

Efficient algorithm for pulmonary nonlinear model online estimation of patients under assisted ventilation

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Abstract: An efficient algorithm to estimate a respiratory system nonlinear model of sedated patients under assisted ventilation is presented. The considered model comprises an airways resistance and a volume-dependant compliance and, for each respiratory cycle, the proposed algorithm provides online the model parameters guaranteeing a minimum accuracy, above a user-defined threshold. Relying on standard nonlinear identification techniques, it exhibits computational burden reduction features, which contribute to its suitability for its online application.

Key-Words: Nonlinear Identification, Mechanical Ventilation, Nonlinear Respiratory Modelling.

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1 Introduction

Continuous respiratory monitoring is an important tool for clinical supervision in the case of patients under assisted ventilation, specially in the case when there is a pathology involving the lungs, airways or some other part of the respiratory system. It is based on a model of the respiratory system and it relies on measuring some biological signals of the patient.

Respiratory system models are an important tool to simulate and assess effects which are hard to evaluate *in vivo*, to contribute to functional diagnosis and, particularly, to determine the best treatment for patients in intensive care, attaining weaning more quickly and safely [1] [2] [3] [4] [5]. The most widespread model of the respiratory system among clinicians is a single compartment lung model which comprises two lumped parameters: resistance and compliance [6]. The first one considers the effect of resistance to pass of the air flow, and the second one takes into account the elastic properties of the tissues and chest wall. Usually, their values are computed considering specific points of the pressure and airflow signals, measured by the respiratory machine at the patient's mouth, P_B and F , respectively [7].

Model-based methods may help clinicians with decisions regarding the most appropriate ventilation strategy to improve the patient's situation and/or to avoid or reduce potential posterior negative effects of mechanical ventilation (MV) [8] [9]. They include finding a lung protective compromise either while a respiratory pathology or while under general anaesthesia [10] [11] [12], detection of asynchronies between the patient and the mechanical ventilation

(MV) [13] [14], or ensuring patient safety regarding high *plateau* pressure values [15]. These models have the potential to enable predictive, personalised, and potentially automated approaches to MV. However, most of the models used in these works are linear, since low computational cost is an important factor to obtain useful information of the patient in real time.

In this work, an algorithm and its user interface are developed, with the objective of providing online the quadratic nonlinear model of the patient's respiratory system with a preset accuracy. The algorithm routines resort to standard nonlinear identification techniques to estimate the model parameters of the patient, using the pressure and flow signals measured at their mouth.

To better deal with online time requirements, a fit check process is run to avoid a new full model estimation at every respiratory cycle. Using the input pressure signal of the current respiratory cycle and the last estimated model, the process computes its output's fit to the real data and compares it to a specified threshold. If the fit is greater than the threshold, a new estimation of the model is omitted, considering that the last one truly represents the patient, i.e. the previous model is kept as valid. The fit check is the mechanism that aims at decreasing the amount of models estimates of the patient, consequently reducing the computational time and burden with respect to the case of continuous estimation. The threshold that defines the minimum acceptable fit can be adjusted online by the clinician, depending on the accuracy required for each particular patient, condition or case under study.

Some results are presented, obtained when using

the algorithm with data measured on twelve sedated patients with COVID-19, two of them measured while undergoing a PEEP titration manoeuvre. Such manoeuvre modifies the breathing and respiratory system condition of the patient, thus making those data appropriate to show the main characteristics of the algorithm.

The paper is structured as follows: Section 2 introduces the models used by the algorithm to describe the respiratory system of sedated patients and, next, Section 3 gives a detailed explanation of the developed algorithm flowchart and the operation of each block; Section 4 then presents some results obtained by using the algorithm with data of real patients and, finally, conclusions and some still ongoing work are pointed out in Section 5.

2 Respiratory system models

This work considers sedated patients under assisted ventilation, which imply on one hand, that they cannot exert any muscular pressure, and on the other, that the pressure and airflow at their mouths, involved in their breathing process, can be measured.

In this section, the linear and nonlinear respiratory system models of a sedated patient under assisted ventilation are presented.

The respiratory system dynamics of a sedated patient can be described via the equation of motion [16]:

$$P_B(t) = \dot{V}_T(t)R_{aw} + P_c(V_T(t)) + PEEP, \quad (1)$$

where V_T is the tidal volume, defined as the amount of air that moves in and out in each respiratory cycle, P_B is the pressure at the patient's mouth, the airflow is $F(t) = \dot{V}_T(t)$, i.e. it corresponds to the time derivative of the volume, and R_{aw} is the airways resistance. P_c , a function of the volume, is the pressure of the chest wall & lung, and $PEEP$ corresponds to the base level pressure value known as Positive End Expiratory Pressure. Note that, as the patient is sedated, there is no pressure term corresponding to muscular activity, and also that $P_B(t)$ and $PEEP$ will be both, in this case, imposed by the ventilator. To simplify notation, the time dependency will not be written in the rest of the paper.

An electric equivalent model of the respiratory system of a sedated patient can be posed according to (1), where pressures and airflow correspond to electric voltages and current, respectively (see Fig. 1). Ground level is the atmospheric pressure, which is normally considered as the zero or reference value.

The most spread and commonly used model both in the literature and by physicians is linear, where R_{aw} is constant and where P_c and the tidal volume are proportional one to the other. In many situations, like

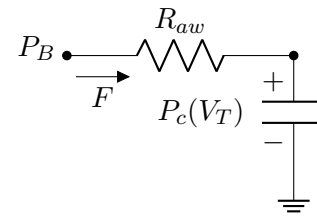


Figure 1: Electrical equivalent model of the patient's respiratory system.

when doing sports, when considering a baby breathing or in case of certain pathologies, a linear description represents poorly the behaviour of the respiratory system. According to the particular condition to be studied, different modifications can be considered to get a better representation of the respiratory dynamics [17] [18] [19]. Two different models have been considered in this work, depending on the description of the $P_c(V_T)$ relation, with R_{aw} constant:

- **Linear Model (LM).** This is the most popular model used among clinicians. It is adequate in case the relation between the chest wall & lung pressure and the tidal volume remains somewhat constant during the respiratory cycle (i.e., the variations of one of them is proportional to the variations of the other). It can be written as:

$$P_c(V_T) = V_T/C, \quad (2)$$

where C is a constant value known as *compliance* of the subsystem and accounts for the elastic properties of the system.

- **Nonlinear Model (NM).** A more accurate characterisation of the relation between P_c and V_T can be obtained by considering a volume dependant compliance [20]. A quadratic description, which is nonlinear but still rather simple, is analysed in this work:

$$P_c(V_T) = \underbrace{(a_1 + a_2 V_T)}_{C^{-1}(V_T)} V_T = a_1 V_T + a_2 V_T^2. \quad (3)$$

Equation (3) gives a better fit than the LM most of the times, particularly when the patient is being ventilated out of the range of normal breathing or presents a respiratory pathology which modifies the lung elasticity [21].

The algorithm developed in this work makes estimations and validation checks aiming to provide an accurate NM for each respiratory cycle of a connected sedated patient, with reduced computational burden.

3 Proposed algorithm

A description of the proposed algorithm is detailed in this section. Fed with data of $P_B(t)$ and $F(t)$ as input signals, both measured at the mouth of the patient, the algorithm computes and provides the set of parameters values of the NM that best describe the patient data for every breathing cycle.

It begins by performing a full complete estimation stage, which consists of quickly estimating the LM parameters' values for a first breathing cycle, and then, using them to establish the NM initial conditions, obtaining the NM parameters values for that first cycle. For the following breathing cycles, instead of repeating the whole process, it checks if the previous obtained NM parameters adjust properly. In case it does, they are kept as the valid NM model for the new cycle, without any other computation.

Only when the patient's condition changes *too much*, the fit to the new data is poor and it is necessary to obtain a new model. To do this, firstly the NM estimation routine is run, but initialised using the last valid NM parameters. Only in case this new NM estimation is not good enough, the complete Full Estimation stage is performed. The minimum accepted level is established by means of the threshold value Γ set by the user in terms of percentage of adjustment.

The flow chart of the algorithm is presented in Fig. 2 and its detailed operation is explained in the following subsections, together with each of its blocks.

3.1 Respiratory cycle acquisition

The proposed algorithm uses digital data of the patient's pressure P_B and tidal volume (V_T) signals to estimate the models and, for that, the latter is obtained indirectly, computed by conditioning and integrating the F signal each respiratory cycle.

The patient's P_B and F digital signals can be obtained either directly from the ventilator that is assisting their breathing or by means of an interconnected external respiratory monitor. In particular, a respiratory monitor FluxMed® GrE [22] has been utilised in this work. This device obtains the pressure signal P_B by using a differential pressure sensor, which measures the pressure at the patient's mouth related to the atmospheric pressure. In the case of the airflow signal F , it uses a fixed orifice pneumotachograph, which measures its value and direction.

3.2 Full estimation

In this block, a full estimation stage is performed, to obtain the nonlinear model of the respiratory system of a patient from their pressure and flow signals in one respiratory cycle. The full stage, explained in detail below, involves a first rapid estimation of the two Linear Model parameters, which allow a rough ini-

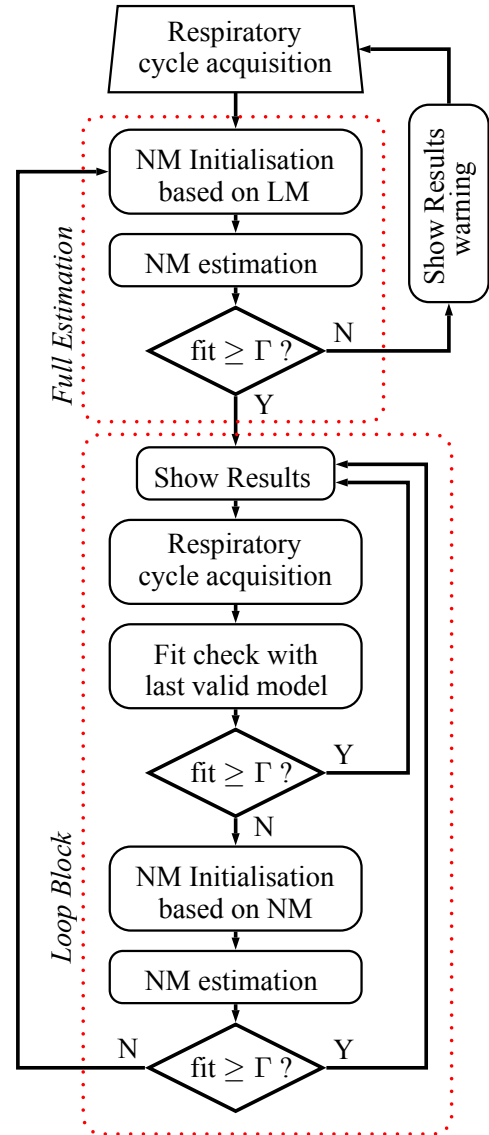


Figure 2: Flow chart of the proposed algorithm.

tialisation of the proper Nonlinear Model estimation routine, performed next.

NM Initialisation based on LM.

Firstly, the LM is computed. To do so, standard routines of the *Matlab® identification toolbox* are used, initialised by calculating R_{aw} and C as indicated in [23]. The identification routine, based on minimisation methods, finds the parameters values that minimise the next quadratic error within the respiratory cycle:

$$M(\theta) = \sum_k \left(\hat{V}_T[k] - V_T[k] \right)^2. \quad (4)$$

\hat{V}_T is the tidal volume computed using the estimated model (1)-(2), with the patient's current cycle P_B

pressure as input signal and parameters $\theta = \theta_L$, where $\theta_L = (C, R_{aw})$, i.e. the parameters of the model at each step of the iterative routine.

Once obtained the LM of current respiratory cycle, its value of resistance is used to generate the initial vector $\theta_N = (R_{aw}, a_1, a_2)$ for the NM estimation of the cycle, together with the values of a_1, a_2 , which are computed via a polynomial fit of (1), rewritten as

$$P_B - FR_{aw} = a_1 V_T + a_2 V_T^2. \quad (5)$$

NM Estimation.

Secondly, the nonlinear identification algorithm is run to obtain the NM of the current respiratory cycle, by minimising (4), with $\theta = \theta_N$. Note that the algorithm utilises the *Levenberg-Marquardt* method [24], although others can be used instead [25].

The goodness of fit obtained by the NM is quantified for the cycle by a normalised root-mean-square error

$$NRMSE\% = 100 \left(1 - \frac{\|V_T - \hat{V}_T\|}{\|V_T - \bar{V}_T\|} \right), \quad (6)$$

where \bar{V}_T is the mean value of V_T . This index equals 100% for a perfect fit between the model prediction and the real data ($\|V_T - \hat{V}_T\| = 0$) and diminishes with poorer adjustment. In case the model prediction is no better than using the average of the data, the error index gives 0%, as $\|V_T - \hat{V}_T\| = \|V_T - \bar{V}_T\|$.

Fit evaluation: fit $\geq \Gamma$?

Finally, the fit of the NM to the data is compared with a threshold value Γ , which corresponds to the accepted ‘percentage of adjustment’, selected and preset by the user.

In case the fit equals or exceeds Γ , the NM is taken as valid for the current respiratory cycle, and the algorithm enters the *Loop Block*.

If, on the contrary, the fit is smaller than Γ , the obtained parameters of the NM are not considered valid and they are shown in a distinctive colour as a warning. A new respiratory cycle is then acquired and a complete estimation stage has to be run on it (the algorithm reenters the *Full Estimation* block).

3.3 Loop Block

Once there is a respiratory cycle with a valid NM, its parameters are added to the plots in the user interface window (description below in *Show Results*), and the algorithm starts a loop in which it is decided, at each respiratory cycle, whether or not to refresh the last valid model.

To make the decision, the data of the next respiratory cycle is acquired and, instead of performing a full

estimation stage, a simpler computation is realised to check how the last valid NM adjusts the real data. In case it is accurate enough, i.e. the calculated fit is higher than Γ , the last NM is considered valid for the new cycle.

In case the NM is not good enough, an *NM Estimation* is performed but, this time, initialised using the last valid NM. It is likely that the patient’s condition has not changed too much, and that those initial conditions allow for a low cost and rapid convergence. A new fit check is realised and, only if this check gives is below Γ , a complete estimation stage is performed with the data, by returning to the *Full Estimation* block.

The idea behind doing these checks in the first place, is to reduce the computational burden and the use of the microprocessor’s resources, while maintaining an accurate tracking of the patient’s respiratory system evolution.

A detailed explanation of the blocks that have not been presented yet, is given below.

Fit check with last valid model

To check how the last valid NM adjusts the real data, the computation of a \hat{V}_T , obtained by feeding the last valid NM with the P_B of the current respiratory cycle as input. Then, (6) is evaluated with that \hat{V}_T and the actual V_T signal (fit check), and this fit is compared with Γ , resulting in two possible actions:

In case the fit is acceptable (fit $\geq \Gamma$), it means the NM is still valid, so there is no need for a re estimation and its parameters are kept as the valid NM for the current cycle. The loop block is thus ready to show the results, acquire the next respiratory cycle data and repeat the fit check process with them.

Otherwise, fit $< \Gamma$ indicates that the last valid NM no longer represents the patient with the required fidelity. Therefore, a new model must be obtained.

NM Initialisation based on NM.

When the last valid NM does not represent the patient anymore, a new estimation has to be performed. However, instead of directly running the full estimation stage, a simplified process is executed.

The parameter vector θ_N of the last valid NM is taken as initial condition and only the *NM Estimation* is performed. Note that the closeness of the initialisation values to the real ones increase the chance of obtaining good results [26] therefore, although the patient’s condition changed, its last valid model seems the best guess.

Show results

When the algorithm finishes processing the current respiratory cycle signals, the results are (optionally) saved and added to the parameters display boxes

in the user interface window. An illustrative presentation of its current version, still a preliminary one, can be seen in Fig. 3.

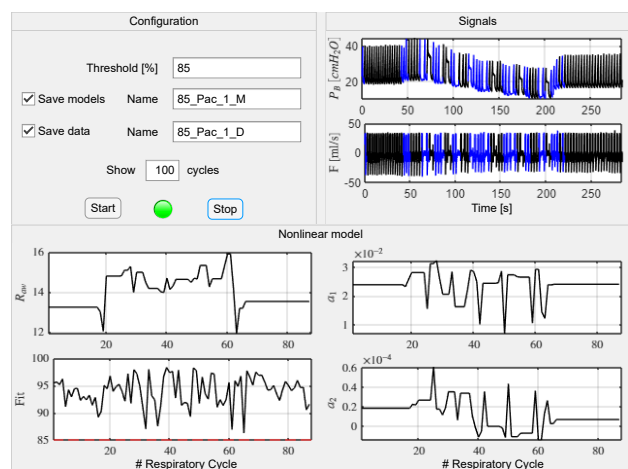


Figure 3: Preliminary user interface.

The window presents three distinguishable areas. One of them is the *Configuration* area, where the user can set the minimum accepted fit threshold, and select some saving (optional) and viewing options. Regarding the latter, the number of cycles to be shown can be chosen, with a default of 100. In case 1 is established, solely the current values of the signals, parameters and associated fit will be shown. The buttons to start and to manually stop the estimation process are also there.

A second area is identified as *Signals*, and both input signals, airflow F and pressure P_B , are shown there, in the time ranges corresponding to the set number of cycles.

Finally, the area at the bottom, headed *Nonlinear Model* displays the values of the valid NM parameters for the chosen range of last cycles, as well as their achieved fit.

In case the algorithm could not reach a fit $\geq \Gamma$, then the resulting ‘invalid’ parameters and the cycle signals are shown to the user, but using a distinctive red colour.

Regarding the displayed graphs, only a first version of the user interface is presented, while an inquiry is currently going on, in order to establish which information to present and how to show it, so that it best helps clinicians.

4 Results using real patient’s data

The main features of the algorithm are demonstrated and analysed through some tests and comparisons performed with data obtained from twelve sedated patients with COVID-19 under assisted ventilation. The

graphical results correspond to patients #1 and #2. Note that, to simplify the presentation and discussions of some results, focusing on some particular aspects, they are not shown within the user interface.

Firstly, the results obtained by the algorithm for 160 respiratory cycles of patient #1 are presented and discussed. Their original $P_B(t)$ and $F(t)$ signals can be seen in Fig. 4. A PEEP titration manoeuvre was

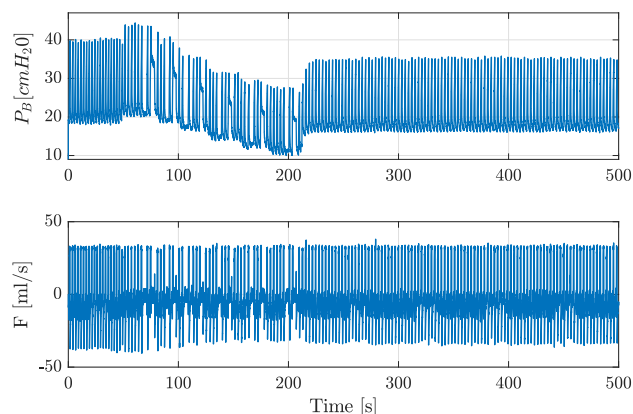


Figure 4: 160 respiratory cycles of patient #1 signals $P_B(t)$ and $F(t)$ to be processed by the algorithm.

performed on the patient during the 50 to 215 second interval. Such treatment consists in increasing the PEEP value in stepped stages until a maximum admissible pressure value is reached, and then decreasing it, making it possible to detect the region of highest compliance in the process [27]. During a manoeuvre of this kind, significant changes in the respiratory mechanics of the patients are produced [28] and, thus, it is expected that the algorithm needs to re estimate the NM at least at each change of the PEEP value.

Additionally, in order to compare results and performance, the same signals are processed using a ‘continuous estimation’ loop, where an estimation of the nonlinear model is performed undoubtedly for every respiratory cycle. Except for the first respiratory cycle, where a Full Estimation is performed, the loop consists in acquiring the next respiratory cycle and performing an NM estimation, initialised based on the last NM. The obtained estimation is taken as the valid NM whichever the fit, unless the rare case where the algorithm fails to converge. Although this did not happen for the tested data, in such a case, the cycle would be discarded and marked as ‘no model available’, and the new cycle would be initialised using the previous NM.

Therefore, the three top boxes in Fig. 5 depict the parameters of the NM of each respiratory cycle obtained when using the developed algorithm with $\Gamma = 85\%$, compared to the ones obtained by estimat-

ing a new model every cycle (continuous estimation). Additionally, the fourth plot indicates whether a new estimation was realised to obtain the NM for the cycle ('on' indication), as opposed to considering valid the previous one after the fit check ('off'). Of course, the indication corresponding to the continuous estimation process is permanently 'on'. Lastly, the fifth row shows the fits obtained in the two cases, together with the selected threshold Γ . As it can be observed

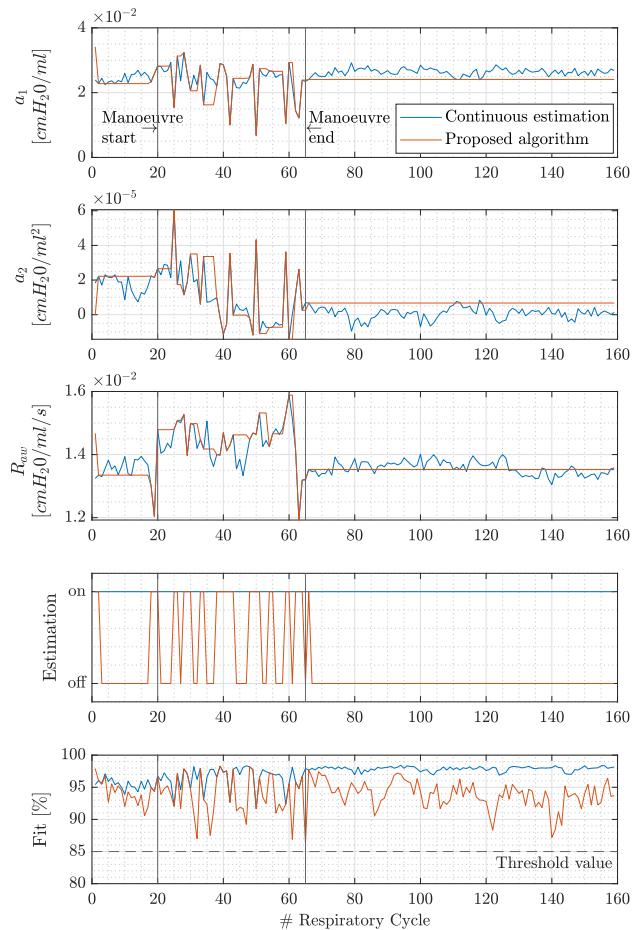


Figure 5: The upper three plots show the parameters values of the NM computed by the algorithm, compared to those obtained by continuous estimation. The fourth plot indicates whether a new estimation was realised to obtain the NM for the cycle. The last plot shows the fit obtained at each respiratory cycle.

by the 'on' indications, there are several re estimations during the PEEP titration manoeuvre but, after it, when the ventilator's configuration is set and left fixed, the estimated NM remains valid for the rest of the interval, with an accuracy higher than Γ . It is expected that the algorithm activates a new model estimation only when there is a significant change in the respiratory system, due to some health condition,

or when an irregular event occurs, i.e. the ventilator makes an inspiratory pause to measure the plateau pressure, the clinician modifies the PEEP or other setting, among others.

As it can be seen, once a new NM is estimated for one respiratory cycle with the proposed algorithm, that NM remains valid for some of the following cycles, where the fit lies between the established threshold and the maximum attainable fit, given by the continuous estimation.

In order to illustrate the advantages of performing only a fit check instead of having to re estimate a model, both the proposed algorithm and the 'continuous estimation' loop were applied to the data corresponding to twelve sedated patients of different characteristics. The times taken to process those two stages were counted, averaged and compared. Thus, Table 1 shows the relation between the average time taken to perform a fit check and the average time taken to run a 'continuous estimation'. As it can be

Patient	$t_{FC}/t_{CE} \cdot 100\%$
#1	4.16%
#2	3.68%
#3	3.94%
#4	4.72%
#5	5.08%
#6	3.87%
#7	4.06%
#8	4.82%
#9	4.02%
#10	3.91%
#11	4.89%
#12	3.29%

Table 1: Average ratio of the time per cycle taken to perform the fit check (t_{FC}) versus the time per cycle taken to perform a 'continuous estimation' (t_{CE}).

appreciated, the fit check requires a very small portion of the processing time required by a 'continuous estimation'. Therefore, it is immediate to infer that the developed algorithm allows a more efficient use of the processing resources, resulting in computational load and time reduction. The improvement of the presented algorithm over the continuous estimation method is notorious, having a favourable impact regarding less energy consumption, i.e. less use of battery and longer equipment service life of the monitoring device.

A second set of tests aims to clarify the role of the threshold Γ , illustrating how an appropriate selection could drastically reduce the required estimation time and resources, while demanding an accuracy too high may result in long-time computations and end with not being able to obtain valid models. To this end, the

algorithm was run using the data set of patient #2 using five different values for the minimum desired accuracy, in particular $\Gamma = 75, 80, 85, 90$ and 95 were selected. A PEEP titration manoeuvre was also performed on the patient, in this case during almost the whole displayed interval (160 respiratory cycles, approx. 500 sec). The $P_B(t)$ signals from each of the cases are shown in Fig. 6.

A respiratory cycle is shown in blue when a valid NM was obtained for it through a complete estimation stage; instead, a cycle is shown in black when the valid NM of the previous cycle was adequate to represent it, and therefore, kept as valid; finally, a red cycle indicates that no valid model could be obtained for that data with the required accuracy.

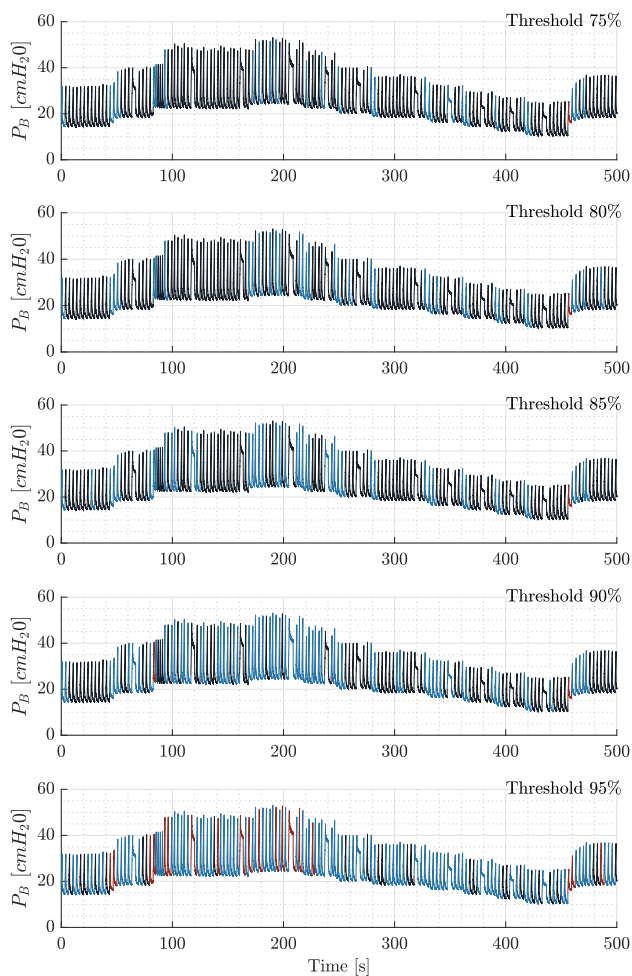


Figure 6: Signal pressure data for five different values of the threshold. The colour code indicates whether a valid NM could be obtained for each cycle, by performing a new estimation (blue) or only by a fit check (black), or not (red).

It can be immediately noted that, when a high accuracy is requested, such as when selecting $\Gamma = 95$,

the algorithm tried to obtain a new model in almost every respiratory cycle, thus increasing the computational burden. What is more, analysing the final fits, it could be noted that when a high value was specified for Γ , there were a large number of cycles where many of the NM, even the re estimated ones, failed to achieve the minimum set fit. For example, in the test with $\Gamma = 95$, only in 88% of the cycles it was possible to obtain a valid NM, and in most of them, 79%, the NM had to be re estimated. But, if Γ is set to 85%, a valid NM was obtained in 99,35% of the cycles, and only 30% of them were re estimated.

To illustrate this situation, Fig. 7 shows a few cycles of the estimated tidal volume signal \hat{V}_T , computed with the models obtained by the algorithm with $\Gamma = 95$, together with the original V_T data of the patient. Although the signals are overlapping and look practically coincident, three of the models could not reach the minimum requested fit (95%), thus the algorithm consider them invalid and they are shown in red.

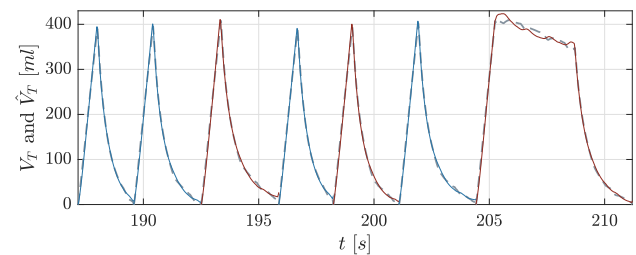


Figure 7: Interval from 187 – 211.2s of the estimated tidal volumes \hat{V}_T of patient #2, together with their original V_T data, corresponding to the test with $\Gamma = 95$ (Fig. 6, fifth row).

On the contrary, when a low value is selected for Γ , the algorithm performs less calculations at the expense of showing parameters values that less accurately represent the patient. When Γ is around 85 or 90%, a good compromise between getting a good model and computational load is achieved. In some cases there is no noticeable improvement, such as during the PEEP titration manoeuvre in the examples, as the patient's description needed to be constantly refreshed and the estimation process was activated at least at each change of PEEP value, no matter the Γ . However, once the manoeuvre was finished and the patient was ventilated with stable P_B and F signals, a new estimation had to be activated only in a few respiratory cycles, except when an almost perfect fit is solicited (see both Figs. 5 and 6).

Note that, during some situations or changes, it is not possible to obtain a valid NM, even with a not so exigent accuracy requirement. This is the case that

can be observed for the time interval 452.5 – 469.5s, where one cycle is shown in red for all the five presented tests (see Fig. 6). The estimated tidal volumes \hat{V}_T for these cycles are shown together with their original V_T data, corresponding to the algorithm test with $\Gamma = 85$ are depicted in Fig. 8. The red cycle, where

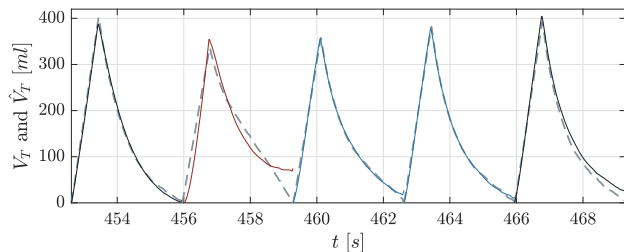


Figure 8: Five-cycles window of the estimated tidal volumes \hat{V}_T of patient #2, together with their original V_T data, corresponding to the time interval 452.5 – 469.5s of the algorithm test with $\Gamma = 85$ (see Fig. 6, third row).

no valid NM could be obtained with any of the tested thresholds, possibly corresponds to the large step set for the PEEP at the end of the PEEP titration manoeuvre.

5 Conclusions

A new method to obtain online the model of the respiratory system of patients under assisted ventilation was presented. Typically, standard equipment rely on linear models, allowing low computational burden for real-time implementation, at the expense of accuracy. Conversely, the proposed algorithm works with a more accurate nonlinear characterisation, and it proved to be able to provide the parameters' values of the nonlinear model ensuring a fit greater than a threshold Γ , without necessity to re-estimate the model in every respiratory cycle.

Therefore, the main advantages of this algorithm are twofold. In the first place, enhanced modelling can be attained with the nonlinear characterisation, and with an accuracy that can be selected by the clinicians in accordance with the required estimation fit. In the second place, after an empirical analysis, it was established that setting the threshold Γ to get a fit between 85% - 90%, resulted in a satisfactory trade-off between good accuracy and reduced computational cost (such percentage can be adjusted, in case it is needed for any particular patient). Effectively, for this range of Γ , it was observed that the estimation was triggered in those respiratory cycles with an irregular event, but during regular cycles the process was rarely activated. The consequent decrease in computation

time, compared to continuous estimation algorithms, contributes to its implementation in actual equipment.

Ongoing work on this research aims to investigate how to improve, not only the algorithm efficiency, but also the user interface. Joint discussions with clinicians are being held, regarding which results to show and the better format for them, to maximise its usefulness while treating a patient. Additionally, an offline analysis of the nonlinear models obtained by using the estimation algorithm with a large group of varied patients is also in progress, in order to draw conclusions on the potential of the tool.

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Contribution of Individual Authors to the Creation of a Scientific Article (Ghostwriting Policy)

The authors equally contributed in the present research, at all stages from the formulation of the problem to the final findings and solution.

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Conflicts of Interest

The authors have no conflicts of interest to declare that are relevant to the content of this article.

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