

Assessing Mechanical Ventilation Asynchrony through Iterative Airway Pressure Reconstruction

Yeong Shiong Chiew¹, chiew.yeong.shiong@monash.edu

Chee Pin Tan¹, tan.chee.pin@monash.edu

J. Geoffrey Chase², geoff.chase@canterbury.ac.nz

Yeong Woei Chiew³, cyeongwoei@yahoo.com

Thomas Desaive⁴, tdesaive@ulg.ac.be

Azrina Md Ralib⁵ azrinar@iium.edu.my

Mohd Basri Mat Nor⁵ m.basri@iium.edu.my

¹School of Engineering, Monash University, Subang Jaya, Malaysia

²Centre for Bioengineering, University of Canterbury, Christchurch, New Zealand

³Lam Hwa EE Hospital, Pulau Penang, Malaysia,

⁴GIGA Cardiovascular Science, University of Liege, Liege, Belgium

⁵Department of Intensive Care, International Islamic University Malaysia Medical Centre,
Kuantan, Malaysia

Corresponding Author: Yeong Shiong Chiew

Abstract:**Background and Objective:**

Respiratory mechanics estimation can be used to guide mechanical ventilation (MV) but is severely compromised when asynchronous breathing occurs. In addition, asynchrony during MV is often not monitored and little is known about the impact or magnitude of asynchronous breathing towards recovery. Thus, it is important to monitor and quantify asynchronous breathing over every breath in an automated fashion, enabling the ability to overcome the limitations of model-based respiratory mechanics estimation during asynchronous breathing ventilation.

Methods:

An iterative airway pressure reconstruction (IPR) method is used to reconstruct asynchronous airway pressure waveforms to better match passive breathing airway waveforms using a single compartment model. The reconstructed pressure enables estimation of respiratory mechanics of airway pressure waveform essentially free from asynchrony. Reconstruction enables real-time breath-to-breath monitoring and quantification of the magnitude of the asynchrony (M_{Asyn}).

Results and Discussion:

Over 100,000 breathing cycles from MV patients with known asynchronous breathing were analyzed. The IPR was able to reconstruct different types of asynchronous breathing. The resulting respiratory mechanics estimated using pressure reconstruction were more consistent with smaller interquartile range (IQR) compared to respiratory mechanics estimated using asynchronous pressure. Comparing reconstructed pressure with asynchronous pressure waveforms quantifies the magnitude of asynchronous breathing, which has a median value M_{Asyn} for the entire dataset of 3.8%.

Conclusion:

The iterative pressure reconstruction method is capable of identifying asynchronous breaths and improving respiratory mechanics estimation consistency compared to conventional model-based methods. It provides an opportunity to automate real-time quantification of asynchronous breathing frequency and magnitude that was previously limited to invasively method only.

Keywords: Mechanical ventilation; asynchrony; respiratory mechanics; asynchronous magnitude.

1.0 Introduction

Model-based estimation of respiratory mechanics has shown increasing potential in intensive care mechanical ventilation (MV). Respiratory mechanics information can be used to guide MV settings, such as setting positive end-expiratory pressure (PEEP) and fraction of inspired oxygen [1, 2]. However, accurate patient-specific respiratory mechanics estimation is a challenging task due to the heterogeneous nature of patient disease state, and patient- and breath- specific response to MV. In particular, respiratory mechanics estimation depends on the identifiability of the mathematical model used, as well as the quality of measured data [3-5]. Inaccurate parameter identification can occur due to asynchronous breathing or any spontaneous breath that is not in synchrony with the ventilator delivered breathing and ventilation mode. These breaths can occur any time, whether the patient is fully or partially ventilated, and significantly alter the breathing waveforms, modifying them to unconventional shapes. These asynchronous, patient-specific inputs and modified waveforms are not able to be modelled, as they are unpredictable. Hence, parameter estimation returns erroneous respiratory mechanics parameters, limiting clinical use of respiratory mechanics estimation in the clinical environment [6].

In addition to parameter estimation failure, asynchronous breathing is often not monitored nor modelled due to lack of real-time monitoring tool, although methods for clinical interpretation and reading of waveforms at the bedside to detect asynchrony as it happens or is observed are reviewed in Georgopoulos et al. [7]. Hence, asynchronous breaths are often analysed retrospectively and manually to obtain the asynchronous index (AI) and to assess MV quality. Asynchronous breaths are thus hidden threats that can increase MV work of breathing, reduce arterial oxygenation, prolong length of MV, increase ventilator dependence, and have other potential adverse outcomes

[8-10]. Thus, there is a need of a method to monitor asynchronous breathing and it is important to account for asynchronous breaths during respiratory mechanics estimation [11]. It is equally imperative these methods are not additionally invasive and do not induce further stress to patients.

Different methods have been examined to overcome such issues. Vicario et al. [12], Chiew et al. [13] and Maes et al. [14] have developed and investigated mathematical models that can capture respiratory mechanics during spontaneous breathing MV. Major et al. and Redmond et al. investigated on models and signal processing methods to predict and obtain reliable data [15, 16]. Similarly, methods have been proposed to automatically monitor asynchronous breathing, but they can be invasive [17-20]. All these methods aimed to improve mechanical ventilation respiratory mechanics monitoring. However, they are also unable to model the magnitude of asynchronous breathing, and thus it is not possible to fully assess the impact of asynchrony on patients and outcomes.

This study presents an airway reconstruction method to better estimate respiratory mechanics of breaths affected by asynchronous events and to quantify its asynchronous magnitude. This method eliminates the effect of asynchrony observed in an asynchronous airway pressure [7] by creating a new airway pressure waveform free from asynchrony. This ‘free’ airway pressure enables a more consistent respiratory mechanics calculation to be performed. In addition, the ‘free’ airway pressure can be compared to the original asynchrony airway pressure to measure the magnitude of asynchrony that occurred. This method allows the magnitude of asynchronous breaths to be quantified, potentially providing unique insight to the frequency and severity of asynchronous breathing that can be used clinically to better manage MV.

2.0 Methods

The airway reconstruction method uses a lung mechanics model to simulate a normal breathing cycle with the aid of existing breathing data. An iterative airway pressure reconstruction (IPR) method attempts to modify the asynchronous breathing cycle to a non-asynchronous cycle using a single compartment linear lung model. The IPR algorithm presented here, is also able to monitor the magnitude of each asynchronous breaths.

2.1 Iterative Pressure reconstruction (IPR)

The IPR method consists of a 3-step iterative process to reconstruct the airway pressure of an asynchronous breathing cycle. It uses maximum original airway pressure and a model generated pressure [21]. Figure 1 shows the sequence of how an asynchronous airway pressure iteratively reconstructed to create an unaffected ‘non-asynchronous’ pressure. The main steps are defined:

Step 1: Model fitting to the asynchronous airway pressure:

The inspiratory airway pressure of an asynchronous breathing cycle is first fit using a single compartment linear lung model defined [22, 23]:

$$P_{aw}(t) = E_{rs}V(t) + R_{rs}Q(t) + P0 \quad (1)$$

Where P_{aw} is airway pressure, t is time, E_{rs} is the respiratory system elastance, V is the air volume, R_{rs} is the respiratory system airway resistance, Q is the flow and $P0$ is the offset pressure. Using the measured airway pressure and flow, the E_{rs} and R_{rs} is calculated using linear regression [2]. It is important to note that the values of E_{rs} and R_{rs} are identified individually for every breath, and

are thus breath-specific and patient-specific. The dotted line in Figure 1a shows the model fit to the asynchronous airway pressure, where the constant E_{rs} cannot account for the unmodelled asynchronous patient breathing effort, reducing the measure pressure.

Step 2: New maximum airway pressure:

The reconstruction process of a new airway pressure waveform uses the intersection between the maximum of asynchronous airway pressure and model fitted pressure. This reconstructed airway pressure begins to ‘fill’ the empty space caused by asynchronous breathing effort, as shown in Figure 1b (Blue Line). The reconstructed airway pressure is then used as a new airway pressure for model fitting using Equation 1 as shown in Figure 1c, improving the modelled pressure waveform towards one typical of a breath unaffected by asynchronous patient effort.

Step 3: Repeat model fitting and pressure reconstruction:

To provide a better approximation of the ‘non-asynchronous’ airway pressure, this process is repeated iteratively, as shown in Figures 1d to 1g for 20 iterations, where the reconstructed airway pressure converges. Figure 1g shows all iterations superimposed together, illustrating how the pressure waveform becomes ‘normal’ and unaffected by asynchrony. The final reconstructed airway pressure is the top-most pressure reconstruction curve of Figure 1g. For comparison, a typical normal airway pressure not affected by asynchrony is shown in Figure 1h.

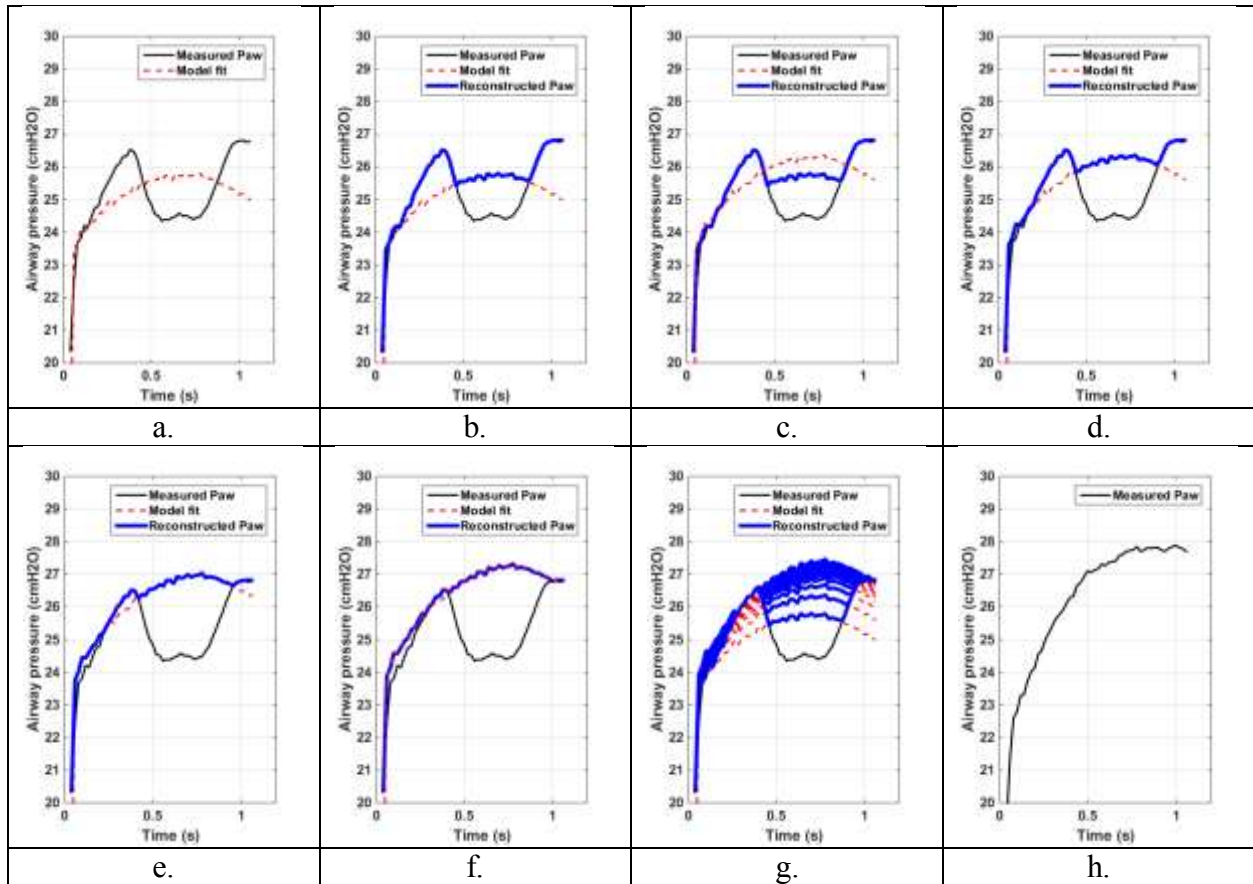


Figure 1: Iterative pressure reconstruction sequence (From (a) to (f)). (g) is the combination of 20 iteration of pressure reconstruction and (h) is the likely airway pressure curve not influenced by asynchronous breathing within 2 minutes.

2.2 Quantifying Respiratory Mechanics and Asynchronous Breathing Magnitudes

The IPR reconstructed airway pressure and original airway pressure are used to estimate respiratory mechanics elastance and resistance. E_{rsRe} and R_{rsRe} are elastance and resistance estimated from the reconstructed airway pressure whereas the E_{rsOri} and R_{rsOri} are estimated from original airway pressure. A student t-test is used to assess difference in the elastance and resistance parameter distributions to determine if the IPR method provides a measureable change in identified values. A p-value of <0.05 is considered significant.

After pressure reconstruction, computing the difference in the areas under the final reconstructed

and original airway pressure waveforms quantifies the magnitude of the patient-specific asynchronous breath input, yielding:

$$M_{Asyn} = \frac{AUC_{Rec} - AUC_{Ori}}{AUC_{Rec}} \times 100\% \quad (2)$$

where M_{Asyn} is the magnitude of the asynchrony for each breathing cycle, AUC_{Rec} is the area under the curve for the reconstructed airway pressure and AUC_{Ori} is the area under the curve of the original airway pressure.

This metric quantifies the extent to which the MV controlled breath is affected by patient-specific asynchronous breathing effort. It thus quantifies the work of this asynchronous breathing input and the severity the asynchrony in the specific breathing cycle. Hence, magnitude and frequency of asynchrony are assessed automatically using this algorithm and computations, enabling a more complete assessment of the impact of asynchrony on patients and outcomes.

2.3 Patient Data

Retrospective data from mechanically ventilated acute respiratory failure patients were used [24]. The patients were ventilated using a Puritan Bennet 840 ventilator with synchronous intermittent mandatory ventilation (SIMV) volume controlled mode using decreasing ramp flow profile (tidal volume = 6-8 ml/kg). The clinical protocol and other details of the patient data used in this study can be found in the studies conducted by Szlavecs et al. [25] and Major et al. [15]. Table 1 shows the details of the subset of patient data used here focusing on the large number of breathing cycles to demonstrate the concept, preparatory to clinical validation over large patient numbers. A total

of >100,000 breathing cycles (over 5 patient days) were analysed. These datasets provide a wide range of asynchronous breaths in shape and size of asynchrony for testing, which thus covers a wide range of observed asynchrony types and shapes. As the ventilation is set under volume controlled mode, it is likely that the asynchronies observed in breaths are ventilation reverse-triggering [26]. All data were sampled at 50 Hz and processed using MATLAB (R2014b, The Mathworks, Natick, MA, USA).

Table 1: Patient data and their cause of respiratory failure

Data No.	Cause of Respiratory Failure	Age and Sex	Number of Breathing Cycles
1	Faecal peritonitis	53 F	52030
2	Cardiac surgery and contracted hospital acquired pneumonia	71 M	33959
3	Pneumonia	60 M	30585

3.0 Results

3.1 Shapes and sizes of asynchronous airway pressure

Asynchronous airway pressure waveforms can have different shapes and magnitudes, as shown in Figures 1-4. However, if effective, the reconstruction through IPR should yield similar unaffected pressure waveform results. Figure 2 shows a second typical airway pressure, where successful pressure reconstruction occurs, in addition to the example of Figure 1.

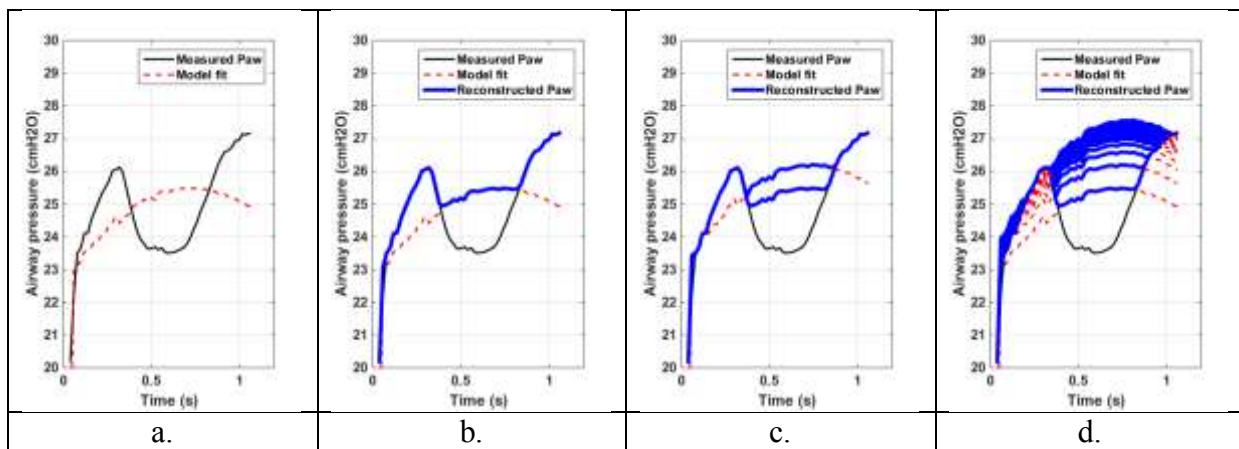


Figure 2: Pressure reconstruction performed iteratively, resulting in a non-asynchronous airway pressure

Figure 3 shows a sample of failed pressure reconstruction due to late asynchrony and how the IPR algorithm overcomes this limitation by incorporating a pressure filling algorithm (Figures 3e-h). Last, Figure 4 shows an early patient triggered breathing cycle and how IPR reconstructs the airway pressure waveform to a passive airway pressure waveform.

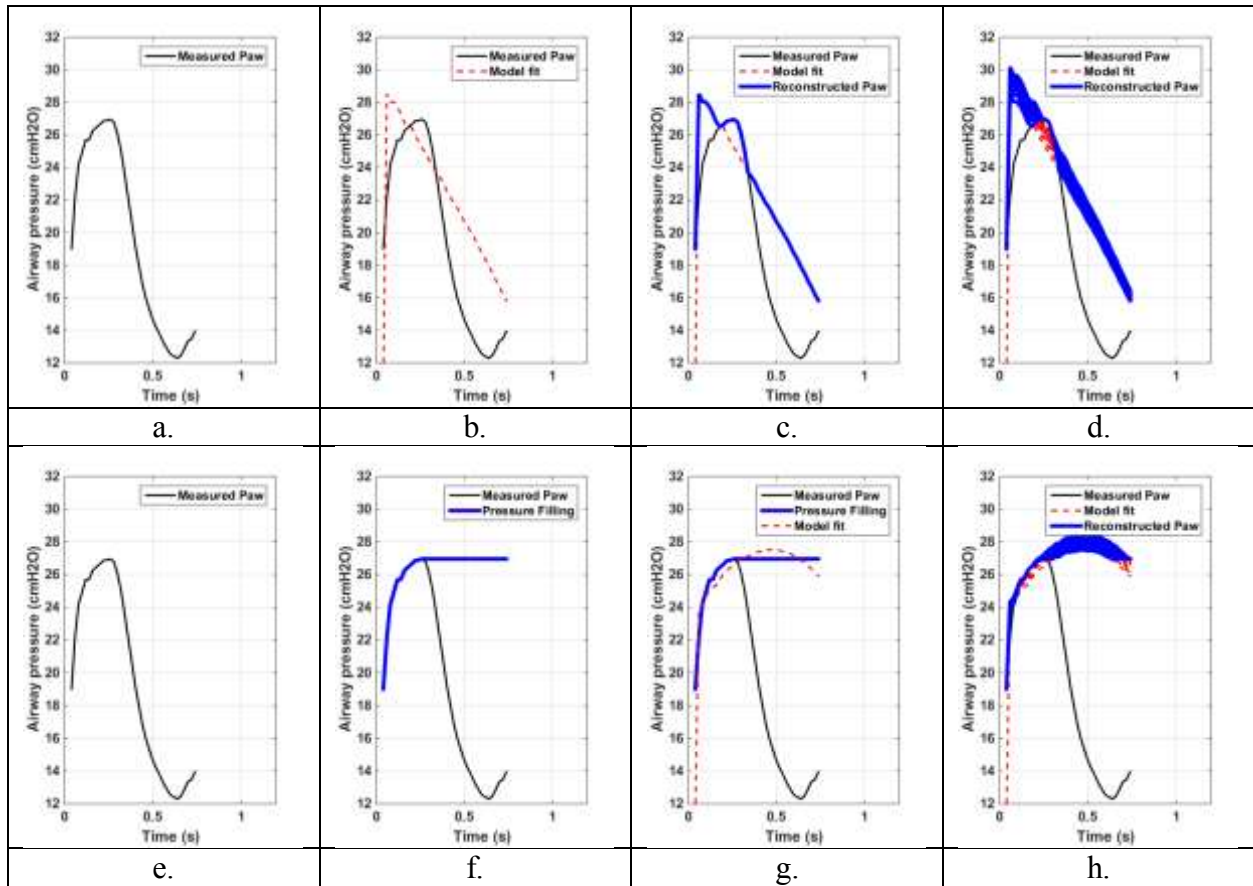


Figure 3: a-d) Fail pressure reconstruction due to missing of end of inspiratory pressure data. e- h) Successful pressure reconstruction with pressure filling.

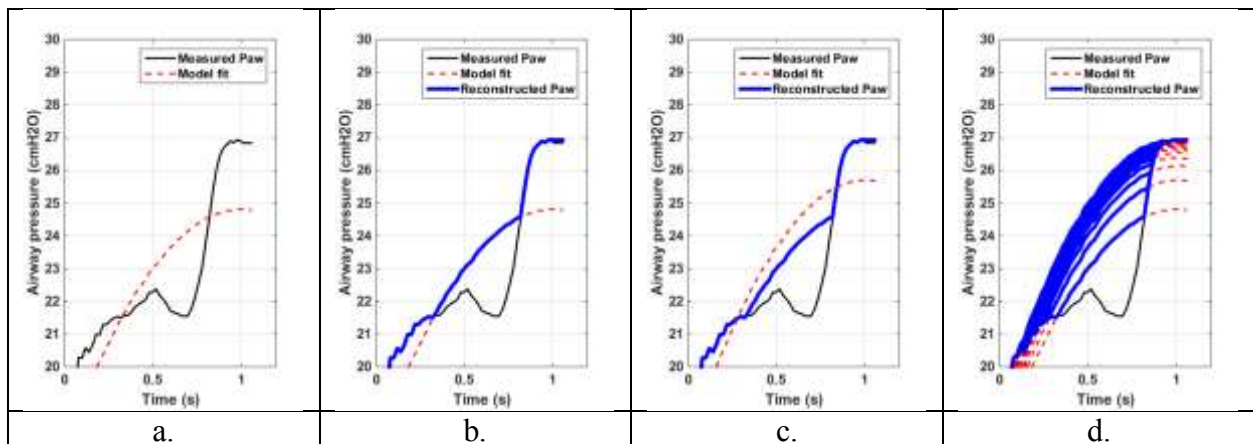


Figure 4: Early asynchrony pressure reconstruction. a) The airway pressure does not show pressure increase as start of breathing cycle due to early asynchrony. b) Pressure reconstruction for the first iteration. c) New model fit using reconstructed pressure. d) Complete pressure reconstruction.

3.2 Asynchrony Level and Respiratory Mechanics

Figure 5 (left) shows the cumulative distribution plot for all M_{Asyn} found in this dataset and Figure 5 (Right) shows the overall M_{Asyn} for the five different patient days. M_{Asyn} for the overall dataset is median 3.8% [IQR: 2.0-10.4].

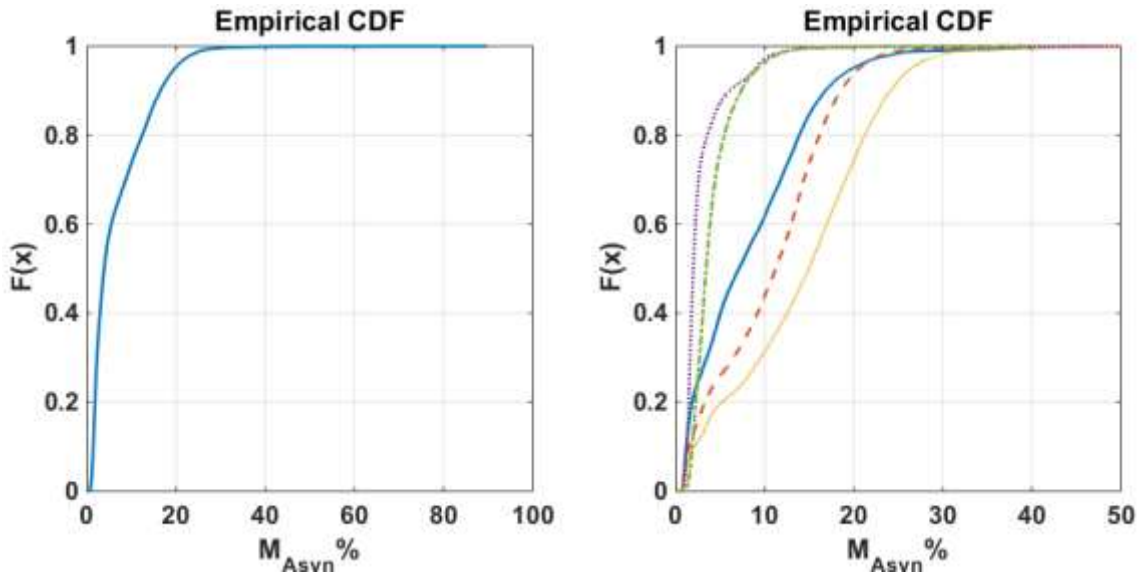


Figure 5: Empirical cumulative distribution plot (CDF) of M_{Asyn} . (Left: all patient data, Right: different patient MV days)

The respiratory elastance and resistance mechanics parameters estimated from the original airway pressure (E_{rsOri} and R_{rsOri}) for each individual breath and for each patient are median 24.9 cmH₂O/l [Interquartile range (IQR): 20.5-29.8] and 7.9 cmH₂O/s [IQR: 5.3-11.3] over 100,000 breaths. Estimated elastance and resistance after pressure reconstruction (E_{rsRe} and R_{rsRe}) are 27.8 cmH₂O/l [IQR: 24.5-31.1] and 9.5 cmH₂O/s [IQR: 7.4-11.4].

For the breathing cycles with $> 5\%$ of M_{Asyn} , which comprises of 42% of the breathing cycle, the E_{rsOri} and R_{rsOri} is 20.8 cmH₂O/l [IQR: 5.7-33.6] and 3.4 cmH₂O/s [IQR: -2.4-14.2]. After pressure reconstruction, the E_{rsRe} and R_{rsRe} are 29.8 cmH₂O/l [IQR: 25.1-34.5] and 10.6 cmH₂O/s [IQR: 6.9-12.1].

4.0 Discussion

4.1 Performance of IPR in different Asynchronies

Case 1: Typical Asynchronies

Figures 1 and 2 show two typical successful airway pressure reconstructions. At each iteration, IPR creates an intersection between old and new pressure, and then overlaying the model fit and the original airway pressure (solid line) to generate a new airway pressure waveform for model identification. As it reconstructs iteratively, the error between the model fit and reconstructed pressure waveform decreases, resulting in a non-asynchronous airway pressure waveform. In this dataset, every typical asynchronous breathing cycle follows these steps during IPR, resulting in a pressure waveform ‘free’ from asynchronous efforts.

Case 2: Late Asynchronies

In some cases, as shown in an example in Figure 3a, asynchronous breathing occurs right at the end of a MV supported breath. This late asynchrony cannot be accurately reconstructed using the typical pressure reconstruction method due to high amount of ‘missing data’ at the end of inspiration, as shown in Figures 3a-d. The reconstruction process depends on the quality of model fit using linear regression, where it attempts a best fit a passive breathing model to the data. However, if most data at the end of a breath are ‘incorrect’ or altered, the first step of pressure reconstruction will not provide a ‘correct trend’ for the iterative reconstruction process. Late asynchronies, detected when the peak pressure is not located at the end of a breathing cycle, are cases when most data are incorrect at the end of the breath requiring this adapted approach.

In late asynchrony cases, the IPR algorithm initiates a pressure filling method [21] to fill up the

asynchronous airway pressure to obtain a peak pressure value. The peak pressure value end of inspiratory pressure is assumed to be at least similar to the maximum observed airway pressure as shown in Figure 3f. Any airway pressure points between the end of inspiratory pressure and the observed peak will be ‘filled’ with an estimated maximum airway pressure, as shown in Figures 3f-g. Using the airway pressure generated through pressure filling method, the standard IPR method has enough data to create a better reconstruction of the final, unaffected airway pressure, as summarised in Figure 3h.

Case 3: Early Asynchronies

Early breathing asynchrony is shown in Figure 4a. This anomaly occurs when the initial pressure step increase due to a step or ramp airway flow increase is not observed. The missing initial airway pressure causes model fitting to fail as the increase in airway pressure is an important feature during parameter identification. During model fitting of the original airway pressure, this lack of an expected increase in pressure results in non-physiological respiratory mechanics parameters, such as negative elastance or resistance [13]. This issue is addressed by enforcing positive minimum parameter values of $E_{rs} = 5\text{cmH}_2\text{O/l}$ and $R_{rs} = 5\text{cmH}_2\text{Os/l}$ in the model identification. These parameter values give a baseline feature of the model airway pressure, resulting in better reconstruction. Figures 4a-d show example of this early asynchrony and its corresponding pressure reconstruction.

4.2 Respiratory Mechanics Estimation and Asynchrony Magnitude through Pressure Reconstruction

In this study, we presented a method to reconstruct asynchrony affected airway pressure into an

airway pressure free from asynchronies. These reconstructed airway pressure can be used to calculate more consistent respiratory mechanics of the patient during MV as they are not influenced by asynchrony. The IQR for E_{rsRe} and R_{rsRe} of the reconstructed airway pressure is smaller compared to original airway pressure. This result implies a more consistent parameter estimation occurred, as the reconstructed airway pressures are ‘free’ from variable and patient-specific asynchronies. E_{rsRe} and R_{rsRe} estimated from reconstructed airway pressure are also found significantly higher than the original unreconstructed values ($p < 0.05$). This result is as expected, where the IPR reconstructs the asynchronous airway pressure to a higher value, resulting in consistent higher respiratory mechanics values. The changes in respiratory mechanics were more apparent, when breathing cycles with 5% or more of asynchrony magnitude were included in the comparison. The $E_{rsRe5\%}$ and $R_{rsRe5\%}$ were also significantly different from $E_{rsOri5\%}$ and $R_{rsOri5\%}$ with $p < 0.05$.”

The reconstruction of the asynchronous affected airway pressure to a ‘free’ airway pressure also enables the quantification of the asynchrony magnitude, M_{Asyn} . This can be done by comparing the reconstructed pressure with original asynchronous airway pressure to estimate the magnitude of asynchrony that occurred during that breathing cycle. From the cumulative distribution plot in Figure 5, it is clear that M_{Asyn} is variable and can differ between patients and patient day. It was found that every breathing cycle has some level of asynchrony using this metric. The magnitudes of each asynchronous breath can range from as low as $<1\%$ or as high as $>25\%$ of the breath. However, it is important to note that low values of M_{Asyn} ($<5\%$) can be due to small reconstruction errors or natural breathing variability, and they may not contribute to actual asynchronous breathing. They constitute approximately 58% of the 100,000 breaths. Larger and more frequent

occurrence of M_{Asyn} may be harmful to patient recovery and thus, it is important to have a metric that can quantify the frequency, as well as the magnitude, of asynchrony for every breathing cycle continuously, which in turn requires an automated or algorithmic approach.

4.3 General

In this study, the patients were fully sedated and ventilated using the Puritan Bennett 840 on SIMV mode as per hospital practice and clinical protocol. Mandatory breaths triggered by the patient will follow the shape of the flow as set in the mechanical ventilator. The key difference is that spontaneous breaths will appear normal and be supported by the ventilator in the same fashion as a partial support mode. The waveforms will thus not be affected with, for example, falling and then rising pressure during the middle of inspiration, as seen for example in Figure 1. In this mode of ventilation (SIMV volume controlled), the shape of the pressure waveform in Figure 1h rises sharply at first, similar to pressure support modes [13, 27-29] due to the linear flow delivered in this volume control mode. Note that the steep section comprises very few points and is due to this controlled flow waveform shape and is thus not a form of pressure support or control mode of ventilation.

Volume controlled modes and SIMV are universally employed with a wealth of options available depending on clinical choice and preference. The reconstructed method presented here is limited to any volume controlled mode where the airway pressure waveforms are deranged by asynchronies. This method does not work on pressure control or support modes where the shape of the airway pressure is largely fixed and dependent on the ventilator output. In the case of pressure control or support mode with asynchronous flow waveform, a similar volume and flow

reconstruction exists for pressure controlled modes where the opposite holds true [30]. Thus, the method presented is generalizable across volume control modes, and the overall approach is generalizable with a different reconstruction algorithm to pressure support modes. Similarly, the method presented in this study is currently limited to asynchrony that occur during the inspiratory process. Asynchronies that occurred during expiration were not considered as the method only reconstruct inspiratory airway pressure. It is however, this method can be expanded to include reconstruction of the expiratory cycle particularly flow using an expiratory time constant model [31] to monitor expiratory asynchrony [17].

In the literature, the quality of patient-ventilator interaction can be assessed directly or indirectly by various metrics such as neural index [32], matching [29], correlation and variation analysis and asynchrony index (AI) [33]. Each index can be computed if certain data and measurements are available. The asynchrony index (AI) is one often-used metric, where it is determined in prior uses through laborious manual inspection of the airway pressure and flow [17]. AI, when it was introduced, focused only on quantifying phase triggering and flow asynchrony and did not include reverse triggering asynchrony until later work of Akoumianaki et al and Major et al. [24, 26]. However, the use of 'asynchrony index (AI)' is not necessarily or definitively limited to phase triggering and can be generalised for all kinds of asynchrony quantification. Equally, the concept is readily generalised to counting all kinds of asynchrony types, where each type could have its own specific index averaged into a greater whole, where this study defined asynchrony for more broadly as any airway pressure altered into nonconventional shape by any type of asynchrony, including but not limited to reverse triggering.

This simulated airway pressure generated from the IPR algorithm follows the single compartment lung model, and is able to model the passive patient airway pressure waveform as if there is no asynchronous effort. However, it is possible that this method may not necessarily reconstruct the airway pressure waveform to an original, true unaffected state. This limitation is due to the fact that the asynchronous affected pressure may have its underlying pressure waveform altered. As seen in Figures 1g and 1h, the reconstructed pressure can have lower peak airway pressure compared to a ‘normal’ breathing cycle that could be expected to be the same. Thus, it may not necessarily be perfect. However, there is no way to be certain, and the reconstructions shown are very similar to surrounding normal breaths, indicating that the reconstruction is likely quite close to the truth.

In particular, there is no means to obtain a direct measurement to compare the reconstructed pressure, and there is no way of knowing the exact airway pressure waveform without a time machine. Invasive measuring tools or specific clinical protocols that require sedation and paralysis may provide an insight to the original airway pressure. As noted in Redmond et al. [34] and Bibiano et al. [35], patient-specific respiratory mechanics are protocol dependent. Thus, only a general trend can be derived from these values and there may be no ‘absolute value’ to be compared with.

The proposed M_{Asyn} in this study is a unique metric that can be used to quantify mechanical ventilation asynchrony automatically and in real time. However, this metric has not been tested and, its impact and clinical relevance requires further investigation. The M_{Asyn} proposed in this study can be monitored at any rate or level desired. The actual use would depend on how it worked

best in the clinical environment it was employed and thus local clinical preference. This information can be used to better manage MV. Clinically, the calculation M_{Asyn} in a breath alone may not be useful, except perhaps as a measure of their effort against the ventilator, but the frequency of asynchrony over a period of time is currently more clinically useful in managing care. This metric can be a useful indicator if it can alert the clinicians that reverse triggering or similar asynchronies are occurring. For example, it provides a warning to the clinicians when continuous MV breaths (10 breaths out of 100) have significant asynchrony magnitude of more than 5%. Figure 6 shows the number of breaths which have $>5\%$ M_{Asyn} at every 100 breaths for the datasets used in this study. For every 100 breath period, each dataset has a different distribution of M_{Asyn} . Dataset 1 shows a consistent trend of high number of $>5\%$ M_{Asyn} breaths. Dataset 2 shows gradual increase of M_{Asyn} whereas Dataset 3 fluctuations between none and high throughout the data collection period. This information is limited to the low patient numbers used in this computational and algorithm proof of concept. However, it shows potential for use by clinicians to manage care at a patient level, but needs to be validated or shown across a larger, more diverse cohort in a clinical validation.

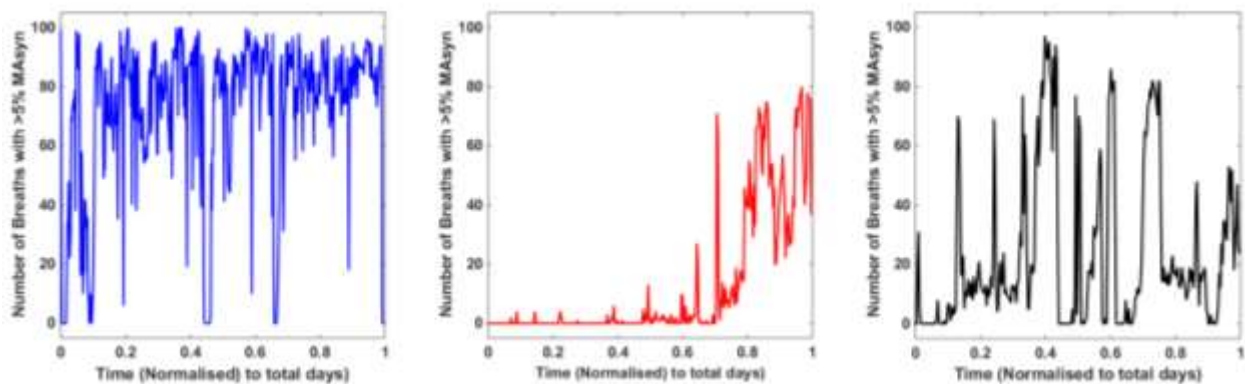


Figure 6: Number of breaths with $>5\%$ M_{Asyn} for every 100 breaths throughout the data collection period. (Left) Dataset 1, (Middle) Dataset 2 and (Right) Dataset 3. The Y-axis shows the number of breaths with $>5\%$ M_{Asyn} where a value of 100 indicates all breaths were affected, and the X-axis shows the normalised time for the whole data collection period.

Currently, there is limited research in automated methods to quantify the magnitude and frequency of asynchronous breathing and thus, it is difficult to assess its true clinical impact. Sinderby et al. [32] have proposed a system to quantify the patient-ventilator interaction, and it can potentially help clinicians to extend knowledge on patient-ventilator interaction [29, 36]. However, this method can only be used with one type of ventilator and it requires an invasive measuring tool. Thus, the IPR method proposed in this study is more generalizable, fully automated in software and can thus be used to automatically monitor mechanical ventilation asynchrony frequency and magnitude independent of any human input or additional devices.

Clinical application of this automated method would be via software with the ventilator or using ventilator signals. Clinically, the ability to monitor the true frequency of asynchrony would be valuable as it is only available via retrospective analysis over shorter periods. Thus, the frequency of occurrence may be much larger than expected. Automated monitoring would enable this value to be monitored and tracked, providing better input as to when to change ventilator settings and care, as well as providing data to assess its true impact on patient condition and recovery. The automated monitoring of asynchrony magnitude enables similar clinical outcomes. Small magnitude events might be ignored, but regular larger events would likely trigger a clinical change in ventilator settings or mode. Equally, the data could also be used to assess the clinical impact on patient condition and outcome. Thus, it is a further means to improve patient care without added clinical effort, or the addition of invasive devices or cost.

A final clinical application note would include that given automated monitoring and management

of asynchrony, as presented here, and other ventilator inputs using model-based identification of the underlying respiratory mechanics [12, 15, 16], there is a significant emerging opportunity for personalized MV management. In particular, the control loop on MV management includes significant clinical input and time, an increasing amount of which could be automated, in essence closing the loop much further, while leaving in clinical oversight. These elements have come together in glycemic control [37] and offer to do so in MV and other major areas of ICU cost, morbidity, and mortality [38].

5.0 Conclusion

An iterative pressure reconstruction (IPR) method is presented and shown to be effective and robust in reconstructing asynchrony affected breaths to enable identification of underlying respiratory mechanics. The resulting estimated respiratory mechanics parameters are more consistent and enable the magnitude of the asynchronous effect to be quantified. Thus, this algorithm offers potential improvements for real-time respiratory mechanics estimation, MV monitoring and insight into patient condition and ventilator interaction.

6.0 Acknowledgements

The authors would like to thank the Monash University Malaysia Advance Engineering Platform (AEP) Health Cluster, Ministry of Higher Education Malaysia (MOHE) Fundamental research grant scheme (FRGS) (Ref: FRGS/1/2016/TK03/MUSM/03/2), the New Zealand Tertiary Education Commission (TEC) and the MedTech Centre of Research Expertise, and the Health Research Council of New Zealand (HRC) (Grant Number: 13/213), for funding and support of this research.

7.0 Conflict of Interest

The authors declare that they do not have conflict of interest.

8.0 References

- [1] M.-C. Pintado, R. de Pablo, M. Trascasa, J.-M. Milicua, S. Rogero, M. Daguerre, J.-A. Cambronero, I. Arribas, M. Sánchez-García, Individualized PEEP Setting in Subjects With ARDS: A Randomized Controlled Pilot Study, *Respiratory Care*, 58 (2013) 1416-1423.
- [2] Y. Chiew, C. Pretty, G. Shaw, Y. Chiew, B. Lambermont, T. Desaive, J. Chase, Feasibility of titrating PEEP to minimum elastance for mechanically ventilated patients, *Pilot and Feasibility Studies*, 1 (2015) 9.
- [3] C. Schranz, P.D. Docherty, Y.S. Chiew, J.G. Chase, K. Moller, Structural Identifiability and Practical Applicability of an Alveolar Recruitment Model for ARDS Patients, *Biomedical Engineering, IEEE Transactions on*, 59 (2012) 3396-3404.
- [4] P.D. Docherty, C. Schranz, Y.-S. Chiew, K. Möller, J.G. Chase, Reformulation of the pressure-dependent recruitment model (PRM) of respiratory mechanics, *Biomedical Signal Processing and Control*, 12 (2014) 47-53.
- [5] P. Docherty, J.G. Chase, T. Lotz, T. Desaive, A graphical method for practical and informative identifiability analyses of physiological models: A case study of insulin kinetics and sensitivity, *BioMedical Engineering OnLine*, 10 (2011) 39.
- [6] L. Brochard, G. Martin, L. Blanch, P. Pelosi, F.J. Belda, A. Jubran, L. Gattinoni, J. Mancebo, V.M. Ranieri, J.-C. Richard, D. Gommers, A. Vieillard-Baron, A. Pesenti, S. Jaber, O. Stenqvist, J.-L. Vincent, Clinical review: Respiratory monitoring in the ICU - a consensus of 16, *Critical Care*, 16 (2012) 219.
- [7] D. Georgopoulos, G. Prinianakis, E. Kondili, Bedside waveforms interpretation as a tool to identify patient-ventilator asynchronies, *Intensive Care Medicine*, 32 (2006) 34-47.
- [8] K.G. Mellott, M.J. Grap, C.L. Munro, C.N. Sessler, P.A. Wetzel, J.O. Nilsestuen, J.M. Ketchum, Patient ventilator asynchrony in critically ill adults: Frequency and types, *Heart & Lung: The Journal of Acute and Critical Care*, 43 (2014) 231-243.
- [9] L. Blanch, A. Villagra, B. Sales, J. Montanya, U. Lucangelo, M. Luján, O. García-Esquirol, E. Chacón, A. Estruga, J. Oliva, A. Hernández-Abadia, G. Albaiceta, E. Fernández-Mondejar, R. Fernández, J. Lopez-Aguilar, J. Villar, G. Murias, R. Kacmarek, Asynchronies during mechanical ventilation are associated with mortality, *Intensive Care Medicine*, 41 (2015) 633-641.
- [10] G. Chanques, J.P. Kress, A. Pohlman, S. Patel, J. Poston, S. Jaber, J.B. Hall, Impact of Ventilator Adjustment and Sedation-Analgesia Practices on Severe Asynchrony in Patients Ventilated in Assist-Control Mode*, *Critical Care Medicine*, 41 (2013) 2177-2187 2110.1097/CCM.2170b2013e31828c31822d31827a.
- [11] A. Szlavecz, Y. Chiew, D. Redmond, A. Beatson, D. Glassenbury, S. Corbett, V. Major, C. Pretty, G. Shaw, B. Benyo, T. Desaive, J. Chase, The Clinical Utilisation of Respiratory Elastance Software (CURE Soft): a bedside software for real-time respiratory mechanics monitoring and mechanical ventilation management, *BioMedical Engineering OnLine*, 13 (2014) 140.
- [12] F. Vicario, A. Albanese, N. Karamolegkos, D. Wang, A. Seiver, N.W. Chbat, Noninvasive Estimation of Respiratory Mechanics in Spontaneously Breathing Ventilated Patients: A Constrained Optimization Approach, *Biomedical Engineering, IEEE Transactions on*, PP (2015) 1-1.
- [13] Y.S. Chiew, C. Pretty, P.D. Docherty, B. Lambermont, G.M. Shaw, T. Desaive, J.G. Chase, Time-Varying Respiratory System Elastance: A Physiological Model for Patients Who Are Spontaneously Breathing, *PLoS ONE*, 10 (2015) e0114847.
- [14] H. Maes, G. Vandersteen, C. Ionescu, Estimation of respiratory impedance at low frequencies during spontaneous breathing using the forced oscillation technique, 2014 36th Annual International Conference of the IEEE Engineering in Medicine and Biology Society, 2014, pp. 3410-3413.
- [15] V. Major, S. Corbett, D. Redmond, A. Beatson, D. Glassenbury, Y.S. Chiew, C. Pretty, T. Desaive, Á. Szlavecz, B. Benyó, G.M. Shaw, J.G. Chase, Respiratory mechanics assessment for reverse-triggered breathing cycles using pressure reconstruction, *Biomedical Signal Processing and Control*, 23 (2016) 1-9.
- [16] D.P. Redmond, Y.S. Chiew, V. Major, J.G. Chase, Evaluation of model-based methods in estimating respiratory mechanics in the presence of variable patient effort, *Computer Methods and Programs in Biomedicine*.
- [17] Y.S. Chiew, C.G. Pretty, A. Beatson, D. Glassenbury, V. Major, S. Corbett, D. Redmond, A. Szlavecz, G.M. Shaw, J.G. Chase, Automated logging of inspiratory and expiratory non-synchronized breathing (ALIEN) for mechanical ventilation, *Engineering in Medicine and Biology Society (EMBC), 2015 37th Annual International Conference of the IEEE, 2015*, pp. 5315-5318.
- [18] S.F. Poole, Y.S. Chiew, D.P. Redmond, S.M. Davidson, N.S. Damanhuri, C. Pretty, P.D. Docherty, T. Desaive, G.M. Shaw, J.G. Chase, Real-Time Breath-to-Breath Asynchrony Event Detection using Time-Varying Respiratory Elastance Model, 19th IFAC World Congress Cape Town, South Africa, 2014, pp. 5629-5634.
- [19] L. Blanch, B. Sales, J. Montanya, U. Lucangelo, O. Garcia-Esquirol, A. Villagra, E. Chacon, A. Estruga, M. Borelli, M. Burgueño, J. Oliva, R. Fernandez, J. Villar, R. Kacmarek, G. Murias, Validation of the Better Care® system to detect ineffective efforts during expiration in mechanically ventilated patients: a pilot study, *Intensive Care Medicine*, 38 (2012) 772-780.
- [20] Q. Mulqueeny, P. Ceriana, A. Carlucci, F. Fanfulla, M. Delmastro, S. Nava, Automatic detection of ineffective triggering and double triggering during mechanical ventilation, *Intensive Care Medicine*, 33 (2007) 2014-2018.
- [21] N.S. Damanhuri, Y.S. Chiew, N.A. Othman, P.D. Docherty, C.G. Pretty, G.M. Shaw, T. Desaive, J.G. Chase, Assessing respiratory mechanics using pressure reconstruction method in mechanically ventilated spontaneous breathing patient, *Computer Methods and Programs in Biomedicine*, 130 (2016) 175-185.
- [22] Y.S. Chiew, J.G. Chase, G. Shaw, A. Sundaresan, T. Desaive, Model-based PEEP Optimisation in Mechanical Ventilation, *BioMedical Engineering OnLine*, 10 (2011) 111.
- [23] E. van Drunen, Y.S. Chiew, C. Pretty, G. Shaw, B. Lambermont, N. Janssen, J. Chase, T. Desaive, Visualisation of time-varying respiratory system elastance in experimental ARDS animal models, *BMC Pulmonary Medicine*, 14 (2014) 33.
- [24] V. Major, C. Simon, D. Redmond, A. Beatson, D. Glassenbury, Y.S. Chiew, C. Pretty, T. Desaive, A. Szlavecz, B. Benyo, G.M. Shaw, J.G. Chase, Assessing Respiratory Mechanics of Reverse-Triggered Breathing Cycles - Case Study of Two Mechanically Ventilated Patients, *IFAC-PapersOnLine*, 48 (2015) 505-510.
- [25] P.a. Pelosi, P.R.M.b. Rocco, To prevent or cure acute respiratory distress syndrome: that is the question! [Miscellaneous], *Current Opinion in Critical Care*, 20 (2014) 1-2.
- [26] E. Akoumianaki, A. Lyazidi, N. Rey, D. Matamis, N. Perez-Martinez, R. Giraud, J. Mancebo, L. Brochard, J.-C.M. Richard, Mechanical ventilation-induced reverse-triggered breaths: A frequently unrecognized form of neuromechanical coupling, *CHEST*, 143 (2013) 927-938.
- [27] J. Spahija, M. de Marchie, M. Albert, P. Bellemare, S. Delisle, J. Beck, C. Sinderby, Patient-ventilator interaction during pressure support ventilation and neurally adjusted ventilatory assist *, *Critical Care Medicine*, 38 (2010) 518-526 510.1097/CCM.1090b1013e3181cb1090d1097b.
- [28] N. Al-Rawas, M. Banner, N. Euliano, C. Tams, J. Brown, A.D. Martin, A. Gabrielli, Expiratory time constant for determinations of plateau pressure, respiratory system compliance, and total resistance, *Critical Care*, 17 (2013) R23.

- [29] K. Moorhead, L. Piquilloud, B. Lambermont, J. Roeseler, Y. Chiew, J.G. Chase, J.-P. Revelly, E. Bialais, D. Tassaux, P.-F. Laterre, P. Jolliet, T. Sottiaux, T. Desaive, NAVA enhances tidal volume and diaphragmatic electro-myographic activity matching: a Range90 analysis of supply and demand, *Journal of Clinical Monitoring and Computing*, 27 (2013) 61-70.
- [30] D.O. Kannangara, F. Newberry, S. Howe, V. Major, D. Redmond, A. Szlavacs, Y.S. Chiew, C. Pretty, B. Benyo, G.M. Shaw, J.G. Chase, Estimating the true respiratory mechanics during asynchronous pressure controlled ventilation, *Biomedical Signal Processing and Control*, 30 (2016) 70-78.
- [31] E. van Drunen, Y.S. Chiew, J. Chase, G. Shaw, B. Lambermont, N. Janssen, N. Damanhuri, T. Desaive, Expiratory model-based method to monitor ARDS disease state, *BioMedical Engineering OnLine*, 12 (2013) 57.
- [32] C. Sinderby, S. Liu, D. Colombo, G. Camarotta, A. Slutsky, P. Navalesi, J. Beck, An automated and standardized neural index to quantify patient-ventilator interaction, *Critical Care*, 17 (2013) R239.
- [33] M. de Wit, S. Pedram, A.M. Best, S.K. Epstein, Observational study of patient-ventilator asynchrony and relationship to sedation level, *J Crit Care*, 24 (2009) 74-80.
- [34] D.P. Redmond, Y.S. Chiew, J.G. Chase, The Effect of Respiratory Manoeuvres for Patient-Specific Respiratory Mechanics Monitoring, *IFAC-PapersOnLine*, 48 (2015) 135-140.
- [35] C. Bibiano, Y.S. Chiew, D. Redmond, J. Kretschmer, P.D. Docherty, J.G. Chase, K. Möller, Effects of Different Models and Different Respiratory Manoeuvres in Respiratory Mechanics Estimation, in: E. Kyriacou, S. Christofides, C.S. Pattichis (Eds.) XIV Mediterranean Conference on Medical and Biological Engineering and Computing 2016: MEDICON 2016, March 31st-April 2nd 2016, Paphos, Cyprus, Springer International Publishing, Cham, 2016, pp. 50-55.
- [36] L. Piquilloud, P. Jolliet, J.-P. Revelly, Automated detection of patient-ventilator asynchrony: new tool or new toy?, *Critical Care*, 17 (2013) 1015.
- [37] J.G. Chase, A. Le Compte, J.-C. Preiser, G. Shaw, S. Penning, T. Desaive, Physiological modeling, tight glyceic control, and the ICU clinician: what are models and how can they affect practice?, *Annals of Intensive Care*, 1:11 (2011).
- [38] J.G. Chase, T. Desaive, J.-C. Preiser, Virtual Patients and Virtual Cohorts: A New Way to Think About the Design and Implementation of Personalized ICU Treatments, in: J.-L. Vincent (Ed.) Annual Update in Intensive Care and Emergency Medicine 2016, Springer International Publishing, Cham, 2016, pp. 435-448.