Design and Characterization of a Volume-Cycled Small Animal Mechanical Ventilator Coupled with a Respiratory System Model

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Abstract— **Small animals such as mice are generally used in experiments that study the behavior of the respiratory system under the influence of drugs, and accurate gas flow measurements are necessary due to the small volumes involved. Based on this need, a mechanical ventilator for small animals was developed using a linear actuator coupled with a 3ml precision glass syringe controlled by a driver. A mechanical load representing a mouse's respiratory system consisting of a rigid plastic cylinder with internal volume of 78ml was ventilated by the machine, and its measured resistance and elastance parameters were compared to values obtained with theoretical mathematical models. A 12.7% maximum deviation was found in the model's elastance in comparison with the predicted value, and the measured resistance did not assume the expected behavior of a linear system, decreasing sharply with the increase of frequency.**

Keywords— **Mechanical Ventilator, Respiratory System Model, Airway Impedance.**

I. INTRODUCTION

Artificial mechanical ventilation is indispensable to the modern medicine, being found in diverse applications such as surgery, emergency care and intensive care units [1]. Respiratory assistance is used when the patient cannot maintain optimal blood oxygenation levels according to clinical criteria, *i.e*, normal breathing is not sufficient for the proper gas exchange with the environment.

Classifying positive pressure ventilators, two types stand out: pressure-cycled and volume-cycled machines [2]. The former type is more common when it comes to ventilation of patients. In these machines, a source of pressurized gas is controlled by a valve which closes when the airway pressure reaches a value determined by the operator. Most hospitals ventilators are pressure-cycled. Volume-cycled ventilators are different, and a predetermined volume of air or gas is injected in the patient.

Great part of the study of the respiratory system's mechanical properties is closely related to tests performed with the aid of mechanical ventilators in animals and humans, measuring and establishing relationships between parameters such as muscle pressure, air flow, and lung volume. Parameters such as gas flow and airway pressure are monitored, and with this data, it is possible to calculate the resistance, impedance, compliance and elastance of the respiratory system [3]. With the aid of these data, one can optimize the airflow and pressure for the ventilated patient, therefore providing an effective respiratory support [4].

It is imperative in this context to better understand the functioning of the respiratory system and to create computational and mathematical models, treating the physiology of this system quantitatively [3]. Therefore, it is common to evaluate the parameters related to animal's respiratory systems using mechanical ventilators [5]. After testing, the animals are usually euthanized, in order to avoid further suffering, mainly because of the tracheotomy procedure recovery.

Small animals such as rats and mice are widely used in experiments that assess the respiratory mechanics in mechanical ventilation because they can be obtained in large numbers and statistically produce more reliable results than larger animals [6]. The challenge of working with mice is that the precision of the devices becomes essential in small tidal volumes and the equipment's total dead space needs to be insignificant in relation to the animal's lung volume. Pneumotachographs, which are usually used in humans and larger animals, are problematic in rats or mice because they cannot precisely measure flow on a small scale. Thus, volume-cycled equipment is usually used with small animals, so that the precision problem can be avoided.

Commercial equipments for the ventilation of small animals can be found in the market, such as the model flexiVent (SCIREQ, Canada). This machine controls the airflow using the movement of linear piston and features volume and pressure control, also performing data acquisition [7]. Another very common device in laboratories is the Harvard Model 683 Small Animal Ventilator (Harvard Apparatus, USA). It is a volume-cycled ventilator with adjustable number of breaths per minute [8].

In this paper, we provide the description of the design and characterization of a small animal mechanical ventilator, and study the frequency behavior of a mechanical load attached to the machine in comparison with the theoretical model of the impedance.

II. METHODS

A. Instrumentation

The small animal mechanical ventilator developed in the project consists of several components and systems, which are depicted in Figure 1:

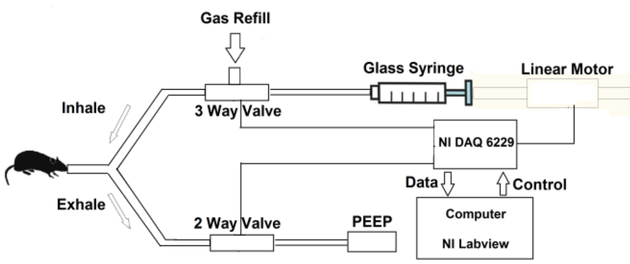

Fig. 1 Constructed mechanical ventilator's block diagram

A linear motor (LM 1207, Faulhaber Minimotor SA, Germany) was utilized to act as an actuator, driving the plunger of a glass syringe forward and backward. The motor presents a PI position feedback controller, and its measured position has a maximum error of 6µm, calculated three with analog Hall sensors. The position of the piston is monitored during ventilation, and its displacement is used to estimate the airflow and volume injected in the model.

A glass syringe was required for the project due to its low friction coefficients in comparison with plastic syringes, and the ventilator was designed to accommodate the use of syringes with various external diameters, ranging from 5mm to 20mm, what permits different flow ranges with the use of the same piston stroke. In the experiments performed for this paper, a syringe with 3ml of internal volume and an external diameter of 11mm (Becton Dickinson, USA) was used.

Two solenoid valves (298A3P1, Mechetronics, England) are responsible for directing or block the airflow to the model and to coordinate the syringe's refill with fresh air according to the movement of the piston (exhalation or inhalation of the animal). The model's pressure is monitored by a Gauge pressure transducer (MPXV7007GP, Freescale Semiconductor, USA), which is located in the model's side.

The system is ultimately controlled by a digital instrumentation platform (LabVIEW 2010, National Instruments, USA) and the input and output of electrical signals is commanded by a multi function analog-digital I/O board (USB DAQ 6229, National Instruments, USA). A sampling frequency of 55.5 Hz was used due to communication restrictions of the linear motor with the RS 232 protocol.

The piston of the linear motor and the syringe are carefully aligned by the rotation of an aluminum block where the syringe was locked, as seen in Figure 2, and all parts were mounted on rigid a 300mm × 150mm × 10mm acrylic plate.

If necessary for experiments, a positive end expiratory pressure (PEEP) can be applied by inserting the expiration tubing in a water recipient under a predetermined height. During regular ventilation, the user can monitor the pressure and flow parameters live on a chart in the control software, and the user is also free to alter any characteristics of the cycles (such as frequency, tidal volume or ration between inhalation and exhalation times) at any moment. Experiments performed for this paper were not done with a live model, but with a 78ml internal volume rigid plastic cylinder (20mm of height), which contained a thin copper wool (occupying 1% of the internal volume) to simulate an isothermal gas exchange. A metallic hypodermic needle, with a total length of 40mm and internal diameter of 1.5mm was used in the connection between tubing and the plastic model.

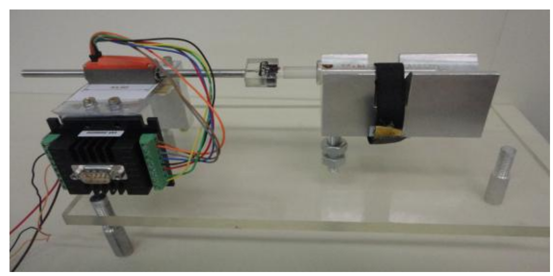

Fig. 2 Partial assembly of the mechanical ventilator, showing the connection between the linear motor's piston and syringe's plunge. Solenoid valves and tubing are not shown

B. Data Analysis

During ventilation, the pressure signal is captured by the pressure transducer, and flow values are estimated by the velocity of the linear motor's piston. Having these parameters, it is possible to calculate the mechanical impedance of a load attached to the machine. A model-dependant approach, depicted in Figure 3, was followed to calculate, with Equation 1, the impedance of the entire apparatus containing the model, tubing and valves, and this approach is later compared to theoretical results considering the isolated model.

In Equation 1, $Z(\omega)$ represents the model's mechanical impedance, $P(\omega)$ is the Fourier transform of the air pressure measured inside the model, and $\dot{V}(\omega)$ is the Fourier transform of the air flow calculated by the displacement of the piston, which is assumed to be the same as the air flow entering the load. Compressibility effects of the air between the syringe and the load have, therefore, been not been considered in this analysis, and results are analyzed in the results and conclusion sessions of this paper.

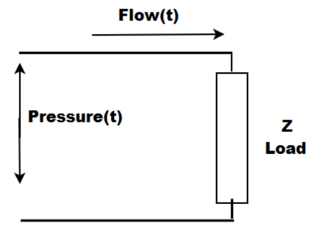

Fig. 3 Visual representation of the mathematical system used to calculate resistance and elastance of the tested system

$$Z_{system}(\omega) = \frac{P_{model}(\omega)}{\dot{V}_{syringe}(\omega)} \quad (1)$$

From the complex impedance found in the experiments, we can calculate the load's mechanical resistance (R), elastance (E), and inertance (I) given by equation 2:

$$Z_{system}(\omega) = R + j * [\omega * \mathrm{I} - \frac{\mathrm{E}}{\omega}] \quad (2)$$

The inertance term in Equation 2 can be neglected at low frequencies [3] because the acceleration of the air inside the tubes is insignificant in comparison with the other terms, and has therefore not been analyzed in this study.

C. Mechanical Load

The ventilator's functioning was validated by the analysis of the mechanical parameters obtained with the ventilation of a physical model. A rigid plastic cylinder with internal radius of 40mm and height of 15.52mm, totaling an internal volume of 78cm^3 was attached to a hypodermal syringe and to tubes connected to the glass syringe. Air pressure was measured inside the rigid container, and the total dead space was estimated to be 2.5ml (resulting in a total volume for the system of 79.72ml).

The model's theoretical elastance can be found with Equation 3, known as Boyle's Law, where the coefficient β can be assumed 1.0, since an isothermal heat exchange can be assumed, considering the low frequencies involved and the copper wool's presence inside the model.

$$\mathrm{E} = \beta * \frac{\mathrm{P_0}}{\mathrm{V_0}} = 11.97 \, \frac{cmH2O}{ml} \quad (3)$$

In Equation 3, P_0 represents the atmospheric pressure (955 cmH_2O measured at the time of the experiments), and V_0 is the chamber's internal volume. The theoretical resistance can also be estimated using laminar flow theory, with Equation 4:

$$\mathrm{R} = \frac{8 * \eta * \mathrm{L}}{\pi * \mathrm{R}^4} \; , \quad (4)$$

where L is the tube's length, R is its radius, and $\boldsymbol{\eta}$ is the air's viscosity. Accounting for the presence of the system's tubing along with the flow resistance caused by the hypodermal syringe, a total resistance R_{total} is expressed in Equation 5:

$$\mathrm{R}_{total} = 0.3341 \, \frac{cmH2O*s}{ml} \quad (5)$$

D. Protocol

For a range of frequencies from 0.167Hz to 3.17Hz, with increments of 0.337Hz between different frequencies, the mechanical load was ventilated, and its experimental parameters calculated.

The pressure transducer was calibrated twice with the use of a water column, and data sets were captured with a duration of 180 seconds, with a sampling frequency of 55.5Hz. The data was later processed in a computer routine (MATLAB, Mathworks, USA), being Fourier-transformed for the calculation of the resistance and elastance parameters for each frequency.

III. Results and Discussion

Figures 4 and 5 display the experimental results obtained with the 78ml rigid plastic cylinder. The values of resistance and elastance calculated at different frequencies are plotted, and the red lines in both graphs represent the theoretical values for the respective parameters calculated in Equations 4 and 6.

As the oscillation's frequency is increased, the resistance value is greatly reduced from about 2.52 cm H_2O*s/ml to 0.117 cm H_2O*s/ml at a frequency of 1.17Hz, and becomes even less significant for the total impedance at a frequency of 3.17Hz, with a magnitude of 0.0194 cm H_2O*s/ml. Even though the expected behavior of a linear system would be a constant value for the resistance, differing from the measured values, this result is similar to other studies [6,9,10] where the resistance magnitude decreases significantly with the increase of frequency. The deviation from theoretical values of resistance is a consequence of several factors including non linearities in the actual system, turbulent air flow in the tubing and neglecting the compressibility of the air.

The model's elastance was found to be practically stable in the frequency range of the experiment, with a mean value of 12.81 cmH_2O/ml, what represents a 7.01% deviation from the predicted value. The maximum deviation was 12.7%, measured at 1.17Hz. This quasi-constant behavior matches the linear model's expected parameters, and was also found in other references [6,9,10].

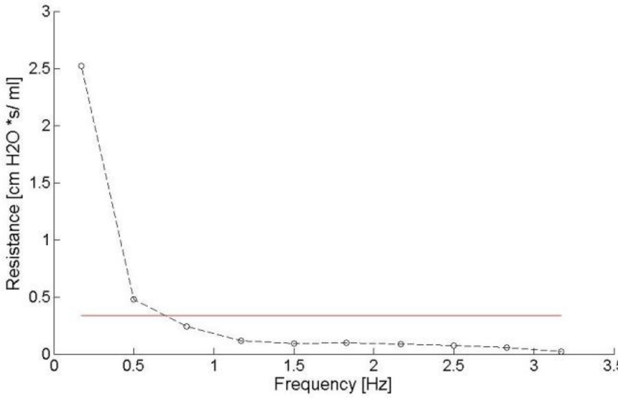

Fig. 4 Real part of load's impedance (resistance). Solid red line: theoretical prediction; plotted dots: experimental results.

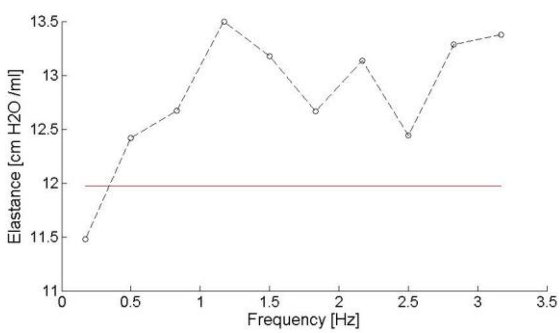

Fig. 5 Imaginary part of load's impedance divided by -ω (elastance). Solid red line: theoretical prediction; plotted dots: experimental results.

IV. CONCLUSIONS

A small animal volume-cycled mechanical ventilator was built, utilizing a linear motor attached to a 3ml precision glass syringe to provide the air flux. The system, controlled by a virtual instrumentation platform in a PC, can provide a sinusoidal flux with frequencies up to 200 cycles per minute.

A mechanical load, consisting of a 78ml rigid plastic cylinder, was ventilated, and its respiratory parameters were calculated based on flux and pressure signals obtained in the experiment. In comparison with the theoretical values, the mean elastance of 12.81 cmH_2O/ml is 7.01% higher than the expected value, and the resistance values presented a sharp decrease as the frequency increased, ranging from 2.52 cm H_2O*s/ml to 0.0194 cm H_2O*s/ml, with an expected value of 0.3341cm H_2O*s/ml.

The results were quantitatively and qualitatively consistent with the predictions and other papers in the same area of study. Further studies will be conducted with this volume-cycled mechanical ventilator considering the system's inertance and air compressibility, in order to obtain more adequate mathematical models for mechanical loads attached to it.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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