

Serial lung model for simulation and parameter estimation in body plethysmography

A. F. M. Verbraak¹ J. M. Bogaard¹ J. E. W. Beneken²
E. Hoorn¹ A. Versprille¹

¹Department of Pulmonary Diseases, University Hospital 'Dijkzigt', Rotterdam, The Netherlands
²Division of Medical Electrical Engineering, Eindhoven University of Technology, The Netherlands

Abstract—A serial lung model with a compressible segment has been implemented to simulate different types of lung and airway disorders such as asthma, emphysema, fibrosis and upper airway obstruction. The model described can be used during normal breathing, and moreover the compliant segment is structured according to more recent physiological data. A parameter estimation technique was applied and its reliability and uniqueness were tested by means of sine wave input signals. The characteristics of the alveolar pressure/flow patterns simulated with the model agree to a great extent with those found in the literature. In the case of absence of noise the parameter estimation routine produced unique solutions for different simulated pathologic classes. The sensitivity of the different parameters depended on the values belonging to each class of pathology. Some more simplified models are presented and their advantages over the complex model in special types of pathology are demonstrated. Noise added to the simulated flow appeared to have no influence on the estimated parameters, in contradiction to the effects with noise added to the pressure signal. In that case effective resistance was accurately estimated. Where parameters had no influence, as for instance upper airway resistance in emphysema or peripheral airway resistance in upper airway obstruction, the measurement accuracy was less. In all other cases, a satisfactory accuracy could be obtained.

Keywords—Body plethysmography, Parameter estimation, Serial lung model, Simulation

Med. & Biol. Eng. & Comput., 1991, 29, 309–317

List of symbols

C	compliance of the lung, litre kPa ⁻¹	R_u	total resistance of the upper airways, kPa litre ⁻¹ s
EE	square error	P_A	alveolar pressure, kPa
K_1	linear resistance of the large airways, kPa litre ⁻¹ s	P_L	elastic lung recoil, kPa
K_2	turbulent resistance of the large airways, kPa litre ⁻² s ²	$P_{L, FRC}$	elastic lung recoil at FRC, kPa
K_3	linear resistance parameter model 2, kPa litre ⁻¹ s	P_{tm}	transmural pressure, kPa
K_4, K_5	linear resistance parameters model 3 for inspiration and expiration, respectively, kPa litre ⁻¹ s	P_{pl}	pleural pressure, kPa
K_6, K_7	linear resistance parameters model 4 for inspiration and expiration, respectively, kPa litre ⁻¹ s	P_s	pressure drop over the small airways, kPa
K_8, K_9	turbulent resistance parameters model 4 for inspiration and expiration, respectively, kPa litre ⁻¹ s ²	V_A	alveolar volume, litre
R_{eff}	effective resistance, kPa litre ⁻¹ s	V_L	alveolar volume + volume of the airways, litre
R_c	linear resistance of the compressible segment, kPa litre ⁻¹ s	V_c	volume of the compressible segment, litre
R_{c0}	weighting constant (see text), kPa litre ⁻¹ s	V_{cN}	maximum volume of the compressible segment for normals, litre
R_p	resistance line trough extreme pressure points, kPa litre ⁻¹ s	V'_A	flow into the alveolar space, litre s ⁻¹
R_s	linear resistance of the small airways, kPa litre ⁻¹ s	V'_m	flow at the mouth, litre s ⁻¹
		V_{c0}	weighting constant (see text), litre
		P_{tms}	point of curvature for the compressible segment, kPa

1 Introduction

A DIRECT calculation of airway resistance from driving pressure and airflow was enabled by body plethysmog-

First received 1st June 1988 and in final form 9th April 1990

© IFMBE: 1991

raphy. Because the difference between the volume displacement at the mouth and the simultaneous change in chest volume are caused by compression or expansion of intrathoracic gas, the plethysmograph can be used for measurements of thoracic gas volume and the alveolar pressure P_A inside the thorax. In 1956, DUBOIS *et al.* re-established the method for routine clinical use.

By plotting P_A against simultaneously measured flow at the mouth V'_m , a pressure/flow loop was obtained. Only when P_A and V'_m yield a linear relationship can airway resistance R be derived directly according to Ohm's law $R = P_A/V'_m$, where ambient pressure is reset to zero. However, for different types of pulmonary pathology, nonlinearities were found between P_A and V'_m , not permitting such a direct derivation of R .

In 1971, MATTHYS made a classification of patterns that were caused by different distributions of elastic and resistive properties of the lung, and by the pressure and flow differences in different parts of the lung.

Usually, estimates of airway resistance are obtained graphically from the body plethysmographic pressure/flow diagrams. REINERT *et al.* (1975) restricted their analysis to the linear parts of pressure/flow curves. Others have estimated airway resistance from a few discrete data, as e.g. total resistance R_t , which is calculated from the line through the two extreme values of pressure in the inspiratory and expiratory part of the curve (ULMER and REIF, 1965) and from lines through mean pressure points at flow rates of $0.5 \text{ litres s}^{-1}$ during inspiration and expiration (GUYATT *et al.*, 1967). In 1975, SMIDT *et al.* proposed to calculate an effective resistance variable, R_{eff} , which was related to the dissipation of energy during the whole respiratory cycle. R_{eff} was defined as the integral of pressure times volume increments divided by the integral of flow times volume increments. This variable is comparable with the effective resistance as defined in alternating current theory. HOLLAND *et al.* (1986) showed that R_{eff} was almost independent of those errors in P_A which were associated with differences in humidity and temperature between inspired and expired air.

System identification and parameter estimation on input/output data receive increasing acceptance in physiological research (BEKEY and BENEKEN, 1978). Until now only a few papers in the field of body plethysmography have dealt with modelling techniques to estimate the physiological variables describing lung mechanics. BANERJEE *et al.* (1976) and CETTL *et al.* (1979) attributed the degree of looping of the $P_A - V'_m$ patterns to parallel inhomogeneity and modelled it by two RC branches in parallel, as described by OTIS *et al.* (1956). Another group of authors (PRIDE *et al.*, 1967, FEINBERG *et al.*, 1970; FEINBERG and CHESTER, 1972; GOLDEN *et al.*, 1973) modelled a serial inhomogeneity, describing the lung as an alveolar compartment, lower and upper airways and a compliant segment in between, allowing a simulation of airway compression during expiration. The serial model of FEINBERG *et al.* (1970) was based on a comprehensive mathematical basis to obtain a quantitative indication of various aspects of lung mechanics. An estimation routine fitted the model to the data obtained during panting. GOLDEN *et al.* (1973) used the same type of model with a restricted number of parameters.

The serial models published so far are dependent on panting manoeuvres to approximate a constant lung volume during the measurements. We have extended the lung model described by GOLDEN *et al.* (1973), with lung compliance dependent on lung volume, to adapt it to the circumstances of normal breathing. Additionally, we have improved the model by giving a better physiological basis

for the compressible segment based on more recent publications. Furthermore, we have evaluated the sensitivity and the uniqueness of the estimated parameters and the influence of noise.

2 Theory and methods

2.1 The serial lung model

For the definition of the model the functional approach of GOLDEN *et al.* (1973) was used. The model (Fig. 1) was restricted to serial inhomogeneity with respect to both resistance and elastic properties of the airways. All alveoli were lumped to one compartment V_A , which was connected to ambient air by a tube representing the lumped airways. This tube consisted of three parts in series: one for the small airways, a compressible segment in between, and one for the large airways. The alveolar compartment and the intrapulmonary airways were influenced by the intrathoracic pressure, which was equal to pleural pressure P_{pl} . GOLDEN *et al.* (1973) assumed static lung recoil P_L to be constant because of the small lung volume changes

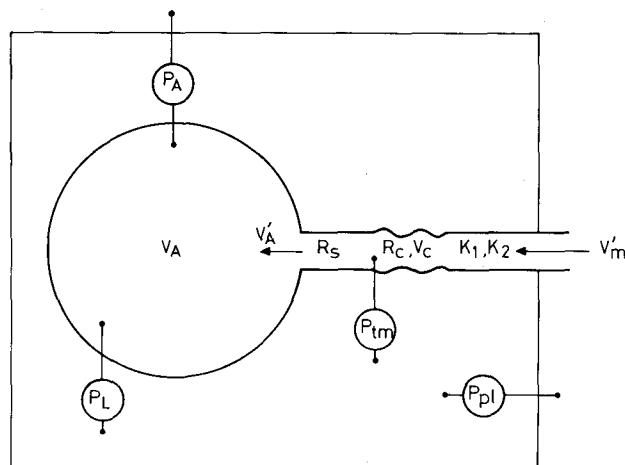


Fig. 1 The serial lung model. For the explanation of the different variables and symbols see list of symbols and text

during the panting manoeuvres. The elastic properties were modelled such that the static lung recoil P_L increased when alveolar volume V_A increased. In the range of normal breathing it was assumed that the increase of P_L against the change in alveolar volume yields:

$$P_L(t) = P_{L, FRC}(0) + 1/C \int_{\sigma=0}^t V'_A(\sigma) d\sigma \quad (1)$$

where C is the compliance of the lung in litre kPa^{-1}

$P_{L, FRC}(0)$ is the $P_L(\text{kPa})$ at functional residual capacity (FRC), which is the lung volume at the end of normal expiration, and thus at the beginning of normal inspiration

$t = 0$ is the moment at which inspiration starts.

$V'_A(\sigma)$ is flow in litres s^{-1} into the alveolar compartment at time $t = \sigma$, giving inspiratory volume V_I at any value of t by integration.

In the case of normal breathing, as in our model, the magnitude of the flow is such that the pressure drop produced by convective acceleration can be neglected, and so airway pressure at different sites in the airways is assumed to be a function of frictional pressure loss only.

2.2 Airway resistances

The resistance of the upper airways R_u was modelled as a rigid part. R_u included a flow-dependent term, and was expressed by the 'Rohrer equation' (ROHRER, 1915):

$$P_u = R_u V'_m = K_1 V'_m + K_2 V'^2_m \quad (2)$$

where P_u is pressure drop in the upper airways
 K_1 is a factor related to the pressure drop due to laminar flow in the upper airways, in kPa litre⁻¹ s
 K_2 is a factor related to the pressure drop due to turbulent flow in the upper airways, in kPa litre⁻² s²
 V'_m is the flow at the mouth, in litre s⁻¹.

The resistance of the peripheral airways R_s was assumed to be constant and we neglected the influence of the lung volume changes during the breathing manoeuvre at volumes above FRC. Based on the dimensions of these airways a Poiseuille flow was assumed. So, the linear pressure drop P_s in these airways is given by

$$P_s = R_s V'_A \quad (3)$$

where R_s is the resistance of the small airways, kPa litre⁻¹ s.

The resistance of the compressible segment represented the resistance in those airway generations, which are susceptible to the changes in transmural pressure P_{tm} being the difference between intrabronchial and pleural pressure. The functional behaviour of the compressible segment was modelled as a nonlinear relationship between P_{tm} and its cross-sectional area. P_{tm} of the compressible segment was located between this segment and the peripheral airways and was assumed to be the same over the whole segment. Furthermore, a constant length and an equal cross-sectional area over its length is assumed. Thus, the cross-sectional area can be expressed in terms of volume V_c . Assuming a laminar flow the resistance in a tube of constant length will be proportional to $1/r^4$ and thus to $1/V_c^2$. V_c was normalised to the maximum volume V_{cN} of the compressible segment for the normal lung, having a recoil tension of 0.5 kPa at FRC-level.

The largest changes in volume will occur for changes in P_{tm} around zero. The site in the segment where P_{tm} equals zero is called the equal pressure point (EPP) (MEAD *et al.*, 1967; HYATT, 1983). The location of the EPP depends on the elasticity of the lung and the peripheral airway resistance R_s . This dependence is described by eqns. (4-7).

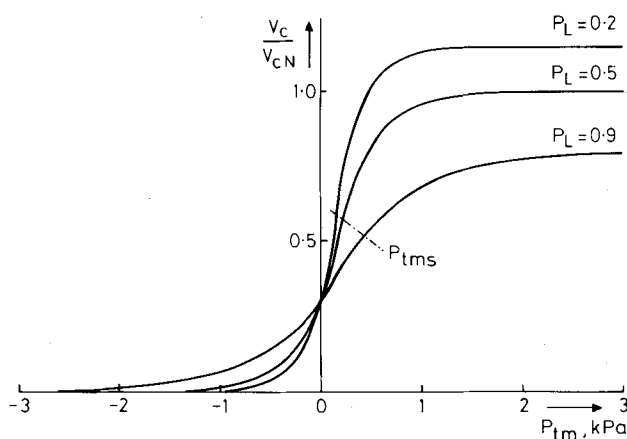


Fig. 2 The relationship between the normalised volume of the compressible segment (V_c/V_{cN}) and the transmural pressure P_{tm} with the elastic lung recoil as parameter. For symbols see list of symbols and text

$$P_{tm}(x) = P_{br}(x) - P_{pl} \quad (4)$$

where $P_{br}(x)$ is intrabronchial pressure (kPa) as a function of the location x in the airways
 P_{pl} is pleural pressure in kPa.

If during breathing eqn. 3 is valid then

$$P_{br}(x) = P_A + R_s(x)V'_A \quad (5)$$

where $R_s(x)$ is the cumulated airway resistance in kPa litre⁻¹ s from the alveolus to the location x in the airways

P_{pl} is the sum of elastic recoil P_L and alveolar P_A

$$P_{pl} = P_L + P_A \quad (6)$$

From eqns. 4, 5 and 6

$$P_{tm}(x) = P_L + R_s(x)V'_A \quad (7)$$

EPP will be found at the location x where $P_{tm}(x) = 0$. Then the driving pressure for the flow is given by P_L and is determined by the peripheral airway resistance $R_s(x)$. This means that the EPP is shifted upstream or downstream, dependent on elastic recoil and/or peripheral airway resistance.

The stiffness of airways increases from the alveoli towards the mouth (LAMBERT *et al.*, 1982). The model described neither the location in detail of the EPP within the tapered serial system with gradually changing R_s , nor the dependence of the airway compliance on generation number. Therefore, it is necessary to find another solution for the modelling of the changing properties of the compressible segment in dependence on the location x of the EPP. A low P_L means a more peripheral located and less stiff compressible segment with a larger volume at maximum distension. Therefore, we modelled the elastic properties of the compressible segment in dependence on the P_L values.

The mathematical description of the volume behaviour of the compressible segment in terms of P_{tm} (Fig. 2) is as follows:

$$P_{tm} \geq P_{tms} \quad \frac{V_c}{V_{cN}} = S - \frac{S^2}{1.2} \times \left[\frac{0.6}{S} \right]^{(P_{tm}/P_{tms})} \quad (8a)$$

$$P_{tm} < P_{tms} \quad \frac{V_c}{V_{cN}} = 0.3 \times \left[\frac{0.6}{S} \right]^{(-P_{tm}/P_{tms})} \quad (8b)$$

$$P_{tms} = 0.15 + 0.05P_L \quad (9a)$$

$$S = 1.25 - P_L/2 \quad (9b)$$

where S is an auxiliary variable to optimise calculations.

Eqns. (8a-9b) describe the relationship between the transmural pressure over the compressible segment and the volume of this segment, with elastic lung recoil as a parameter. These relationships are adapted from the literature and have been based on measurements in dogs and extrapolated to humans (MARTIN and PROCTOR, 1958; HYATT and FLATH, 1966; MARTIN *et al.*, 1965; MACKLEM and MEAD, 1968; MURTAGH *et al.*, 1971). For mathematical convenience the curves were considered to be sigmoidal and split up into an upper and a lower part with an intersection at $P_{tm} = P_{tms}$, where P_{tms} is the point of curvature. P_{tms} depends on elastic lung recoil (eqn. 9a). A continuous set of curves was used over the whole range of static lung recoil values. The volume of the compressible segment V_{c0} at maximum transmural pressure for $P_L = 0.5$ kPa was chosen as 0.125 litre and the resistance of the compressible airways R_{c0} was chosen as 0.06 kPa litre⁻¹ s, as an estimate for the airway generations 2-10 (LAMBERT *et al.*,

1982). The choice of these generations within the 23 generations of the bronchial tree is also based on the experimental evidence for the location of the EPP. In Fig. 2 the normalised values of V_c are plotted against P_{im} for three values of P_L (0.2, 0.5 and 0.9).

The flow at the mouth is dependent on the peripheral airway resistance R_s , the resistance of the compressible segment R_c , the upper airway resistance R_u and alveolar, pleural and elastic recoil pressures P_A , P_{pl} and P_L . For the complete mathematical description of the lung model with a compressible segment, lung model 1 is represented by the following equations, which can be derived:

Model 1:

$$P_{pl} = P_A - P_L \quad (10)$$

$$P_L - P_{im} + R_s V'_A = 0 \quad (11)$$

$$P_{im} + P_{pl} + (R_c + K_1)V'_m + K_2(V'_m)^2 = 0 \quad (12)$$

$$R_c = R_{c0}(V_{c0}/V_c)^2 \quad (13)$$

where R_c is the resistance of the compressible segment in $\text{kPa litre}^{-1} \text{s}$. V_c is the volume of the compressible segment in litres. R_{c0} and V_{c0} are model constants as defined before. R_{c0} defines the overall magnitude of R_c , and V_{c0} determines the relative volume of the compressible segment at which R_c will be of influence.

$$V_c(t) = V_c(0) + \int_{\sigma=0}^t (V'_m - V'_A) d\sigma \quad (14)$$

$$P_L(t) = P_{L, FRC} + 1/C \int_{\sigma=0}^t V'_m d\sigma \quad (15)$$

$$P_{im} = f(V_c, P_L) \quad (8a-9b)$$

where V'_A is the flow into the alveolar compartment litre s^{-1}

V'_m is the flow at the mouth, litre s^{-1}

R_s, P_L, K_1 and K_2 are the model parameters.

2.3 Simplified models

In cases where the influence of compressibility of the airways could be neglected, e.g. stiff lungs and normal lungs at low flow, simpler models were used with a restricted number of parameters if compared with the basic model. Models 2, 3 and 4 were defined by an absence of compressibility and different dominant properties determining the behaviour of model 1.

Model 2: a linear resistance parameter K_3 ($\text{kPa litre}^{-1} \text{s}$) for inspiration and expiration is introduced:

$$P_A = K_3 V'_m \quad (16)$$

Model 3: different linear resistances parameters K_4 and K_5 ($\text{kPa litre}^{-1} \text{s}$) for inspiration and expiration are introduced:

$$P_{A, in} = K_4 V'_{m, in} \quad (17)$$

$$P_{A, ex} = K_5 V'_{m, ex} \quad (18)$$

where $P_{A, in}$ is alveolar pressure during inspiration in kPa

$P_{A, ex}$ is alveolar pressure during expiration in kPa

Model 4: different linear and turbulent resistance parameters (K_6 and K_7 , $\text{kPa litre}^{-1} \text{s}$, and K_8 , K_9 , $\text{kPa litre}^{-2} \text{s}^2$) are used for inspiration and expiration, respectively:

$$P_{A, in} = K_6 V'_{m, in} + K_8 V'^2_{m, in} \quad (19)$$

$$P_{A, ex} = K_7 V'_{m, ex} + K_9 V'^2_{m, ex} \quad (20)$$

2.4 Parameter estimation

The parameter estimation technique and the simulation of the serial lung model were connected in the way indicated in Fig. 3. With the serial lung model (simulation) an output signal V'_m was calculated for a given P_A . Based on the same stimulus P_A and with use of one of the described mathematical models (1, 2, 3 or 4) the computer calculated (estimation) a predicted response V'_{pred} for a given set of start parameters. Then, a new set of parameters was computed to reduce the difference in square error EE between V'_{pred} and the known V'_m . This was continued either for a maximum predefined number of 20 iterations or for a smaller number when the difference in square error EE between the two responses was reduced below 0.0001.

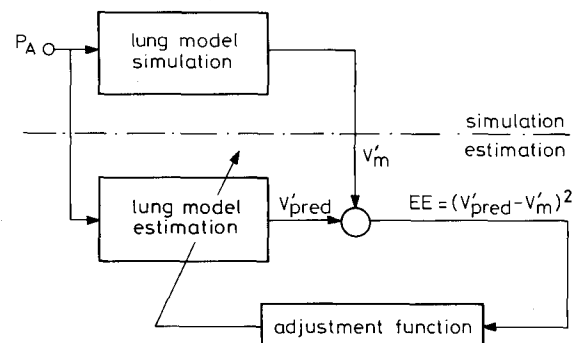


Fig. 3 The parameter estimation process; for explanation see text

For the parameter estimation technique the Marquardt algorithm (MARQUARDT, 1963) was applied, which is a modified Gauss-Newton algorithm. The loss function $EE = (V'_{pred} - V'_m)^2$ was minimised. With the Marquardt algorithm the step size of each adjustment can be influenced by means of a factor μ . By changing μ after each iteration it was possible to control dynamically the convergence of the estimation ($\mu = 0$, Gauss Newton; $\mu = \infty$ steepest descent with step size zero). At the start of the estimation μ was set at 0.1. If the error was smaller in the next iteration, μ was adjusted to 0.4μ , and if the error was larger the last iteration was repeated after μ was changed to 10μ . The factors 0.4 and 10 were found empirically.

2.5 Forcing the serial model with simulated signals

First the serial model was stimulated by a sinusoidally changing P_A . Because of unequal inspiratory and expiratory resistances (models 1, 3 and 4) the sinusoidal alveolar pressure curve had to be corrected to minimise the difference (ΔV) between the lung volume at the start ($\sigma = 0$) and that at the end ($\sigma = t$) of the simulated respiratory cycle below 0.01 litre. The change in lung volume ΔV between the start and end of the respiratory cycle was found from the value obtained after integration of the output V'_m over the whole respiratory cycle. The minimisation of ΔV was realised by the introduction of an offset in the zero line of the sinusoidal alveolar pressure signal.

A higher expiratory than inspiratory resistance needed a shift of the zero line into the direction of the inspiratory pressure curve, giving a larger amplitude and duration of the expiratory pressure curve. For the inspiratory part of the curve the opposite changes occurred. The offset in the zero line was calculated, from the volume shift ΔV and the overall resistance R_{eff} (HOLLAND *et al.*, 1986), by an iterative process.

2.6 Choice of parameters for testing the simulation

The parameter values for model 1 were divided into five classes: the normal lung (*N*), the emphysematous lung (*E*), the fibrotic lung (*F*), the asthmatic lung (*A*) and the lung with a large increase in upper airway resistance (*U*). The characteristic values for the various parameters were chosen from reviews of pulmonary pathophysiology (PRIDE *et al.*, 1967; PRIDE 1971; COTES, 1975; OTIS *et al.*, 1956, and those for upper airway resistance for class *U* were derived from patients with bilateral vocal cord paralysis (BOGAARD *et al.* 1987a; b).

Emphysema was modelled by a lower value of the elastic recoil $P_{L,FRC}$ and thus an increased lung compliance (*C*). Because of a lower $P_{L,FRC}$ the traction on the walls of the respiratory bronchioles is smaller and consequently pleural pressure will be less negative with respect to alveolar pressure (eqn. 6), causing a narrowing of the small airways and therefore an increase in R_s . In fibrosis the characteristic physiological disorder is the increased stiffness of the lung tissue, which was modelled by an increase of $P_{L,FRC}$ and a decrease of *C*. In asthma both upper and peripheral airway resistances are increased, which was reflected in increased values for K_1 , K_2 and R_s . To simulate patients with an upper airway obstruction only K_1 and K_2 were greatly increased, according to the results obtained from patients with bilateral vocal-cord paralysis as mentioned above.

2.7 Uniqueness

The validity of the parameters obtained by a parameter estimation technique depends on the uniqueness of the parameter values. To evaluate the uniqueness, simulations were made for the five classes *N*, *E*, *F*, *A* and *U* as mentioned in Table 1. The uniqueness of the calculated parameter set and the convergence of the iterative estimation procedure were analysed by estimating the parameters of a class when starting from the parameter values belonging to the other classes, e.g. simulation of *N*, and starting of parameters *E*, *F*, *A* and *U*, respectively.

Table 1 Values for the parameters (K_1 , K_2 , R_s and P_L) and lung compliance *C* for the different groups *N*, *E*, *F*, *A* and *U*

	K_1 , kPa litre ⁻¹ s	K_2 , kPa litre ⁻² s ²	R_s , kPa litre ⁻¹ s	$P_{L,FRC}$, kPa	<i>C</i> , litre kPa ⁻¹
<i>N</i>	0.05	0.02	0.03	0.5	2.0
<i>E</i>	0.05	0.02	0.3	0.1	5.0
<i>F</i>	0.05	0.02	0.03	0.9	1.0
<i>A</i>	0.1	0.06	0.3	0.5	2.0
<i>U</i>	0.29	4.6	0.03	0.5	2.0

2.8 Sensitivity

The squared error $EE = (V'_{pred} - V'_m)^2$ was determined after application of stepwise changes in the parameters in order to study the sensitivity of the parameter estimation technique. This was done in two ways:

- (i) by determination of the interdependence of pairs of parameters
- (ii) by studying the influence of fluctuations in each of the parameters on the resulting squared error.

2.9 Noise

Random noise was applied to the input signal of alveolar pressure and to the output signal of flow of the serial lung model. The mean noise level was 0.02 kPa for the pressure and 0.02 litre s⁻¹ for the flow. The deviation of

the parameter estimates in the different classes from the selected input parameter values with which the simulation was performed was investigated by starting with values of the class itself and values obtained from the normal situation. For the normal situation the starting values for the emphysema class were also applied. The noise was generated by a noise generator of Digital Equipment Corporation which was implemented in the Fortran-IV library belonging to the RT-11 operating system.

3 Results

The results of simulations of the different pathological classes as defined in Table 1 are presented in Fig. 4. These simulations were based on a sinusoidal alveolar pressure change with an amplitude of 0.5 kPa for classes *N*, *E*, *A* and *U* and 0.2 kPa for class *F*, all at a rate of 0.5 Hz. The lower values of alveolar pressure in class *F* are necessary for the calculation of the segment volume with the Runge Kutta algorithm in the case of an almost stiff compressible segment because of high P_L values. The difference between the maximum of alveolar pressure in inspiration and that in expiration for emphysema (Fig. 4E) was caused by a shift of the zero line in the alveolar pressure. This shift was necessary to obtain an equal inspiratory and expiratory volume, as mentioned before. The characteristics of the simulated curves were in agreement with recordings of normals and patients, as documented among others by MATTHYS *et al.* (1971; 1979).

For each curve the resistance R_i and the effective resistances for inspiration ($R_{eff,i}$), expiration ($R_{eff,e}$) and total ventilatory cycle (R_{eff}) were calculated. To illustrate the mechanical behaviour of a lung with emphysema, the input variable P_A , the output variable V'_m and the resulting variables P_{tm} and R_c were plotted as a function of time for both classes *E* and *N* (Fig. 5). The offset in the zero line of alveolar pressure (Fig. 5a) compensated for a higher overall expiratory resistance (Fig. 5d) leading to a smaller peak flow V'_m (Fig. 5b). In case of emphysema P_{tm} was around zero during a part of the expiratory phase (Fig. 5c). In this part the calculated resistance (R_c) of the collapsible segment was relatively large (Fig. 5d) For the fibrotic case, not shown, the resistance R_c was almost constant during the respiratory cycle.

In the estimation procedure the parameters used in the simulations could be determined, independent of the start parameters.

For classes *E* and *F* the dependence between the parameters is shown in Fig. 6. In this figure the contour lines where parameter combinations have the same loss function EE , were plotted. In each plot the parameters K_1 and R_s fluctuated around their optimal values of 0.05 and 0.3, respectively. The parameter P_L had different values, 0.1 and 0.9, respectively. The parameter K_2 was 0.02 and was constant in both cases. In the simulation of fibrosis the contour lines were almost straight, whereas in emphysema they were more elliptical. This implied that for fibrosis K_1 and R_s were almost completely interdependent, i.e. cannot be estimated separately.

Fig. 7 presents the EE changes for the *N* and *F* class, after individually changing the four parameters between 50 per cent and 150 per cent of their optimal values for each class. From this figure it can be noticed that the influence of a change in the parameter values K_1 , K_2 and R_s on the squared error was different for the two classes *N* and *E*. For the normal lung the parameters had more or less an equal influence on the resulting squared error, whereas for the emphysematic lung the parameters K_1 and K_2 were far less important for reducing the squared error.

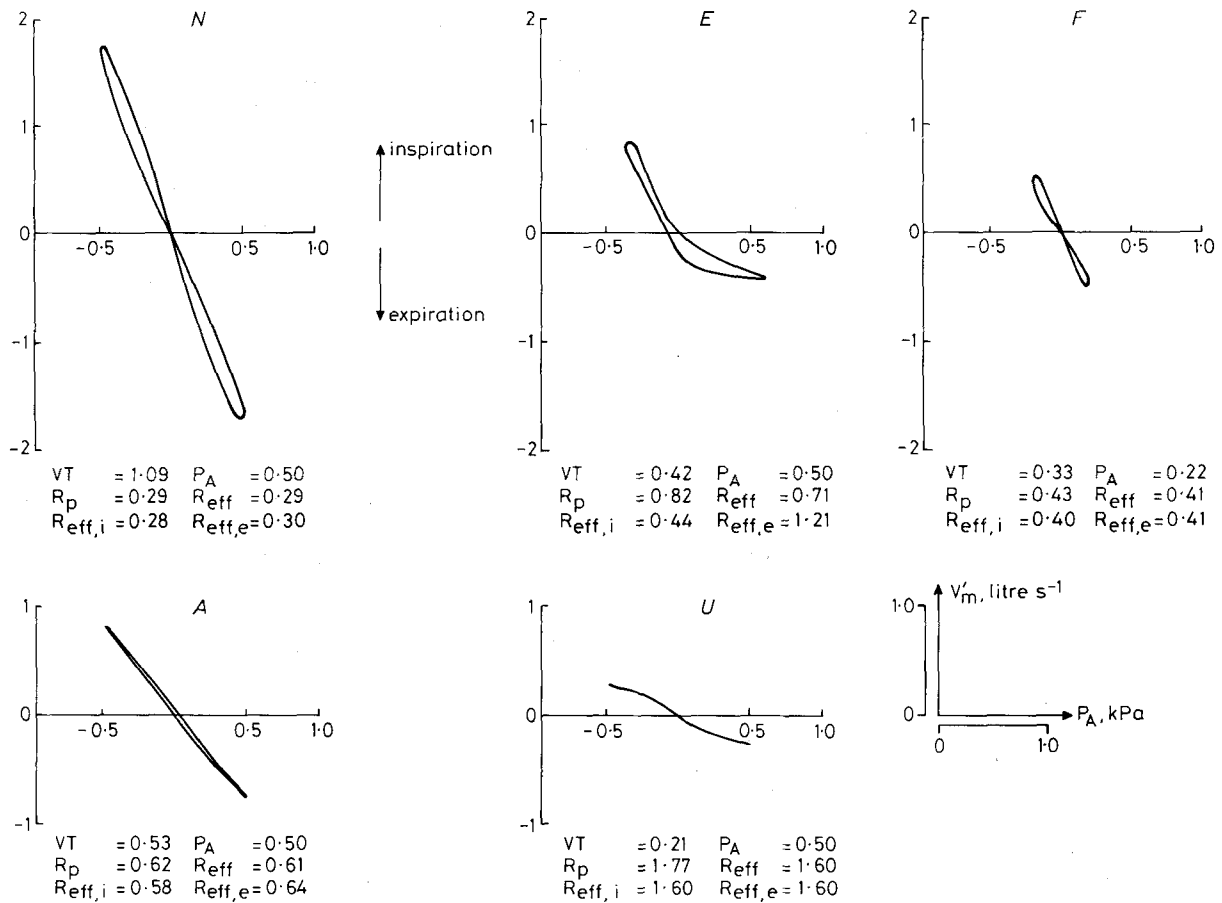


Fig. 4 Simulations performed with model 1 and the parameters of Table 1 for the different groups N, E, F, A and U (R in kPa s litre^{-1}). V_T is tidal volume, P_A is the amplitude of the simulated pressure curve, R_p is the resistance calculated by means of the peak pressure and the associated flow value. R_{eff} is calculated for the total curve as well as for the inspiratory ($R_{eff,i}$) and expiratory ($R_{eff,e}$) part separately. For symbols see list of symbols and text

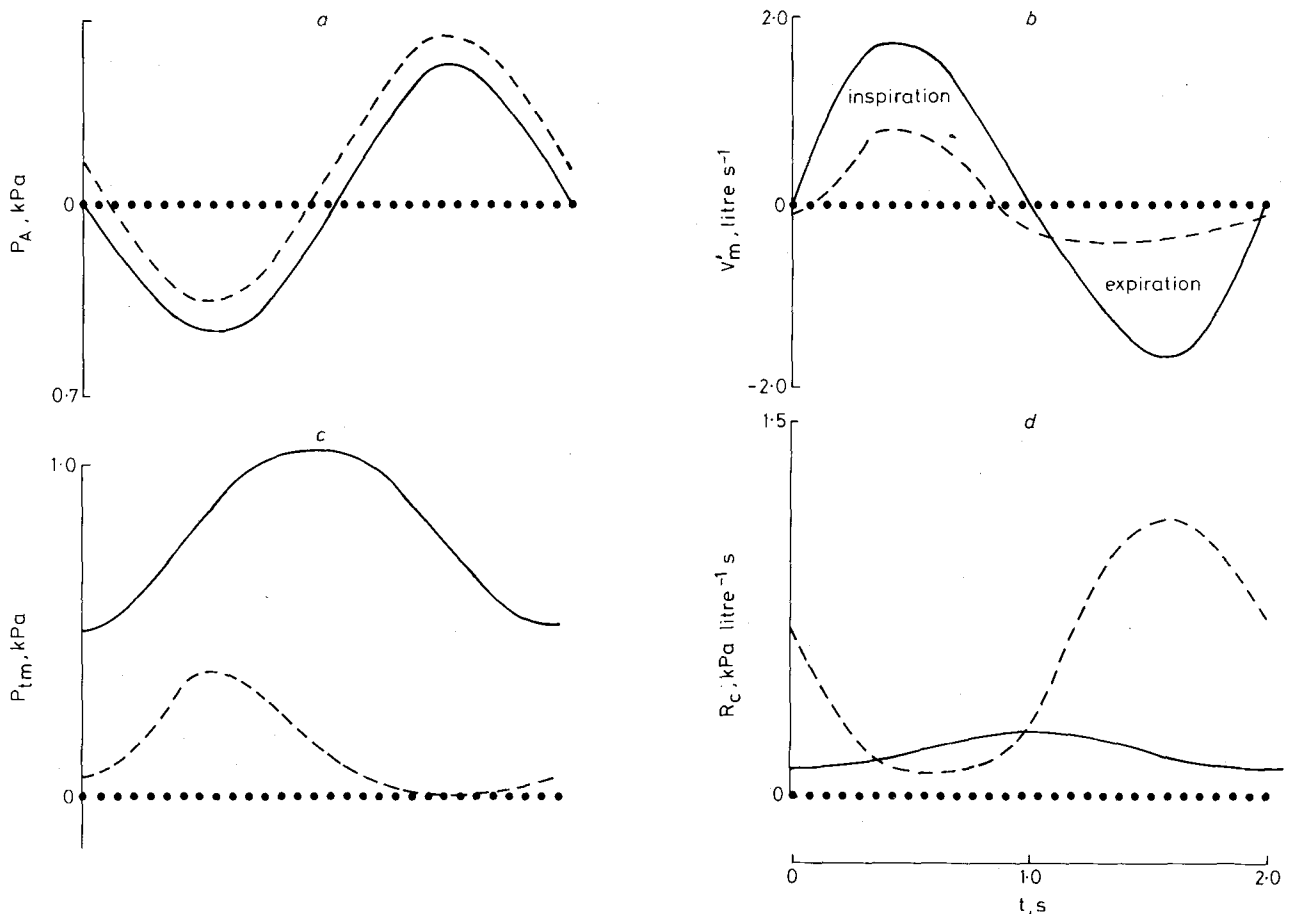


Fig. 5 The variation of different values with time as calculated with model 1 in normal (—) and emphysema (----) during normal breathing. For symbols see list of symbols and text

Noise superimposed on the model output V'_m gave no appreciable influence on the parameter estimates. This was not the case when noise was added to the input variable P_A , as is shown in Table 2. If the starting values were chosen from the same pathology class or from the normal class the total resistance from the bronchial tree, as given

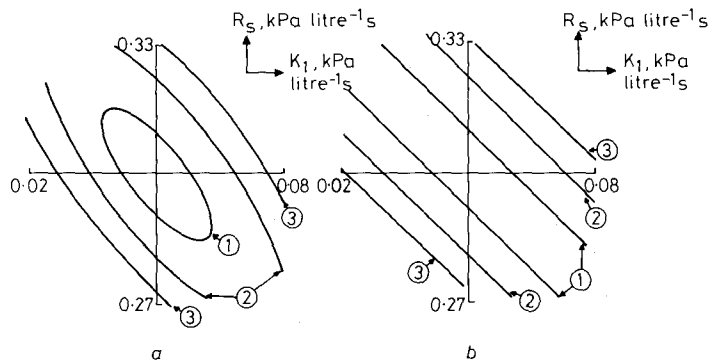


Fig. 6 Plots of contour lines (1: $EE = 0.01$; 2: $EE = 0.05$, 3: $EE = 0.1$) as function of parameters K_1 and R_s for a highly collapsible ($P_L = 0.1$) and a stiff compressible segment ($P_L = 0.9$), respectively. Optimal parameter values: $K_1 = 0.05$; $K_2 = 0.02$; $R_s = 0.3$ and $P_L = 0.1$ in (a) and $P_L = 0.9$ in (b). For these calculations the influence of volume changes on P_L was neglected ($1/C = 0$). In both figures: x-axis $0.02 < K_1 < 0.08$ ($\text{kPa litre}^{-1} \text{s}$); y-axis $0.27 < R_s < 0.33$ ($\text{kPa litre}^{-1} \text{s}$). For symbols see list of symbols and text

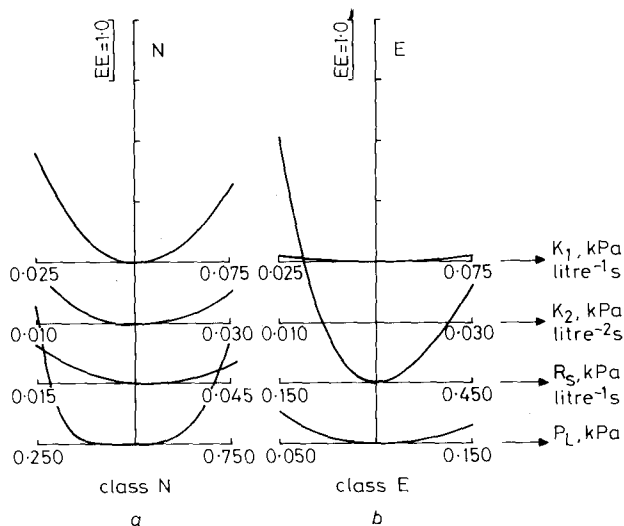


Fig. 7 Plots of EE as function of a perturbation plus and minus 50 per cent of the parameter for the normal and emphysema case. Remaining parameters have the value belonging to the class value. For these calculations the influence of volume change on change in P_L was neglected ($1/C = 0$). (a) Class N; (b) class E. For symbols see list of symbols and text

Table 2 Residual square error (EE), parameter estimates (K_1 , K_2 , R_s and P_L) and effective resistance estimate (R_{eff}) with and without addition of random noise of 0.02 kPa to the input signal P_A and of $0.02 \text{ litre s}^{-1}$ to V'_m . In the table the class of which the start parameters were taken is indicated. For each pathology class input parameters were as defined in Table 1 and starting values were chosen both according to the same class and to the normal class. For further explanation see text

Simulate class	N			E			F			A			U		
Noise level	0	0.2	0.2	0	0.2	0.2	0	0.2	0.2	0	0.2	0.2	0	0.2	0.2
Start class	N	N	E	E	E	N	F	F	N	A	A	N	U	U	N
EE	0.00	0.33	0.33	0.00	0.27	0.26	0.00	0.18	0.18	0.00	0.20	0.17	0.00	0.03	0.03
K_1	0.05	0.05	0.04	0.05	0.05	0.01	0.05	0.05	0.04	0.10	0.13	0.20	0.20	0.29	0.40
K_2	0.02	0.02	0.03	0.02	0.03	0.08	0.02	0.05	0.05	0.06	0.09	0.10	4.6	4.6	4.14
R_s	0.03	0.03	0.03	0.30	0.30	0.30	0.03	0.02	0.02	0.30	0.26	0.19	0.03	0.03	0.00
P_L	0.50	0.50	0.50	0.10	0.10	0.10	0.90	0.90	0.90	0.50	0.40	0.34	0.50	0.50	0.55
R_{eff}	0.29	0.29	0.29	0.71	0.72	0.72	0.41	0.41	0.41	0.61	0.61	0.61	1.60	1.60	1.59

by the effective resistance, appeared to be not influenced by random noise. For the N , E and F classes hardly any differences were found in all parameters. The A and U classes showed somewhat larger differences for all parameters. Except for the A and U class, it was possible to obtain an accurate P_L estimate in all situations. The same was true for the N class if the E -parameters were taken as starting values; although, as mentioned above, R_{eff} was not influenced by the separation in R_s and upper airway resistance. This last value as characterised by K_1 and K_2 was less accurate.

Table 3 shows the parameter estimates for the complex model (1) and those of the three simplified models. The parameters of the simplified models (2, 3 and 4) were obtained by fitting these models to the curves simulated with the complex model (1). This was done for the five separate classes (N , E , A , F and U). In these simulations noise was not superimposed. The estimation with model 1 agrees with the values given in Table 2 in the case of absence of noise. Except for the application of model 2 (one linear resistance) in the emphysema case, in all other simplified model fits the estimate for the effective resistance of the total respiratory cycle was close to the effective resistance calculated with the complex model. Because of asymmetries of the inspiratory and expiratory part of the curve in the emphysema class a separate resistance for each part (model 3) was necessary to obtain a reliable estimate of the effective resistance for the whole cycle.

Although most obvious for the U class, in all cases model 4 with a linear and tubulent resistance parameter for inspiration and expiration gave a good fit based on the square error (EE). Only for the class U curve and the expiratory part of the class E curve were the parameters for the turbulent resistance part (K_7 and K_9) markedly larger than those for the linear part (K_6 and K_8). In the emphysema case the expiratory curve was largely determined by airway compression. In all other cases the turbulent resistance parameters were much smaller than the linear ones.

4 Discussion

Estimation of pulmonary parameters based on model fitting of body plethysmographic pressure/flow tracings has been performed by a small number of investigators (FEINBERG *et al.*, 1970; GOLDEN *et al.* 1973). These attempts provided a better understanding of body plethysmographic alveolar pressure/flow data. In this present study an extended version of the serial lung model of GOLDEN *et al.*, (1973) has been used.

The aim of this present study was (1) to evaluate a physiologically well defined serial lung model with respect to its ability to simulate patient curves, and (2) to study the

Table 3 Results of the estimation process for the primary (1) and the simplified (2, 3 and 4) models, performed on signals generated by means of a simulation with mode 1. Indicated are for each class and each fitted model the resulting square error, the total effective resistance (R_{eff}), the effective resistance for inspiration and expiration separately ($R_{eff, in}$ and $R_{eff, ex}$) and the resistance line through the extreme points (R_p)

Class	Model	Parameter values	EE	R_{eff}	$R_{eff, in}$	$R_{eff, ex}$	R_p
N	1	$K_1 = 0.05$ $K_2 = 0.02$ $R_s = 0.03$ $P_1 = 0.50$	0.00	0.29	0.28	0.30	0.29
	2	$K_3 = 0.29$	3.69	0.29	0.29	0.29	0.29
	3	$K_4 = 0.29$ $K_5 = 0.30$	3.55	0.29	0.29	0.30	0.29
	4	$K_6 = 0.29$ $K_7 = 0.00$ $K_8 = 0.28$ $K_9 = 0.01$	3.54	0.29	0.29	0.30	0.30
E	1	$K_1 = 0.05$ $K_2 = 0.02$ $R_s = 0.30$ $P_L = 0.10$	0.00	0.71	0.44	1.21	0.82
	2	$K_3 = 0.98$	11.2	0.98	0.97	0.97	0.98
	3	$K_4 = 0.45$ $K_5 = 1.32$	2.06	0.75	0.45	1.32	0.79
	4	$K_6 = 0.45$ $K_7 = 0.01$ $K_8 = 0.01$ $K_9 = 3.29$	1.52	0.74	0.45	1.27	0.81
F	1	$K_1 = 0.05$ $K_2 = 0.03$ $R_s = 0.03$ $P_L = 0.90$	0.00	0.41	0.40	0.41	0.43
	2	$K_3 = 0.43$	1.36	0.43	0.43	0.43	0.43
	3	$K_4 = 0.42$ $K_5 = 0.43$	1.36	0.43	0.42	0.43	0.43
	4	$K_6 = 0.37$ $K_7 = 0.10$ $K_8 = 0.43$ $K_9 = 0.00$	1.35	0.42	0.42	0.43	0.43
A	1	$K_1 = 0.10$ $K_2 = 0.06$ $R_s = 0.30$ $P_L = 0.50$	0.00	0.61	0.58	0.64	0.62
	2	$K_3 = 0.61$	0.32	0.61	0.61	0.61	0.61
	3	$K_4 = 0.58$ $K_5 = 0.64$	0.14	0.61	0.58	0.64	0.61
	4	$K_6 = 0.53$ $K_7 = 0.07$ $K_8 = 0.60$ $K_9 = 0.06$	0.12	0.61	0.58	0.64	0.61
U	1	$K_1 = 0.20$ $K_2 = 4.60$ $R_s = 0.30$ $P_L = 0.50$	0.00	1.60	1.60	1.60	1.76
	2	$K_3 = 1.62$	0.15	1.62	1.62	1.62	1.62
	3	$K_4 = 1.62$ $K_5 = 1.62$	0.15	1.62	1.62	1.62	1.62
	4	$K_6 = 0.51$ $K_7 = 4.34$ $R_8 = 0.26$ $K_9 = 5.43$	0.00	1.59	1.59	1.60	1.77

uniqueness and sensitivity of a parameter estimation technique for the fitting of the simulated curves.

The behaviour of the serial model was studied by simulating different combinations of parameters (Table 1). The model produced patterns (Fig. 4) for the different types of pathology which agreed quite well with the patterns as defined by MATTHYS (1971). In the classes representing the normal condition and patients with fibrosis, asthma and an increased upper airway resistance, a nonlinear behaviour of the model was virtually absent because the influence of the compressible segment is negligible, since either R_s was small or P_L was relatively large. For emphysema, where both R_s was increased and the P_L was decreased the effect of the compressible segment was more pronounced. Large differences in the time course of some output variables were found (Fig. 5) between the classes for the normal condition and for emphysema, respectively:

- (i) the transmural pressure in class E was below zero during part of the breathing cycle, which indicates the presence of a marked compression even during the normal breathing
- (ii) the area of the compressible segment in class E decreased greatly, and, therefore, resistance R_c was much larger during expiration than it was during expiration in the normal case (Fig. 4e).

Also the difference in the values of effective resistance, calculated for the inspiratory ($R_{eff, in}$) and expiratory ($R_{eff, ex}$) resistance, showed this effect of large expiratory airway compression. The model appeared to be sufficiently accurate for simulation of the characteristic loop patterns, related to pulmonary pathology, in spite of a (for practical purposes necessary) simplified description of the compressible segment.

For simulations without additional noise the parameter estimation routine gave unique solutions for the parameter values belonging to each class. It was shown that the sensitivity of the parameter estimation technique depended on the values of the parameters of each class (Fig. 7). In the normal condition (class N) the sensitivity for the different parameters was more or less the same. For emphysema (class E) the parameters R_s and P_L were much more important than K_1 and K_2 . Thus K_1 and K_2 appeared to

be of little importance in reducing the error in the parameter estimation scheme. Therefore, the accuracy of the estimation of K_1 and K_2 will be smaller than that of both other parameters (Table 2, Figs. 6a and 6b). The application of noise confirmed the results on the sensitivity of the model fit for the various parameters in dependence on the pathology class. In the case of upper airway obstruction the factor K_2 has such a dominant influence that the other parameters have almost no influence on the resulting effective resistance and on the shape of the curve.

In circumstances where the influence of the compressible segment was minimal, the serial long model could be simplified. In such situations, a good estimation of the different parameter values in model 1, which characterised the resistance of the serial connection of the segments, was not possible. Then a model with only one serial resistance element with a laminar and a turbulent term could be used, as was shown in Table 3. This did not hold for the E case where the four models yield appreciably different estimates.

We conclude that the serial lung model is able to fit curves which are influenced by a serial mechanical inhomogeneity, especially defined by the behaviour of the compressible segment. Moreover, parameter estimation was able to recognise in the cases described, even in the presence of noise on the model input, the most relevant aspects of the lung mechanical behaviour.

Acknowledgment—This study was supported by a grant from the Dutch Asthma Foundation.

References

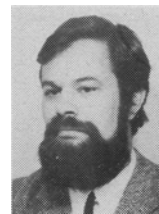
- BANERJEE, M., EVANS, J. N. and JAEGER, M. J. (1976) Uneven ventilation in smokers. *Respirat. Physiol.*, **27**, 277–291.
- BEKEY, G. A. and BENEKEN, J. E. W. (1978) Identification of biological systems: a survey. *Automatica*, **14**, 41–47.
- BOGAARD, J. M., PAUW, K. H., VERSPRILLE, A., STAM, H., VERBRAAK, A. F. M. and MAAS, A. J. J. (1987a) Maximal expiratory and inspiratory flow-volume curves in bilateral vocal-cord paralysis. *ORL*, **49**, 35–41.
- BOGAARD, J. M., PAUW, K. H. and VERSPRILLE, A. (1987b) Flow

- limitation in upper airway obstruction (theoretical analysis). *Ibid.*, **49**, 42-47.
- CETTL, L., DVORAK, J., FELKEL, H. and FEUEREISL, R. (1979) Results of simulation of nonhomogeneous ventilatory mechanics for a patient-computer arrangement. *Int. J. Bio-Med. Comput.*, **10**, 67-74.
- COTES, J. E. (1975) *Lung function. Assessment and application in medicine*. Blackwell Scientific Publications.
- DUBOIS, A. B., BOTELHO, S. Y. and COMROE, J. H. Jr. (1956) A new method for measuring airway resistance in man using a bodyplethysmograph values in normal subjects and in patients with respiratory disease. *J. Clin. Invest.*, **35**, 327-335.
- FEINBERG, B. N., CHESTER, E. H. and SCHOEFFLER, J. D. (1970) Parameter estimation: a diagnostic aid for lung diseases. *Instrum. Technol.*, 40-46.
- FEINBERG, B. N. and CHESTER, E. H. (1972) A dynamic model of pulmonary mechanics to simulate a panting maneuver. *Bull. Physio-path. Respirat.*, **8**, 305-322.
- GOLDEN, J. F., CLARK, J. W. Jr., and STEVENS, P. M. (1973) Mathematical modeling of pulmonary airway dynamics. *IEEE Trans.*, **BME-20**, 397-404.
- GUYATT, A. H., ALPERS, J. H., HILL, I. D. and BRAMLEY, A. C. (1967) Variability of plethysmographic measurements of airway resistance in man. *J. Appl. Physiol.*, **22**, 383-389.
- HOLLAND, W. P. J., VERBRAAK, A. F. M., BOGAARD, J. M. and BOENDER, W. (1986) Effective airway resistance: a reliable variable from bodyplethysmography (A theoretical analysis and an application in COLD patients). *Clin. Physics & Physiol. Meas.*, **7**, 319-331.
- HYATT, R. E. and FLATH, R. E. (1966) Influence of lung parenchyma on pressure-diameter behaviour of dog bronchi. *J. Appl. Physiol.*, **21**, 1448-1452.
- HYATT, R. E. (1983) Expiratory flow limitation. *J. Appl. Physiol.: Respirat. Environ. Exercise Physiol.*, **55**, 1-8.
- LAMBERT, R. K., WILSON, T. A., HYATT, R. E. and RODARTE, J. R. (1982) A computational model for expiratory flow. *Ibid.*, **52**, 44-56.
- MACKLEM, P. T. and MEAD, J. (1968) Factors determining maximum expiratory flow in dogs. *J. Appl. Physiol.*, **25**, 159-169.
- MARQUARDT, D. W. (1963) An algorithm for least-squares estimation of nonlinear parameters. *SIAM J.*, **11**, 431-441.
- MARTIN, H. B. and PROCTOR, D. F. (1958) Pressure-volume measurements on dog bronchi. *J. Appl. Physiol.*, **13**, 337-343.
- MARTIN, C. J., YOUNG, A. C. and ISHIKAWA, K. (1965) Regional lung mechanics in pulmonary disease. *J. Clin. Invest.*, **44**, 906-913.
- MATTHYS, H. (1971) Ganzkörperplethysmographie. *Pneumology I*, **146**, 216-231.
- MATTHYS, H., FISCHER, J., ULRICHS, H.Ch. and RÜHLE, K. H. (1979) Functional patterns of different lung diseases for computer-assisted diagnostic procedures. *Progr. Respirat. Res.*, **11**, 188-201.
- MEAD, J., TURNER, J. M., MACKLEM, P. T. and LITTLE, J. B. (1967) Significance of the relationship between lung recoil and maximum expiratory flow. *J. Appl. Physiol.*, **22**, 95-108.
- MURTAGH, P. S., PROCTOR, D. F., PERMUTT, S., KELLY, B. L. and EVERING, S. (1971) Bronchial mechanics in excised dog lobes. *Ibid.*, **31**, 403-408.
- OTIS, A. B., MCKERROW, C. B., BARTLETT, R. A., MEAD, J., MCILROY, M. B., SELVERSTONE, N. J. and RADFORD, E. P. Jr (1956) Mechanical factors in distribution of pulmonary ventilation. *J. Appl. Physiol.*, **8**, 427-433.
- PRIDE, N. B., PERMUTT, S., RILEY, R. L. and BROMBERGER-BARNEA, B. (1967) Determinants of maximal expiratory flow from the lungs. *Ibid.*, **23**, 646-662.
- PRIDE, N. B. (1971) The assessment of airflow obstruction (role of measurements of airway resistance and of tests of forced expirations). *Br. J. Dis. Chest.*, **65**, 135-169.
- REINERT, M., HEISE, D. and TRENDELENBURG, F. (1975) Zum Auswertemodus phasenverschobener Resistancekurven. *Pneumologie*, **152**, 147-156.
- ROHRER, F. (1915) Der Strömungswiderstand in der menschlichen Atemwegen und der Einfluss der unregelmässigen Verzweigung des Bronchialsystems auf der Atmungsverlauf in verschiedenen Lungenbezirken. *Pflügers. Arch. Ges. Physiol.*, **162**, 225-259.
- SMIDT, U., FINKENZELLER, P. and RENNINGS, C. (1975) On-line Computereinsatz in der Ganzkörperplethysmographie zur Berechnung der mittleren Resistance. *Pneumologie*, **151**, 223-231.
- ULMER, W. T. and REIF, E. (1965) Die obstruktiven Erkrankungen der Atemwege. Klinische Bedeutung und objektiver Nachweis mit der Ganzkörperplethysmographie. *Dtsch. Med. Wschr.*, **90**, Jg. 41.

Authors' biographies



Ton F. M. Verbraak was born in Tilburg, The Netherlands in 1946. He received a MEE degree from Eindhoven University of Technology, Division of Medical Electrical Engineering, in 1976. He works in the Pulmonary Function Department of the University Hospital Rotterdam. The present paper is part of a thesis on signal processing in pulmonary function and simulation and parameter estimation in body plethysmography. His fields of interest are signal processing, physiological modelling and patient monitoring.



Jan M. Bogaard was born in The Hague in 1936. He worked for 15 years as chemical engineer (Ing.) in the Department of Lung Function & Exercise Testing at the University of Leiden. During the same period he became an experimental physicist at this university. From 1974 he worked in Rotterdam where he received his Ph.D. degree in 1980 for work on random walk modelling of indicator-dilution curves. His fields of interests are development and application of methods on pulmonary function, regulation of breathing and exercise physiology.



Jan E. W. Beneken received a MEE degree from Delft University of Technology in 1958 and a Ph.D. degree in Experimental Physics from the University of Utrecht. He is presently Professor and Chairman of the Division of Medical Electrical Engineering of Eindhoven University of Technology with research interests in physiological modelling, patient monitoring, AI applications in medicine, ultrasound transmission tomography and communication aids for the handicapped. He is Chairman of the Bioengineering Committee (COMAC-BME) of the European Community.



Ed Hoorn was born in Rotterdam, The Netherlands in 1955. He received his Ing. degree in Physical Engineering. In 1980 he worked at the Pathophysiological Laboratory of the Erasmus University. Currently he works at the Central Department of Automation & Information of the University Hospital Rotterdam, where he is involved in the development of computer programs for clinical routine and research. His fields of interest are computerised data acquisition and data analysis.



Professor Adrian Versprille is a full professor in clinical respiratory physiology and head of the research laboratory of the Department of Pulmonary Diseases, Erasmus University, Rotterdam and head of the pulmonary laboratory University Hospital 'Dijkzigt'. The field of mechanical ventilation and the development of diagnostic and therapeutic methods as a spinoff of his basic research are his main interests.