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IFAC PapersOnLine 56-2 (2023) 8215–8220

An Estimation Perspective on Breathing Effort Disturbances in Mechanical Ventilation

Lars van de Kamp [*,**] **Bram Hunnekens** [*]
Nathan van de Wouw [**,***] **Tom Oomen** [**,****]

[*] *Demcon Advanced Mechatronics, Best, 5600, MB Eindhoven, Netherlands.*
[**] *Department of Mechanical Engineering, Eindhoven University of Technology, 5612, AZ Eindhoven, Netherlands*
[***] *Department of Civil, Environmental and Geo-Engineering, University of Minnesota, Minneapolis, MN 55455 USA*
[****] *Delft Center for Systems and Control, Delft University of Technology, 2628, CD Delft, Netherlands*

Abstract: Estimation of relevant lung parameters and the breathing effort of a ventilated patient is essential to keep track of the patient's clinical condition. The aim of this paper is to investigate the major challenges of estimating the patient's condition with parametric models. The main method is a linear regression framework, where identifiability and persistence of excitation aspects are clearly unraveled. Different approaches for improving estimation accuracy are outlined. As an illustration, one of the solution strategies is implemented, which leads to accurate estimates of the breathing effort and relevant lung parameters.

Keywords: mechanical ventilation, linear regression, parameter estimation, respiratory systems, system identification

1. INTRODUCTION

Mechanical ventilators are mechatronic systems used for life-saving therapy in Intensive Care Units (ICUs) to support patients who cannot fully breathe independently. The main goal of mechanical ventilation is to ensure oxygenation and carbon dioxide elimination for the patient as stated in Warner and Patel (2013). Especially during the flu season or a world-wide pandemic such as the COVID-19 pandemic, mechanical ventilation has proven to be a life-saver for many patients around the world, see Wunsch (2020). Patients that are *fully sedated* completely rely on mechanical ventilation, while patients that are *spontaneously breathing* are only supported by the ventilator.

Information about the patient's clinical condition is crucial to achieving optimal treatment for every individual patient. For individual treatment plans, it is necessary to track the patient's condition over time. The patient's clinical condition cannot be measured directly. Insight into the patient's condition can be obtained with parametric patient models. By estimating the parameters in such models, the well-being of the patient can be insightfully quantified. Parametric lung models, for example the linear one-compartmental lung model as described in Bates (2009), enable estimation of the patient's lung compliance and the resistance of the patient's airway. The estimates can be obtained for *fully sedated patients* using recursive least squares algorithms as demonstrated by Borrello (2001) and Avanzolini et al. (1997). These methods produce inaccurate results for the parameter estimation when the patient is *spontaneously breathing* because the breathing is not taken into account in the passive patient models as stated by Redmond et al. (2019).

From an estimation perspective, it is essential to include the unknown *spontaneous breathing effort* of the patient in the estimation process to obtain more accurate estimates fo the patient parameters. Besides that, clinically, information about the patient's breathing effort is also essential. It helps to monitor the patient and also helps to detect and eventually prevent patient-ventilator asynchrony Holanda et al. (2018). In Blanch et al. (2015), patient-ventilator asynchrony is associated to increased mortality rates. Summarizing, accurate estimates of the patient parameters and the breathing effort are relevant to determine the patient's clinical condition and thereby improve the patient's treatment.

One class of approaches to estimate the patient's characteristics and the breathing effort simultaneously involves only the existing measurement signals, such as the airway pressure and the patient flow. This can only be accomplished if prior knowledge in the form of constraints on the patient's breathing effort are enforced. In Vicario et al. (2016), the lung resistance, the lung compliance, and the patient effort are estimated in a non-invasive fashion through linear regression techniques by enforcing stringent conditions on the patient effort, i.e., a monotonic decrease during inspiration and a monotonic increase during expiration of the patient effort. This may be considered a too stringent assumption in practice. In Schauer and Simanski (2021), the patient parameters and the breathing effort are estimated non-invasively by parameterizing the breathing effort with radial basis functions. A constraint is enforced on the breathing effort; namely that the effort is periodic, which is a too stringent assumption in practice. In Reinders et al. (2022), the patient parameters and the breathing effort are estimated, also non-invasively by enforcing sparsity on the second derivative of the breathing effort. In practice, the breathing effort is often more smooth, i.e., a non-sparse second derivative of the breathing effort, which leads to inaccurate estimates.

Another class of approaches to estimate the patient's characteristics and the breathing effort simultaneously

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10.1016/j.ifacol.2023.10.1003

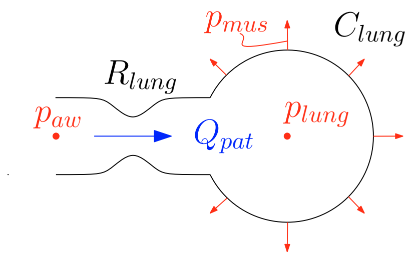

Fig. 1. Schematic representation of a linear one-compartmental lung model.

involves using extra measurement signals, which makes the estimation less challenging but possibly more expensive, error-prone, and uncomfortable for the patient. In Navajas et al. (2000), the inspiratory pressure level of a single breath is increased to estimate the lung resistance and compliance over multiple breaths. This estimation method is only accurate if the breathing effort stays the same over multiple breaths, which may be considered a too stringent assumption in practice. In Petersen et al. (2020), the shape of the breathing effort is constrained by surface electromyographic (sEMG) measurements, which makes it is possible to estimate the patient parameters and breathing effort with linear regression. However, the placement of the sEMG sensors is error-prone and might intervene with the patient's treatment.

Although a range of different methodologies have been developed to estimate the patient's clinical conditions in a non-invasive manner, the methods achieve sub-optimal performance either due to the fact that too stringent constraints are added to the shape of the breathing effort or that treatment of the patient must be altered, in the form of extra measurements or ventilation maneuvers.

The main contribution of this paper is an estimation perspective on combined patient parameter and breathing effort estimation, encompassing a range of methods involving both prior knowledge and additional measurements. As sub-contributions, a mathematical explanation is given why estimating the patient characteristics and breathing effort simultaneously is a challenging identification problem and a simulation case-study is conducted for a possible solution of the estimation problem. These contributions are a stepping stone for future research on patient estimation with the presented estimation perspective, for example estimation using information of multiple breaths.

In this paper, the contributions are touched upon as follows. First, in Section 2, the considered patient and patient breathing model is presented. In Section 3, the linear regression framework for estimation of the patient characteristics and breathing effort is introduced. Thereafter, in Section 4, a simulation case-study of a spontaneously breathing patient is presented to analyze a possible solution that fits within the estimation framework. Finally, conclusions and recommendations for future work are presented in Section 5.

2. PATIENT AND BREATHING EFFORT MODELING

The patient model that is used in this paper is the linear one-compartmental lung model as described in Bates (2009). This model is the simplest description of the lungs and airways, but is very intuitive for clinicians due to the physiological parameters as lung resistance, R_{lung}, and lung compliance C_{lung}. A schematic overview with all important signals and parameters is shown in Figure 1. The model is considered to be a grey box model with certain patient parameters, which is derived below. Finally, an input-output model is given, where the inputs, outputs, and exogenous disturbance are defined.

The model consists of two components: the lungs and the airway. The lung model describes how the lung pressure changes due to the volume inside the lungs together with the patient's breathing effort. The airway model describes the pressure drop over the airway and the flow moving in or out of the lungs. The pressure inside the patient's lungs is modeled as

$$p_{lung}(t) = \frac{1}{C_{lung}} V_{pat}(t) + p_{lung}(t_0) + p_{mus}(t), \quad (1)$$

where $V_{pat}(t) := \int_{t_0}^{t} Q_{pat}(\tau) d\tau$ is the volume inside the patient's lungs, C_{lung} the average compliance over the lungs, $Q_{pat}(t)$ the flow towards the patient's lungs, $p_{lung}(t_0)$ the initial lung pressure, and $p_{mus}(t)$ is the patient's time-varying breathing effort. The breathing effort p_{mus} changes the lung pressure p_{lung} due to contraction and relaxation of the respiratory muscles. Therefore, it is modeled as an additive exogenous disturbance in (1).
The airway of the patient is modeled with a linear resistance, which gives the relation between the airway pressure, lung pressure, and the patient flow:

$$Q_{pat}(t) = \frac{p_{aw}(t) - p_{lung}(t)}{R_{lung}}, \quad (2)$$

where R_{lung} is the linear airway resistance. Combining expressions of the lung pressure (1) and the patient flow (2) gives the following expression for the airway pressure p_{aw}:

$$\begin{aligned} p_{aw}(t) = \frac{1}{C_{lung}} \; & V_{pat}(t) + R_{lung} Q_{pat}(t) + \\ & p_{lung}(t_0) + p_{mus}(t). \end{aligned} \quad (3)$$

The lung compliance C_{lung}, the lung resistance R_{lung}, the initial lung pressure $p_{lung}(t_0)$, and the breathing effort $p_{mus}(t)$ are typically unknown in practice. The measured signals are the airway pressure $p_{aw}(t)$, the patient flow $Q_{pat}(t)$, and the volume $V_{pat}(t)$. Equation (3) is algebraic, therefore, the discrete time equivalent is

$$\begin{aligned} p_{aw}(k) = \frac{1}{C_{lung}} \; & V_{pat}(k) + R_{lung} Q_{pat}(k) + \\ & p_{lung}(1) + p_{mus}(k), \end{aligned} \quad (4)$$

where k denotes the discrete sampling number and $p_{lung}(1)$ denotes the initial lung pressure. The discrete time variant forms the foundation for the estimation problem as presented in Section 3.

A more generic structure for the model that we use for the estimation is:

$$y(k) = G(\xi) \boldsymbol{u}(k) + d(k), \quad (5)$$

where, for the modeled as described in (4), $y(k) := p_{aw}(k)$ is a measured output, $G(\xi)$ the transfer from $\boldsymbol{u}$ to y with $\xi = [\xi_1 \; \xi_2] := [1/C_{lung} \; R_{lung}]$, which includes the patient parameters, $\boldsymbol{u}(k) := [V_{pat}(k) \; Q_{pat}(k)]^\top$ the measured input signals, and $d(k) := p_{lung}(1) + p_{mus}(k)$ the unknown exogenous disturbance. In the next section, we develop an estimation perspective to identify the patient parameters in $G(\xi)$ and the exogenous disturbance $d(k)$ simultaneously.

3. ESTIMATION PERSPECTIVE ON SPONTANEOUSLY BREATHING PATIENTS

In this section, an estimation perspective on spontaneously breathing patients is presented. In Section 3.1, a linear regression framework for the breathing effort estimation is proposed. In Section 3.2, the uniqueness of the estimated parameters is discussed. In Sections 3.3, 3.4, and 3.5, multiple, alternative solutions are proposed to solve the non-uniqueness of the formulated breathing effort estimation problem.

3.1 Linear regression framework for breathing effort estimation

The estimation goal is to accurately find estimates of the patient parameters and the exogenous disturbances in the chosen grey box model presented in (5). These estimates are important for adjusting the treatment according to the patient's condition. The goal must ideally be achieved by only using the measured signals at hand, i.e., the airway pressure $p_{aw}(k)$, the patient $Q_{pat}(k)$, and the patient volume $V_{pat}(k)$. We adopt the perspective that we measure these signals for a single breath, by which we define the following model structure:

$$\mathcal{M}_\beta : X \to Y, \quad Y = X\beta \tag{6}$$

with

$$Y = \begin{bmatrix} p_{aw}(1) \\ \vdots \\ p_{aw}(N) \end{bmatrix}, X = \begin{bmatrix} V_{pat}(1) & Q_{pat}(1) & 1 & & 0 \\ \vdots & \vdots & & \ddots & \\ V_{pat}(N) & Q_{pat}(N) & 0 & & 1 \end{bmatrix},$$

$$\beta^\top = \begin{bmatrix} \frac{1}{C_{lung}} & R_{lung} & \bar{p}_{mus}(1) & \dots & \bar{p}_{mus}(N) \end{bmatrix} \in \mathbb{R}^{N+2}, \tag{7}$$

where $\bar{p}_{mus}(k) = p_{mus}(k) + p_{lung}(1)$ denotes the sum of the patient effort and the initial lung pressure and N denotes the number of samples in a single breath. The data set of a single breath is captured by $\mathcal{D} = \{X, Y\}$. We assume that the lung resistance R_{lung} and compliance C_{lung} do not change over the data set $\mathcal{D}$. Note that we aim to estimate β.

In the estimation procedure, we want to select the member in the set $\mathcal{M}_\beta$ that reflects the patient in the best way possible given the dataset $\mathcal{D}$. For now, the assumption is made that the linear model in (3) can fully describe the patient. In that case, the true parameter vector is defined as β_o. Hence, measurements of the true system are described by:

$$Y = X\beta_o + v, \tag{8}$$

where the measurement noise v on the output Y is assumed to be normally distributed with $v \sim \mathcal{N}(0, \sigma^2)$, where σ^2 is the sample variance. To estimate the parameters, we define a least-squares cost function:

$$J = \sum_{k=1}^{k=N} (p_{aw}(k) - \hat{p}_{aw}(k))^2 = \|Y - \hat{Y}\|_2^2 \tag{9}$$

with $p_{aw}(k)$ the measured airway pressure and $\hat{p}_{aw}(k)$ the estimated airway pressure via the model (4) with the estimated lung resistance $\hat{R}_{lung}$, the estimated lung compliance $\hat{C}_{lung}$, and the estimated breathing effort $\hat{p}_{mus}(k)$. The parameter vector that minimizes the cost function is found by analytically calculating the derivative of the cost function and equating that to zero. It is well known, e.g., in Hastie et al. (2009), that the solution of the parameter vector is given by

$$\hat{\beta} = (X^\top X)^{-1} X^\top Y. \tag{10}$$

Note that the solution $\hat{\beta}$ is only unique if $(X^\top X)$ is invertible, which is not the case for the estimation problem as defined above. This non-uniqueness can have two different causes as stated in Ljung (1999). One is that two different regressors β give identical input-output properties in the model, i.e., the model structure is *not identifiable*. The other cause is that the dataset $\mathcal{D}$ is *not informative enough* to distinguish between different regressors β in the model structure $\mathcal{M}_\beta$. In Section 3.2, a more in-depth analysis of the two causes is given in the scope of the estimation problem for mechanical ventilation.

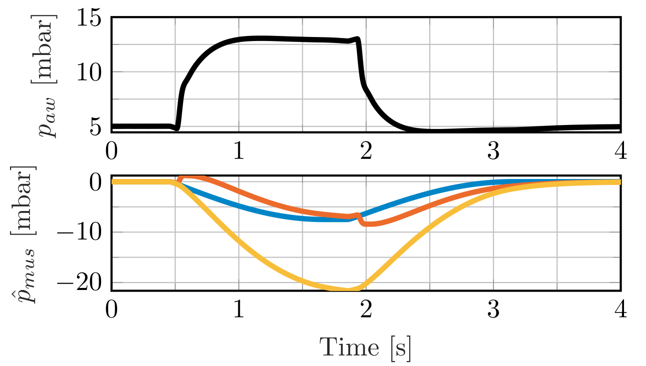

Fig. 2. Three combinations of $\hat{C}$, $\hat{R}$, ($\hat{C} = 80$ [ml/mbar], $\hat{R} = 0.083$ [mbar s /ml](—)), ($\hat{C} = 80$ [ml/mbar], $\hat{R} = 0.042$ [mbar s/ml](—)), ($\hat{C} = 40$ [ml/mbar], $\hat{R} = 0.083$ [mbar s/ml](—)) with accompanying breathing effort $\hat{p}_{mus}$ leading to the same airway pressure p_{aw} (—). The model structure in (7) is not identifiable.

3.2 Non-unique patient parameter estimation

The estimation problem with the cost function as formulated in (9) does not give a unique solution for the parameter vector $\hat{\beta}$. This can be related to problems concerning *identifiability* of the model structure or the *informativeness* of the input signals. First, the identifiability of a model structure is defined as:

Definition 1. The parameterization $\mathcal{M}_\beta$ is identifiable if for all β_1 and β_2 it holds that

$$\mathcal{M}_{\beta_1} = \mathcal{M}_{\beta_2} \Rightarrow \beta_1 = \beta_2, \tag{11}$$

where the model equality is defined as

$$\mathcal{M}_{\beta_1} = \mathcal{M}_{\beta_2} \Leftrightarrow \mathcal{M}_{\beta_1}(X) = \mathcal{M}_{\beta_2}(X) \quad \forall X. \tag{12}$$

The identifiability is a property of the model structure and is independent of the data. For all inputs in X, we find that $X^\top X$ is not full rank (the rank drops with two because the last N rows of $X^\top X$ summed together are a linear combination of the first two rows). In other words, we are able to find infinite many different β vectors that result in the same output. Therefore, it is concluded that the chosen parameterization is not identifiable. An interpretation of the lack of identifiability can be given using (4). It is observed that if we choose a combination of $\hat{C}_{lung}$ and $\hat{R}_{lung}$, then it is possible to find a breathing effort $\hat{p}_{mus}(k)$ such that $p_{aw}(k) = \hat{p}_{aw}(k)$ $\forall k \in [1, N]$, namely $\hat{p}_{mus} = p_{aw}(k) - \left(\frac{1}{\hat{C}_{lung}} V_{pat}(k) + \hat{R}_{lung} Q_{pat}(k) + \hat{p}_{lung}(1)\right)$, even if the parametric estimates $\hat{R}_{lung}$ and $\hat{C}_{lung}$ are wrong. In Figure 2, three different combinations are shown that result in the same airway pressure. Again, we conclude that the parameterization is not identifiable.

Secondly, the informativeness of the inputs is made explicit with the condition of persistent excitation as follows:

Definition 2. A dataset $\mathcal{D}$ is persistently exciting with respect to the identifiable parametrization $\mathcal{M}_\gamma$ if, for any two realizations $\mathcal{M}_{\gamma_1}$, $\mathcal{M}_{\gamma_2}$ satisfy

$$\mathcal{M}_{\gamma_1}(X) - \mathcal{M}_{\gamma_2}(X) = 0, \tag{13}$$

implies that $\gamma_1 = \gamma_2$.

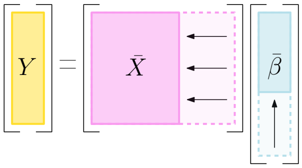

Fig. 3. Enforcing constraints on the breathing effort shape reduces the amount of parameters to be estimated $\bar{\beta}$, e.g., basis functions, sparse estimation.

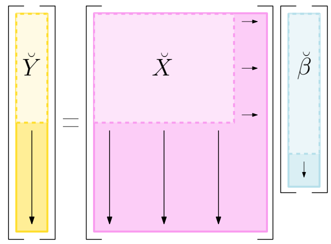

Fig. 4. Estimation over multiple breaths with constraints over subsequent breaths to increase information, e.g., a breath does not vary from the previous breath(s).

Note that the parameterization $\mathcal{M}_\beta$ is not identifiable; hence, it is not possible to conclude whether the inputs are persistently exciting. To show the concept of persistently exciting signals, we change the linear regression problem slightly in the following example.

Example 3. Assume that the patient is fully sedated such that it is known that there is no breathing effort ($p_{mus}(k) = 0 \ \forall k$). The regression problem then simplifies to:

$$\underbrace{\begin{bmatrix} p_{aw}(1) \\ \vdots \\ p_{aw}(N) \end{bmatrix}}_{Y} = \underbrace{\begin{bmatrix} V_{pat}(1) & Q_{pat}(1) \\ \vdots & \vdots \\ V_{pat}(N) & Q_{pat}(N) \end{bmatrix}}_{X} \underbrace{\begin{bmatrix} \frac{1}{C_{lung}} \\ R_{lung} \end{bmatrix}}_{\beta}. \tag{14}$$

In this regression problem, we find that the model structure is identifiable, because each parameter vector β gives a different output Y for inputs X under the assumption that the columns of $X^\top X$ are linearly independent.

The input signals are not persistently exciting if $X^\top X$ has linearly dependent columns. In the patient estimation case, the patient flow Q_{pat} and volume V_{pat} are only linearly dependent when the flow is zero. This might happen in the continuous positive airway pressure (CPAP) mode of the ventilator where a constant airway pressure is delivered, which results in a zero patient flow Q_{pat} and a constant volume V_{pat}. In this case, the input signals are not persistently exciting. All other airway pressure profiles, e.g., the pressure profile in Figure 2, are persistently exciting, because the rank of $X^\top X$ remains full.

In the next sections, possible adjustments are proposed to end up with an identifiable model structure. This can be achieved by imposing constraints on the breathing effort over a single breath or by imposing constraints on the breathing effort over multiple breaths.

3.3 Possible solutions within the estimation framework

Identifiability of the model structure $\mathcal{M}_\beta$ can be guaranteed in different ways. One option to change the model structure is shown in Figure 3, where the parameter vector β is reduced $\bar{\beta}$ by including *prior knowledge on a single breathing effort*. Another option is visualized in Figure 4, where the amount of data in the input $\breve{X}$ is increased, compared to the input in X, by using *prior knowledge over multiple breaths* which also increases $\breve{\beta}$ in some cases.

The prior knowledge of the breathing effort is related to the shape of the breathing effort. Constraints that we consider to be practically feasible can be enforced to reduce the possible realizations of the breathing effort. It is necessary to define a subset of breathing efforts, which include the true breathing effort, that leads to an identifiable model structure. In the following sections, we introduce two new model structures, one where prior knowledge is applied to a single breath and one where prior knowledge is applied to multiple breaths.

3.4 Prior knowledge on a single patient breath

Let us parameterize the breathing effort $\hat{p}_{mus}$ as follows:

$$\hat{p}_{mus}(k) = \theta^\top \boldsymbol{q}(k), \tag{15}$$

where $\theta \in \mathbb{R}^n$ are the parameters that determine the shape of the breathing effort and $\boldsymbol{q}(k) \in \mathbb{R}^n$ the signals of the parameterized breathing effort. This extra prior knowledge enables us to define a new model structure:

$$\bar{\mathcal{M}}_\beta : Y = \bar{X}\bar{\beta} \tag{16}$$

with

$$\begin{aligned} Y^\top &= \left[\, p_{aw}(1) \cdots \ p_{aw}(N) \,\right], \\ \bar{X} &= \begin{bmatrix} V_{pat}(1) & Q_{pat}(1) & q_1(1) & \cdots & q_n(1) \\ \vdots & \vdots & \vdots & & \vdots \\ V_{pat}(N) & Q_{pat}(N) & q_1(N) & \cdots & q_n(N) \end{bmatrix}, \\ \text{and } \bar{\beta}^\top &= \begin{bmatrix} \frac{1}{C_{lung}} & R_{lung} & \theta_1 & \ldots & \theta_n \end{bmatrix} \in \mathbb{R}^{n+2}. \end{aligned} \tag{17}$$

The parameterization of the breathing effort significantly decreases the amount of estimated parameters in $\bar{\beta}$ (compared to β) because the breathing effort without parameterization equals the number of samples n within one breath. Possible models for the breathing effort are for example polynomial basis functions (with $\boldsymbol{q}(k) = [1 \ t(k) \ \cdots \ t^n(k)]$), radial basis functions as in Schauer and Simanski (2021), or a sinusoidal half-wave model (see Section 4). The signal $\boldsymbol{q}(k)$ can also be a measured signal as in Petersen et al. (2020). A stricter parameterization results in a smaller subset of possible breathing efforts and less parameters θ that need to be estimated. At least, it would be beneficial for the estimation if the amount of estimated parameters $\beta \in \mathbb{R}^{N+2}$ is reduced to $\theta \in \mathbb{R}^n$ where $n \ll N+2$. However, too stringent constraints may result in a selected subset that does not include the true breathing effort.

3.5 Prior knowledge on multiple patient breaths

Instead of enforcing constraints on the shape of a single patient breath, it is possible to use information over multiple breaths and constrain the variation of breathing effort between breaths as done in Navajas et al. (2000). We conjecture that constraints on multiple breaths can be formulated such that they are less stringent compared to some constraints on single breaths. If we assume that the breathing effort stays equal over m breaths of length N, then

$$\breve{\mathcal{M}}_\beta : \breve{Y} = \breve{X}\breve{\beta} \tag{18}$$

with

$$\begin{aligned} \breve{Y}^\top &= \left[\, p_{aw}(1) \cdots \ p_{aw}(mN) \,\right], \\ \breve{\beta}^\top &= \begin{bmatrix} \frac{1}{C_{lung}} & R_{lung} & \bar{p}_{mus}(1) & \ldots & \bar{p}_{mus}(N) \end{bmatrix} \in \mathbb{R}^{N+2}, \end{aligned}$$

$$\breve{X} = \begin{bmatrix} V_{pat}(1) & Q_{pat}(1) & 1 & & 0 \\ \vdots & \vdots & & \ddots & \\ V_{pat}(N) & Q_{pat}(N) & 0 & & 1 \\ \vdots & \vdots & & & \\ V_{pat}((m-1)N+1) & Q_{pat}((m-1)N+1) & 1 & & 0 \\ \vdots & \vdots & & \ddots & \\ V_{pat}(mN) & Q_{pat}(mN) & 0 & & 1 \end{bmatrix} \tag{19}$$

This parameterization leverages information from multiple breaths where we assume that the lung resistance R_{lung}, compliance C_{lung}, and the breathing effort $p_{mus}(k)$ stay the same over multiple breaths. This does not decrease the amount of estimated parameters but increases the amount of data points compared to a single breath if and only if each of the m ventilator breaths are distinct.

4. SIMULATION CASE-STUDY OF PARAMETER ESTIMATION OF SPONTANEOUS BREATHING PATIENTS

Parameterization of the breathing effort helps to define a new estimation problem with a unique solution as presented in Section 3.4 and 3.5. With the parameterization we select a subset in which we can find the true breathing effort by solving a optimization problem. In this simulation case study, we compare three different methods to parameterize the breathing effort:

(i) Enforcing sparsity on the second derivative of the breathing effort;
(ii) Parameterizing the breathing effort with a sinusoidal flipped halfwave, as defined in Reinders et al. (2021), with estimated breathing start times of the patient;
(iii) Parameterizing the breathing effort with a sinusoidal flipped halfwave, as defined in Reinders et al. (2021), with the true breathing start times of the patient.

In method (i), we minimize the cost function:

$$\begin{aligned} &\min_{\hat{\beta}} \|Y - \hat{Y}\|_2^2 + \lambda \|\hat{\ddot{p}}_{mus}\|_0 \\ &\text{subject to} \quad \hat{p}_{mus} \leq 0 \ \ \forall k, \end{aligned} \tag{20}$$

where $\hat{Y}$ is the estimated output of the model defined in (6) and (7) and λ a weighting parameter. The rationale of the constraint is that the patient's inspiration and expiration are only passive. The regularization term restricts the shape of the breathing effort to a shape that only has a sparse second derivative. We apply ℓ_1-relaxation to make the optimization problem convex. The algorithms to find a solution for this estimation problem are available in Reinders et al. (2022).

In method (ii) and (iii), we parameterize the breathing effort with a sinusoidal halfwave model, which is defined in Reinders et al. (2021), and is equal to

$$\alpha p_{mus}(t) = \begin{cases} 0, & t < T_{pi} \\ -\alpha \sin\left(\dfrac{\pi(t-T_{pi})}{2(T_{pih}-T_{pi})}\right), & T_{pi} \leq t < T_{pih} \\ \alpha, & T_{pih} \leq t < T_{pe} \\ \alpha \sin\left(\dfrac{\pi(t-T_{pe})}{2(T_{peh}-T_{pe})}\right) - \alpha, & T_{pe} \leq t < T_{peh} \\ 0, & T_{peh} \leq t \end{cases}, \tag{21}$$

where α denotes the amplitude of the breathing effort, T_{pi} the start of the patient inspiration, T_{pih} the start of the patient inspiration hold, T_{pe} the start of the patient expiration, and T_{peh} the start of the patient expiration hold which are visualized in Figure 5.

The breathing start times of the patient are unknown in practice. Thus, this breathing effort parameterization can only be used if the patient's breathing start times are estimated. In this simulation case study, we have two ways to determine these starting times. In method (ii) we obtain the start times by extracting them from the estimated breathing effort obtained with method (i). In method (iii), we use the true patient's breathing start time because they are available in the simulation environment.

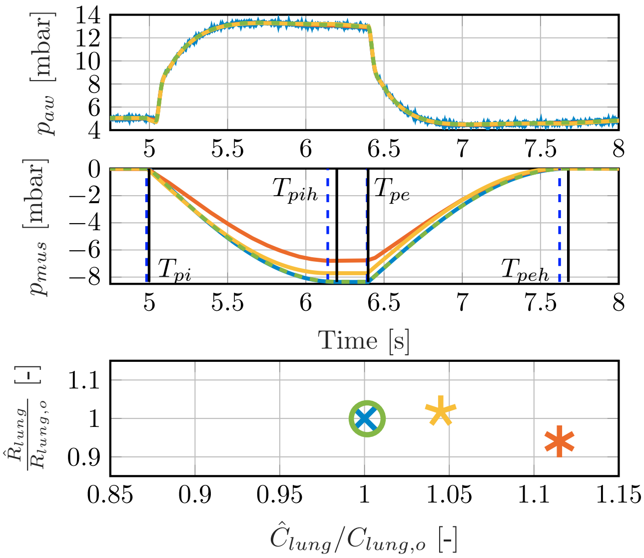

Fig. 5. Simulation results of three different estimation methods. The true airway pressure p_{aw} and breathing effort p_{mus} (—) are compared to method (i) (—) (∗), method (ii) (—)(⋆) with the patient breathing start times from the sparse estimation (- -), method (iii) (- -)(○) with the true patient breathing start times (—). Re-estimation with the parameterized breathing effort (method (ii)) improves the parameter estimates compared to sparse estimation (method (i)), but not converges the true values due to the inaccurate estimates of the patient's breathing start times.

The sinusoidal halfwave parameterization enables us to present a new model structure:

$$\mathcal{M}_{\bar{\beta}} : \bar{X} \to Y, \quad Y = \bar{X}\bar{\beta} \tag{22}$$

with

$$Y = \begin{bmatrix} p_{aw}(1) \\ \vdots \\ p_{aw}(N) \end{bmatrix}, \bar{X} = \begin{bmatrix} V_{pat}(1) & Q_{pat}(1) & p_{mus}(1) \\ \vdots & \vdots & \vdots \\ V_{pat}(N) & Q_{pat}(N) & p_{mus}(N) \end{bmatrix}, \\ \text{and } \bar{\beta}^\top = \begin{bmatrix} \dfrac{1}{C_{lung}} & R_{lung} & \alpha \end{bmatrix}. \tag{23}$$

The methods (ii) and (iii) fit within the possible solutions presented in Section 3.4, where we parameterize the breathing effort. In this case, we obtain that $\theta^\top \boldsymbol{q}(k) := \alpha p_{mus}(k)$. This reduces the amount of estimated parameters from $N+2$ to 3. A unique solution for this estimation problem can be found because $(\bar{X}^\top \bar{X})$ is invertible for all nonzero inputs except if $Q_{pat}(k) = c p_{mus}(k)$ $\forall k$ or $V_{pat}(k) = c p_{mus}(k)$ $\forall k$, where c is a constant. These exceptions do not occur in practice because those inputs signals do not comply with clinician set ventilation signals. Thus, the model structure is identifiable in practice.

In Figure 5, results of a simulation case study are shown, where we compare the estimation results of method (i) with methods (ii) and (iii) as explained above. It can be seen that method (ii) results in more accurate estimates than method (i). However, the estimated breathing effort amplitude $\hat{\alpha}$ did not converge exactly to the true value due to a mismatch in the start of the patient's breathing times. We only converge to the true parameter set when the breathing times can be estimated exactly. This is shown with method (iii), where the green line in Figure 5 is on the true breathing effort. For other start times, a different combination of lung resistance R_{lung}, lung compliance C_{lung}, and breathing effort p_{mus} is found, because the subset of the breathing effort, due to the parameterization, does not contain the true breathing effort.

The estimates of parameter vector $\bar{\beta}$ with the sparse estimation can thus be improved by conducting a re-estimation method where the breathing effort is parameterized by a sinusiodal halfwave model. However, it is important to mention that the re-estimation only improves the estimation results when the breath timings (e.g., T_{pi}, T_{pih}) are estimated accurately. Convergence to the true parameter set and exogenous disturbance can be enforced with stringent constraints, e.g, parameterization of the shape with one parameter.

5. CONCLUSIONS AND RECOMMENDATIONS

In this paper, a linear regression framework for estimation of the ventilated patient's clinical condition is proposed. With the framework it is shown that the model structure based on a linear one-compartmental lung model to estimate the patient's characteristics and breathing effort is not identifiable. Furthermore, different possible solutions are briefly discussed to change the model structure within the linear regression framework. One of the solutions is to parameterize the patient's breathing effort with a sinusoidal halfwave. In the simulation case study, it was shown that re-estimation with the parameterized breathing effort leads to more accurate estimates of the patient's characteristics and breathing effort under the condition that the patient's breathing times are estimated accurately and that the shape of breathing effort can be mimicked with the parameterezation.

The parameterization of the sinusoidal halfwave is rather stringent because not all patients breathe with this shape. However, the used method gives a good indication that when we know the shape of the breathing effort, the amplitude of the effort together with the patient's characteristics can be estimated. Future research includes estimation with measured signals that are related to the breathing effort. Furthermore, we want to research estimation over multiple breaths by enforcing constraints on subsequent breaths. In Figure 6, the breathing effort and patient's characteristics are estimated based on two breaths with the assumption that the breathing is exactly the same across breaths but the shape is free. These initial simulation results indicate that it is a promising research area. Furthermore, we should explore methods with less stringent assumptions on subsequent breaths.

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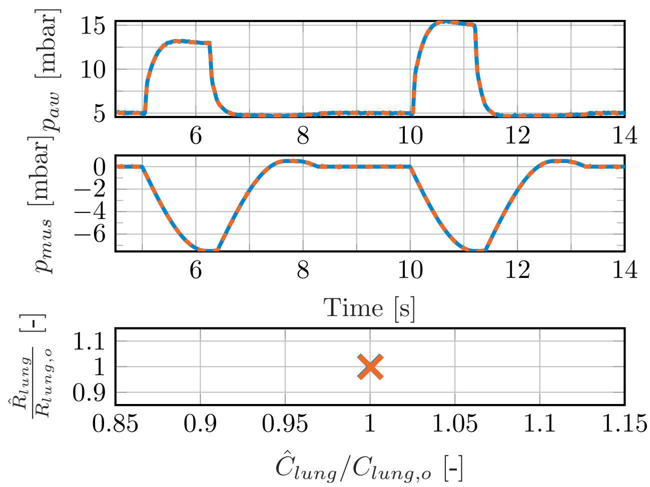

Fig. 6. Simulation results of a two breath estimation approach where the breathing effort is equal across two efforts and the pressure support is adjusted. The true airway pressure p_{aw} and breathing effort p_{mus} (—) are compared to the airway pressure and breathing effort of a two breath estimation procedure (- -).

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