Implementation of a Non-Linear Autoregressive Model with Modified Gauss-Newton Parameter Identification to Determine Pulmonary Mechanics of Respiratory Patients that are Intermittently Resisting Ventilator Flow Patterns

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Abstract: Modelling the respiratory system of intensive care patients can enable individualized mechanical ventilation therapy and reduce ventilator induced lung injuries. However, spontaneous breathing (SB) efforts result in asynchronous pressure waveforms that mask underlying respiratory mechanics. In this study, a nonlinear auto-regressive (NARX) model was identified using a modified Gauss-Newton (GN) approach, and demonstrated on data from one SB patient. The NARX model uses three pressure dependent basis functions to capture respiratory system elastance, and contains a single resistance coefficient and positive end expiratory pressure (PEEP) coefficient. The modified GN method exponentially reduces the contribution of large residuals on the step in the coefficients at each GN iteration. This approach allows the model to effectively ignore the anomaly in the pressure waveform due to SB efforts, while successfully describing the shape of normal breathing cycles. This method has the potential to be used in the ICU to more robustly capture patient-specific behaviour, and thus enable clinicians to select optimal ventilator settings and improve patient care.

Keywords: Autoregressive Models, Parameter Identification, Biomedical Systems, Nonlinear Systems

1. INTRODUCTION

Acute respiratory distress syndrome (ARDS) patients in the intensive care unit (ICU) require mechanical ventilation (MV) for breathing support (Esteban *et al.*, 2002). MV pushes air into the lungs and ensures gas exchange is maintained (Girard and Bernard, 2007). Positive end expiratory pressure (PEEP) is a key MV therapy setting (Gattinoni *et al.*, 2010). A PEEP that is too high can damage healthy alveoli (Ricard *et al.*, 2002), and a PEEP that is too low can result in insufficient oxygenation, and cyclic opening and closing of alveoli with each breath (Baumgardner *et al.*, 2013). When sub-optimal ventilator settings cause injury to the lungs, this is known as ventilator induced lung injury (VILI) (Slutsky and Ranieri, 2013). A lung model that captures patient-specific behaviour could enable individualised mechanical ventilation, reduce the incidence of VILI, and help reduce patient morbidity and mortality (Fenstermacher and Hong, 2004) (Rees *et al.*, 2006).

Spontaneously breathing (SB) patients apply their own inspiratory efforts on top of a ventilator supported breathing cycle. These SB efforts can result in abnormal airway pressure curves, or 'M' shaped pressure curves (M-waves), (Akoumianaki *et al.*, 2013), as shown in Fig. 1. The M-wave pressure curve masks the underlying respiratory mechanics from identification since the exact SB effort is unknown and effectively random. Therefore, a method is required to overcome the impact of the M-waves to provide a consistent model-based estimation of respiratory mechanics for clinical use.

A nonlinear autoregressive (NARX) model of the respiratory system has been proposed by Langdon *et al.* (2015) that successfully describes pressure curves in patient data across increasing PEEP steps. The model uses pressure dependent elastance by incorporating basis functions, and uses multi-valued resistance terms to capture lung relaxation during an end-inspiratory pause. In this paper, the NARX model is applied to M-wave data in conjunction with a modified version of the Gauss-Newton (GN) parameter identification algorithm. The modified GN method has previously been used to ignore contributions from outlying data by finding the parameter set that fits the majority of the data points, rather than the least squares optima for all data points (Docherty *et al.*, 2014). The aim was to use these two approaches to model respiratory mechanics while effectively ignoring M-waves in the pressure signal.

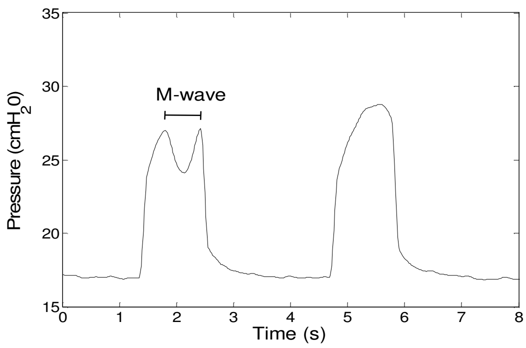

Fig. 1. Pressure data containing an M-wave and a normal breath.

2. MATERIALS AND METHODS

2.1 Data

Data were obtained from a respiratory failure patient diagnosed with pneumonia and ventilated with a Puritan Bennett 840 (PB840) ventilator. The available data spans approximately 80 minutes, where the patient was ventilated using a synchronous mandatory ventilator (SIMV) in volume controlled mode at a respiratory rate of 15-16 breathing cycles per minute. Over 65% of the breathing cycles contained some degree of M-wave shape. PEEP was constant at P_0 = 17 cmH_2O. The airway pressure and flow signals from the ventilator were recorded using specialised software (Szlavecz *et al.*, 2014). Approval for the use of this data was given by the New Zealand South Regional Ethics Committee (Ethics no: 13STH84).

2.2 Respiratory Models

The first order model (FOM) is a simple model that captures the respiratory system in an elastic and resistive component:

$$P(t) = R\dot{V}(t) + EV(t) + P_0, \tag{1}$$

where P is the measured airway pressure (cmH_2O), t is time (s), R is the Poiseuille airway resistance (cmH_2Os/L), $\dot{V}$ is the airway flow rate, E is the pulmonary elastance (cmH_2O/L), V is the inspired volume (L), and P_0 is the offset pressure (cmH_2O).

The FOM was used as a comparison with the NARX model, which is described:

$$P(t) = \sum_{i=1}^{M} a_i \emptyset_{i,d}\big(P(t)\big)V(t) + \sum_{j=0}^{L} b_j \dot{V}(t_{-j}) + P_0 \tag{2}$$

where a_i and b_j, are the parameters to be identified. M is the number of basis-functions to be used, $\emptyset_{i,d}$ is a particular basis function of degree d, a_i is the coefficient for a given basis function, and $\emptyset_{i,d}\big(P(t)\big)$ is the basis function value for a given pressure measurement. The sum of the basis functions multiplied by their a_i coefficients represent elastance through pressure. There are L b_j coefficients that represent the effect of airway resistance to flow and changes in flow. The FOM can be replicated with $M = L = 1$, and $d = 0$.

Hence, the pressure dependent elastance can be defined:

$$E(P) = \sum_{i=1}^{M} a_i \emptyset_{i,d}\big(P(t)\big) \tag{2a}$$

Zeroth order basis-functions ($d = 0$) are square functions:

$$\emptyset_{i,0}(P) = \begin{cases} 1 & if\ P_i \le P < P_{i+1} \\ 0 & otherwise \end{cases} \tag{3}$$

where P_i are division points (also known as knots) that subdivide the interval $0 \le P \le P_{\max}$. Basis functions of higher degrees are defined recursively (de Boor, 1972):

$$\emptyset_{i,d}(P) = \frac{P - P_i}{P_{i+d} - P_i}\emptyset_{i,d-1}(P) + \frac{P_{i+d+1} - P}{P_{i+d+1} - P_{i+1}}\emptyset_{i+1,d-1}(P) \tag{4}$$

In previous work, the NARX model parameter values were M = 5, d = 1, L = 350 to provide a good fit to the data (Langdon *et al.*, 2015). The large L value allowed an end-expiratory pause to be captured. However, the M-wave data set does not contain this pause, and thus L = 1 is appropriate for this study.

First degree basis functions are appropriate in this case as previous work indicated an improvement over zeroth degree functions, and no significant difference in outcomes for second degree functions. The choice of M depends on the range of pressures in the data. As the M-wave data set contains a constant PEEP, the range of pressures is limited. Thus, a smaller number of basis functions can be used. An M value of 3 was used in this analysis as it provided a robust result for the smaller pressure range data (Fig. 2).

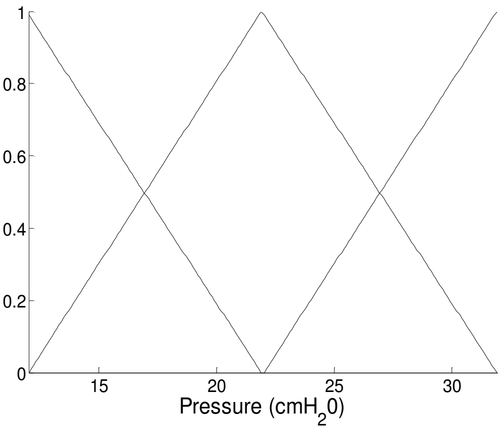

Fig. 2. First degree basis functions for $12 \le P \le 32$ with $P_i \in [12, 22, 32]$ cmH_2O.

2.3 Modified Gauss-Newton

The original Gauss-Newton parameter identification method uses an iterative process which updates the parameter set at each iteration, i:

$$\mathbf{x}_{i+1} = \mathbf{x}_i - (\mathbf{J}^{\mathrm{T}}\mathbf{J})^{-1}\mathbf{J}^{\mathrm{T}}\boldsymbol{\psi} \tag{5}$$

where:

$$\mathbf{J} = \left[\frac{\delta\psi_j}{\delta x_k}\right] = \begin{bmatrix} \frac{\delta\psi_1}{\delta x_1} & \frac{\delta\psi_1}{\delta x_2} & \cdots & \frac{\delta\psi_1}{\delta x_n} \\ \frac{\delta\psi_2}{\delta x_1} & \frac{\delta\psi_2}{\delta x_2} & \cdots & \frac{\delta\psi_2}{\delta x_n} \\ \vdots & \vdots & \ddots & \vdots \\ \frac{\delta\psi_m}{\delta x_1} & \frac{\delta\psi_m}{\delta x_2} & \cdots & \frac{\delta\psi_m}{\delta x_n} \end{bmatrix} \tag{6a}$$

$$\boldsymbol{\psi} = [\psi_j] = [\,P(\mathbf{x}_i, t_j) - P_{M,j}\,] = \begin{bmatrix} P(x_i, t_1) - P_{M,1} \\ P(x_i, t_2) - P_{M,2} \\ \vdots \\ P(x_i, t_m) - P_{M,m} \end{bmatrix} \tag{6b}$$

and P_M is the measured pressure, $\mathbf{x}$ is the vector of model parameters, $\boldsymbol{\psi}$ is the residual vector, $\mathbf{J}$ is the Jacobian of $\boldsymbol{\psi}$, j is the sample index (j = 1…m), k is the parameter index (k = 1…n), $P(\mathbf{x}_i, t_j)$ is the simulated value of P at $t = t_j$, and $P_{M,j}$ is the measured value of P at $t = t_j$.

The original GN method leads to a least squares optimisation. The adapted method replaces $\boldsymbol{\psi}$ with $\widehat{\boldsymbol{\psi}}$:

$$\widehat{\boldsymbol{\psi}} = [\hat{\psi}_j] = \psi_j e^{\frac{-|\psi_j|}{\beta|\tilde{\psi}|}} \tag{7}$$

where $|\tilde{\psi}|$ is the median of the absolute values of the residuals, and β is a scaling factor. It is important to note that the Jacobian is a function of the residual vector $\boldsymbol{\psi}$, but not a function of $\widehat{\boldsymbol{\psi}}$.

$\widehat{\boldsymbol{\psi}}$ changes how each residual error value contributes to the magnitude of the step to adjust **x**, compared to the original GN method. In the original GN, the contribution to the change in **x** at each iteration increases with the square of the error. Therefore, if undesired outliers exist in the data, they have a large effect on the direction of convergence, and the resulting model may not represent the majority of the data points.

When $\widehat{\boldsymbol{\psi}}$ is used, the contribution of residuals greater than a certain value decreases exponentially. Therefore, large outliers will not greatly affect the result. The value of β determines where the exponential decrease becomes influential, with respect to model residuals at the *i*th iteration. A β value of infinity means that the original GN method is applied as ψ_j is multiplied by one. However, if β is small, the approach will ignore important characteristics that define the system (Docherty *et al.*, 2014).

2.4 Analysis

The FOM and the NARX model were identified using the entire ~80 minutes of ventilation data. The β parameter was varied to determine an optimal number for ignoring M-waves, and results were compared to the original GN method (β = Inf) for both the FOM and NARX model. The GN initial values were chosen by evaluating the FOM and the NARX model via direct inversion. All analysis was undertaken on an i7 quad core PC with 16GB RAM using 64 bit MATLAB, version 2014a (MathWorks, Natick, MA).

3. RESULTS

Figs. 3 and 4 show a section of the data containing both M-wave breaths and normal breaths. The FOM produced similar results with the original GN method and modified GN with β = 4. In comparison with the FOM, the NARX model was able to better match the peak pressure in normal breaths and better fit the expiration curve in all breaths. The NARX model with β = 4 is also able to successfully ignore M-waves. When β = Inf, the NARX model provides a better fit to the data than the FOM, as expected, because the NARX model is more complex as it contains a larger number of identified parameters. However, in this case, this improvement is undesirable because our aim is to ignore M-waves rather than capture them.

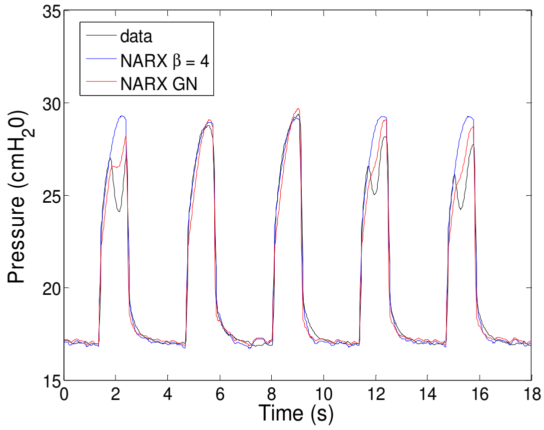

Fig. 3. M-wave pressure data and the NARX model identified with original GN method (β = Inf) and modified GN method (β = 4).

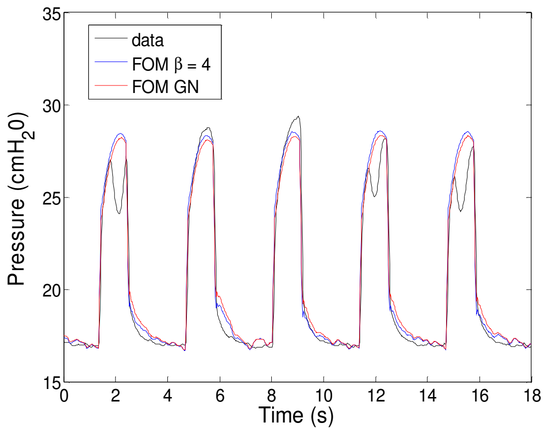

Fig. 4. M-wave pressure data and the FOM identified with original GN method (β = Inf) and modified GN method (β = 4).

Fig. 5 shows the effect of varying β on the NARX model output pressure. A β value that is too low means that the model is unable to capture the shape of the inspiratory curve, and unable to reach the peak pressure in the breath. If β is too high the model tends to start following the M-wave curve rather than ignoring it, and also tends to slightly undershoot the inspiratory curve. In this analysis, β = 4 was the optimal number that allowed the model to capture the shape of normal breaths as well as ignore M-waves.

Of note, for the NARX model, 2000 GN iterations were required for coefficient convergence for β = 2, whereas 150 iterations were sufficient for β = 4, 6, and 8. For the original GN method, only two iterations were required. For β = 1, the coefficients did not converge when tested up to 3000 iterations. Fig. 6 verifies that the NARX model coefficients have converged after 150 iterations of the modified GN algorithm. 150 iterations took approximately 12.5 seconds to complete.

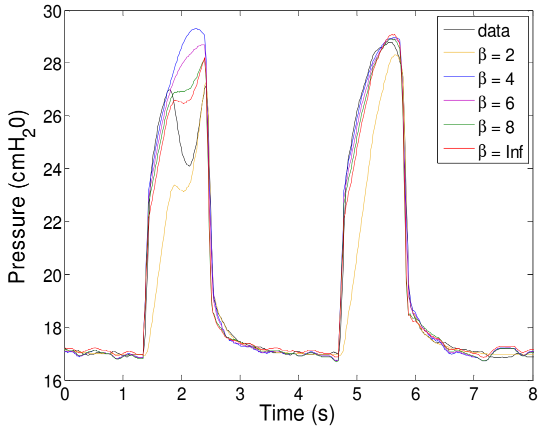

Fig. 5. Airway pressure data and the NARX model identified with GN for β = 2, 4, 6, 8, and Inf.

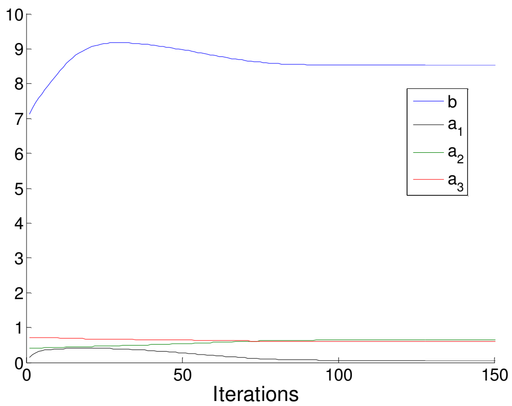

Fig. 6. Convergence of NARX model coefficients with β = 4.

Table 1 presents the root mean square (RMS) residuals for both the NARX model and FOM for the original and modified GN methods. Table 2 shows the identified coefficient values. Both methods applied to the FOM resulted in similar coefficients and residuals, giving rise to the similar plots in Fig. 4. The FOM resistance coefficients are 25% or more higher than the corresponding NARX model resistance coefficients. Fig. 7 shows how the elastance coefficients in the NARX models change through pressure. In contrast, one elastance parameter exists for all pressure in the FOM.

Table 1. FOM and NARX RMS residuals for the original and modified GN

	RMS residual (cmH_2O)
NARX β = Inf	0.853
NARX β = 4	1.123
FOM β = Inf	1.128
FOM β = 4	1.182

Table 2. FOM and NARX model coefficients for the original and modified GN

	Elastance (cmH_2O/L)			Resistance (cmH_2Os/L)
NARX β = Inf	0.254	0.428	0.733	7.286
NARX β = 4	0.055	0.644	0.606	8.521
FOM β = Inf	0.521			9.547
FOM β = 4	0.525			10.765

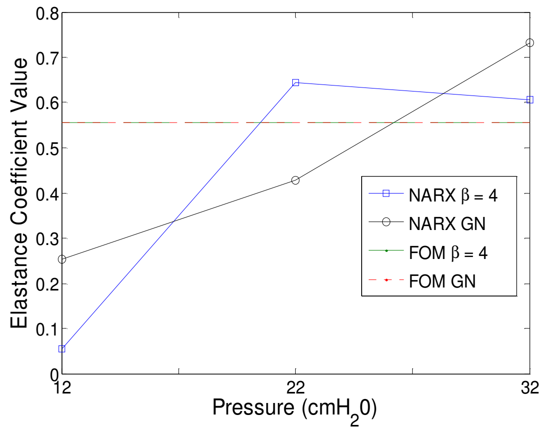

Fig. 7. Elastance coefficients through pressure for the NARX and FOM models.

Fig. 8 (a) and (b) shows undesirable behaviour in expiration that the models sometimes exhibit. The behaviour corresponds with oscillation in the flow measurements that are caused by the patient's SB efforts when the ventilator is in expiration mode (Fig. 8 (c)). The upwards blips in the airway pressure during expiration exists in both the FOM and NARX models, and with both the original and modified GN methods.

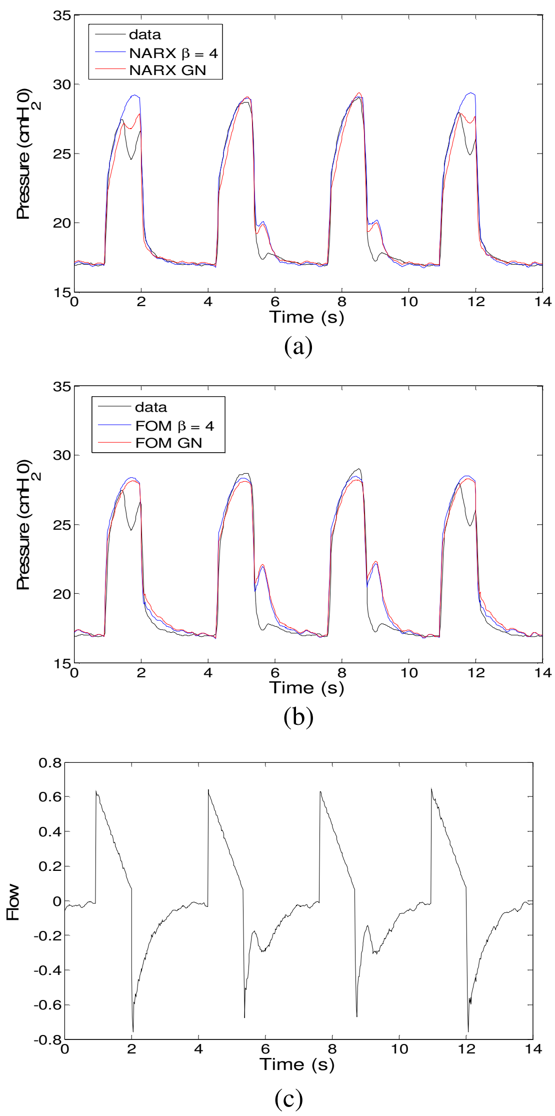

Fig. 8. Airway pressure with undesired model behaviour in expiration for the NARX (a), and FOM (b), and the corresponding flow measurement data (c).

4. DISCUSSION

The NARX model was successfully fitted to the patient data using the modified GN method with $\beta = 4$. The approach was able to effectively describe the shape of inspiration in normal breaths and ignore the M-waves in breaths where SB occurred. In comparison to the FOM, the NARX model was able to better capture the expiratory curve, and fit to the peak pressure of each normal breath, as shown in Fig. 3 and Fig. 4.

Fig. 5 indicates that $\beta = 4$ was optimal in this analysis for effectively ignoring M-waves. Assuming the residual error is normally distributed, the value of β equals the number of standard deviations (SD) of the error distribution that is between the peaks of the objective contribution shape (Docherty *et al.*, 2014). For example, when $\beta = 2$, the largest contribution to the step in $\mathbf{x}$ happens for residuals that are two SDs from the mean. For residuals smaller than two SD, the contribution increases with the square of the residual, and for errors larger than two, the contributions decrease exponentially. Thus, when β was small, the contribution of much of the valuable information was small and the model was not able to capture the shape of the breaths. However, when β is large, the contributions from only very large residuals are preferentially reduced by GN, so the method approaches the original GN method, and the model becomes a better fit to the measured data so M-waves begin to be followed rather than ignored.

Table 1 indicates that the NARX model with the original GN method was better than the FOM at providing a best fit to the data, according to least squares criterion. This outcome is primarily facilitated by the use of three elastance coefficients that depend on pressure, compared to the single elastance FOM coefficient (Table 2, Fig. 7). The difference in resistance coefficients of over 25% between the FOM and NARX model would have also played a role. These factors allowed the NARX model to partially capture M-waves (Fig. 3), which the simpler FOM was unable to do (Fig. 4).

The NARX model with the modified GN method resulted in a larger RMS residual value compared to the original GN method (Table 1). This outcome is an expected and desired result because the modified GN method has allowed the M-waves in the data to be ignored. The model follows the shape of normal inspiration in breaths where M-waves exist. Thus, the model residuals are large in these regions. Since most breaths contain some degree of M-wave, the NARX RMS residual for the modified GN method is significantly larger than for the NARX identified with the original GN.

The NARX model with $\beta = 4$ resulted in an RMS residual that was similar to those of the FOM models. This result occurred because the FOM similarly did not fit the M-waves, as the model is too simple to capture this type of behaviour. However the FOM was not able to reach the peak inspiratory pressure in normal breaths, and also tended to provide a worse fit to the data during expiration, compared to the NARX model. Thus, the NARX model with $\beta = 4$ had a slightly lower RMS residual.

Assuming the residuals are normally distributed, use of the modified GN method should have no negative effects when outlier behaviour does not exist in the data, and the result in this case should closely match the outcome of the original GN method (Docherty *et al.*, 2014). Thus, the method could safely be used to provide clinicians with patient-specific information in situations where the patient is not spontaneously breathing, as well as when SB is present. A small time penalty would occur due to the extra calculations per iteration, in order to compute $\widehat{\boldsymbol{\psi}}$, but this would be negligible over the small number of GN iterations that are required for coefficient convergence.

Fig. 7 showed that oscillations in the flow measurements cause the models to fail to capture the appropriate expiratory curve. This flow characteristic is caused by the patient's spontaneous breathing efforts while the ventilator is in the expiration part of the breathing cycle. As the inspiratory pressure curve is the important part of the breath used by clinicians to determine ventilator settings, this effect is not a significant problem. A method to smooth out the flow oscillation before identifying the model could be employed in future work, e.g. by using the expiratory time constant calculated from other breaths (Van Drunen *et al*., 2013).

The patient had many instances of SB during the ventilation period, as over 65% of breaths contained an M-wave. The success of the method under these conditions suggests it could be useful in monitoring many SB patients, though it is not clear whether the approach would still be useful in situations where an even larger percentage of breaths contain M-waves. The β value or NARX model parameters could potentially be adjusted to allow the model to successfully fit other situations such as this.

The modified GN method cannot be used to identify the model across data where the patient state changes, e.g. due to lung recruitment or over-distension caused by a PEEP increase. The reason for this limitation is because breaths that have different characteristics to the majority of data will be treated as outliers and will not be tracked by the model. This issue could be reduced by accounting for known PEEP changes in the model and identification, though investigation with a larger patient cohort is required to further establish the efficacy of the method.

The method requires only the use of airway pressure and flow data which are typically measured for each patient in the ICU, and it was identifiable in real time with only 150 GN iterations (Fig. 6), taking 12.5 seconds. Therefore the method is simple enough to be used in the ICU to track patient state. The output pressure data could be used by clinicians to set patient-specific ventilator settings, leading to improved patient care and outcomes. Comparing the output pressure with the original M-wave pressure curves could also give clinicians an indication of the breathing effort of the patient, which can be useful in determining when to extubate the patient (Boles *et al*., 2007).

5. CONCLUSION

A nonlinear autoregressive model was used to model the airway pressure curve in a patient breathing spontaneously on top of mechanical ventilation support. The model was identified using a modified Gauss-Newton parameter identification method, which allowed M-waves caused by SB efforts to be successfully ignored. The NARX model provided an improvement over the FOM, which was unable to match the peak pressure in normal breaths. The successful elimination of M-waves allows respiratory mechanics to be more accurately estimated, which could enable patient-specific ventilation, and thus improve conditions for patients.

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