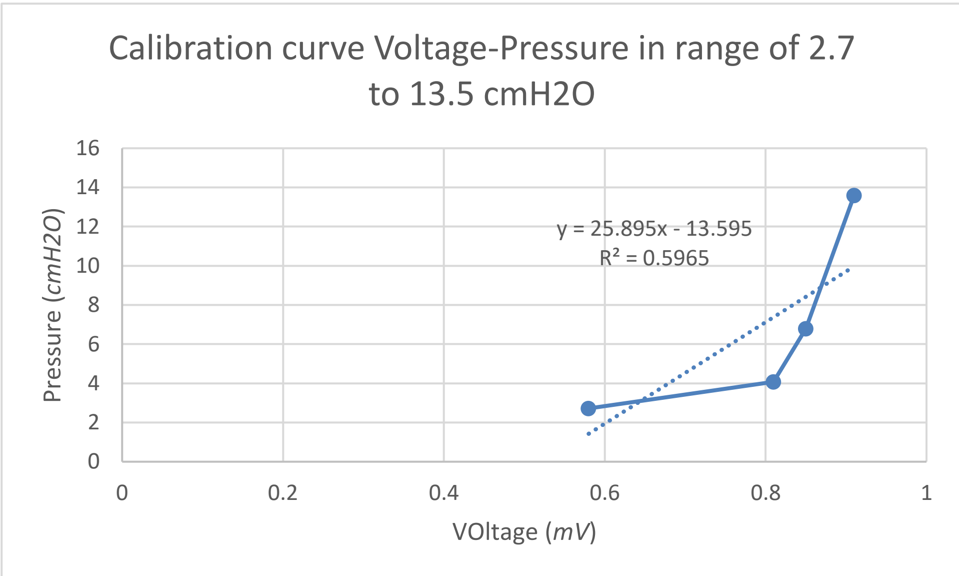


Figure 5.3 Calibration curve Voltage-Pressure in range of 2.7 to 13.5 cmH2O

5.6 Pressure oscillations at different levels of expiratory tube immersion and flow rate

The first part of this subchapter from 5.61 to 5.6.2 is composed of the tables and figures which describes the pressure oscillations at depth of expiratory tube immersions and flow rates.

The second part of subchapter from 5.6.3-5.6.7 is mainly consisting of the screenshots from the Simulink Model, which represent the waveforms of pressure oscillation. Pressure oscillations are captured at different levels of expiratory tube immersion and at different flow rates. More specifically, the pressure oscillations were measured at immersion depth 3, 5, 7 and 10 cmH_2O of expiratory tube under the water and the flow rate at 5, 8, 10, 15 *L/min.* The vertical axes in the figures represent as a voltage amplitude of the pressure oscillations in *mV*, and horizontal axis is a time axis in seconds. The time is negative because we are observing the oscillations which were recorded a few seconds ago. Each figure is composed of 4 screenshots from Simulink Model. The photos categorized according to the immersion of expiratory tube level. In addition, each screenshot in one figure is labeled by the flow rate which was used.

5.6.1 Pressure oscillations' mean, amplitude, maximum and minimum in *mV*

The 5.6.1 consist of 4 tables, where the pressure oscillations are in units of *mV*. The tables 5.9-5.12 represent the mean value, amplitude, maximum and minimum of the pressure oscillations in *mV*. In tables there are two independent variables influencing the pressure measured by pressure transducer. The Flow is set at range from 5 to 15 L/min. In order to save space in a tables, the pressure level which is defined by expiratory tube immersion depth is referred as Pressure. In the center of the tables there are values of the pressure oscillation measured by the pressure transducer.

Table 5.9 Pressure oscillation's mean in mV at different level of expiratory tube immersion (3, 5, 7 and 10 cmH2O) and flow (5, 8, 10, 15 L/min)

	Pressure 3 (*cmH₂O*)	Pressure 5 (*cmH₂O*)	Pressure 7 (*cmH₂O*)	Pressure 10 (*cmH₂O*)
Flow 5 (*L/min*)	0.70 *mV*	0.85 *mV*	0.89 *mV*	0.90 *mV*
Flow 8 (*L/min*)	0.82 *mV*	0.88 *mV*	0.92 *mV*	0.89 *mV*
Flow 10 (*L/min*)	0.85 *mV*	0.91 *mV*	0.92 *mV*	0.94 *mV*
Flow 15 (*L/min*)	0.95 *mV*	0.91 *mV*	0.93 *mV*	0.98 *mV*

Table 5.10 Pressure oscillation's amplitude in mV at different level of expiratory tube immersion (3, 5, 7 and 10 cmH2O) and flow (5, 8, 10, 15 L/min)

	Pressure 3 (*cmH₂O*)	Pressure 5 (*cmH₂O*)	Pressure 7 (*cmH₂O*)	Pressure 10 (*cmH₂O*)
Flow 5 (*L/min*)	0.274 *mV*	0.260 *mV*	0.345 *mV*	0.380 *mV*
Flow 8 (*L/min*)	0.512 *mV*	0.410 *mV*	0.503 *mV*	0.478 *mV*
Flow 10 (*L/min*)	0.593 *mV*	0.440 *mV*	0.410 *mV*	0.439 *mV*
Flow 15 (*L/min*)	0.515 *mV*	0.570 *mV*	0.490 *mV*	0.494 *mV*

Table 5.11 Pressure oscillation's maximum in mV at different level of expiratory tube immersion (3, 5, 7 and 10 cmH2O) and flow (5, 8, 10, 15 L/min)

	Pressure 3 (*cmH₂O*)	Pressure 5 (*cmH₂O*)	Pressure 7 (*cmH₂O*)	Pressure 10 (*cmH₂O*)
Flow 5 (*L/min*)	8.364 *mV*	12.297 *mV*	14.565 *mV*	15.321 *mV*
Flow 8 (*L/min*)	14.936 *mV*	15.184 *mV*	17.562 *mV*	16.394 *mV*
Flow 10 (*L/min*)	16.875 *mV*	16.421 *mV*	16.284 *mV*	17.232 *mV*
Flow 15 (*L/min*)	18.552 *mV*	18.209 *mV*	17.659 *mV*	19.089 *mV*

Table 5.12 Pressure oscillation's minimum in mV at different level of expiratory tube immersion (3, 5, 7 and 10 cmH2O) and flow (5, 8, 10, 15 L/min)

	Pressure 3 (*cmH_2O*)	Pressure 5 (*cmH_2O*)	Pressure 7 (*cmH_2O*)	Pressure 10 (*cmH_2O*)
Flow 5 (*L/min*)	0.830 *mV*	5.147 *mV*	5.078 *mV*	4.872 *mV*
Flow 8 (*L/min*)	0.857 *mV*	3.910 *mV*	3.731 *mV*	3.250 *mV*
Flow 10 (*L/min*)	0.569 *mV*	4.322 *mV*	5.010 *mV*	5.161 *mV*
Flow 15 (*L/min*)	4.391 *mV*	2.535 *mV*	4.185 *mV*	5.505 *mV*

5.6.2 Pressure oscillations' mean, amplitude, maximum, and minimum converted to cmH_2O

The 5.6.2 consist of 5 tables and 1 figure, where the pressure oscillations are in units of cmH_2O. The tables 5.13-5.16 represent the mean value, amplitude, maximum and minimum of the pressure oscillations in cmH_2O. The table 5.17 is a table for results of two-way Anova test.

Table 5.13 Pressure oscillation's mean in cmH2O at different level of expiratory tube immersion (3, 5, 7 and 10 cmH2O) and flow (5, 8, 10, 15 L/min)

	Pressure 3 (*cmH_2O*)	Pressure 5 (*cmH_2O*)	Pressure 7 (*cmH_2O*)	Pressure 10 (*cmH_2O*)
Flow 5 (*L/min*)	4.597 cmH_2O	8.722 cmH_2O	9.822 cmH_2O	10.097 cmH_2O
Flow 8 (*L/min*)	7.897 cmH_2O	9.547 cmH_2O	10.647 cmH_2O	9.822 cmH_2O
Flow 10 (*L/min*)	8.722 cmH_2O	10.523 cmH_2O	10.647 cmH_2O	11.197 cmH_2O
Flow 15 (*L/min*)	11.472 cmH_2O	10.372 cmH_2O	10.922 cmH_2O	12.297 cmH_2O

Table 5.14 Pressure oscillation's amplitude in cmH2O at different level of expiratory tube immersion (3, 5, 7 and 10 cmH2O) and flow (5, 8, 10, 15 L/min)

	Pressure 3 (*cmH_2O*)	Pressure 5 (*cmH_2O*)	Pressure 7 (*cmH_2O*)	Pressure 10 (*cmH_2O*)
Flow 5 (*L/min*)	7.534 cmH_2O	7.149 cmH_2O	9.487 cmH_2O	10.449 cmH_2O
Flow 8 (*L/min*)	14.079 cmH_2O	11.274 cmH_2O	13.831 cmH_2O	13.144 cmH_2O
Flow 10 (*L/min*)	16.306 cmH_2O	12.099 cmH_2O	11.274 cmH_2O	12.072 cmH_2O
Flow 15 (*L/min*)	14.161 cmH_2O	15.674 cmH_2O	13.474 cmH_2O	13.584 cmH_2O

Table 5.15 Pressure oscillation's maximum in cmH2O at different level of expiratory tube immersion (3, 5, 7 and 10 cmH2O) and flow (5, 8, 10, 15 L/min)

	Pressure 3 (cmH_2O)	Pressure 5 (cmH_2O)	Pressure 7 (cmH_2O)	Pressure 10 (cmH_2O)
Flow 5 (*L/min*)	8.365 cmH_2O	12.297 cmH_2O	14.566 cmH_2O	15.322 cmH_2O
Flow 8 (*L/min*)	14.937 cmH_2O	15.184 cmH_2O	17.563 cmH_2O	16.394 cmH_2O
Flow 10 (*L/min*)	16.875 cmH_2O	16.422 cmH_2O	16.284 cmH_2O	17.233 cmH_2O
Flow 15 (*L/min*)	18.553 cmH_2O	18.209 cmH_2O	17.659 cmH_2O	19.089 cmH_2O

Table 5.16 Pressure oscillation's minimum in cmH2O at different level of expiratory tube immersion (3, 5, 7 and 10 cmH2O) and flow (5, 8, 10, 15 L/min)

	Pressure 3 (cmH_2O)	Pressure 5 (cmH_2O)	Pressure 7 (cmH_2O)	Pressure 10 (cmH_2O)
Flow 5 (*L/min*)	0.830 cmH_2O	5.148 cmH_2O	5.079 cmH_2O	4.873 cmH_2O
Flow 8 (*L/min*)	0.858 cmH_2O	3.91 cmH_2O	3.731 cmH_2O	3.25 cmH_2O
Flow 10 (*L/min*)	0.569 cmH_2O	4.323 cmH_2O	5.01 cmH_2O	5.161 cmH_2O
Flow 15 (*L/min*)	4.391 cmH_2O	2.535 cmH_2O	4.185 cmH_2O	5.505 cmH_2O

Table 5.17 Two-way Anova

Source of Variation	Sum of Squares	Degrees of freedom	Mean of squares	P-value
	18.7678	3	6.255933	0.029962
Pressure	17.03446	3	5.678154	0.038387
Flow	11.87096	9	1.318996	
Total	47.67322	15		

The Figure 5.4 illustrates the sizes of the pressure oscillations according to the expiratory tube depth immersion in cmH_2O referred as CPAP and flow in *L/min*. The Figure is supposed to be rotated anticlockwise to 90 degree. The axis Pressure cmH2O represents the pressure measured by pressure transducer and converted from *mV* to cmH_2O. The graph is a bar chart, where each element represents the amplitude of the pressure oscillation at certain flow and expiratory tube depth immersion. For better understanding, I connected the bottom, middle and top points of each element. It allows the reader to better understand the trends of mean values and amplitudes.

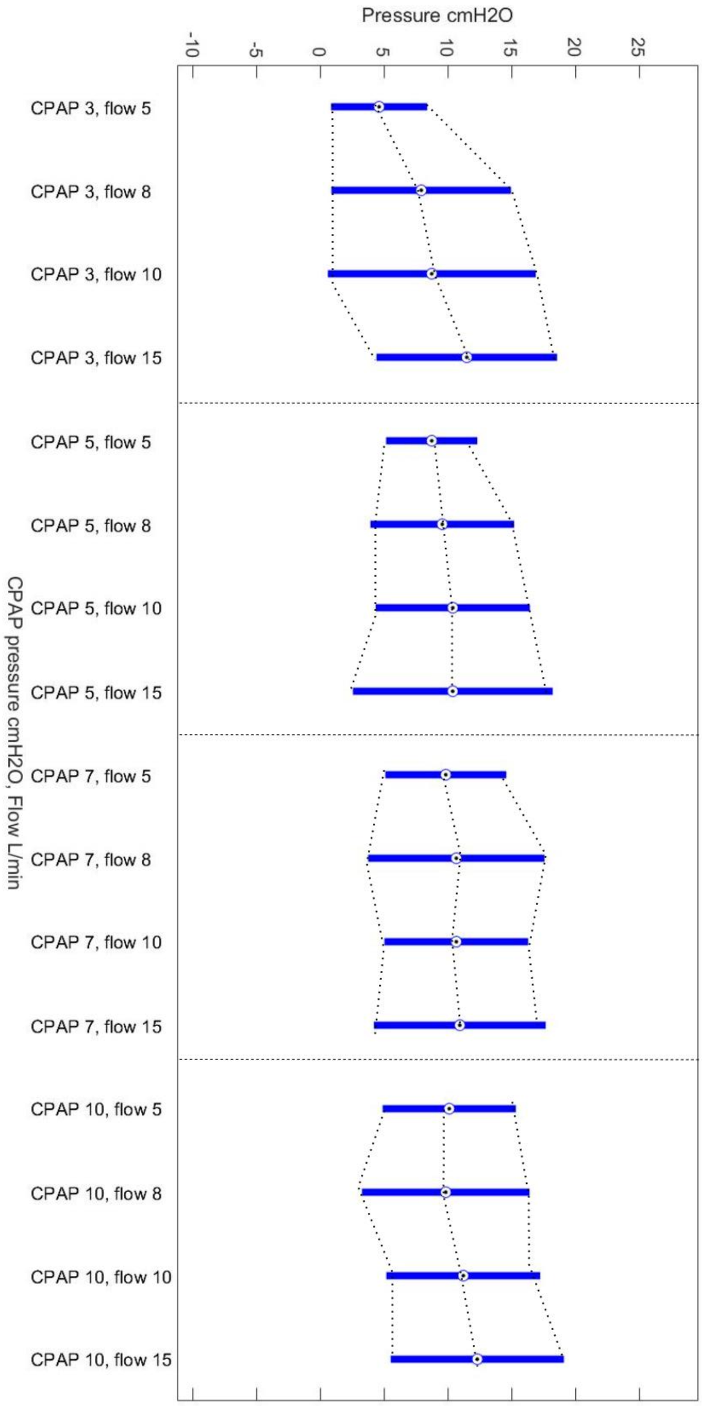


Figure 5.4 Box chart of pressure oscillations' amplitudes at different levels of CPAP pressure and flow (rotate anticlockwise to 90 degree)

5.6.3 Pressure oscillations at PEEP 3 cmH_2O and flow rate 5, 8, 10, 15 L/min

Figure 5.5 represents the pressure oscillations waveform in *mV* in some period of time at PEEP 3 *cmH2O* and flow rate 5, 8, 10, 15 *L/min*.

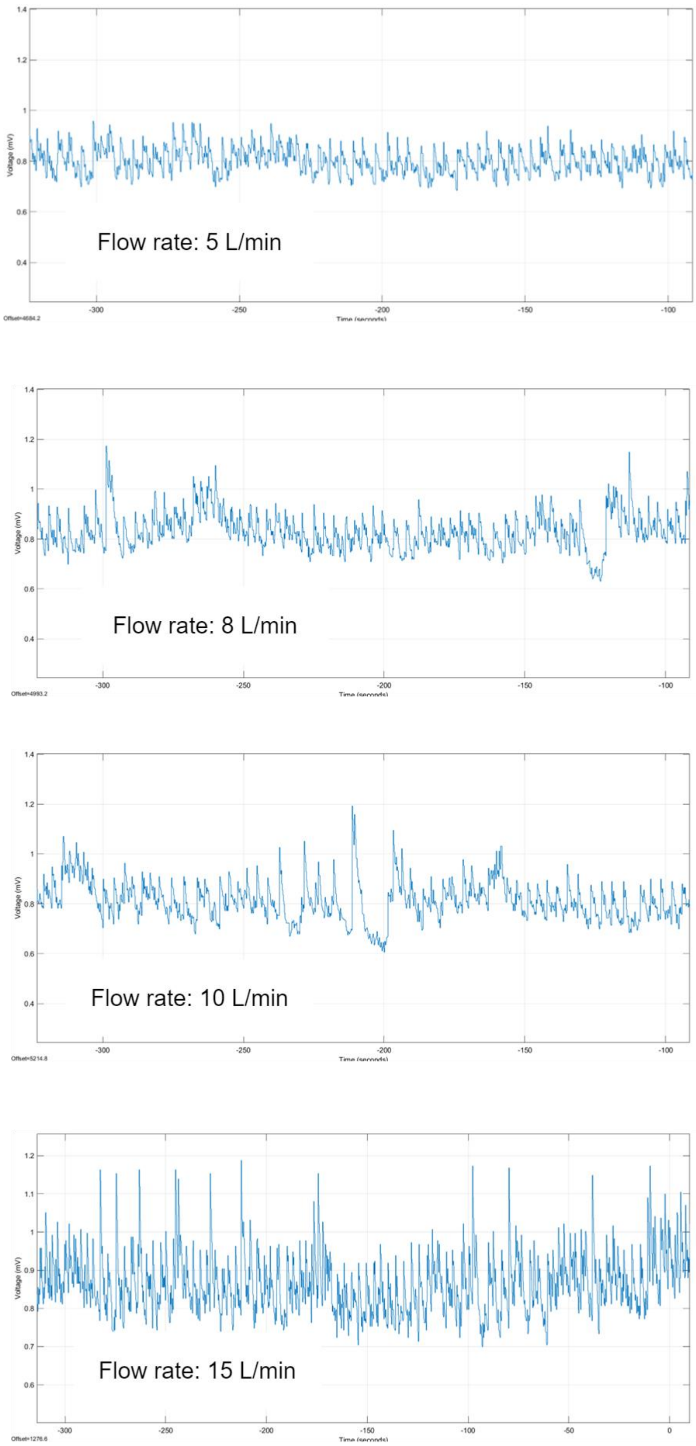


Figure 5.5 Pressure oscillations at PEEP 3 cmH2O and flow rate 5, 8, 10, 15 L/min

5.6.4 Pressure oscillations at PEEP 5 cmH$_2$O and flow rate 5, 8, 10, 15 L/min

Figure 5.6 represents the pressure oscillations waveform in *mV* in some period of time at PEEP 5 *cmH2O* and flow rate 5, 8, 10, 15 *L/min*.

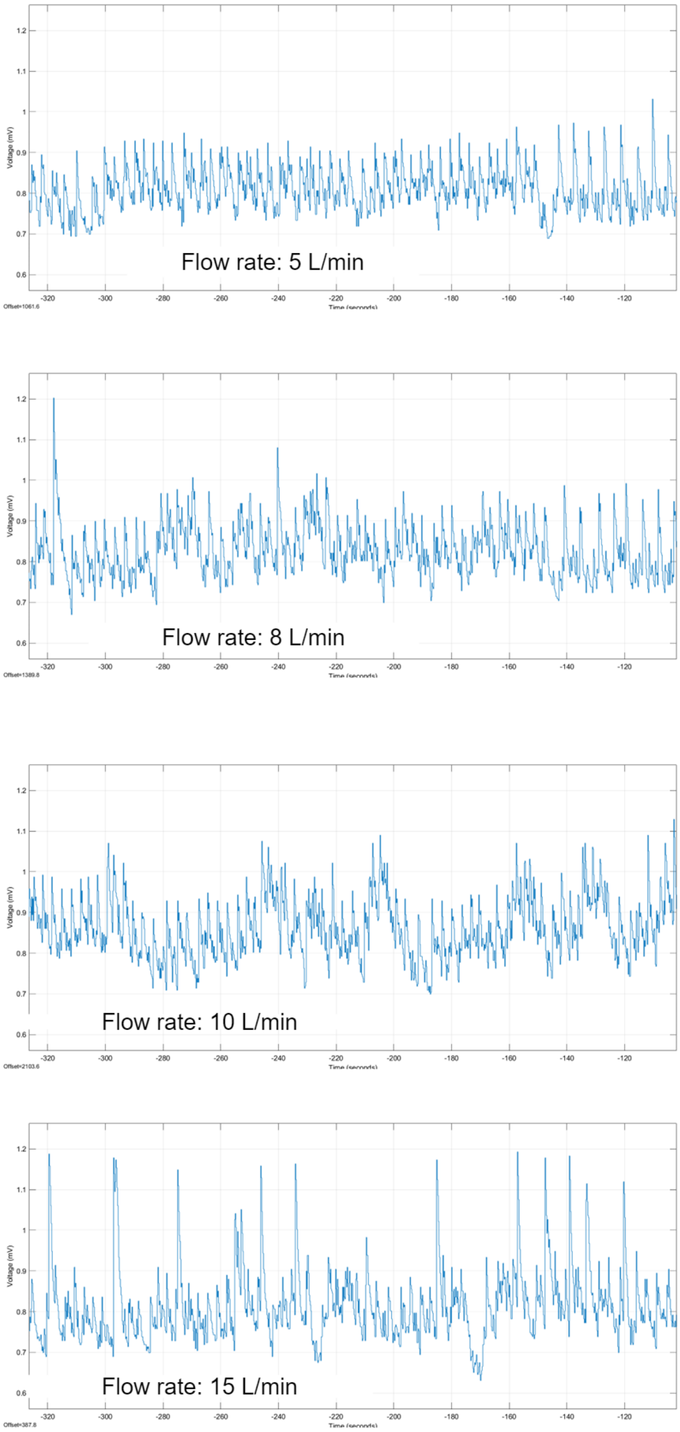


Figure 5.6 Pressure oscillations at PEEP 5 cmH2O and flow rate 5, 8, 10, 15 L/min

5.6.5 Pressure oscillations at PEEP 7 cmH_2O and flow rate 5, 8, 10, 15 L/min

Figure 5.7 represents the pressure oscillations waveform in *mV* in some period of time at PEEP 7 *cmH2O* and flow rate 5, 8, 10, 15 *L/min*.

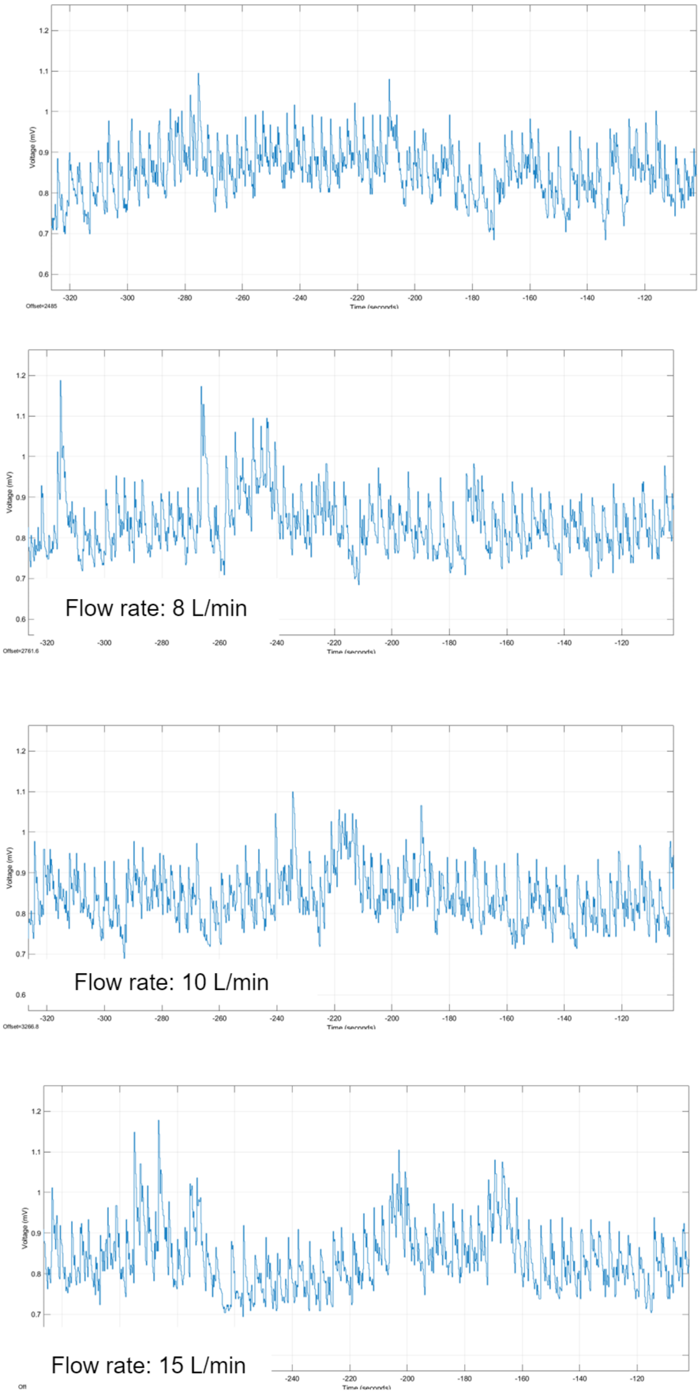


Figure 5.7 Pressure oscillations at PEEP 7 cmH2O and flow rate 5, 8, 10, 15 L/min

5.6.6 Pressure oscillations at PEEP 10 cmH_2O and flow rate 5, 8, 10, 15 L/min

Figure 5.8 represents the pressure oscillations waveform in *mV* in some period of time at PEEP 10 *cmH2O* and flow rate 5, 8, 10, 15 *L/min*.

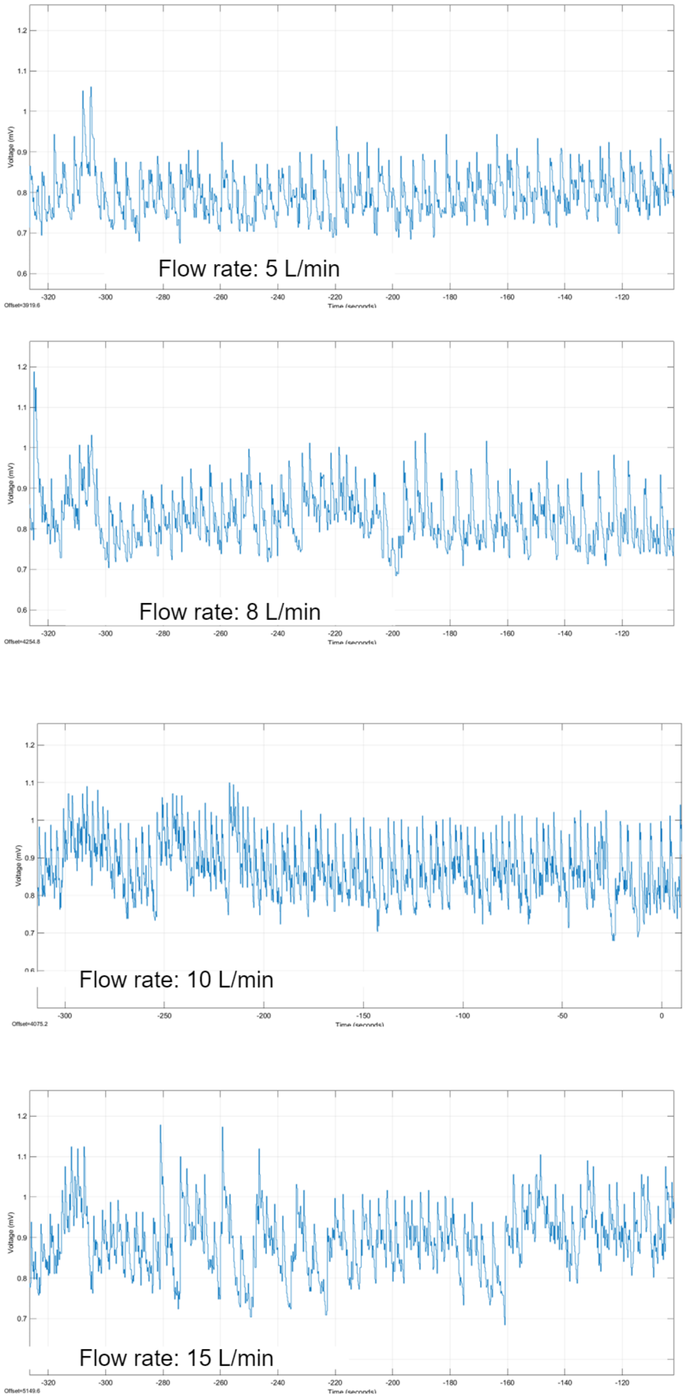


Figure 5.8 Pressure oscillations at PEEP 10 cmH2O and flow rate 5, 8, 10, 15 L/min

6 Discussion

According to the results of bachelor thesis bubble CPAP, the designed bubble CPAP is working and is able to control flow and read pressure oscillations, however with some limitations related to the hardware part of the project.

The results of a subchapter PWM block verification where the PWM signal sent by Simulink Model to the microcontroller is verified. The PWM signal is showing consistently correct work and behaves at it is expected. In Table 5.1 we can see that when setting half of the maximum voltage, the duty cycle of PWM is 50%. Whereas when setting the full voltage, the duty cycle is 100%. We can observe the maximum value of pulse width of PWM at state “0”. The duration of state “0” decreases, as we increase the voltage. Meanwhile, the pulse width of state “1” increase proportionally to the raise of input voltage.

The next subchapter Arduino Input signal verification verifies the functioning of Arduino Input of Simulink Model, therefore, the pressure display functionality. I set the known value by source and recorded displayed values on Pressure Display. The set values of voltage and voltage displayed did not differ much. Therefore, the Pressure Display reads the values correctly.

The results of subchapter Verification of DC signal examined the DC signal which was obtained by conversion of PWM signal. The measurements of DC signal were performed by oscilloscope and digital multimeter. Oscilloscope verified the shape of the signal, whereas digital multimeter – the voltage value. The type A uncertainty shows the error of the multimeter. The maximum error of multimeter is at set voltage 1.50. However, this error is still insignificant. The standard deviation within the sample shows how voltage differs within one sample which were categorized according to set voltage.

The subchapter Calibration curve for flow mass controller: flow and voltage. Five different measurements for comparing the set voltage and displayed flow was conducted. Then, the average of this 5 measurements were taken to build a calibration curve. Calibration curve in Figure 5.1 is almost linear. The curve supposed to be linear, since the step of change of set voltage was fixed. The maximum voltage which I was able to set is 0.60 *V* which correlates to almost 15 *L/min*. If I increased the voltage and therefore the flow, the alarm system was turned on. It was discussed in the Current State of the Art, that bias flow in one of the parameter which influence the pressure oscillation. And according to the study “High Bias Gas Flows Increase Lung Injury in the Ventilated Preterm Lamb” high amplitude of pressure oscillations has a positive effect on lung protection, the bias flow close to 18 *L/min* [26] is becoming dangerous. The alarms in monitoring system were turned on after I reached the flow 15 *L/min*.

The results of subchapter Calibration curve for pressure transducer: pressure and voltage shows the pressure in *mmHg*, *cmH2O* and voltage in *mV*. The Figure 5.2 shows the calibration curve of Voltage and Pressure in cmH2O. The observed can hardly to be called linear. The graph experience rapid increase in voltage after the pressure of 15 *cmH2O* which corresponds to the pressure of 10 *mmHg*. The pressure transducer which was used is Edwards pressure transducer. The transducer is usually used for much higher ranges of pressure, so the possibility of low accuracy at low values of pressure exists.

The possible way of solution is to amplify the signal from the pressure transducer with amplifier. The output signal received from sensing elements requires amplification before digital conversion. Generally, sensing elements are in range of mV. The suitable type of amplifier is an instrumentation amplifier since it gives the required amplification without much noise and good CMRR. Instrumentation amplifier is a differential amplifier. The element which makes it suitable for measurement equipment is input buffer amplifiers. For example, INA823 instrumentation amplifier can be used. Due to time constriction, I could not perform such actions but in the future it will be beneficial to amplify the signal from pressure transducer.

The results of subchapter 5.6.1 and 5.6.2 represent the mean, amplitude, maximum and minimum of pressure oscillation detected by the Pressure Display at different depth of immersion of expiratory tube and different flow.

First of all, I want to discuss the results of the two-way Anova test. As was mentioned before, the p value of 0.05 is considered to be significant. If the p value is more than 0.05, we fail to reject the null hypothesis. If p value is less than 0.05, we can reject the null hypothesis. In this test we evaluated the influence of flow and immersion depth of expiratory tube to the mean pressure of pressure oscillations. The P value is less than 0.05, therefore, we can reject the null hypothesis. We can say that both factors, flow and immersion depth of expiratory tube, influence the mean pressure. However, I would point out that not enough data was collected to confidently reject the null hypothesis. In the future it will be beneficial to perform same test with step of the bias flow 0.5 or 1 *L/min* in range of 3 to 15 *L/min* and different levels of immersion of expiratory tube in water.

Further discussion will be comparing the results of change of pressure oscillations in my project and in other studies which were dedicated to change of pressure oscillations. In the study “Effects of Flow Rate on Delivery of Bubble Continuous Positive Airway Pressure in an In Vitro Model” the mean pressure was observed at different flow rates. [25] However, there was no studies performed which simultaneously compared change in oscillations influenced by two independent factors (flow rate and level of immersion of expiratory tube).

As can be seen in the Figure 6.1, the results of external study showed the increase of the pressure mean as the flow increased. Before more rapid increase from 18 *L/min* the average of pressure oscillation was relatively steady in the range from 2 to 10 *L/min*.

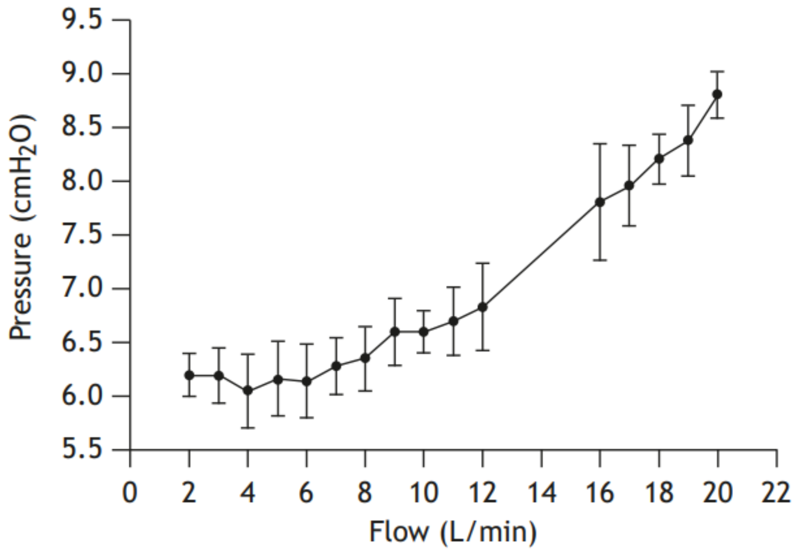


Figure 6.1 Flow-Pressure relation graph

In my project as it can be seen on Figure 5.4, at each immersion of tube level, the mean value of pressure oscillation in most of the cases is increasing respectively to the increase of bias flow. It is important to note, that at higher levels of expiratory tube immersions and at higher flow rates, the change of the mean value was insignificant. At immersion level of expiratory tube 10 cmH_2O the mean pressure was higher at flow 5 *L/min* than at 8 *L/min*. If we compare the pressure oscillation mean at flow 15 *L/min* at different level if immersion, we can find out, that the highest mean pressure is at immersion level 3 and 10 cmH_2O. The problem might me in detection of the peaks of oscillations. It will be discussed with conjunction to change of amplitude. Overall, in my project the trend of increasing of mean oscillation pressure, as the flow increases is present. Also, if we compare the means of oscillation pressure at some definite flow rate and at different immersion depths of expiratory tube, we can see, that mean of pressure oscillation is shifting up. However, the displayed pressure is higher than the set pressure by expiratory tube which might be the problem of calibration.

The shape of the signal will be compared to the results of the in-vitro study "Bubble CPAP: Is the Noise Important? An In Vitro Study", where the pressure oscillations were studied across a range of lung model compliance (0.1–1.6 *mL/cm* H_2O) at each of three different flows (2, 6, and 10 $_{L/min}$). We are interested in Pao (Pressure in airway openings) since we have not done in-vitro tests. The Figure 6.2 represents the oscillation over time. If we compare it with pressure oscillations in my project at Figures 5.5, 5.6, 5.7, 5.8 the shapes resembling each other.

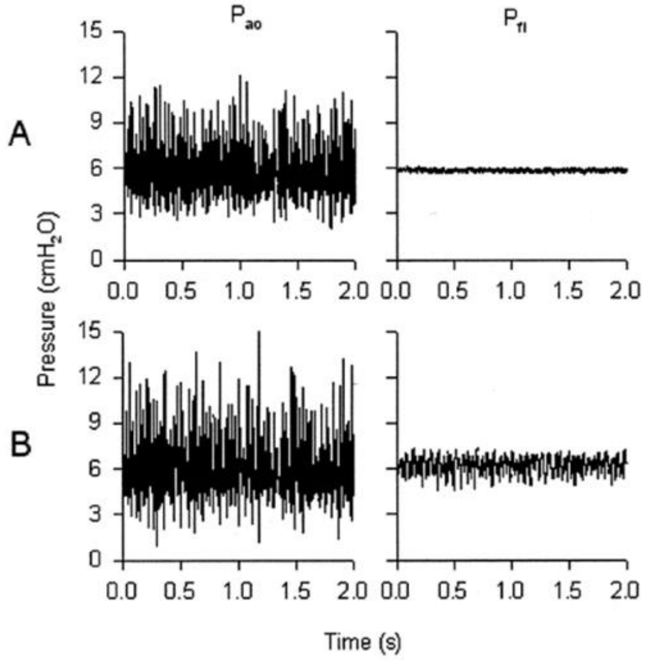


Figure 6.2 Pressure waveform during bubble CPAP

Another parameter of pressure oscillations which needs to be discussed is an amplitude of pressure oscillation. According to findings of the study "Bubble CPAP: Is the Noise Important? An In Vitro Study" the amplitude should increase with the flow. In Figure 5.4 we can observe that at immersion depth of expiratory tube 3 and 5 *cmH2O*, as we increase the flow from 5 to 15 *L/min*, the amplitude is slightly increasing as well with shifting up of mean pressure. However, at higher level of immersion of expiratory tube, the amplitude is stagnating or even decreasing. During measurements I was observing the work of bubble CPAP, the bubbling was more intensive at higher immersion levels and higher flow values. Therefore, the problem is not in creation of bubbling. At immersion level of expiratory tube 7 cmH_2O, the amplitude is higher at flow 7 *L/min* than at 10 and 15 *L/min*. The sampling frequency of Arduino Uno might be a possible problem for detecting a pressure oscillations swings at the higher oscillation amplitudes. In a further studies instead of Arduino more powerful microcontroller board might be chosen. For example, Arduino Mega.

Although the system is less accurate at higher bubbling rates, the designed project follows the main principles and patterns of bubble CPAP. The present design has limitation in hardware which can be further improved. The device has a great potential to be a tool for education about bubble CPAP. The project can regulate the continuous and steady flow in range of 0-12 *L/min* with step less than 0.5 *L/min* from flow mass controller by Simulink Model. It can read and display pressure values as a voltage in a Simulink Model, although it might be limited at high frequency bubbling.

7 Conclusion

The main goal of this bachelor thesis was developing the teaching tool bubble CPAP. The main requirements for such design are that bubble CPAP will be controlled by the Simulink software and be able to control the flow in certain range and read and display the pressure. The data presented above proving that the system designed in this project is working and effective. Flow can be control with high precision, and the pressure can be displayed in Simulink software. However, the project has limitations in reading the pressure in high frequency range.

Bubble CPAP is a great teaching tool since it relatively simple in use and has a lot of room for improvement. For today, there are plethora unsolved problems related to the bubble CPAP. It is already known from the State of the Art that accumulation of the condensate in the expiratory tube causes the significant increase in pressure delivered to the neonates [33]. Only a few models of existing bubble CPAP have pressure releasing valve which prevents high pressure from damaging the neonates. However, this method is not the best and the safest protective measure. In the future the problem has to be solved. One of the possible solution for that is the microcontroller which will react to accumulation of condensate and excessively high pressure and will redirect the air to the expiratory tube.

On the other hand, the promising studies with model of the lungs and change of its compliance was done. In-vitro models of lungs showed that bubble CPAP pressure waveform which fluctuates around the 5 to 20 and 40 to 100 *Hz*, changes with the compliance of the lungs. The changes in amplitude and frequency of the pressure waveform associated with lung’s low-pass mechanical filtering effect. The question is whether it is possible that frequency and amplitude change is a natural filter which optimizes the amount of noise delivered to the lung during CPAP. [25]

Therefore, there are a lot of technical and physiological challenges which requires a solution regarding bubble CPAP.

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Attachment A: Formatting requirements

Figure 7.1 represents connection of power supply to pressure transducer

Figure 7.1 Connection of power supply to pressure transducer

Attachment B: MATLAB script for Figure 5.4 Box chart of pressure oscillations' amplitudes at different levels of CPAP pressure and flow (rotate anticlockwise to 90 degree)

```
%%cpap3
cpap3flow5=[0.830374; 8.364826];
cpap3flow8=[0.857872; 14.936848];
cpap3flow10=[0.569143; 16.875457];
cpap3flow15=[4.391365; 18.552835];

%%cpap5
cpap5flow5=[5.14756; 12.29704];
cpap5flow8=[3.91015; 15.18433];
cpap5flow10=[4.32262; 16.42174];
cpap5flow15=[2.53525; 18.20911];

%%cpap7
cpap7flow5=[5.078815; 14.565625];
cpap7flow8=[3.731413; 17.562907];
cpap7flow10=[5.01007; 16.28425];
cpap7flow15=[4.18513;17.65915];

%%cpap10
cpap10flow5=[4.87258; 15.32182];
cpap10flow8=[3.250198; 16.394242];
cpap10flow10=[5.161309; 17.232931];
cpap10flow15=[5.505034; 19.089046];

figure
boxplot([cpap3flow5 cpap3flow8 cpap3flow10 cpap3flow15
cpap5flow5 cpap5flow8 cpap5flow10 cpap5flow15 cpap7flow5
cpap7flow8 cpap7flow10 cpap7flow15 cpap10flow5 cpap10flow8
cpap10flow10 cpap10flow15], 'PlotStyle', 'Compact',
'Labels', {'CPAP 3, flow 5', 'CPAP 3, flow 8', 'CPAP 3,
flow 10', 'CPAP 3, flow 15', 'CPAP 5, flow 5', 'CPAP 5,
flow 8', 'CPAP 5, flow 10', 'CPAP 5, flow 15', 'CPAP 7,
flow 5', 'CPAP 7, flow 8', 'CPAP 7, flow 10', 'CPAP 7, flow
15', 'CPAP 10, flow 5', 'CPAP 10, flow 8', 'CPAP 10, flow
10', 'CPAP 10, flow 15' });
ylabel('Pressure cmH2O')
xlabel('CPAP pressure cmH2O, flow L/min')
```