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Identification of Respiratory Mechanics during Mechanical Ventilation

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Abstract

The master thesis deals with modeling of the human respiratory mechanics during mechanical ventilation. This field is becoming increasingly interesting since the computer development has now made it possible to perform powerful simulations and data analysis. This makes it possible to simulate changed ventilator settings before implementing them on the actual patient. This gives the opportunity of obtaining optimal ventilator settings that better meet the goals of the treatment but with smaller risks of permanent damage to the lungs. Today's settings are often made based on general practical experience rather than the actual conditions of the patient.

In this thesis a method for model construction based on subspace identification and curve fitting from data series of three to five normal breaths is developed and tested on a number of different data sets. The model is also identified and tested on a few data sets where data have been collected before, during and after a known change in the settings.

It is shown that it is possible to obtain good, although not perfect models, of the respiratory mechanics from just three to five normal breaths, using this method. This accuracy might be sufficient for the purpose of simulation.

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1 Preface

This report is the result of a master thesis work made during the spring of1999 at the department of Automatic Control at Lund University in co-operation with the department of Clinical Physiology at Lund University hospital. It deals with the subject of modelling the human respiratory system under mechanical ventilation.

It should be pointed out that a report of this kind is supposed to be readable for a last year engineering student. Some of the medical facts and terminology are therefore simplified which might disturb a reader with solid medical background. Despite this, I hope that the methods and results are interesting enough to make the report useful for the more qualified readers as well.

Chapter 2 contains some background information, including a brief introduction to the human lung physiology, an explanation of the forces acting on the human respiratory system and a description of the uses and risks with mechanical ventilation. In Chapter 3 the objectives of the work are found and Chapter 4 contains the mathematical modelling, the equipment used and the experiments that was carried out. Chapter 5 contains the results and discussions and conclusions are found in Chapters 6 and 7. Finally, some suggestions of further work are found in Chapter 8.

I am very grateful to my supervisor at the department of Clinical Physiology, Professor Björn Jonson, for giving me the opportunity to work with such an interesting and for me completely new subject and also for his help and support. I would also like to thank my two supervisors from the department of Automatic Control, Professor Rolf Johansson and Professor Per Hagander, for great support and feedback.

Leif Uttman and Björn Drefeldt at the department of Clinical Physiology have also helped me a lot in understanding the mysteries of the respiratory system, the previous work in the area and the technology behind mechanical ventilation. Last but definitely not least I want to thank Anna Blomberg for all her encouragement and for useful help with the structure and language of the report.

2 Background

Mechanical ventilation is a necessary, life-supporting aid in modern intensive care. The human body might in certain situations, due to diseases as well as accidents, be unable to utilise the lungs to such an extent that life can be sustained. The mechanical ventilator is then used to inflate the lungs with external aid so that the normal gas exchange between alveolar and blood in the lungs can occur as usual.

The drawback with mechanical ventilation is that it is difficult to adapt the settings to individual needs and the goal of the treatment since the characteristics of the lungs are very individual. A bad choice of settings might cause permanent damage to the respiratory system and the settings are therefore often made based on rules of thumb which ensure the safety but does not necessarily improve the health of the patient.

The development in the computer area has made it possible to perform fast and accurate simulations of complex physical systems. This suggests that it should be possible not only to model the respiratory system of each individual based on sampled data from the ventilator, but also to simulate changed ventilator settings in the computer before applying them. A physician should, based on knowledge and experience, be able to state goals with the treatment as well as constraints in the ventilator settings. Optimisation algorithms could then be used to find the best possible ventilator settings. If the physician finds the suggested settings reasonable they can then be implemented on the actual ventilator.

For such a system to be accepted by medical professionals, working under great pressure in intensive care, it is important that it is easy to use and able to model and simulate in close to real-time. From a technical point of view there is an obvious possibility to create a complete control system. The computer could then be connected directly to the ventilator and implement the settings at once. Even the use of direct feedback to reach the wanted goals stepwise is possible. This is probably not a wise approach if clinical acceptance is expected.

2.1 The respiratory system

This section is intended to give a very brief overview of the properties of the human respiratory system. A more thorough exposition on the subject can be found in [1] or [2].

2.1.1 Introduction and definitions

Each litre of air that is inhaled and exhaled can provide the blood with 40-45 ml oxygen and eliminate the same amount of carbon dioxide. If the metabolism of the body is changed the ventilation must be changed proportionally so that the new requirements are met. This is normally controlled through changing the *tidal volume* (volume per breath) or changing the frequency.

The human respiratory system basically consists of the *trachea* (air passage) and the lungs. Air is moved in and out of the lungs by interaction between the opposite elastic forces of the lung and the *thorax* (chest). The difference in pressure that is induced between lung and thorax is called *pleural pressure*, P_{pl}.

In the lungs, the trachea passes into the *main bronchi*, one for each lung. The bronchi are divided into smaller and smaller branches and finally end in the *alveoli* where the actual gas exchange between the air and the blood occurs. Gas is exchanged by diffusion through the alveolar wall so that oxygen is added to the blood and carbon dioxide is removed.

2.1.2 Elastic properties of the respiratory mechanics

The term *respiratory mechanics* usually refers to the interactions between lungs and thorax during breathing and the forces involved are mainly elastic and resistive.

The elastic properties of the respiratory mechanics depend on the elasticity of the lungs and chest and are crucial for the functionality of the lung, in health as well as in disease. There is a difference in pressure between the inside and the outside of the lung. This is due to the fact that the pressure in the alveolar is higher than the pleural pressure. This difference in pressure is called elastic pressure, P_{el}, and is volume dependent. The properties of the elastic pressure can be described in a pressure/volume-curve (P/V-curve), such as the one, showing one complete breath, found in Figure 1.

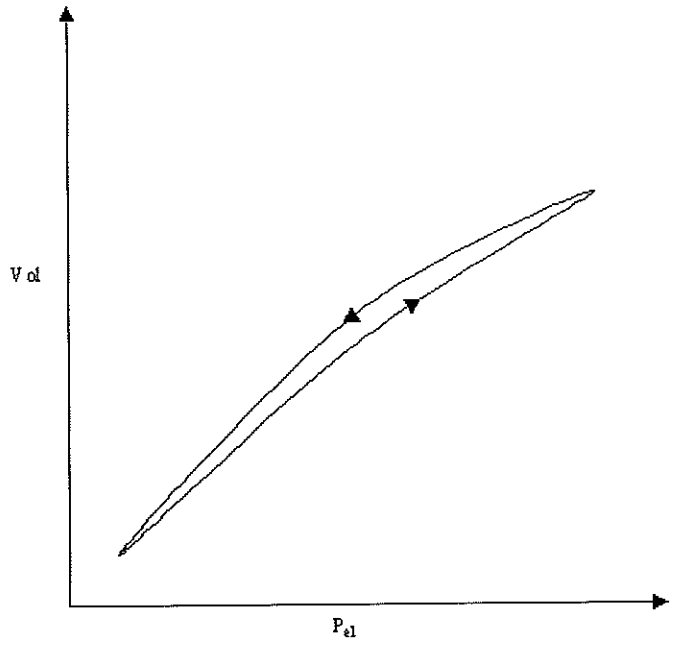

Figure 1. Volume as a function of elastic pressure (P_{el}). The lower limb shows the inspiration and the upper part the expiration.

This figure indicates a small hysteresis between inspiration and expiration. For normal breaths this effect is usually found to be very small and it has been slightly exaggerated here for illustration. The reason for the hysteresis is simply that the elastic forces in the lung are larger during inspiration than during expiration [1, Ch. 2]. This effect is enlarged for deeper breaths.

The slope of the non-linear function is referred to as compliance, C, and shows the volume change of the lung per unit of pressure change. This is measured as l/cm H_20, which equals 0.0102 $m^3/(N/m^2)$ in SI units. A person's age as well as various diseases affect the elasticity of the lung and consequently the shape of the P_{el}/V-curve.

2.1.3 Resistive properties

Airway resistance dominates the resistive properties of the respiratory system. The pressure drop in the airways is called resistive pressure, P_{res}, and is defined as

$$P_{res} = R\dot{V} \tag{1.1}$$

where R is the resistance, often measured as cm $H_20/(l/s)$ which in SI units equals 98 $(N/m^2)/(m^3s)$.

Resistance occurs due to internal friction in the trachea and depends mainly on the length and radius of the airways. An individual's tracheal length is constant whereas the radius may vary and thus affect the resistance. Turbulence may occur and increase the resistance if the flow is large compared to the radius.

The resistive properties vary for different individuals and also for a single individual in health and disease. Especially due to certain obstructive diseases such as asthma, inspiratory and expiratory resistance may differ a lot and be very volume dependent. Without resistance the total, tracheal pressure would follow the elastic pressure/volume-curve exactly. The resistance causes the tracheal pressure to make a larger loop, where the distance to the elastic curve depends on the resistance. This can be seen in Figure 2 where the inner loop is the same as in Figure 1 and the outer loop is the volume behaviour for the total pressure.

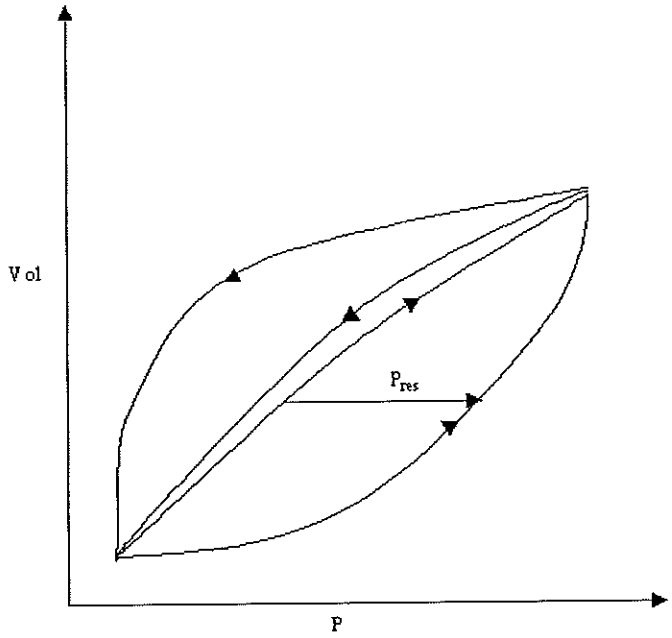

Figure 2. Volume as a function of elastic (inner loop) and total tracheal (outer loop) pressure.

2.1.4 Gas exchange and CO_2-level

The purpose of the lungs is to provide enough oxygen to the body while maintaining a specific pH value by keeping a certain partial pressure of CO_2 in arterial blood (P_aCO_2). The pH value of the body is determined by the amount of dissolved CO_2 in the blood since the main buffers for pH control, carbon acid (H_2CO_3) and bicarbonate (HCO_3) are created according to [1, p. 55]

$$CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^- . \tag{1.2}$$

The value of P_aCO_2 is thus vital for the body to function correctly. Two factors, namely ventilation and metabolism, determine P_aCO_2. Thus, an increased production of CO_2 in the body is normally compensated automatically by increasing the elimination through changed ventilation. When using mechanical ventilation, the normal ventilation is externally overtaken and it is therefore of extreme importance that the P_aCO_2 is monitored when changing the settings of the ventilator.
Normally there is diffusion equilibrium between air and blood in the alveolar. The partial pressure of oxygen in arterial blood (P_aO_2) therefore mainly depends on the oxygen pressure in the air. Under normal air pressure, with P_aCO_2 kept at normal levels, the alveolar oxygen pressure is high enough to provide necessary amounts of oxygen to the body. The body does therefore not need a control system for the oxygen levels, like the one controlling P_aCO_2. Since it is not harmful for the body with a modest change of the oxygen level, there is consequently no particular need to model P_aO_2 when simulating the respiratory system during mechanical ventilation. This work will thus not deal with oxygen modelling.

2.2 Mechanical ventilation

The Servo Ventilator 900C (Siemens-Elema AB, Solna, Sweden) is a widespread ventilator used in intensive care all around the world and referred to in this study. The ventilator has a number of user choices that can be set to adjust it to the patient's condition and needs:

- Pressure or volume control:
  The ventilator can be set to either keep a certain pressure during inspiration or to inspire a certain amount of air each minute. Depending on the choice made a desired pressure or a desired minute volume is also set.
- Breathing frequency:
  The number of breaths per minute.
- Inspiratory time:
  The duration (in % of the total breath) of the inspiration.
- Pause time:
  The duration (in % of the total breath) of a post-inspiratory time. Using this setting produces a pause between inspiration and expiration.
- Positive end expiratory pressure (PEEP):
  The pressure that should be reached at the end of the expiration.

2.2.1 Risks with mechanical ventilation

Mechanical ventilation is as mentioned often a necessary, life-supporting action that is used with rules of thumb that are known to work but not necessarily prevent permanent damage to the patients' respiratory system. A reason for this might be that it is considered better if a person survives with some permanent damages than not at all. The main problem of risk is that the peak pressure is too high, causing serious injury to the respiratory system. Another problem is that a too low pressure can collapse the lung, which can cause the lungs to stick together. Large shear forces will then act on the lung walls when trying to inflate the lungs again. This can also cause severe injuries.

3 Objectives

The objective of this master thesis is to identify the human respiratory mechanics under mechanical ventilation and thus to obtain a model that can predict the behaviour when changing the ventilator settings. For the identification and the not yet implemented simulation of changed settings to be accepted in clinical use it is important that it is fast, easy and safe. One important goal of the work must therefore be to make it possible to identify relevant models from normal breaths, thus avoiding the use of a special sequence that might interfere with the ventilator settings chosen by the medical professionals. It is also preferable if the parameters of the model can be determined in a short time and that the process is easy to use and requires none or only very limited knowledge of the underlying mathematics.

The goal in the long run, although beyond the aim of this thesis, is to use the obtained model for simulation and optimisation as a tool in intensive care. Using simulation is a good way of testing changed ventilator settings in the computer before applying them to the actual ventilator. Thus it is possible to find settings where, for instance, the peak pressure is less harmful without changing the P_aCO_2 too much and with a reduced number of experiments on the actual ventilator and patient.

The work can be defined as consisting of the following parts.

- Study of literature on the medical background and previous work in the field.
- Adoption of the available data to a format that can be used in Matlab.
- Trying out different identification methods to find a suitable one for the purpose of this thesis.
- Development of a complete modelling and verification environment in Matlab.
- Verification of the model with as much data as possible.
- Analysis of the result and error estimation to be able to draw conclusions.

4 Materials and methods

4.1 Mathematical modelling

4.1.1 Model of the respiratory mechanics

According to the background in Chapter 2, the tracheal pressure (P_{tr}) can be described as consisting of one resistive (P_{res}) and one elastic part (P_{el}). The elastic part is dependent of the volume of the lungs, but since it is the flow that is measurable from the ventilator it is better to model the elastic pressure as a function of flow rather than volume. Since the volume is the integral of the flow this is an equivalent representation. Assuming that a 1st order model is sufficient a differential equation for the elastic pressure is

$$\frac{dP_{el}}{dt} + \omega P_{el} = \xi \dot{V} \tag{3.1}$$

where ω is assumed to be the damping that causes the hysteresis in the elastic pressure/volume curve in Section 2.1.2. ξ is the flow equivalence of the compliance. Using Laplace transformation, the transfer function from flow to pressure becomes

$$G_{el} = \frac{P_{el}}{\dot{V}} = \frac{\xi}{s+\omega}. \tag{3.2}$$

The resistive pressure, P_{res}, is direct proportional to the flow, according to Equation 1.1. The actual resistance, R, is a non-linear and volume-dependent parameter that often is different for inspiration and expiration. It can be modelled as a polynomial of a certain degree and based on previous work [3] the degrees where chosen so that

$$R_{insp} = r_{i0} + r_{i1}V \tag{3.3}$$

and

$$R_{\exp} = r_{e0} + r_{e1}V + r_{e2}V^2 \tag{3.4}$$

for inspiration and expiration respectively.
To summarise, the tracheal pressure, Ptr, is

$$P_{tr} = R\dot{V} + \frac{\xi}{s+\omega}\dot{V} = \begin{cases} \left(r_{i0} + r_{i1}V + \frac{\xi}{s+\omega}\right)\dot{V} & \dot{V} \geq 0 \\ \left(r_{e0} + r_{e1}V + r_{e2}V^2 + \frac{\xi}{s+\omega}\right)\dot{V} & \dot{V} \leq 0. \end{cases} \tag{3.5}$$

The elastic part can be modelled with a larger model order but it is always possible to separate the two parts since it is only the resistive one that is direct proportional to the flow.

4.1.2 Model of alveolar CO_2-pressure

It is important to have a good model of the arterial CO_2-pressure, P_aCO_2, to be able to determine what happens to the CO_2 elimination when the tidal volume is changed.. Since the arterial blood is in diffusion equilibrium with the alveolar air the alveolar CO_2-pressure (P_ACO_2) and the arterial CO_2-pressure (P_aCO_2) the two pressures can be assumed to be equal. It is therefore reasonable to model P_ACO_2 instead since this Information is available from the ventilator.

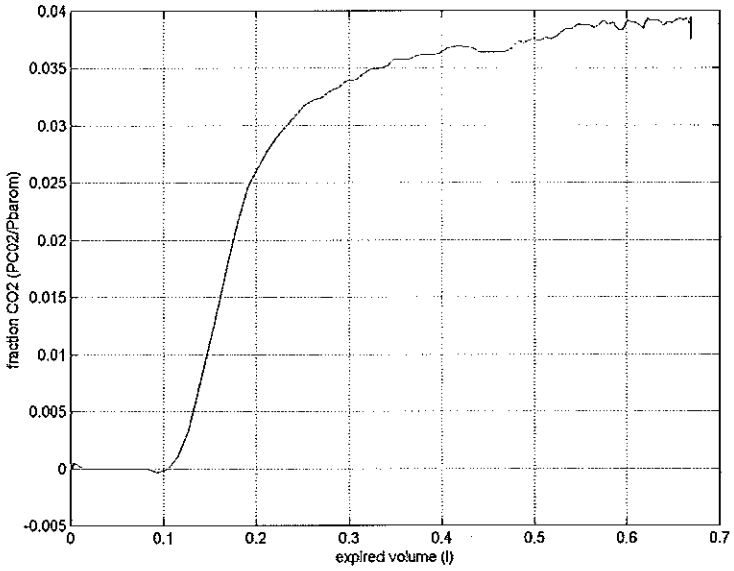

Figure 3. The fraction of CO2 of the total alveolar pressure as a function of expired volume.

Figure 3 shows the fraction CO_2, F_{CO2}, (P_aCO_2/P_{barom}) as a function of expired volume in one breath so that the volume at the right endpoint of the curve equals the tidal volume. If this curve is integrated the volume CO_2 per breath is found. To be able to evaluate how this volume is changed when the tidal volume is raised or lowered, the upper part of the curve must be parameterised. One possible parameterisation is [3]

$$F_{CO_2} = b + m\ln(V_{\exp}). \tag{3.6}$$

4.2 Equipment and data gathering

All data was collected from patients ventilated with the Servo Ventilator 900C (Siemens-Elema AB, Solna, Sweden). This ventilator allows external control which can override the settings made on the front panel for some of the parameters, e.g. breathing frequency, minute volume, and level of positive end-expiratory pressure (PEEP). A personal computer was connected to the ventilator via AD/DA-converters for external control and data acquisition. Data was gathered with a constant sampling period of 0.02 seconds.

Muscle forces acting on the respiratory system affect pressures measured at the airway openings and therefore disturb a good determination of the respiratory mechanics. Muscle relaxation was used in all cases to avoid this kind of disturbances.

4.3 Experiments

A data sequence consisting of a number of normal breaths, typically three to five, from a patient ventilated with known settings, is constructed. The total length of the sequence depends on the number of breaths and the breathing frequency but a typical size would be approximately 1000 samples. Available signals are time (t), flow ($\dot{V}$) and pressure (P_{tot}) in the ventilator and the alveolar CO_2-pressure (P_ACO_2). Because of tube resistance and compliance this is not the actual flow and pressure in the trachea. The parameters of the tube are measured in vitro and the real input and output signals to be used in the identification are calculated as [4]

$$\begin{cases} \dot{V}_{tr}(t) = \dot{V}_{tot}(t) - C_{tube}\dfrac{dP_{tot}}{dt} \\ P_{tr}(t) = P_{tot}(t) - \left(K_1\dot{V}_{tr}(t) + K_2\dot{V}_{tr}^2(t)\right) \end{cases} \tag{3.7}$$

where C_{tube} is the tube compliance and K_1 and K_2 describes the resistance of the tube, corresponding to the polynomial representation of the tracheal resistance in Equations 3.3 and 3.4.

For example, due to small differences in the flow transducers and different composition of the air during inspiration and expiration the given measurements of inspiratory and expiratory flow are not comparable. It is therefore necessary to calculate a correction factor that can be multiplied with either of the flows. The inspired and expired volume of one breath is obtained from integrating the inspiratory and expiratory flows. For a normal breath these volumes should be equal. By dividing the volumes a correction factor is obtained. The first breath in the series should not be used since the starting point does not necessarily occur at the exact beginning of a breath and the inspired volume would then not be a full breath. Instead the difference between the first inspiration and the first expiration is used to calculate the initial volume of the lung. This information is important when the coefficients of the resistance polynomials of Equations 3.3 and 3.4 should be decided.

The model described in Section 4.1 is continuous but most identification tools are designed for discrete modelling. Since the data is sampled it is reasonable to design a discrete time model and try to convert the parameters to continuous time afterwards. A prerequisite for the discrete representation is that the flow is piecewise constant, i.e. does not change between the sampling points.

A 1st order discrete transfer function

$$H(z) = \frac{\beta_0 z + \beta_1}{z + a_1} \tag{3.8}$$

between tracheal flow and pressure is determined with Matlab and the SMI toolbox [5]. A 1st order model has proven adequate in all subjects tested.

To isolate the elastic part of the transfer function a polynomial division is performed, resulting in the transfer function

$$H(z) = R + \frac{b_0}{z + a_1}. \tag{3.9}$$

The problem with the obtained model is that it is very sensitive to linear trends in the data. If data contains linear trends the model output becomes unstable. This problem can be solved if both flow and pressure data are detrended before used in the identification. Detrending calculates the mean value of all data points and subtracts this from each data point. This removes linear trends and places the data symmetrically around zero.

Using detrended data with the same identification method as above, a stable model can be obtained but the hysteresis effect discussed in Section 2.1.2 is amplified to a degree that had no biological explanation. It was found that it is the direct term of the transfer function (R) that is affected most by the linear trends, whilst the elastic parameters are almost equal for detrended and normal data series. To avoid the hysteresis problem a combined approach can be used. Two identifications are performed, one without and one with detrending of data. The elastic parameters (a_1 and b_0) are taken from the first model and the resistive parameter (R) from the second, detrended model.

Typical combined model output (tracheal pressure) and actual output in response to flow are found in Figure 4. Note that the mean value of the original actual pressure has been added to both series to return to original values.

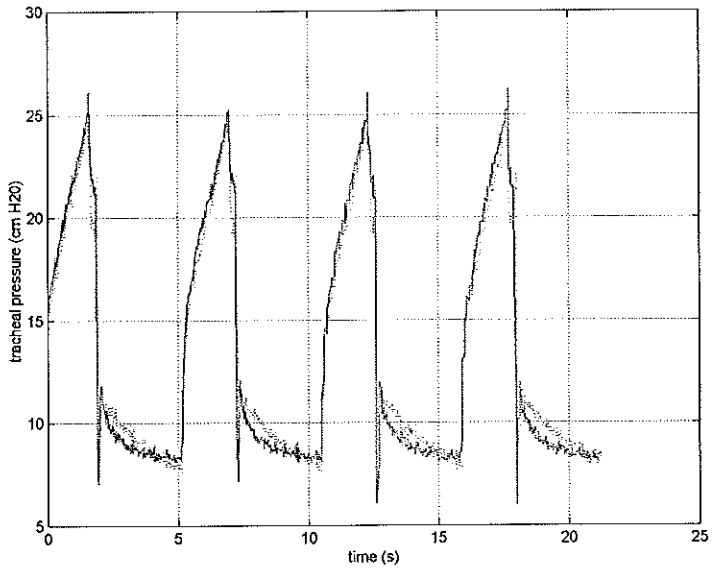

Figure 4. Actual (solid) and model (dotted) output from data Bf. The parameters of this data set is found Table 4.

The resistive part of the obtained model is just a constant, which is not sufficient since inspiratory and expiratory resistances usually differ, especially in certain diseases. This is for instance the case in some obstructive diseases where the inspiratory resistance is large but the expiratory resistance even larger.

Using the transfer function in Equation 3.9 it is easily seen that the resistive pressure can be obtained by subtracting the model elastic pressure from the actual tracheal pressure. If the elastic parameters are correct the remaining part can be assumed to be the actual resistive pressure. The coefficients in the expressions for R_{insp} and R_{exp} from Equations 3.3 and 3.4 can then be determined by minimising the difference between the functions and the actual resistive pressure in a least-square sense. This is done with a non-linear curve fitting routine in Matlab. A typical resistance function is found in Figure 5.

All parts of the tracheal pressure from Equation 3.5 are now known and the elastic and resistive parts of the pressure can be calculated separately. A plot showing actual and model tracheal pressure and model elastic pressure is found in Figure 6.

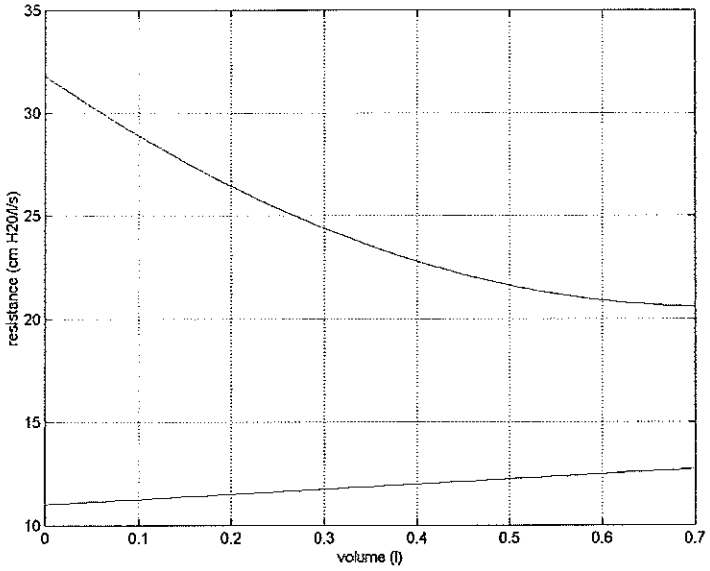

Figure 5. Inspiratory (lower) and expiratory (upper) resistance as a function of volume for data Bf.

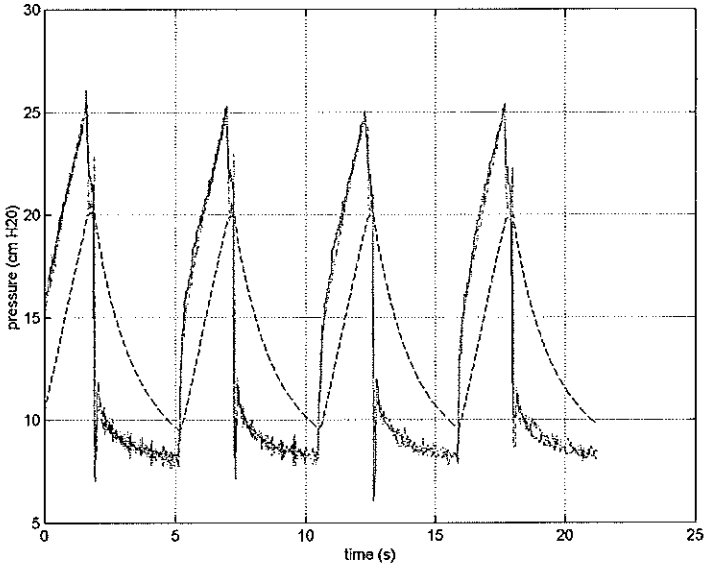

Figure 6. Tracheal pressure (solid) and elastic pressure (dashed) for data Bf. The tracheal pressure is plotted both as model and actual output but the model follows the actual output so well that it is difficult to separate them.

For the physician to be able to draw conclusions about the patients' condition this model must be presented in a familiar form. This can be done with for instance a P/V-curve, like the one in Figure 7. This curve shows all breaths in the identification data but it is of course possible to select just one breath and present this.

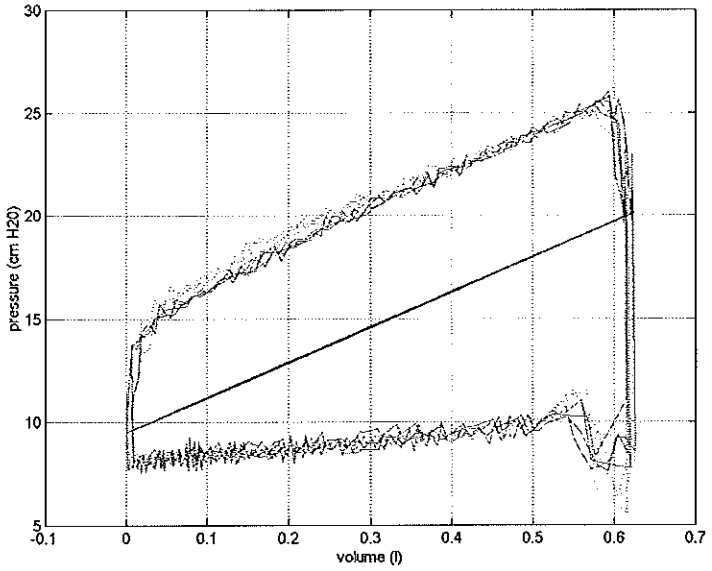

Figure 7. Total model tracheal pressure (outer loop) and elastic pressure (inner loop) of data Bf. The dotted loop is actual tracheal pressure.

To estimate the parameters in the alveolar CO_2-pressure the volume of the first expiration in the data series is found through integration of the flow. The fraction CO_2 is obtained by simply dividing the given CO_2-pressure by the normal air pressure (P_{barom}). A curve-fitting routine is then used to fit the function in Equation 3.6 to the upper part of the curve. The curve from Figure 1 with the mentioned function included is found in Figure 8.

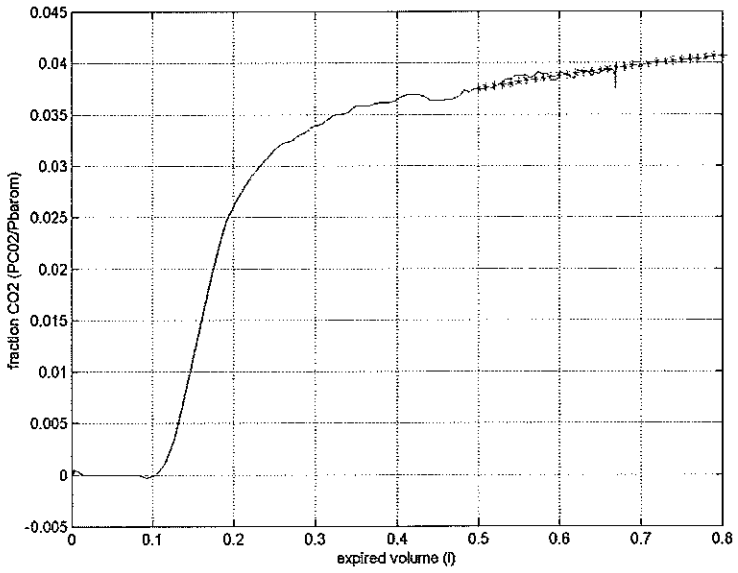

Figure 8. Fraction CO_2 as a function of expired volume (solid) and the mathematical model from Equation 3.6 (stars).

4.4 Continuous representation

So far, all the modelling has been performed in discrete time. At this stage it is possible to convert the transfer function to continuous time since no more identification is necessary. It is difficult to perform a correct transformation between discrete and continuous time but it is done to be able to represent the model as a differential equation, which is much more intuitive to understand than a discrete transfer function.

The total continuous transfer function from flow to tracheal pressure is

$$G_{tr}(s)=\frac{\gamma_0 s+\gamma_1}{s+\omega}=R+\frac{\xi}{s+\omega}. \tag{3.10}$$

To obtain a relation between the continuous parameter vector $\delta=[\omega\ \gamma_0\ \gamma_1]$ and its discrete equivalence $\theta=[a_1\ \beta_0\ \beta_1]$ a few calculations are required. These can be found in Appendix A. Comparing the state-space realisations from Appendix A with the transfer function in 3.8 and 3.10 results in a relationship between the continuous and discrete parameters

$$g(\theta)=\begin{cases} \omega=\frac{1}{h}a_1 p_0-p_1 \\ \gamma_0=\beta_0 \\ \gamma_1=-\frac{1}{h}p_1\beta_0+\frac{1}{h}p_0\beta_1 \end{cases} \tag{3.11}$$

where p_0 and p_1 are derived in Appendix A.

A relationship between the divided parameter set $\lambda=[\omega\ R\ \xi]$ and the original continuous parameters $\delta=[\omega\ \gamma_0\ \gamma_1]$ is easily established as

$$\begin{cases} \omega=\omega \\ \gamma_0=R \\ \gamma_1=R\omega+\xi \end{cases} \Leftrightarrow \begin{cases} \omega=\omega \\ R=\gamma_0 \\ \xi=\gamma_1-\gamma_0\omega \end{cases} \tag{3.12}$$

or in matrix form

$$\begin{bmatrix} \omega \\ R \\ \xi \end{bmatrix}=\begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & -\omega & 1 \end{bmatrix}\begin{bmatrix} \omega \\ \gamma_0 \\ \gamma_1 \end{bmatrix}. \tag{3.13}$$

Please note that the resistive part is equal in discrete and continuous representation. This is the reason for the using the letter R in both cases.

4.5 Errors in the estimated parameters

To be able to evaluate the correctness of the model it is important to have some kind of measurement of the errors in the estimated parameters. This section deals with the variance of the parameters from the identification, i.e. not the resistance parameters found with curve fitting.

A more detailed description of the expressions in this section can be found in [6], from which most of the material is taken.

4.5.1 Variance in the discrete representations

The original model from Equation 3.8 describes the time series

$$P_{trk} = -a_1 P_{trk-1} + \beta_0 \dot{V}_k + \beta_1 \dot{V}_{k-1} + v_k = \begin{bmatrix} -P_{tr_{k-1}} & \dot{V}_k & \dot{V}_{k-1} \end{bmatrix} \begin{bmatrix} a_1 \\ \beta_0 \\ \beta_1 \end{bmatrix} + v_k = \varphi_k \theta + v_k \qquad (3.14)$$

where v_k is the error between observation at time k and the model output at time k. φ_k is referred to as the regressor vector.

In matrix notation the total vector of observations can be described as

$$P_{tr_N} = \begin{bmatrix} P_{tr_1} \\ P_{tr_2} \\ \cdots \\ P_{trN} \end{bmatrix} \qquad (3.15)$$

if N is the total number of observations. The total regressor matrix and total error vector is

$$\phi_N = \begin{bmatrix} \varphi_1 \\ \varphi_2 \\ \cdots \\ \varphi_N \end{bmatrix}, \quad \varepsilon(\theta) = \begin{bmatrix} P_{tr_1} - \varphi_1 \theta \\ P_{tr_2} - \varphi_2 \theta \\ \cdots \\ P_{tr_N} - \varphi_N \theta \end{bmatrix} = P_{tr_N} - \phi_N \theta \,. \qquad (3.16, 3.17)$$

The sum of the squared error between observations and model output can now be described as

$$V(\theta) = \frac{1}{2} \varepsilon^T \varepsilon = \frac{1}{2} \left(P_{tr_N} - \phi_N \theta \right)^T \left(P_{tr_N} - \phi_N \theta \right). \qquad (3.18)$$

If $\hat{\theta}$ is an unbiased estimation of θ, its covariance matrix is

$$\Sigma_\theta \approx \sigma^2 \left(\phi_N^T \phi_N \right)^{-1} \qquad (3.19)$$

An unbiased estimate of σ^2 in Equation 3.19 is

$$\hat{\sigma}_\theta^2 = \frac{2}{N-p} V\left(\hat{\theta}\right) \qquad (3.20)$$

where p is the number of parameters, in this case p=3.

An estimation of the covariance matrix of $\theta=[a_1\ \beta_0\ \beta_1]^T$ is thus

$$\Sigma_\theta = \frac{2}{N-p} \; V\left(\hat{\theta}\right) \left(\phi_N^T \phi_N \right)^{-1} \qquad (3.21)$$

and the variances of the three parameters a_1, β_0 and β_1 are the diagonal elements of this matrix.

To estimate the variances of the three discrete parameters R, a_1 and b_0 it is assumed that the covariance of a general vector function of variables with known variance can be calculated as

$$\Sigma_{f(\theta)} = \frac{\partial f}{\partial \theta} \Sigma_\theta \left(\frac{\partial f}{\partial \theta} \right)^T . \tag{3.22}$$

The relation between the original parameter vector, $\theta=[a_1\ \beta_0\ \beta_1]^T$, and the divided set, $\mu=[a_1\ R\ b_0]^T$ is

$$\begin{cases} a_1 = a_1 \\ \beta_0 = R \\ \beta_1 = Ra_1 + b_0 \end{cases} \Leftrightarrow \begin{cases} a_1 = a_1 \\ R = \beta_0 \\ b_0 = \beta_1 - \beta_0 a_1 \end{cases} \tag{3.23}$$

or in matrix form

$$\begin{bmatrix} a_1 \\ R \\ b_0 \end{bmatrix} = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & -a_1 & 1 \end{bmatrix} \begin{bmatrix} a_1 \\ \beta_0 \\ \beta_1 \end{bmatrix} \tag{3.24}$$

where it can be assumed that

$$\begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & -a_1 & 1 \end{bmatrix} = \frac{\partial f}{\partial \theta} . \tag{3.25}$$

so that, using Equation 3.22, the variance of the new discrete parameter vector $\mu=[a_1\ R\ b_0]^T$ can be determined as the diagonal elements of the covariance matrix

$$\Sigma_\mu = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & -a_1 & 1 \end{bmatrix} \Sigma_\theta \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & -a_1 & 1 \end{bmatrix}^T \tag{3.26}$$

with Σ_θ from Equation 3.21.

4.5.2 Variance in the continuous representations

The variance of the continuous parameter vector $\delta=[\omega\ \gamma_0\ \gamma_1]^T$ is also estimated using Equation 3.22. Differentiating Equation 3.11 gives, with p_0 and p_1 from Appendix A,

$$\frac{\partial g}{\partial \theta} = \begin{bmatrix} \frac{1}{h} p_0 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & -\frac{1}{h} p_1 & \frac{1}{h} p_0 \end{bmatrix} \tag{3.27}$$

which inserted to Equation 3.22 gives

$$\Sigma_\delta = \begin{bmatrix} \frac{1}{h}p_0 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & -\frac{1}{h}p_1 & \frac{1}{h}p_0 \end{bmatrix} \Sigma_\theta \begin{bmatrix} \frac{1}{h}p_0 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & -\frac{1}{h}p_1 & \frac{1}{h}p_0 \end{bmatrix}^T \tag{3.28}$$

with Σ_θ from Equation 3.21 and p_0 and p_1 from Equation A.7. The diagonal elements of Σ_δ are now the variances of the parameter vector $\delta=[\omega\ \gamma_0\ \gamma_1]^T$.
The variance of the divided set $\lambda=[\omega\ R\ \xi]^T$ is calculated from the variance of $\delta=[\omega\ \gamma_0\ \gamma_1]^T$ in the same way as for the discrete equivalents. From Equation 3.13 it can be assumed that

$$\begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & -\omega & 1 \end{bmatrix} = \frac{\partial f}{\partial \delta} \tag{3.29}$$

so that, using Equation 3.22, the variance of $\lambda=[\omega\ R\ \xi]^T$ can be determined as the diagonal elements of the covariance matrix

$$\Sigma_\lambda = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & -\omega & 1 \end{bmatrix} \Sigma_\gamma \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & -\omega & 1 \end{bmatrix}^T \tag{3.30}$$

with Σ_δ from Equation 3.28.

5 Results

5.1 Model of respiratory mechanics

The model has been used and validated in two different ways, with a large material (12 patients) and with a small material where data has been recorded both before and after a known change in ventilator settings. With the second data set it is possible to test if the model can handle changes in tidal volumes and breath frequencies. This is of course very important since it indicates if the model can be used for simulating changed settings and still be valid.

Note that the mean value of the actual pressure, i.e. what is subtracted when detrending, is added to the model pressures of all plots in this section to obtain figures as close to reality as possible.

5.1.1 Validation with large material

Models have been identified using data from 12 patients with different lung diseases. The parameters are found in Table 1, 2 and 3. The names of the sets are the initials of the patients and used just for convenient labelling. In all cases models were determined with one data set and verified with another. Table 1 contains the values of the discrete elastic pressure parameters with variance. The last column in the table describes a simple visual characterisation of the fitting between model and data. In case the fitting between model identification data and verification data respectively differed much this is also mentioned, as well as when the curve fitting to resistance polynomials has affected the result noticeable. The corresponding continuous time parameters are found in Table 2. Table 3 contains the original, constant value of R with variance as well as the parameters of the resistance polynomials found with curve fitting.

Data	a_1	Var(a_1)	b_0	Var(b_0)	Characterisation
Al	-0.9994	9.19×10^{-5}	0.3702	5.19×10^{-3}	Good agreement with data
Be	-0.9999	3.03×10^{-5}	0.6045	1.31×10^{-2}	OK agreement with data
Cc	-0.9998	9.45×10^{-5}	0.9076	7.58×10^{-2}	OK agreement with data
Di	-0.9986	3.20×10^{-4}	0.7046	1.35×10^{-1}	Bad agreement with data
Fd	-0.9992	6.07×10^{-5}	0.6301	1.58×10^{-2}	Good data fit, OK verification
Go	-1.0001	3.86×10^{-5}	0.6344	1.50×10^{-2}	OK agreement with data
Gv	-0.9993	8.27×10^{-5}	0.4656	1.12×10^{-2}	Good agreement with data
Je	-0.9994	4.96×10^{-5}	0.5058	9.99×10^{-3}	Good agreement with data
Jm	-0.9996	1.02×10^{-4}	0.4058	1.17×10^{-2}	OK agreement with data
Jm76	-0.9991	3.76×10^{-4}	0.9296	3.94×10^{-1}	Very good after R-fitting, bad original identification
Ma	-0.9994	4.98×10^{-5}	0.6070	2.06×10^{-2}	Very good
Pv	-0.9987	2.01×10^{-4}	0.8240	1.18×10^{-1}	Good after R-fitting, OK original identification

Table 1. Discrete elastic parameters with variance and characterisation of the identification and verification.

Data	ω	Var(ω)	ξ	Var(ξ)
Al	0.0296	3.68×10^{-8}	18.517	32.932
Be	0.0049	1.21×10^{-8}	30.228	27.498
Cc	0.0100	3.78×10^{-8}	45.386	189.60
Di	0.0704	1.28×10^{-7}	35.254	336.69
Fd	0.0382	2.43×10^{-8}	31.517	39.652
Go	-0.0066	1.54×10^{-8}	31.720	37.464
Gv	0.0363	3.31×10^{-8}	23.289	28.004
Je	0.0326	1.98×10^{-8}	25.297	25.012
Jm	0.0189	4.10×10^{-8}	20.294	42.942
Jm76	0.0450	1.51×10^{-7}	46.501	985.27
Ma	0.0299	1.99×10^{-8}	30.359	51.765
Pv	0.0639	8.06×10^{-8}	41.226	297.01

Table 2. Continuous elastic parameters with variance.

Data	R	Var(R)	r_{I0}	r_{I1}	r_{e0}	r_{e1}	r_{e2}
Al	5.901	0.817	7.520	-0.833	5.591	4.851	2.817
Be	10.027	0.518	9.958	-1.088	7.534	1.130	8.397
Cc	17.331	3.317	24.598	-17.210	9.432	-9.063	4.640
Di	8.459	5.298	23.207	-13.277	8.378	-38.115	74.610
Fd	4.088	0.519	1.454	6.286	0.947	26.940	-29.616
Go	5.8159	0.863	3.946	-1.788	6.420	-5.159	13.225
Gv	2.866	0.855	2.244	2.163	1.540	7.999	1.332
Je	3.801	0.687	3.461	0.263	2.772	5.778	3.959
Jm	5.756	1.047	3.682	7.462	4.770	10.226	-6.158
Jm76	24.950	12.231	34.988	-23.834	44.203	-121.48	194.17
Ma	11.513	1.007	11.658	2.503	13.473	-0.086	5.114
Pv	11.870	4.377	21.026	-29.032	28.641	-70.446	87.415

Table 3. Constant resistive parameter with variance and coefficients of the resistance polynomials.

In almost all cases a model with close matching to the actual data was obtained and also verified with new data sets with good results.

Even if the parameters exhibit large individual variations two main groups can be identified, the ones with large resistance, i.e. obstructive cases, and those with smaller, more normal, values of the resistances. P/V curves showing typical behaviour of the two cases are found in Figure 9. Note that there is a small hysteresis in the elastic pressure. To some extent this can be explained by the detrending of data. A linear increase in volume occurs in the right end of the curve. In the original data set there is a post-inspiratory pause that should have caused a vertical pressure drop under constant volume at the end of the inspiration. The detrending has lifted the actual zero-flow to a positive value, which naturally increases the volume. The actual respiratory system does of course not exhibit this behaviour.

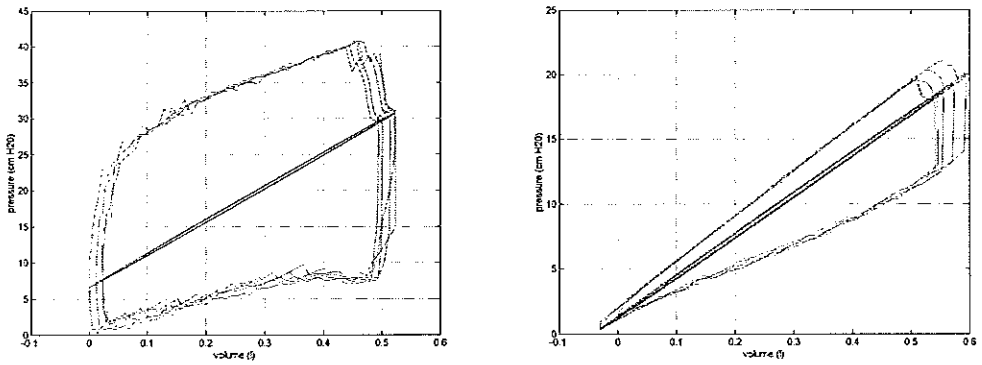

Figure 9. P/V-plots of typical obstructive data (left) and less resistive data (right). The inner loop of each plot is the model elastic pressure and the outer is the model tracheal pressure.

Some of the identified parameters have very bad variance, especially in the ξ-parameter. All those cases also exhibit bad model behaviour even if the curve fitting of the resistance polynomials of Equations 3.3 and 3.4 sometimes improves the result. Figure 10 and 11 illustrates the identification data for Cc and Jm76 before and after the polynomial fitting. It is clearly seen that the original identification can not handle the last part of the expiration very well but that the final model of Jm76 is good despite this.

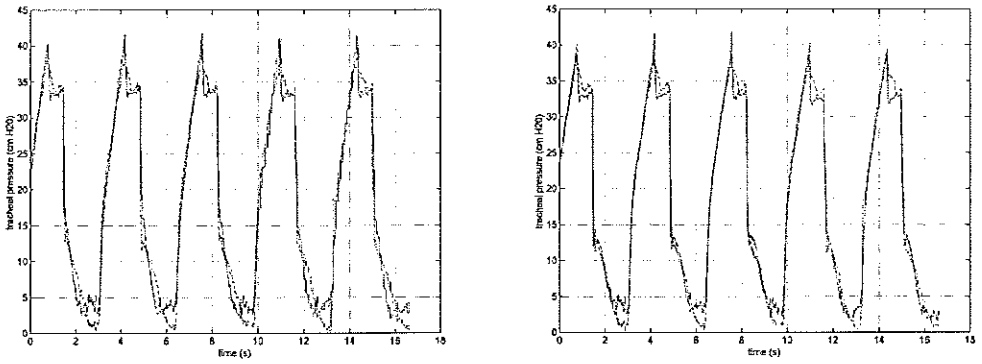

Figure 10. Identification data for Cc before (left) and after (right) the fitting of the resistance polynomials. The solid line is model output and the dashed line is actual output.

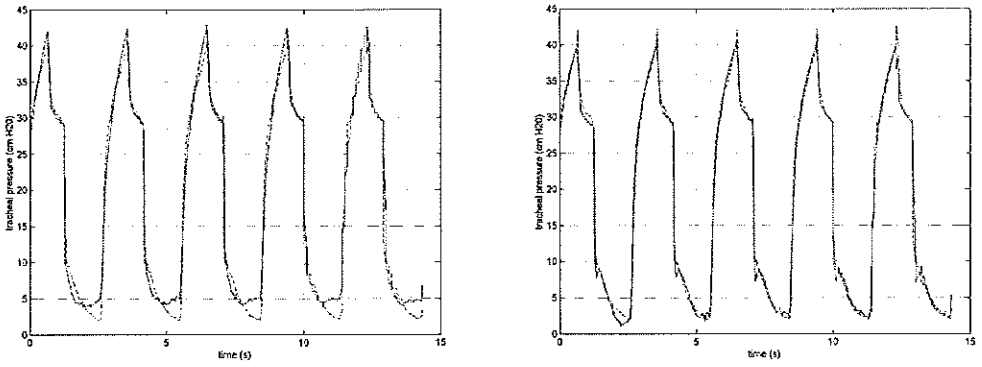

Figure 11. Identification data for Jm76 before (left) and after (right) the fitting of the resistance polynomials. The solid line is model output and the dashed line is actual output.

5.1.2 Validation with known changes in ventilator settings

There were a number of data sets available where recordings had been made both before and after some known change in the ventilator settings, for example increased inspiratory time or frequency. Models were first determined with data from the original settings. Those models could then be verified by comparing model output and actual output from data series recorded during or after the parameter change. The parameters are found in Table 4 to 6.

Data	a_1	Var(a_1)	b_0	Var(b_0)
Np	-0.9998	$2.53\text{x}10^{-4}$	0.3600	$6.42\text{x}10^{-2}$
Bf	-0.9999	$1.18\text{x}10^{-4}$	0.3405	$5.51\text{x}10^{-2}$
Tm	-0.9999	$7.22\text{x}10^{-5}$	0.6131	$8.22\text{x}10^{-2}$

Table 4. Discrete elastic parameters with variance.

Data	ω	Var(ω)	ξ	Var(ξ)
Np	0.0083	$1.02\text{x}10^{-7}$	18.001	160.68
Bf	0.0060	$4.74\text{x}10^{-8}$	17.027	137.73
Tm	0.0063	$2.89\text{x}10^{-8}$	30.656	205.58

Table 5. Continuous elastic parameters with variance.

Data	R	Var(R)	r_{i0}	r_{i1}	r_{e0}	r_{e1}	r_{e2}
Np	11.855	0.888	13.235	3.780	5.864	48.899	-71.184
Bf	17.883	0.480	15.141	5.500	25.197	-2.788	-10.340
Tm	27.308	1.022	25.694	-5.065	44.656	-75.025	94.344

Table 6. Constant resistive parameter with variance and coefficients of the resistance polynomials.

As can be seen from the plots in Figures 12 to 14 the model can handle changes in ventilator settings quite well. A slight exception can be seen for the changed settings of data tm where it seems as though the model cannot handle the last part of the expiration as well as in the other cases.

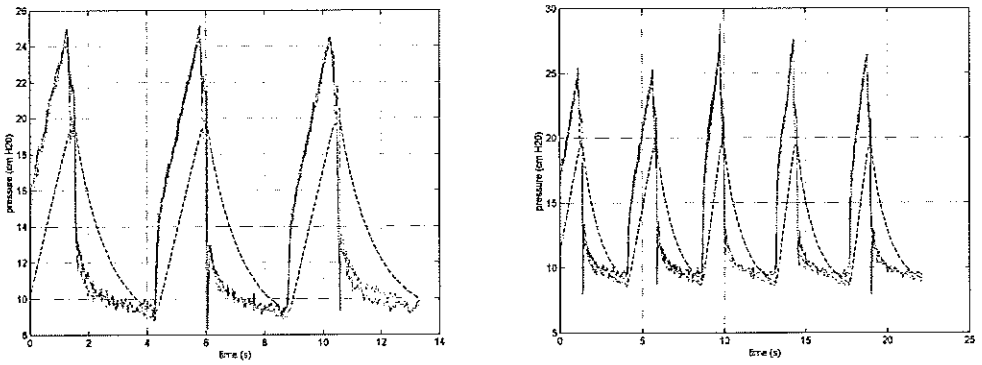

Figure 12. Data Np before (left) and during (right) a change in inspiratory time from 33% to 25%.

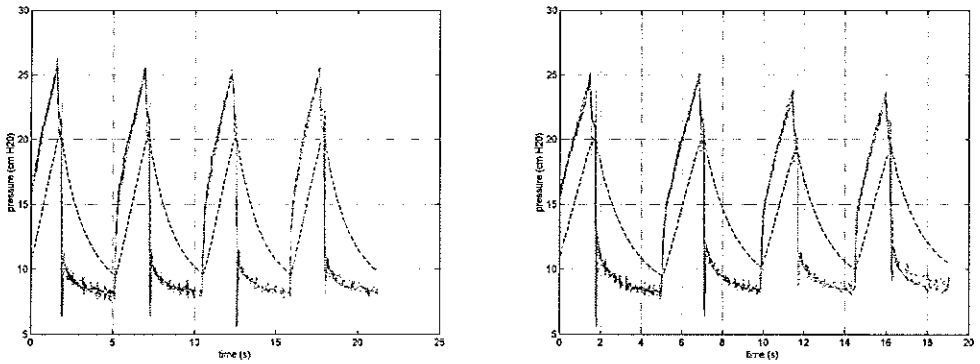

Figure 13. Data Bf before (left) and during (right) a change in frequency from 11 to 13 breaths/minute.

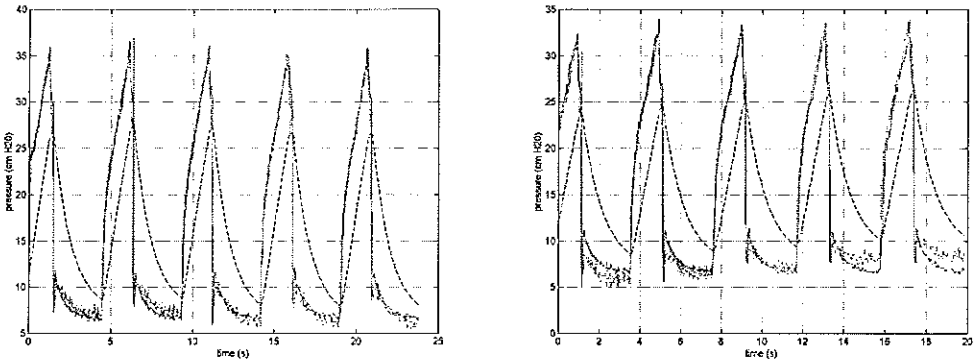

Figure 14. Data tm before (left) and during (right) a 25% increase in frequency.

5.1.3 Parameter errors

The parameters with standard deviations are visualised in the left diagram of Figure 15 to 19. The numbers on the x-axis corresponds to the data sets according to Table 7. The right diagram in Figure 15 to 19 is a cumulative plot of each parameter.

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Al	Be	Cc	Di	Fd	Go	Gv	Je	Jm	Jm 76	Ma	Pv	Np	Bf	Tm

Table 7

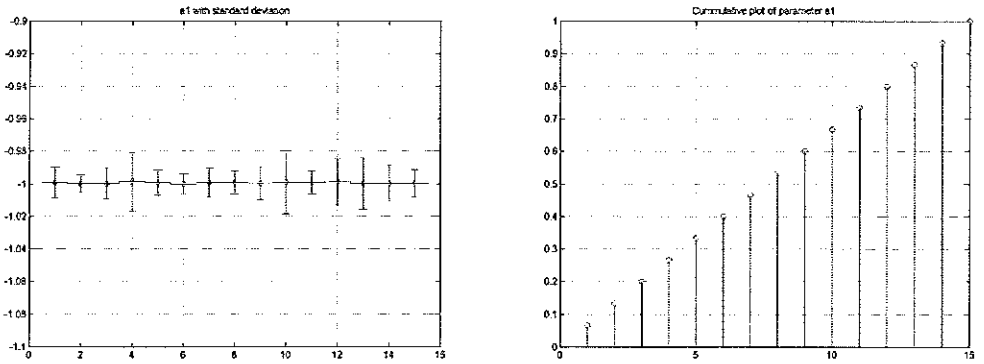

Figure 15. Discrete time parameter a_1 with standard deviations (left) and as cumulative plot (right) for all data sets.

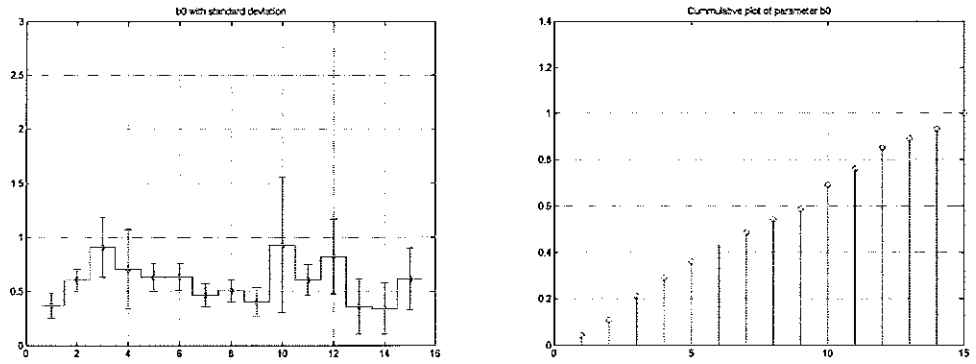

Figure 16. Discrete time parameter b_0 with standard deviations (left) and as cumulative plot (right) for all data sets.

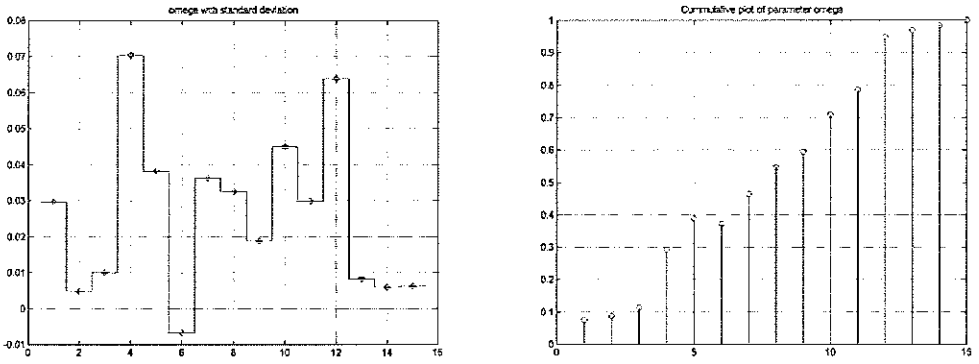

Figure 17. Continuous time parameter ω with standard deviations (left) and as cumulative plot (right) for all data sets.

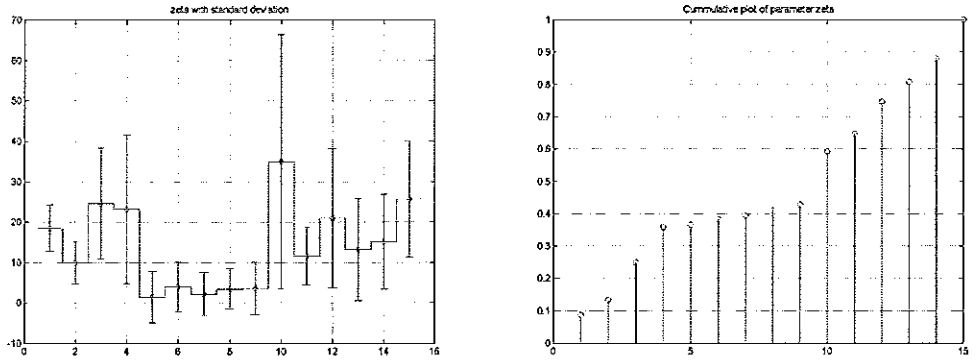

Figure 18. Continuous time parameter ξ with standard deviations (left) and as cumulative plot (right) for all data sets.

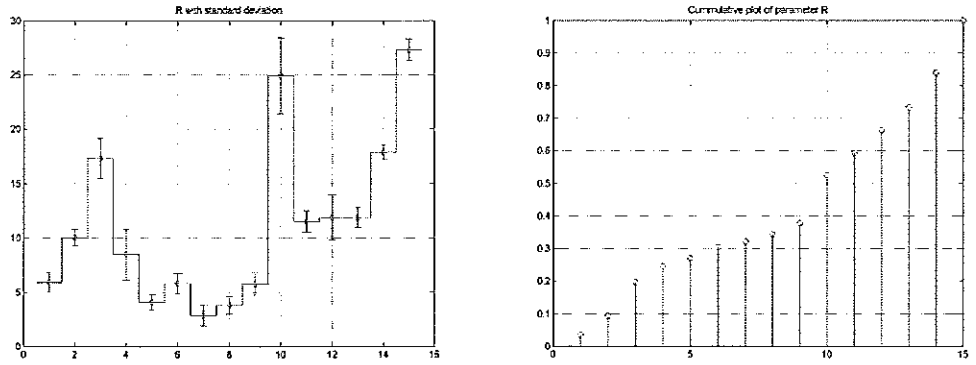

Figure 19. Parameter R with standard deviations (left) and as cumulative plot (right) for all data sets.

5.1.4 Residual tests

The residuals of a model can be calculated as the difference between model output and actual output in each point. If the model is sufficient there should be no structure in a sequence of residuals. Uncorrelated residuals indicate that the error is white noise, independent of previous inputs. There are thus no remaining dependencies in the error of the model. By the central limit theorem, such residual sequences are asymptotically normally distributed.

Autocorrelation and cross-correlation are two ways to test the residuals of a model. The first test calculates the correlation between the residual at time zero and residuals at later times. If the correlation is kept within a 99%-confidence interval for a normal distribution it can be concluded that the residuals are normal distributed white noise. The cross-correlation test is similar but test the independence between the input at a certain time and the residuals of earlier and later samples.

Due to lack of time it has not been possible to perform these tests on the complex model with resistance polynomials, since this would have required changes in the available Matlab-routines. The tests were instead performed on the model with constant resistance, acquired for detrended data. This could at least be an indication of the reliability of the model. A typical result from the test is found in Figure 18 and all data sets exhibit similar results.

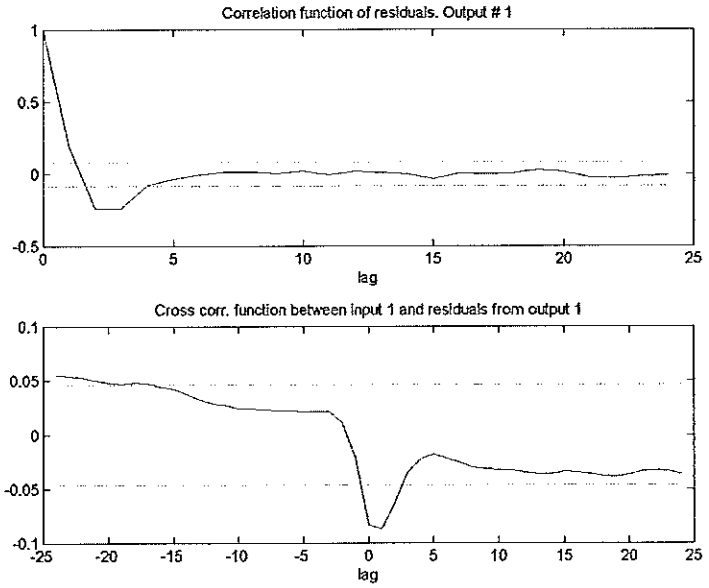

Figure 20. Autocorrelation (upper) and cross-correlation (lower) tests for data Ma.

Two simple possibilities to test the residuals of the total model with resistance polynomials are to calculate VAF (variance accounted for) and NQ (the quote between the norm of the difference between model and actual output and the norm of the actual output),

$$VAF = \left(1 - \frac{\mathrm{var}\left(P_{tr,actual} - P_{tr,model}\right)}{\mathrm{var}\left(P_{tr,actual}\right)}\right) * 100\% \tag{5.1}$$

$$NQ = \frac{\left\| P_{tr,actual} - P_{tr,model} \right\|}{\left\| P_{tr,actual} \right\|} * 100\% . \tag{5.2}$$

VAF should be as large as possible, VAF is 100% for two equal signals, and NQ should be as low as possible. Both VAF and NQ have meaningful ranges of 0-100%.

Table 8 contains VAF and NQ for all data sets tested.

Data	VAF (%)	NQ (%)
Al	98.4	5.78
Be	98.88	5.81
Cc	98.64	6.83
Di	95.64	12.51
Fd	97.65	9.71
Go	98.05	8.21
Gv	98.36	6.47
Je	98.86	5.61
Jm	96.35	9.75
Jm76	98.51	7.34
Ma	98.57	6.73
Pv	98.72	6.51
Np	95.36	7.52
Bf	97.18	7.01
Tm	97.56	8.70

Table 8 VAF and NQ for all data sets.

5.2 Model of alveolar CO_2-pressure

The parameters b and m in Equation 3.6 were determined for all available data sets. The values are found in Table 9.

Data	b	m
Al	0.042	0.007
Be	0.053	0.012
Cc	0.045	0.004
Di	0.078	0.017
Fd	0.066	0.008
Go	0.055	0.013
Gv	0.044	0.009
Je	0.049	0.012
Jm	0.038	0.010
Jm76	0.057	0.016
Ma	0.059	0.018
Pv	0.055	0.011
Np	0.075	0.027
Bf	0.047	0.014
Tm	0.047	0.013

Table 9 Parameters b and m from all data sets.

A curve fit similar to the one in Figure 8 was obtained for all data tested, indicating that the proposed modelling is good enough.

6 Discussion

6.1 Model of respiratory mechanics

The results show that a good discrete model can be obtained from a data series of just three to five normal breaths. The model is not perfect in all cases but it should be good enough for the purpose of simulation. This section focuses on some of the important features and limitations of the proposed model structure and determination procedure.

6.1.1 Elastic properties

It seems as though the elastic properties of the respiratory system are well modelled with the suggested method, even if the results might differ slightly from previous work, especially concerning hysteresis. This is treated more in detail below.
Otherwise it is always possible to obtain parameters that seem reasonable and none of the tested data exhibits unexpected behaviour. There are ways to measure the elastic pressure but such information was not available for the data used in this work. It is therefore difficult to claim that the elastic pressure from the model is the actual elastic pressure. Since the total model pressure follows the total actual pressure well in most cases it is reasonable to believe that all parts of the original identified model are correct.

6.1.2 Resistive properties

As mentioned above it is not sufficient to model the resistive properties as a simple constant, equal for inspiration and expiration. This is the reason for modelling it as a volume-dependent polynomial. The results of this are unfortunately not always that good. For some cases the original identification does not work as well as expected but the curve fitting finds good resistance parameters leading to a total model output that follows the actual output well. There are however also cases where a relatively good original identification is practically unchanged or even a bit worse after the curve fitting. This and the large variation in resistance parameters might indicate that either the resistive modelling chosen or the numerical method used is not optimal.
Another problem with the proposed resistance modelling is that it seems as though the curve fitting is dependent on the data series starting at full inspiratory flow and not at zero for a good result. This makes it important not to make the cut too early in the original data sets. In this work this problem have been solved by calculating the initial volume and adding this to the integrated volume wherever it is necessary. It is nevertheless important to keep this in mind.

6.1.3 Detrending

The detrending of data is necessary to get a correct model of the resistive properties. The drawback is that it places the data points symmetrically around zero, raising an actual zero flow (i.e. during a pause) above zero, causing an increase in volume that has no physical relevance. This should not be a problem as long as detrending is used consistently for a particular patient since all data then will be treated in the same way.

6.1.4 Hysteresis

Previous work [7] has shown a non significant hysteresis in the elastic pressure during normal breaths and therefore used the same elastic pressure model for inspiration and expiration. That model was determined by using a long sinusoidally modulated inspiratory flow to which a model with three linear segments was fitted. Using the simpler model of this work a small but yet relevant hysteresis is found. By using identification methods it is quite simple to get a model that is equal for inspiration and expiration but still recognises the differences. The suggested

modelling method is can also be used with data from normal breaths. It is worth mentioning that the hysteresis effect in the P-V curves is amplified because of detrending since, as mentioned above, an actual zero flow is lifted above zero causing an increase in volume that is not physically relevant.

6.1.5 Continuous parameters

Equation 3.11 is a linear approximation that describes the relationship between continuous and discrete parameters. This is the normal way to transform discrete models to continuos time and it usually works fine. The problem with the parameters estimated in this work is that a_1 is very close to 1. This causes the denominator in the expressions for p_0 and p_1 in Equation A.7 to be almost zero since λ_2 in that equation equals 1 and $\lambda_1=-a_1$. Both p0 and p1 then becomes very large and since both are used in Equation 3.1 it can be concluded that this linear approximation is not valid for the identified model.

There are a number of solutions to the problem of obtaining correct continuous parameters, a problem that is important since, as mentioned earlier, it is easier to understand a continuous expression. Unfortunately it has not been possible to examine those options within the time available for this master thesis but some suggestions are presented here. One solution is obviously to identify a continuous model initially. This can be done using other identification methods and might require faster sampling so that the data series can be assumed to be continuous. Another solution might be to just change the sample rate and thus avoiding the dangerous value of a1. A third possibility is to use other, more advanced, conversions from discrete to continuous time.

A simple solution is of course never to present the actual parameter values, neither in discrete nor continuous time. It might be enough for the physician to just see a graphical representation of the model.

6.1.6 Parameter errors

The parameter variance is not too good, especially in continuous time. This might of course suggest that the chosen identification method or model structure is not suitable for the respiratory system.

The variance of b_0, the nominator of the discrete elastic model, is rather bad. One possible reason might be that the assumption of a constant flow between the sample points is not valid. This can be solved by using a faster sampling rate or using a continuous time model where it is not necessary to make such assumptions. Another problem is that the calculation of the covariance matrix in Equation 3.19 assumes that the estimated parameters are unbiased estimations of the actual parameters. This might not be the case.

The variance of the continuous parameters is not reliable since it is calculated using approximations that are not valid according to the discussion on continuous parameters above.

Despite the bad variance a good model is found in most cases and it can also be verified using other data sets. This indicates that the model is acceptable after all, at least for the purpose of predicting the behaviour for small changes in the ventilator settings. The residual tests performed supports this.

The values of VAF and NQ are very good, showing that the estimated model agrees well with actual data. The autocorrelation and cross-correlation tests are not quite satisfactory since the curves do not stay within the confidence intervals for all values. It should be remembered that those tests where performed on the model with constant parameters. This and the good results on the other test suggest that the results of the autocorrelation and cross-correlation tests are acceptable.

All tested data sets where the original identification produces poor result also exhibits larger variance even for the discrete parameters. It can therefore be concluded that the discrete variance is a good measurement of how well the identification has worked. For some of these sets the fitting to resistive polynomials

has produced a final result that is really good or at least better than originally. This is one more indication that it is not sufficient to model the resistance with just one constant parameter.

6.1.6 Limitations

The proposed model has been tested on 15 subjects. This is of course a too small population for statistically satisfactory conclusions to be drawn from the results. Nevertheless there are certain trends that could explain why the identification and the curve fitting works more or less well for different data. Almost all data where the model is not reasonably good seems to have been recorded with a rather large maximum flow, typically more than 0.5-0.6 l/s, indicating that it is good if the flow can be kept below 0.5 l/s to ensure a good identification. Comparing the flow from two data sets with very similar ventilator settings and identified parameters but with different results confirms this. This is a model limitation that needs to be examined thoroughly and must be considered when using the model.

Another limitation seems to be that the identification cannot handle obstructive cases as well as other cases. This is sometimes handled by resistance polynomials but more examination of this is necessary.

There is no guarantee that the model used is globally valid, which the experiments with changed settings could be an evidence of. Some of those sets might have had too large changes for the model to be valid. Examples of this can be found in Figure 12 where the model does not follow the data for the changed settings particularly well, especially at the end of the expiration. The change in this case is a 25% increase in frequency and this is obviously a very large step. There might of course be other explanations such as bad choice of starting point for the validation series but validity in a larger area is a limitation of this model. When using the model for simulation purposes this must be kept in mind, avoiding large changes in ventilator settings.

6.2 Model of alveolar CO_2-pressure

It is possible to model the alveolar CO_2-pressure very well with the simple function in Equation 3.6. Of course curve fitting is not a complete way to model a physical behaviour but the purpose of this model is to be able to track relative changes from the original value rather than determine an absolute correct new pressure.

To illustrate the purpose of finding a model for the upper part of the alveolar CO_2-pressure curve, it is here shown how the partial pressure for a new tidal volume or a new breathing frequency can be calculated, using the two parameters b and m.

The volume CO_2 exhaled during each breath (V_tCO_2) equals, as mentioned above, the area under the curve in Figure 3. If the tidal volume is changed, the end point of the curve is moved either to the left or to the right, changing the total area. The new V_tCO_2 is calculated as

$$V_tCO_2^{new} = V_tCO_2^{old} + \int_{V_t^{old}}^{V_t^{new}} (b + m\ln(V))dV \tag{6.1}$$

where V_t^{old} is the original tidal volume and V_t^{new} is the wanted tidal volume. This is correct if the upper part of the curve indeed can be described by Equation 3.6. The new alveolar CO2-pressure can now be calculated as

$$P_ACO_2^{new} = P_ACO_2^{old} \frac{V_tCO_2^{old} RR^{old}}{V_tCO_2^{new} RR^{new}} \tag{6.2}$$

where RR^{old} and RR^{new} are the old and new breathing frequencies respectively and $V_tCO_2^{old}$ is the original volume CO_2 per breath.

If the two parameters b and m are correct, it is possible to keep good track of changes in the alveolar CO_2-pressure. As mentioned in Section 4.1.2 this pressure is equal to the arterial CO_2-pressure. According to Section 2.1.4, information about changes in the arterial CO_2-pressure is very important for the physician.

7 Conclusions

It is obvious that identification methods are very valuable to create simple yet useful discrete models of the human respiratory system with data sets of just a few ordinary breaths and with a rather small amount of time and computer work needed. It should also be possible to obtain correct continuous time models as well even if this is not shown in this thesis.

The major drawbacks seem to originate from the fact that curve fitting must be used at one stage since two different models should be applied for inspiration and expiration to model the physical behaviour correctly. This can probably be solved by using another parameterisation of the respiratory forces or by using different numerical methods.

The model is developed for a certain tidal volume, breathing frequency and minute volume and there is no guarantee that it is globally valid since the lung physiology is very dependent on those parameters. Changed settings should therefore be handled with care so that the changes are kept relatively small. It is probably better to make a model for a certain setting, find a new but similar setting, implement this and then make a new model rather than trying to reach a goal far away in just one step.

8 Suggestions for further work

In this work one step towards an increased use of computers in ventilator care has been taken. This section contains some suggestions for improvements of the proposed model as well as further work towards good simulation and optimisation tools.

A better model for resistance, more based on physical principles of, for instance, turbulence and flow, would make an improvement of this model that could perhaps give really good results in more cases than in the present one. An example of such resistance modelling can be found in [8].

A method for standardisation of extraction of suitable data from the recorded series could be a possible solution to the problem of finding a good starting point.

The best use of the proposed model is probably to create a user-friendly simulation and optimisation tool that can be used in a clinical situation where medical professionals can state therapeutic goals and limits with the treatment and the best possible settings can be found. The optimisation and graphical user-interface routines in Matlab can be used for this work as well.

9 References

[1] Jonson B, Westling H, White T, Wollmer P (eds.). *Klinisk fysiologi med nuklearmedicin och klinisk neurofysiologi.* Liber AB, Stockholm, Sweden, 1998.

[2] Sonesson B, Sonesson G. *Människans anatomi och fysiologi.* Almqvist & Wiksell Medicin, Stockholm, Sweden, 1993.

[3] Jonson B, Uttman L. "Optimisation of mechanical ventilation on the basis of physiological measurements" in *Dialogues on anaesthesia and intensive care.* University of Naples "Federico II", Naples, Italy, 1999.

[4] Jonson B, Richard J C, Straus C, Mancebo J, Lemaire F, Brochard L. "Pressure-volume curves in acute lung injury" *Am J Respir Crit Care Med,* Vol. 159, pp 1172-1178, 1999.

[5] Haverkamp B, Verhagen M. SMI Toolbox: *State Space Model Identification Software for Multivariable Dynamical Systems.* Delft University of Technology, Faculty of Information Technology and Systems, Department of Electrical Engineering, Systems- and Control Engineering Group, Delft, The Netherlands, 1997.

[6] Johansson R. *System Modeling and Identification.* Prentice-Hall, Inc., Englewood Cliffs, NJ, 1993.

[7] Svantesson C. *Respiratory mechanics during mechanical ventilation in health and in disease.* Doctoral dissertation, ISRN LUMEDW/MEFL—1013—SE. Department of Clinical Physiology, Lund University, Sweden, 1997.

[8] Liu C H, Niranjan S C, Clark, JR. J W, San K Y, Zwischenberger J B, Bidani A. "Airway mechanics, gas exchange, and blood flow in a nonlinear model of the normal human lung" in *J. Appl. Physiol.* 84(4) pp 1447-1469, 1998.

[9] Åström K J, Wittenmark. B *Computer controlled systems: theory and design, 2nd edition.* Prentice-Hall International Inc., Englewood Cliffs, NJ, 1990.

Appendix A. State-space realisation and the inverse of sampling.

The subspace identification method used in this thesis produces a model in state-space realisation. A brief introduction to this format is given in this section and it is also shown how it relates to the transfer function. To perform a correct conversion between discrete and continuous time, the inverse of sampling, the state-space realisation is necessary and how the conversion can be done using the Caley-Hamilton theorem is also presented.

A state-space realisation for a continuous system is given as

$$\begin{cases} \frac{dx}{dt} = Ax(t) + Bu(t) \\ y(t) = Cx(t) + Du(t) \end{cases} \Leftrightarrow G(s) = \frac{Y}{U} = C(sI - A)^{-1}B + D \tag{A.1}$$

and for a discrete system

$$\begin{cases} x(k+1) = \Phi x(k) + \Gamma u(k) \\ y(k) = Cx(k) + Du(k) \end{cases} \Leftrightarrow H(z) = \frac{Y}{U} = C(zI - \Phi)^{-1}\Gamma + D \tag{A.2}$$

where C and D are equal for the two systems. According to the theory of zero-order hold sampling [9, Ch. 3.2] the parameters of the discrete system are given in matrix form by (h is the sampling period)

$$\begin{bmatrix} \Phi & \Gamma \\ 0 & 1 \end{bmatrix} = \exp\left\{ \begin{bmatrix} A & B \\ 0 & 0 \end{bmatrix} h \right\} \tag{A.3}$$

This expression can be reversed to obtain a possible conversion from discrete to continuous time as

$$\begin{bmatrix} A & B \\ 0 & 0 \end{bmatrix} = \frac{1}{h} \ln \begin{bmatrix} \Phi & \Gamma \\ 0 & I \end{bmatrix}. \tag{A.4}$$

If it is assumed that A, B, Φ and Γ are all of size 1x1, the Caley-Hamilton theorem [9, App. B] can be used to evaluate the matrix logarithm function. According to the theorem a matrix satisfies its own characteristic equation so that

$$\ln \begin{bmatrix} \Phi & \Gamma \\ 0 & I \end{bmatrix} = p\left(\begin{bmatrix} \Phi & \Gamma \\ 0 & I \end{bmatrix} \right) = p_0 \begin{bmatrix} \Phi & \Gamma \\ 0 & I \end{bmatrix} + p_1 I \tag{A.5}$$

where *I* is the identity matrix and p satisfies

$$\begin{cases} p(\lambda_1) = \ln \lambda_1 \\ p(\lambda_2) = \ln \lambda_2 \end{cases} \tag{A.6}$$

if λ_1 and λ_2 are the eigenvalues of the matrix. In this case, $\lambda_1 = \Phi$ and $\lambda_2 = 1$. The values of p_0 and p_1 are obtained by solving equation 6 so that

$$\begin{cases} p_0 = \dfrac{\ln\lambda_2 - \ln\lambda_1}{\lambda_2 - \lambda_1} \\ p_1 = \ln\lambda_1 - \lambda_1 \dfrac{\ln\lambda_2 - \ln\lambda_1}{\lambda_2 - \lambda_1} \end{cases} \tag{A.7}$$

Now A and B can be determined from equation 4 as

$$\begin{cases} A = \dfrac{1}{h}\left(p_0\Phi + p_1\right) \\ B = \dfrac{1}{h} p_0\Gamma. \end{cases} \tag{A.8}$$