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Model-in-the-Loop Simulation of Mechanical Ventilation in Neonates

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Abstract: Preterm neonates often require mechanical ventilation due to immaturity of the respiratory system at birth. Physiological Closed-Loop Control (PCLC) has the potential to improve therapy and relieve clinical staff. We present an integrated model of the patient and mechanical ventilation setup for Model-in-the-Loop simulation of PCLC ventilation in neonates. The model uses settings of pressure-controlled mechanical ventilation as inputs and generates simulated measurements of airway pressure, airway flow, and time capnograms as outputs. We compare the model outputs with measurements from the ventilation of preterm lambs. The results are promising and we expect the model to enable a future X-in-the-Loop validation pipeline for PCLC ventilation of neonates.

Keywords: X-in-the-Loop Testing, Physiological Closed-Loop Control, Capnography

1 Introduction

Preterm neonates are often in need of mechanical ventilation. Among the very low-birth weight infants, up to 80% are intubated in the delivery room [1]. Automatically adjusting mechanical ventilation based on physiological measurements, so-called physiological closed-loop control (PCLC), can potentially relieve medical staff and improve patient care. PCLC ventilation systems for neonates are currently only available for control of oxygenation, while systems for control of CO_2 elimination, are yet under research [2, 3]. In the latter case, the control variable is the arterial partial pressure of carbon dioxide ($PaCO_2$). Because measuring $PaCO_2$ requires blood-sampling, $PaCO_2$ is usually approximated by end-tidal partial pressure of CO_2 ($PetCO_2$), which can be measured noninvasively in the breathing gas using capnography devices.

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PCLC ventilation systems are safety critical and require a corresponding safety-centered development process, as employed in other safety-critical domains as aviation or autonomous driving. Model-based development in the sense of X-in-the-Loop testing can contribute to increasing safety and system reliability, as well as reducing animal trials. Setting up a model-based validation pipeline involves process modeling with increasing complexity. In the case of PCLC the development requires modeling of the technical mechanical ventilation system and the physiological patient system. Especially in preterm neonates, where tidal volumes may easily be as small as 10 ml or smaller, the influence of apparatus deadspace and resistance should not be neglected.

Recent contributions in the field of model-based validation of PCLC-based ventilation systems include a concept for testing [4] and a Hardware-in-the-Loop test bench for adults [5]. Also, physical capnography simulators for adults [6] and neonates [7] have been presented. However, published models of neonatal mechanical ventilation have so far been focused on simulating either gas exchange without modeling of the actual pressure waveforms generated by mechanical ventilation [8, 9] or modeling of lung mechanics without consideration of gas exchange [10, 11]. As the first step towards an X-in-the-Loop testing pipeline of PCLC-based ventilation ventilationin neonates we present an integrated model of a ventilated neonatal patient and a mechanical ventilation setup including simulated capnograms.

2 System Model

An overview of the model is given in Fig. 1. We will present the physiological patient model first, before detailing the technical model of the ventilation circuit including the modeling of capnograms.

2.1 Patient Model

The patient model consist of a lung mechanics model, a gas exchange model, and a $PetCO_2$ estimator. Further, it is accounted for airway deadspace ($V_{d^{AW}}$) in the trachea and alveolar deadspace (V_{d^A}) in the lung by $V_l = V_A + V_d$, where V_l is the tidal lung volume, V_A is the alveolar lung volume, and $V_d = V_{d^{AW}} + V_{d^A}$. The linear one compartment model is

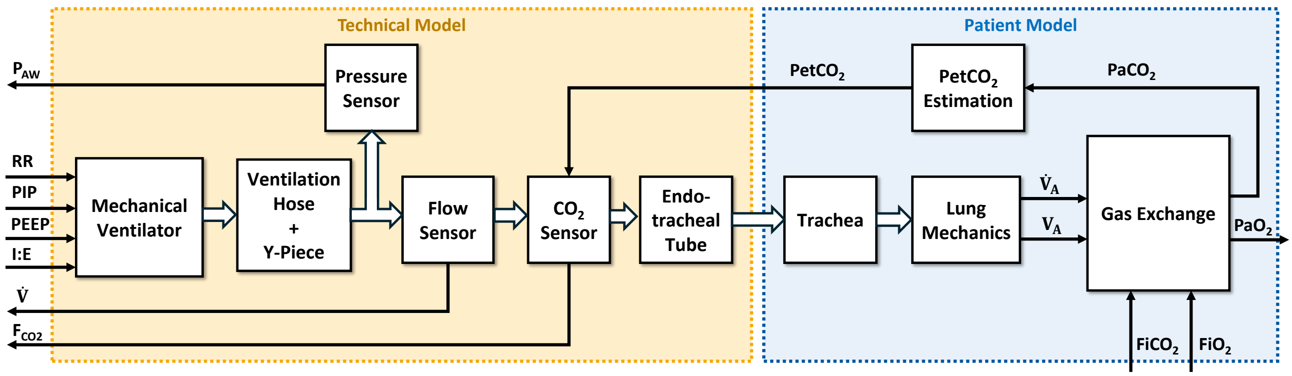

Fig. 1: Overview of the system model consisting of a technical model of the mechanical ventilation circuit and a physiological patient model. Double arrows represent the ideal gas phase with its states pressure and flow.

chosen for the lung mechanics

$$P_l(t) = R_{rs}(t) \cdot \dot{V}_l(t) + \frac{1}{C_{rs}(t)} \cdot V_l(t) + PEEP(t) \qquad (1)$$

with $P_l(t)$ being the pressure after the trachea, PEEP being the positive end-expiratory pressure, and $R_{rs}(t)$ and $C_{rs}(t)$ being the resistance and compliance of the respiratory system, respectively. The gas exchange model is taken from Tehrani [12], and comprises four compartments: lungs, body, brain, and cerbrospinal fluid. The original model also contained a part for autoregulation of breathing which was removed as proposed in [8] to let the ventilation instead be controlled by the mechanical ventilator. The inputs to the gas exchange model are alveolar lung volume and alveolar lung flow together with the inspiratory fractions of CO_2 and O_2, $FiCO_2$ and FiO_2, respectively. As output $PaCO_2$ is received and used to estimate $PetCO_2$ based on [13]

$$PetCO_2 = PaCO_2 \cdot (1 - 0.595 \cdot \frac{V_d}{V_l}) \qquad (2)$$

under the assumption that $PaCO_2$ is equilibrated with the alveolar partial pressure of CO_2. $PetCO_2$ is then used to model time capnograms, which will be described in the upcoming section.

2.2 Technical Model

The technical model represents the ventilator together with the ventilation circuit and sensors found in a PCLC ventilation setup. The mechanical ventilator acts as a pressure source which can be parametrized by the typical settings of pressure controlled mechanical ventilation, i.e. respiratory rate (RR), peak inspiratory pressure (PIP), positive end-expiratory pressure (PEEP), and inspiration to expiration ratio (I:E). A rectangular pressure signal c(t) is generated to match the given ventilation settings in a time-triggered continuous mandatory ventilation mode. Based on c(t) the output pressure differential of the ventilator P_{vent} is then given by

$$P_{vent}(t) = PEEP(t) + (PIP(t) - PEEP(t)) \cdot (c(t) * h(t)), \qquad (3)$$

where h(t) is a transfer function that is applied as a convolution to c(t) to allow for a rise time of the pressure in the ventilator. The ventilator has an inspiratory and expiratory side (not shown in Fig. 1 for brevity) with valves directing pressure flow. During inspiration, P_{vent} represents the positive ventilation pressure, whereas during expiration it represents PEEP. The ventilation hose and endotracheal tube are modeled as frictional pipes using the Pipe element of MATLAB Simscape for ideal gases to represent the pressure loss in the narrow tubes of the ventilation setup. The Y-Piece, the flow sensor and the CO_2 sensor are modeled as frictionless dead spaces. The outputs of the model are the airway pressure (P_{aw}), the airway flow ($\dot{V}$), and the fraction of CO_2 in the breathing gas (F_{CO2}) read from the pressure sensor, the flow sensor, and the CO_2 sensor, respectively. Each sensor samples the corresponding continuous-time signals at 50 Hz. Whereas pressure and flow sensor directly return the sampled signal, the CO_2 sensor models time capnograms as described in the next paragraph.

A time capnogram represents the fraction of CO_2 in the breathing gas (FCO_2) over the time course of one breath. Based on the FCO_2 at the end of expiration $PetCO_2$ can be derived. A volumetric capnogram, which corresponds to FCO_2 over the volume course of one breath, can be used quantify $V_{d^{AW}}$ and V_{d^A} and achieve further insight into the individual effectiveness of gas exchange [14]. We therefore believe that future PCLC ventilation systems will make use of online analyses of time capnograms and volumetric capnograms beyond the mere determination of $PetCO_2$. Thus, we present a simple way of approximating time capnograms with our model.

Because our model is supposed to be running in a real-time simulation, only a single gas is considered in the technical model instead of the gas mixture resulting from breath-

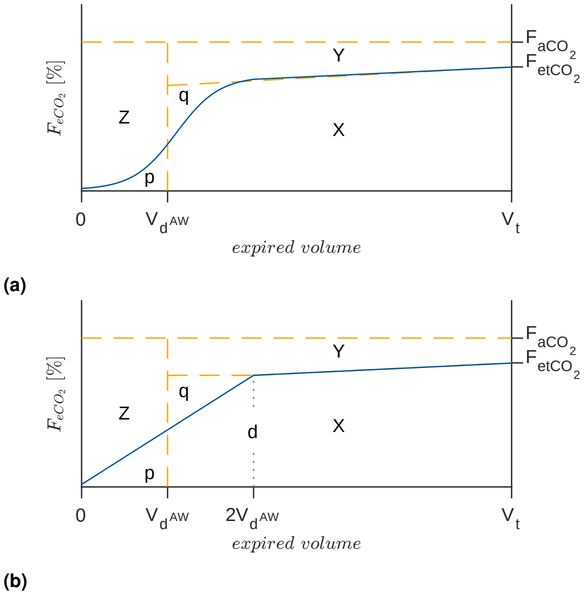

Fig. 2: Modeling of the expiratory phase in a volumetric capnogram as piecewise linear function (Fig. 2a inspired by [14])

ing. Therefore, the capnogram cannot be derived from simply sampling FCO_2 in the breathing gas. Instead, we make use of the fact that V_{dAW} and V_{dA} are parameters of our model and therefore known along with $PetCO_2$ and $PaCO_2$, computed by our model. We use this knowledge to first construct a simplified volumetric capnogram, which can then be evaluated over the expired volume at each simulation time step to receive the time capnogram. PCLC algorithms under test can then analyse this time capnogram, but also a meaningful volumetric capnogram, when evaluating the modeled FCO_2 over the integral of $\dot{V}$. Fig. 2a shows the expiratory phase of an idealized volumetric capnogram, which is characterized by (i) a phase of F_{CO2} close to zero due to the empyting of the airways(omitted in Fig. 2), (ii) a phase with an S-shaped upswing in which the transition from airway gas to alveolar gas happens, and (iii) a plateau caused by the alveolar gas rich in CO_2. By extending the plateau to the left and placing a perpendicular to the upswing to create two equally sized areas p and q, the areas X, Y, and Z can be identified [14]. X represents the effective elimination of CO_2, whereas Y and Z correspond to the ineffective ventilation due to alveolar deadspace and airway deadspace, respectively. Based on these relationships we approximate the volumetric capnogram as piecewise linear function, as shown in Fig. 2b, by interpolating between three characteristic points: the beginning of expiration, where FCO_2 equals $FiCO_2$, the end of expiration, where FCO_2 equals $FetCO_2$ (determined from $PetCO_2$), and the intersection point between the rising edge (approximated phase(ii)) and the plateau phase. With the assumption, that the expired volume at the transition point equals twice airway deadspace, FCO_2 at this volume (denoted as d in Fig. 2b) can be found geometrically.

3 Results

To demonstrate the functionality of the whole model we compared data from two animal trials with outputs of the model. The animal trials where part of a study on evaluating a PCLC ventilation for neonates [2, 3] and involved pressure controlled ventilation of preterm lambs. The used mechanical ventilation setup and interconnection of devices for automatic data logging are described in [15]. Two passages of stationary mechanical ventilation with different ventilation settings as shown in Tab. 1 were used. The model was parameterized with measured time series data of the subjects' dynamic C_{rs}. All other parameters of the patient model were taken from [12].

Figure 3 shows the simulated measurements in comparison to the measurements from each animal trial. It can be found that the modeled data of P_{aw}, $\dot{V}$, and tidal volume (received by integrating the modelled $\dot{V}$) match the measured data very closely for both animals. Regarding the modeled capnograms it can be observed that they compare well with the measurement regarding the signal timing and general shape, but have a considerable gap in the signal amplitude. This mismatch results from a difference in the equilibria of metabolic CO_2 production and CO_2 elimination between the modeled patient and each individual animal. These results show, that a prediction of $PetCO_2$ without a priori knowledge of interindividual parameters of gas exchange is difficult and model calibration is desirable.

Tab. 1: Subject and ventilation parameters of comparator data.

Subject	C_{rs} [ml/mbar]	PIP [mbar]	PEEP [mbar]	RR [1/min]	I:E [-]
(a)	1.3	27	8	30	1:5
(b)	1.7	19	8	70	1:2

4 Conclusion

An integrated model of pressure controlled mechanical ventilation of neonates was presented including detailed modeling of the mechanical ventilation setup and a simple approach to modeling time capnograms. Waveform signals including airway pressure, flow, and volume of mechanical ventilation were accurately modeled. The model appears promising for use in a future X-in-the-Loop simulation pipeline for PCLC-based ventilation of neonates.

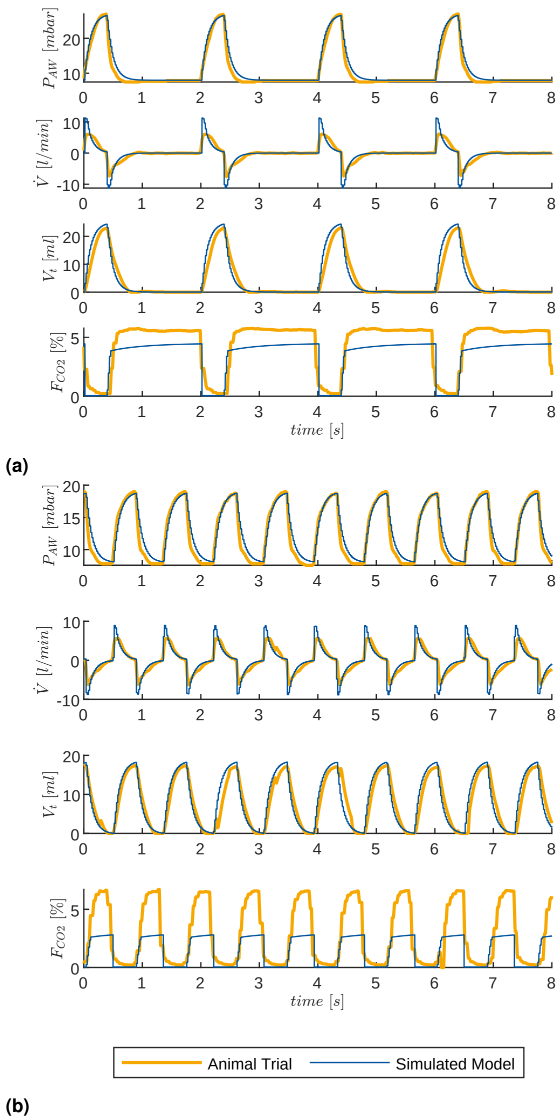

Fig. 3: Measured ventilation waveforms from animals trials compared to modeled ventilation waveforms

Author Statement

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