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A Model-based Approach to Generating Annotated Pressure Support Waveforms

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***Abstract*— During pressure support ventilation, every breath is triggered by the patient. Mismatches between the patient and the ventilator are called asynchronies. It has been reported that large numbers of asynchronies may be harmful and may lead to increased mortality. Automatic asynchrony detection and classification, with subsequent feedback to clinicians, will improve lung ventilation and, possibly, patient outcome. Machine learning techniques have been used to detect asynchronies. However, large, diverse and high-quality training and verification data sets are needed. In this work, we propose a model for generating a large, realistic, labeled, synthetic dataset for training and testing machine learning algorithms to detect a wide variety of asynchrony types. Next to a morphological evaluation of the obtained waveforms, validation of the proposed model includes a test with a machine learning algorithm trained on clinical data.**

***Index Terms*— patient-ventilator interactions, asynchronies, pressure support ventilation**

I. INTRODUCTION

Mandatory positive pressure mechanical ventilation is a form of life support. It is difficult to optimize the ventilator settings for a patient and ventilator-induced lung injury remains a major concern. When there is a spontaneous breathing effort, support modes may be used whereby the patient can control tidal volumes. In the pressure support mode (PSV), the patient triggers each breath and the ventilator supports this effort by a positive pressure during the inspiration phase. Mismatches between the patient's effort and the mechanical ventilator support are called asynchronies. A high rate of asynchronies is associated with adverse outcomes such as an increased mortality [1]. However, the detection, classification and resolvement of these asynchronies is challenging for bedside ICU clinicians, even for the more experienced ones. Besides, continuous monitoring of the mechanical ventilation is not feasible in clinical practice.

Many studies have been conducted on the detection of asynchronies [1]. Especially neural networks provide an interesting opportunity to elevate the quality of automated asynchrony detection and incorporate more types of asynchronies [2]. However, studies suffer from having too little data to improve training, testing, and comparison of these machine learning algorithms, since a large, diverse, labeled dataset is not available. Ideally this dataset would contain data of patients with different types of respiratory diseases, from different hospitals, measured with different types of devices, and would include different types of asynchronies. At the moment, obtaining such a dataset is difficult since manual labeling and advanced monitoring are required, which is time-consuming, operator-dependent, and prone to errors.

We propose to use a model-based approach to generate a diverse synthetic dataset including pressure, flow and tidal volume curves of a diverse ICU population during PSV. Generating a synthetic dataset or augmenting a dataset with synthetic data to help training and testing of machine learning algorithms is well known in other fields [3].

We study the feasibility of generating a suitable dataset using a physiological model that is similar to Bates' model [4] and comprises the main features that are needed to model pressure, flows and tidal volume curves. The original model has parameter sets for four healthy individuals, we use measured lung/airway parameters obtained in clinical studies to hand-tune the parameters to model different lung dysfunctions. We add a simple mechanical ventilator model that incorporates the main features to model waveforms at the airway opening. We validate the results by comparison with measured data, feedback from one of the authors, and reuse of a machine learning algorithm trained on clinical data to test the validity of the model.

II. METHODS

A. Patient model

Multi-compartment lung models are an option to model lung heterogeneity, however the determination of a large number of parameters is a challenge. Therefore, we selected the advanced non-linear one-lung model of Athanasiades [5] which was validated using data obtained during forced inspiration and expiration tests on healthy test persons. This model is an extension of the model of Bates [4] and includes turbulence, nonlinear models for resistances and volumes, peripheral airway collapse and visco-elastic tissue properties. Model parameters for patients with different disease types were chosen such that calculated total airway resistance, lung-chest wall volumes and compliances agree with measured clinical data of the relevant patient groups. Note that the same one-lung model of Bates was used in many clinical studies to extract the above parameters.

The model (see Fig. 1) consists of three variable resistances modeling the upper airways (R_u), collapsible airways (R_c), and small airways (R_s).

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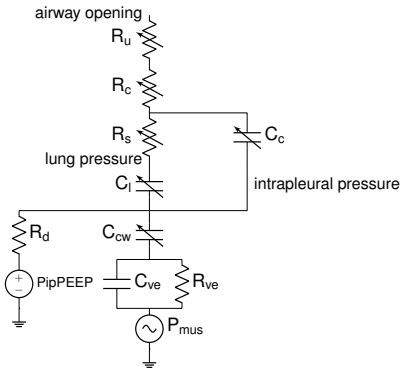

Fig. 1. The lung model which is an adapted version of [5]. Note that the components have nonlinear dynamics and are coupled with each other through these dynamics.

The resistance of the upper airway is given by a nonlinear flow dependent Rohrer resistor, which accounts for the turbulence:

$$R_u = A_u + K_u \mid \dot{V}_{cw} \mid, \tag{1}$$

where A_u is the linear resistance of the upper airways, K_u is a constant, and $\dot{V}_{cw}$ the airflow rate. The resistance of the collapsible airway varies with the volume of the collapsible airway segment V_c, and is given by:

$$R_c = K_c(V_{cmax}/V_c)^2, \tag{2}$$

where K_c is a constant and V_{cmax} is the maximum volume of the collapsible airways.

The resistance of the small airways captures the dependency of the small airway resistance on the lung volume V_l [5]:

$$R_s = A_s e^{K_s(V_l - RV)/(V^* - RV)} + B_s, \tag{3}$$

where A_s, K_s, B_s, and V^* are constants and RV is the residual volume of the lung.

The variable capacitor C_c models the compliance of the collapsible airway segment. In Athanasiades et al. [5], this is modeled by a piece-wise continuous function. We replace this function by a completely continuous and twice differentiable function, which has the same (sigmoidal) shape in the physiological region:

$$V_c = V_{cmax}/(1 + e^{-A_c(P_c - B_c)})^{D_c} \ , \tag{4}$$

where V_{cmax} is the maximum volume of the collapsible airways, A_c, B_c, and D_c are patient dependent constants and P_c is the pressure over the capacitor C_c.

C_{cw} is the compliance of the chest wall, and the volume is modeled by:

$$V_{cw} = \frac{TLC - RV}{0.99 + \exp\frac{-(P_{cw} - A_{cw})}{B_{cw}}} + RV \ , \tag{5}$$

where TLC is the total lung capacity, RV the residual volume, P_{cw} the pressure in the chest wall and A_{cw} and B_{cw} are patient dependent constants.

For diseased persons, the original equation for V_l in [5] does not describe the lung volume. Instead, we employ the exponential curve determined empirically by Venegas et al. [6] which is valid for multiple types of patients, and use this equation:

$$V_l = A_l/(1 + e^{-B_l(P_t - D_l)}) \ , \tag{6}$$

where A_l, B_l and D_l are patient dependent constants and P_t is the transmural pressure. Together with C_l, the linear C_{ve} and R_{ve} form a nonlinear kelvin body that mimics the viscoelastic properties of the lung. C_{ve} and R_{ve} are constants and are chosen in such a way to resemble available literature.

$\mathrm{P_{mus}}$ describes the effect of the respiratory muscle activity. The last modification consisted of adding the voltage source $\mathrm{PipPEEP}$ and a very high resistance R_d, to ensure correct initial conditions.

The model originally came with parameter sets of four healthy individuals fitted to experimental data. We hand-tune ten new parameter sets for each individual representing four lung dysfunctions (Obese, ARDS, COPD and idiopathic fibrosis) with three different disease severities for ARDS and COPD, and two types of severity for obesity, resulting in 40 new parameter sets. Model parameters are changed such that airway resistance, lung and chest wall compliance and lung volumes are in line with available data. The most important changes we made to model these diseases, can be summarized as follows:

- In obesity, due to closure of the peripheral airways and due to the diaphragm being pressed in cranial direction in supine position, the lung volumes are lower, therefore the lung and chestwall compliance is also reduced. The upper airway resistance is strongly increased mostly due to increased turbulence.
- For ARDS patients, we use the "baby lung concept". RV and TLC are strongly reduced, and the airway resistance moderately increased.
- COPD is characterized by high airway resistance and low lung elastic recoil. This results in high compliance of the lung tissue and high lung volumes. The expiratory resistance is much higher due to excessive central airway collapse during expiration.
- In idiopathic fibrosis, the lung tissue has low compliance (stiff). RV, FRC, and TLC are all lower compared to healthy individuals. Airway resistance is smaller or comparable to healthy.

B. Ventilator model

The ventilator model is shown in Fig. 2. The model ventilator has ideal pressure sources. The impedance of the ventilator tubing is modeled with a RLC lumped element model, the resistance is modeled using Rorher's equation.

The pressure and flow are measured near the airway opening, before the Y-piece. The flow dependent resistance of the tubing is often higher than the airway resistance. For this reason, the pressure drop over the tube resistance is very important for modeling the specific waveform characteristics at the airway opening.

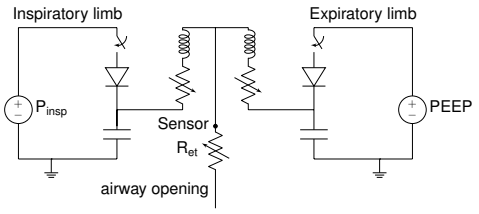

Fig. 2. Equivalent circuit of the ventilator model. Note that the endotracheal tube and the resistances modeling the tubing system are not simple resistances.

C. Validation methods

To test whether the model parameters are tuned correctly, we compare Rinsp, Rexp, compliances and lung volumes in the model, to values encountered in literature. RV and TLC can directly be observed from the model parameters. FRC can be calculated by calculating the volume at $P_l + P_c = -P_{cw}$. We define Rexp and Rinsp as the sum of R_u, R_c, and R_s during expiration and inspiration. Ctot is calculated by taking the slope of the combined lung-chestwall pressure-volume curve of the model at FRC. We report the values using zero end-expiratory pressure (ZEEP), except for COPD where we report the values using PEEP and P_{insp}.

After this, the patient-ventilator circuit is implemented in LT Spice XVII [7]. Triggering and cycling is done within the LTSpice simulation. Triggering was done at 1-2 cmH2O below PEEP. Cycling off is done a a fraction of peak inspiratory flow (range 10-80 percent).

The input muscle waveform $\mathrm{P}_{\mathrm{mus}}$ is generated by MATLAB R2019b [8]. $\mathrm{P}_{\mathrm{mus}}$ is a rounded trapezoid with a different rising and falling edge. By varying $\mathrm{P}_{\mathrm{mus}}$, the rise and fall times, and the patient type, we were able to generate different types of asynchronies naturally in our data: delayed inspiration (DI, the ventilator triggers too late), late cycling (LC, the ventilator cycles too late), early cycling (EC, the ventilator cycles too early), and ineffective efforts (IE, the ventilator does not trigger). The amplitude was in the range 5-10 cmH2O except for the delayed trigger and ineffective efforts where average values 4 cmH2O and 2 cmH2O were used respectively. Typical rise and fall times were 0.5 s and 0.3 seconds. For the delayed trigger and early cycling breaths longer rise times, up to one second, were used. The maximum amplitude and rise and fall times are as observed in clinical data. Breathing rates, start time of a breath, muscle pressure, rise and fall times and PEEP and maximum ventilator pressure were given random variations. White low-pass filtered noise (BW 15Hz) was added to the simulated waveforms.

Using this method a synthetic dataset with more than 300.000 breaths is created, the breaths are automatically annotated since the timing of the patient and ventilator are saved. A subset of this dataset is checked visually whether important features are present and compared to clinical data. The clinical data was obtained after cardiac surgery (no lung diseases reported) [9]. The experimental procedures for collecting this clinical data were approved by the Institutional Review Board.

In the first test using machine learning, a subset of 5000 breaths is randomly selected. We apply the machine learning algorithm proposed in [10] to the subset. The algorithm is a modified version of the u-net architecture that is trained on a small annotated clinical dataset. The goal of the algorithm is to find the timing of the start and end of patient inspiration. The machine learning architecture obtained high performance when it was trained and tested on the same clinical dataset, however, it is unclear how well it generalizes when it is applied to a different dataset.

III. RESULTS

Table I shows the range of Rinsp, Rexp, Ctot, and the lung volumes reported in literature for the different disease archetypes (the target values) and values obtained from the model. The model is sufficiently close to the target values for our application, and for the next validation step the waveforms are studied.

Fig. 3 provides a comparison of clinical waveforms of a patient with normal lungs after cardiac surgery [9], and four simulated patient archetypes with various types of asynchronies. The cycling threshold in the simulations is slightly wrong, such that asynchronies are present. The features in the figure correspond well to clinical data.

The machine learning algorithm detected the start of patient inspiration with a median error of 0.19 s, the detection of the end of patient inspiration had a median error of 0.44 s. The algorithm detected whether patient effort was present with 0.99 precision and a recall of 0.973.

IV. DISCUSSION AND CONCLUSION

In this study, we presented a model-based method based on a previously validated lung model for healthy test subjects, adjusted it for the main disease archetypes, combined it with a new ventilator model, to automatically generate annotated PSV waveforms.

We started by creating more parameter sets than the original four that were provided. Table I shows that the new parameter values show sufficient correspondence to the target values found in literature.

Fig. 3 shows that the simulated waveforms are very close to the clinical waveforms and show the most important features of the diseases and asynchronies. The increase in pressure during inspiration is caused by the decreasing inspiratory flow. This causes the flow dependent resistance of the tubing to decrease, which leads to an increase in pressure at the airway opening. The flow has a rounded peak, which is one of the signs that patient effort is present. Expiratory flow limitation (EFL) and airtrapping are observed in obese and COPD simulations. ARDS and especially fibrosis show features of archetypes with low compliance, low lung volumes, low resistance and stronger and longer duration inspiratory effort: the flow rises and decays faster than in other archetypes. In the simulations IE, LC, and DI emerged more often in obese and COPD archetypes. EC was more observed in ARDS and fibrosis archetypes. This corresponds

TABLE I

COMPARISON OF TARGET VALUES OF LUNG VOLUMES, CTOT AND RESISTANCES IN LITERATURE TO MODEL VALUES

	Normal		Obese		ARDS		COPD		Fibrosis	
	Target	Model	Target	Model	Target	Model	Target	Model	Target	Model
RV (L)	1.2	1.6±0.4	0.5±0.3	0.35±0.05	0.5±0.2	0.044±0.004	f(height,age)	3.3±0.08	1.1±0.2	1.25±0.15
FRC at ZEEP (L)	2.4	3.2±1.2	1.1±0.3	1.3±0.3	1.3±0.3	1.6±0.5	>normal	4.6±0.6	1.6±0.2	1.9 ±0.2
TLC (L)	6.0	6.7± 1.5	5.1±1.5	5.2±1.2	4.8±1	5.4±1.2	2*RV	6.6±0.4	3.4±0.3	3.25±0.15
Rinsp (cmH2O/L/s)	2±1	3±1	6±2.5	7±1	5±3	6.3±1	7.5±2.5	6.5±2.5	2±1	2.1±0.1
Rexp (cmH2O/L/s)	2±1	3±1	6±2.5	7±1	5±3	6.3±1	15±5	14±6	2±1	2.1±0.1
Ctot at FRC (L/cmH2O)	0.15±0.05	0.15±0.05	0.1±0.05	0.06±0.01	0.045±0.02	0.044±0.004	>0.15	0.165±0.03	0.025±0.01	0.029±0.03

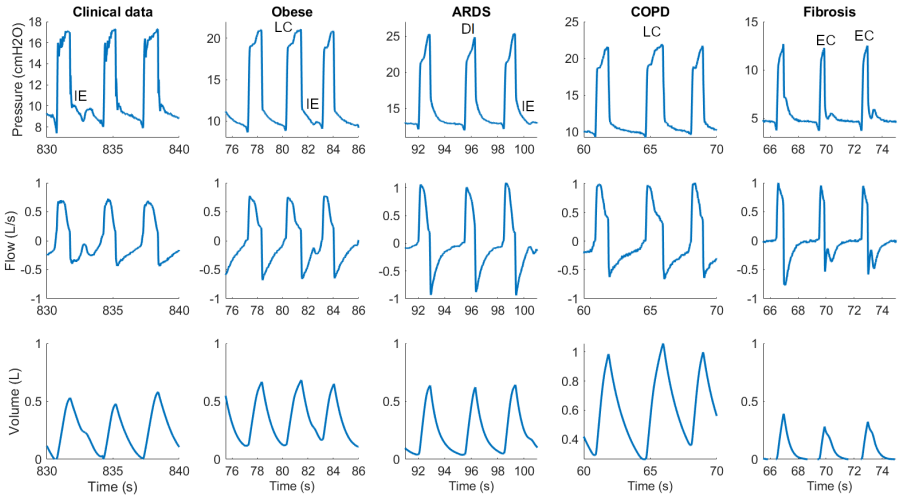

Fig. 3. The column on the left shows a clincal waveform of normal pulmonary function during PSV [9]. It includes an ineffective effort (IE). The remaining four columns show the simulated waveforms for obese, ARDS, COPD and idiopathic fibrosis archetypes. They also show early cycling (EC), late cycling (LC), ineffective effort (IE) and delayed inspiration (DI).

to clinical observations. During LC after the rounded peak in the flow, the flow starts decreasing exponentially. This is a sign that the patient has stopped inspiration, and thus that the ventilator cycles too late. This is both observed in the simulations and in clinical data. The EC asynchronies show the typical flow characteristics for EC when the maximum of the patient effort lies after the cycling time. IE show the typical drop in the pressure waveform and rise in flow waveform, that are caused by a breath of the patient that is not sufficient to reach the trigger threshold of the ventilator.

The first tests to identify the patient inspiration in the simulated waves using machine learning, give excellent results. The machine learning algorithm trained on clinical data, was able to recognize most patient inspirations in the simulated data with high precision. Especially IE were difficult to detect, and sometimes skipped. Also a combination of DI and EC was hard to detect, since this type of breath was not present in the clinical training set. These results indicate the feasibility to use a synthetic dataset to augment clinical patient-ventilator waveforms.

In future work, a survey will be conducted amongst experienced intensivists, to check whether they are able to distinguish the clinical data and simulations. The impact of including the synthetic data during the training phase of a machine learning algorithm for asynchrony detection will be investigated. The model will also be used to test and validate (new) methods relevant for lung protective ventilation.

REFERENCES

[1] Candelaria de Haro et al. “Patient-ventilator asynchronies during mechanical ventilation: current knowledge and research priorities”. In: *Intensive care medicine experimental* 7.1 (2019), p. 43.

[2] Lingwei Zhang et al. “Detection of patient-ventilator asynchrony from mechanical ventilation waveforms using a two-layer long short-term memory neural network”. In: *Computers in Biology and Medicine* (2020), p. 103721.

[3] Sebastian Abt and Harald Baier. “A plea for utilising synthetic data when performing machine learning based cyber-security experiments”. In: *Proceedings of the 2014 Workshop on Artificial Intelligent and Security Workshop*. 2014, pp. 37–45.

[4] Jason H. T. Bates. “The linear single-compartment model”. In: *Lung Mechanics: An Inverse Modeling Approach*. Cambridge University Press, 2009, pp. 37–61. DOI: 10.1017/CBO9780511627156.004.

[5] A Athanasiades et al. “Energy analysis of a nonlinear model of the normal human lung”. In: *Journal of Biological Systems* 8.02 (2000), pp. 115–139.

[6] José G Venegas, R Scott Harris, and Brett A Simon. “A comprehensive equation for the pulmonary pressure-volume curve”. In: *Journal of Applied Physiology* 84.1 (1998), pp. 389–395.

[7] Laurence W. Nagel and D.O. Pederson. *SPICE (Simulation Program with Integrated Circuit Emphasis)*. Tech. rep. UCB/ERL M382. EECS Department, University of California, Berkeley, Apr. 1973. URL: http://www2.eecs.berkeley.edu/Pubs/TechRpts/1973/22871.html.

[8] MATLAB. *version 9.7.0.1216025 (R2019b) Update 1*. Natick, Massachusetts: The MathWorks Inc., 2019.

[9] Ashley JR De Bie et al. “Fully automated postoperative ventilation in cardiac surgery patients: a randomised clinical trial”. In: *British Journal of Anaesthesia* 125.5 (2020), pp. 739–749.

[10] Tom Bakkes et al. “A Machine-Learning Method for Automatic Detection and Classification of Patient-Ventilator Asynchrony”. In: *2020 42nd Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)*. IEEE. 2020.