RICE UNIVERSITY

ANALOG COMPUTER SIMULATION OF SELECTED PULMONARY FUNCTION TESTS

by

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ABSTRACT

Analog Computer Simulation of Selected Pulmonary Function Tests

Mark Francis Olender

A mathematical model previously derived by Golden, et al. (1973) is developed and extended to allow for the simulation of a wide range of pulmonary function tests. The model parameters include large airway resistance, small airway resistance, collapsible airway resistance, collapsible airway compliance, and lung compliance. And, the model is driven by a variable pleural pressure waveform.

The simulation is implemented on an analog computer for ease of parameter manipulation. The effects of changes in model parameters on selected pulmonary function tests are observed and discussed. Simulations of diseased states (emphysema, asthma, and fibrosis) are presented and analyzed.

It is concluded that the model properly simulates breathing maneuvers associated with the clinical assessment of pulmonary function. In addition the model structure is much simpler than the ventilatory system models of Fry (1968) and Pardaens, et al. (1972), yet yields the same information in a diagnostic sense.


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ACKNOWLEDGEMENTS

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My deepest expression of gratitude goes to my wife, Judy, who supplied the support, assistance, and love without which I could not have attempted to start.
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CHAPTER 1

Introduction

A lumped parameter approach to the modeling of pulmonary airway dynamics is advantageous in that it reduces the complexity of analysis and frequently allows the interpretation of clinical data that are generally obtained via measurements on the system as a whole (i.e., the measurement is in itself a summation of the responses from an inherently distributed system and only certain measurements are feasible from a clinical standpoint.

Numerous models of airway dynamics have appeared in the literature, many differing considerably in their ability to describe the mechanics of this system. One would expect that for a well-formulated model, both model complexity and dimensionality would increase with the amount of anatomical and functional detail incorporated into the model. There are two general approaches to this modeling problem: first, a "fundamental" approach wherein the investigator attempts to describe lung-airway mechanics in considerable detail from a fluid mechanical standpoint, and second, a "functional" approach wherein the more general aspects of the lung-airway behavior are considered. Typical of models in this latter category is the model of Rohrer (1915) who first described the relationship between alveolar pressure ($P_{ALV}$) and airflow at the mouth ($V_{AO}$) (see equation (1)). While this model adequately describes inspiratory flows of less than 5 liters/second, it fails to predict expiratory flow limitation due to airway compression
1-2

(Bouhuys and Jonson (1967)). More sophisticated models have since been developed that include lumped upstream and downstream airway resistances as well as peripheral airway compliance.

Thus, "fundamental" models as described above usually have an entirely different set of modeling objectives than the more clinically oriented goals of "functional" models. Given the same clinical objective, for example simulating (a) pulmonary function data obtained from the execution of a panting maneuver in a body-plethysmograph or (b) patient data obtained from a forced expiratory maneuver, the approaches taken would differ considerably:

(1) The "fundamental" model would most probably take into account the morphometry of the bronchial tree. Weibel (1963) has developed a symmetrical model that assumes a regular dichotomous branching and this study has been utilized in other modeling studies of lung-airway dynamics (e.g., Fry (1968) and Pardaens, et al. (1972)).

(2) The "functional" model would contain rather gross lumpings of pulmonary resistance and compliance subject to the constraints that the parameters have a physical basis and the fit to observed subject data is adequate. The overriding concern here is the ability to specify a model structure that makes sense physically, and yet with only a relatively small number of parameters is able to adequately mimic patient data (e.g., Golden, et al. (1973), Feinberg, et al. (1970), Pride, et al. (1967), and Yamabayashi, et al. (1970)).
Here the "fundamental" model would be of considerable use in studying (for a given set of parameters) the basic fluid mechanical aspects of the airflow in the bronchial tree. It would have utility as a teaching aid and as a research tool since parameter manipulation could be made at any level in the tree and effects on respiratory variables observed. The rather large number of parameters involved, however, preclude the use of parameter identification techniques (e.g., Graupe (1972)) for the determination of the model parameters for a given patient for diagnostic purposes. These latter objectives can possibly be achieved using an adequately specified "functional" model containing many fewer model parameters. Viewed in this pragmatic context, additional model complexity is warranted only if it lends additional diagnostic insight into lung-airway behavior.

This work extends the simple lumped parameter "functional" model of Golden, et al. (1973) (which simulates the special case of the panting maneuver executed in a body plethysmograph) to the simulation of a wider range of pulmonary function tests that include the production of pressure-flow curves, maximum expiratory flow-volume (MEFV) curves, and isovolume pressure-flow (IVPF) curves. The model is programmed on an analog computer which allows fast realization and convenient parameter manipulation. The results indicate the effectiveness of using a lumped parameter, multiple resistance model to mimic the full range of dynamic pulmonary function tests. In addition to the resistance parameters, the airway and lung compliance
curves must also be specified. Thus, the simulation indicates the influence of a number of airway and lung parameters on the nature of expiratory flow limitation.
In this chapter, a mathematical model that has been previously developed (Golden, et al. (1973)) is presented and extended to allow for the simulation of panting and maximum expiratory maneuvers. The physiological properties of the ventilatory system are considered, the mathematical model is derived, and the equations that comprise the model are presented.

The ventilatory system is a highly complex organization that accomplishes the task of moving air from the mouth to the over 500 million alveoli that comprise the exchange surface with the blood. Ventilation is achieved by the production of a pressure gradient between the alveoli and the mouth, and airflow results.

Because of the highly complex nature of the ventilatory system, especially near the alveolar level, some simplifying assumptions must be made and a lumped representation must be considered if any analysis is to be achieved. Also, since clinical tests are derived by considering a lumped ventilatory system, any analysis obtained from clinical data can only be interpreted by considering the ventilatory system as a lumped parameter system.

The lumped parameter model of Golden, et al. (1973) is shown in Figure 1. It consists of a single, but variable airway that connects the mouth with the lumped alveolar space. The alveolar space and most of the airway are surrounded by the
Figure 1 Lumped parameter model for the pulmonary ventilatory system (from Golden, et al. (1973))
pleural cavity. The airway is comprised of three sections: the large airway section, the collapsible airway section, and the small airway section.

The alveolar space is characterized by the compliance of the lung tissue. Under static conditions, the lung volume is determined by the pressure (lung elastic recoil) across the lung tissue wall. The normal static lung compliance curve is shown in Figure 5. Under dynamic conditions, there is no longer a single relationship between lung volume and lung elastic recoil. During expiration (and inspiration) a hysteresis develops in which the pressure generated at a specific lung volume is less than (and greater than) the pressure needed to maintain that lung volume under static conditions. To a large extent, dynamic lung hysteresis is a function of the alveolar surface film as demonstrated by the large decrease in hysteresis when the lungs are filled with saline and the air-liquid interface is eliminated. An additional component that contributes to the hysteretic behavior of the lung is the visco-elastic nature of the lung as seen in isolated lung tissue studies (Sugihara, et al. (1972), Glaister, et al. (1973), and Clements, et al. (1961)). So, under dynamic conditions the volume of the lung is a function of the lung elastic recoil, the effort of expiration (or inspiration), and the past history of the lung inflation. Maximum expiratory lung elastic recoil for the vital capacity maneuver is also shown in Figure 5.

In the model, between the lungs and the chest wall is an
artificial space. Changes in the pressure within this space are transmitted to the alveoli and are responsible for the formation of the pressure gradient between the mouth and the alveoli, and the resulting ventilation.

The airway is comprised of three lumped sections that are intended to model the changes that occur from the large airways near the mouth to the small airways near the alveoli. The large, rigid part of the airway is modeled by a nonlinear "Rohrer resistor" characterized by the following pressure-flow relation:

\[ P = K_1 V_{A0} + K_2 V_{A0}^2 \]  

(1)

Here, \( K_1 V_{A0} \) is the laminar flow term containing the viscosity of the gas and the tubular geometry, while the second term, \( K_2 V_{A0}^2 \), is an additional resistance term which becomes significant at higher flow rates where turbulent flow is likely to occur. The mid-section of the airway, having no cartilaginous support, is normally held distended by the pressure gradient across the wall of the airway. However, when this transmural pressure passes from positive to negative (which can occur during forced expiration), the airway tends to collapse. So the mid-airways of the ventilatory system are modeled by a pressure-dependent resistance \( R_C \) characterized as a cylinder of constant length whose radius, and hence volume \( V_C \), varies with transmural pressure \( P_{TM} \). According to Poiseuille's law, a rigid tube having a radius \( r \) and a length \( L \) will have a resistance \( R \) to laminar flow that is inversely proportional to \( r^4 \):

\[ R = \frac{8 \mu L}{\pi r^4} \]
where $\mu$ is the viscosity of the fluid. So, the resistance of the collapsible segment varies inversely with the square of the cross-sectional area, for a segment of constant length. Poiseuille's law is then used in the development of the following expression for the resistance of the collapsible segment:

$$ R_C = f(V_C) = K_3(K_4/V_C)^2 \quad (2) $$

Here $K_3$ and $K_4$ are weighting constants; $K_3$ determines the overall magnitude of $R_C$ and $K_4$ determines the relative volume of the collapsible segment at which $R_C$ will be the dominant component of the overall airway resistance. Finally, the small part of the airway represents the smaller peripheral airways located within the lung tissue. These airways are held distended by the overlying lung tissue at high lung volumes, but tend to collapse with the lung tissue at low lung volumes. Thus the small part of the airway is modeled by a nonlinear resistance whose magnitude is a function of lung volume (Figure 3):

$$ R_S = f_1(V_L) \quad (3) $$

The electrical analog of the model is shown in Figure 2. Using Kirchoff's voltage and current laws, the following equations are obtained:

$$ P_{ALV} = P_{EL} + P_{PL} \quad (4) $$

$$ 0 = P_{EL} - P_{TM} + R_S V_L \quad (5) $$

$$ 0 = P_{TM} + P_{PL} + (R_C + K_1 + K_2 V_A 0 ) \dot{V}_A 0 \quad (6) $$

$$ V_C(t) = V_C(0) + \int_0^t (\dot{V}_A 0 - \dot{V}_L) dt \quad (7) $$

$$ V_L(t) = V_L(0) + \int_0^t (\dot{V}_A 0 - \dot{V}_L) dt \quad (8) $$

Here, $P_{TM}$ is a nonlinear function of $V_C$ (Figure 4):

$$ P_{TM} = f_2(V_C) \quad (9) $$
Figure 2 Electrical equivalent model of the pulmonary ventilatory system (shown in Figure 1)
Figure 3 Relationship between small airway resistance and lung volume for the normal and increased small airway resistance cases
Figure 4  Airway compliance for the normal case
and lung elastic recoil ($P_{EL}$) is a nonlinear function of $V_L$ and $P_{PL}$, as determined by the maneuver effort (see Figure 5):

$$P_{EL} = f_3(V_L, P_{PL}).$$

(10)

Thus, equations (1) through (10) comprise the mathematical model for the ventilatory system.
Figure 5 Lung compliance (both static and dynamic expiratory) for the normal case
CHAPTER 3
Computational Aspects

In this chapter, the block diagram of the computer program for the model is presented. The parameter values and relationships are developed from those reported in the literature. The pleural pressure waveform is modified to generate each respiratory maneuver that is simulated. The parameters are varied one at a time to observe their primary effect. And, disease state conditions are implemented and MEFV curves are produced.

The mathematical model of pulmonary airway dynamics was programmed on an Electronics Associates, Inc. MiniAc analog computer system and was run at ten times real time to allow for the slow response time of the plotter. A block diagram of the computer program is given in Figure 6.

Typical resistance and compliance values for a normal subject were taken from the literature. Specifically, values for large airway resistance ($K_1$ and $K_2$) were adapted from Bouhuys and Jonson (1967) and Mead (1961). The values of $K_1$ and $K_2$ were taken to be $K_1 = 0.5 \text{ cm H}_2\text{O}/(\text{L/sec})$ and $K_2 = 0.2 \text{ cm H}_2\text{O}/(\text{L/sec})^2$. Values for collapsible airway resistance ($K_3$ and $K_4$) were also adapted from the literature. Mead, et al. (1967) found that increased large airway resistance had no discernible influence on maximal flow at volumes below 50% vital capacity (VC). Furthermore, Bouhuys (1974) states that the MEFV curve represents flows that correspond to plateaus.
Figure 6  Block diagram for the analog computer system - variable function generators (VFGs) include VFG₁ (transmural pressure \( P_{TM} \) as a function of collapsible airway volume \( V_C \)), VFG₂ (lung elastic recoil \( P_{EL} \) as a function of lung volume \( V_L \)), and VFG₃ (small airway resistance \( R_S \) as a function of lung volume \( V_L \))
Figure 6

[Diagram of a control system with various components and equations.]
on IVPF curves at lung volumes below about 80% VC. These results were approximated when values $K_3 = 0.6 \text{ cm H}_2O/(1/\text{L} \cdot \text{sec})$ and $K_4 = 0.125$ were utilized. The nonlinear function for small airway resistance was adapted from data reported by Macklem and Mead (1967) and Bouhuys (1974) and is shown in Figure 3. $R_s$ is small and approximately constant (equal to $0.3 \text{ cm H}_2O/(\text{L}/\text{sec})$) above 40% VC, but increases rapidly below 40% VC.

Physiological data published by Murtaugh, et al. (1971) and Hyatt and Flath (1966) was used in the formulation of the compliance curve for the collapsible segment (Figure 4). Likewise, pressure-volume data published by Colebatch, et al. (1973) was used in the formulation of the static lung compliance ($P_{EL}$-static) curve (Figure 3). The dynamic lung compliance ($P_{EL}$-dynamic) curve (Figure 5) was formulated using the static lung compliance curve and data published by Glaister, et al. (1973) and Clements, et al. (1961). The choice of lung elastic recoil was found dependent on respiratory maneuver.

The pleural pressure driving function was also found to vary with particular respiratory maneuver. For the panting simulation, a high frequency (1.6 Hz), low volume (<0.1L) sinusoid, offset by a negative static pleural pressure was programmed to react with the static lung elastic recoil function. For the maximum expiratory maneuver, a filtered, two-break point temporal waveform (Figure 11a) and the dynamic lung elastic recoil function were implemented. This $P_{PL}$ waveshape was adapted from patient data recorded in The Methodist Hospital Pulmonary Function Laboratory, Houston, Texas.
(Figure 7), as well as data reported by Milic-Emili, et al. (1964). In the MEFV maneuver, peak pleural pressure (due to expiratory muscular effort) is found to be highly variant from subject to subject due to normal physical variables (age, height, sex) and, in addition, training for the maneuver (Milic-Emili, et al. (1964)). This accounts for the significant variability in peak expiratory flow (for normal subjects) seen in the literature, since flow is generally considered to be limited by peak pleural pressure in this range (Bouhuys (1974)). Figure 7 shows actual patient data for a representative untrained normal subject who was able to generate a pleural pressure that is slightly in excess of +60 cm H₂O. Because of this high degree of variability, the choice of peak pleural pressure used in association with the driving waveform \( P_{PL}(t) \) for the maximum expiratory maneuver in the model is somewhat arbitrary. Therefore, a value of 100 cm H₂O (considered as an intermediate value) for peak pleural pressure was used in this study. To generate IVPF curves, the methods employed by Hyatt, et al. (1958) were mimicked. These involved sequentially increasing expiratory effort until maximum effort (and therefore pleural pressure) at that volume was achieved. So, in the simulation a ramp-to-plateau pleural pressure waveform (Figure 11b) was utilized. The slope of the ramp and the dynamic nature of the lung elastic recoil (with \( P_{EL} \) static and \( P_{EL} \) dynamic in Figure 5 indicating the extremes corresponding to minimum and maximum effort, respectively) were increased sequentially until maximum pleural pressure at that volume was
Figure 7 Patient data for a typical normal case showing temporal waveforms (flow at the mouth ($V_A^0$), relative lung volume (lung volume ($V_L$) minus residual volume ($RV$)), and pleural pressure ($P_{PL}$)) for the MEFV maneuver (recorded at The Methodist Hospital, Pulmonary Function Laboratory, Houston, Texas).
achieved. Flow at the mouth and alveolar pressure were recorded for each case. Table 1 shows the other values (arbitrarily chosen) that are used for the normal case.

Physiological data published by Colebatch, et al. (1973) was used in the formulation of the static lung compliance ($P_{EL}^{\text{static}}$) curves for the emphysematic, the asthmatic, the asthmatic after in halation of a bronchodilator (aerosol isoproterenol), and the normal case as shown in Figure 16. The static lung compliance for the fibrotic case was taken from Ruch and Patton (1965) and is also included in Figure 16. The dynamic expiratory lung compliance ($P_{EL}^{\text{dynamic}}$) curve (Figure 16) for each case was formulated using the static lung compliance for that case and the data published by Glaister et al. (1973) and Clements, et al. (1961) concerning hysteresis exhibited by isolated lung tissue.

The compliance of the airways was also found to be dependent on the disease state, but to a lesser degree. Static compliance curves for the airways (Figure 17) were therefore derived and utilized using data published by Murtaugh, et al. (1971), Hyatt and Flath (1966), and Fry (1968).

The simulation of the MEFV maneuver for various diseased states was accomplished by driving the specific case with the appropriate pleural pressure waveform from total lung capacity to residual volume. Corresponding changes in lung compliance, airway compliance, and airway resistance are made according to the specific disease state. Table 2 indicates the parameter changes according to the disease state.
### TABLE 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal Value</th>
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<tr>
<td>TLC</td>
<td>6.5 liters</td>
</tr>
<tr>
<td>RV</td>
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</tr>
<tr>
<td>VC</td>
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</tr>
<tr>
<td>FRC</td>
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</tr>
<tr>
<td>$V_c$ MAX</td>
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<tr>
<td>$R_{LAW}$</td>
<td>$0.7$ cm H$_2$O/(L/sec) *</td>
</tr>
<tr>
<td>$K_1$</td>
<td>$0.5$ cm H$_2$O/(L/sec)</td>
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<tr>
<td>$K_2$</td>
<td>$0.2$ cm H$_2$O/(L/sec)</td>
</tr>
<tr>
<td>$K_3$</td>
<td>$0.6$ cm H$_2$O/(1/L·sec)</td>
</tr>
<tr>
<td>$K_4$</td>
<td>$0.125$</td>
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* - at a flow of 1 L/sec
### TABLE 2

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal</th>
<th>Asthma</th>
<th>Asthma(PI)</th>
<th>Emphysema</th>
<th>Fibrosis</th>
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<tbody>
<tr>
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<td>7.8 L</td>
<td>7.8 L</td>
<td>7.8 L</td>
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</tr>
<tr>
<td>RV</td>
<td>1.5 L</td>
<td>4.4 L</td>
<td>3.6 L</td>
<td>3.6 L</td>
<td>1.5 L</td>
</tr>
<tr>
<td>VC</td>
<td>5.0 L</td>
<td>3.4 L</td>
<td>4.2 L</td>
<td>4.2 L</td>
<td>3.1 L</td>
</tr>
<tr>
<td>$R_{L_{AW}}^*$</td>
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<td>2.1</td>
<td>0.7</td>
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<tr>
<td>$K_1^{**}$</td>
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<td>0.5</td>
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<tr>
<td>$K_2^{**}$</td>
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<tr>
<td>$R_S^{***}$</td>
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<td>increased</td>
<td>normal</td>
</tr>
<tr>
<td>$C_{AW}^{****}$</td>
<td>normal</td>
<td>normal</td>
<td>normal</td>
<td>flacid</td>
<td>stiff</td>
</tr>
</tbody>
</table>

* - in cm H$_2$O/(L/sec) at a flow of 1 L/sec
** - in cm H$_2$O/(L/sec)
*** - as shown in Figure 3
**** - as shown in Figure 17
The asthmatic case is characterized by a decrease in lung elastic recoil (an increase in lung compliance—Figure 16), an increase in large airway resistance due to smooth muscle contraction in the large airways, and an increase in small airway resistance due to mucus accumulation and mucosal swelling in the small airways. So, for the asthmatic case corresponding dynamic expiratory lung elastic recoil curve (Figure 16) was utilized, large airway resistance was tripled by tripling the individual $K_1$ and $K_2$ parameters (this corresponds to an increase of $1.4 \text{ cm H}_2\text{O}/(\text{L/sec})$ at a flow of $1\text{L/sec}$), and small airway resistance was increased $1.4 \text{ cm H}_2\text{O}/(\text{L/sec})$ by simply shifting the curve upward (Figure 3). The normal pleural pressure waveform (Figure 11a) was utilized.

The asthmatic (post inhalation) case is characterized as the asthmatic except with large airway resistance decreased due to the inhalation of a vaso-relaxor agent, and a slight change in the lung compliance curve. So, for this case the corresponding dynamic expiratory lung elastic recoil curve (Figure 16) was utilized, large airway resistance was returned to its normal value, and small airway resistance remained increased (Figure 3). The normal pleural pressure waveform was utilized.

The emphysematic case is characterized by a large increase in lung compliance, an increase in airway compliance, and an increase in small airway resistance due to mucus accumulation and mucosal swelling in the small airways. So, for the emphysematic case, the corresponding dynamic expiratory lung elastic
recoil curve (Figure 16) was utilized, the flacid airway compliance curve (Figure 17) was utilized, and the increased small airway resistance curve (Figure 3) was utilized. Because of the extreme loss of lung elastic recoil the pleural pressure driving waveform had to be altered to allow for deflation to residual volume. This involves increasing the time duration of the final phase of the waveform (Figure 21-insert) and corresponds to pleural pressure waveform produced by an emphysematic during a clinical MEFV maneuver (Figure 22).

The fibrotic case is characterized by a large decrease in lung compliance and a corresponding decrease in airway compliance. So, for the fibrotic case the corresponding dynamic expiratory lung elastic recoil curve (Figure 16) and the stiff airway compliance curve (Figure 17) were used. The normal pleural pressure driving function was used also.
RESULTS

The results of the simulations of various pulmonary function tests are presented in this chapter. The panting maneuver is reproduced to indicate the proper function of lumped airway compliance and resistances. Maximum expiratory maneuvers are simulated to: (1) indicate the correlation between data presented in MEFV and IVPF curves, (2) indicate the effects of individual parameter manipulations, and (3) indicate the ability of the model to simulate various disease states.

At the present time, a battery of tests is used to assess the pulmonary function of a patient. Airway resistance measured during a panting maneuver in a body plethysmograph (usually at functional residual capacity (FRC)) is one of the component tests. An increase in total airway resistance (normal total airway resistance is less than 2.0 cm H$_2$O/(L/sec)) usually indicates an increase in large airway resistance. A normal total airway resistance is not, however, conclusive that a subject is normal since small airway resistance contributes less than 25% of the total. Large increases in small airway resistance are necessary to significantly affect total airway resistance.

Maximum expiratory maneuvers represent another pulmonary function test. Figure 8 indicates exemplary MEFV curves for several disease states. As shown, with obstructive lung disease vital capacity is reduced, flow rates are low (especially near
Figure 8  Typical MEFV curves for normal and diseased cases (from Bouhuys (1974))
residual volume), and the descending portion of the MEFV curve is convex to the volume axis; with restrictive lung disease vital capacity is reduced even more than in the obstructive case, flow rates are high, and the descending portion of the MEFV curve is concave to the volume axis. The entire curve, or measurements taken from the curve (such as volume expired during the first second of expiration and the mean flow during the expiration of the middle 50% of the forced vital capacity) can be used in formulating a diagnosis.

Further tests such as the response to bronchodilators, gas and blood gas analysis, the dynamic nature of lung compliance, and others are used to give a more complete picture to the state of the pulmonary system of a patient.

The accurate simulation of these tests helps justify the use of the model in the interpretation of pulmonary respiratory dynamics. Unless the model is capable of indicating the results of parameter manipulation and the simulation of various disease states, the model itself cannot be considered a valid representation of pulmonary function.

Figure 9 demonstrates the ability of the model to mimic the shallow panting maneuver performed in a body plethysmograph by normal and diseased patients. Each maneuver is driven by a sinusoidal pleural pressure that produces variations of ± 5 cm H2O in alveolar pressure. Each patient simulation is conducted at three different lung volumes (90%, 50%, and 10% vital capacity) and therefore, three different values of lung elastic recoil. Since total airway resistance is reflected as
Figure 9  Simulated panting maneuvers at representative lung volumes (the driving pleural pressure waveform is a small amplitude sinusoid varying about a mean value)

(a) Normal airway resistance values

(b) Tripled large airway resistance ($K_1 = 1.5 \text{ cm H}_2\text{O}/(\text{L/sec})$, $K_2 = 0.6 \text{ cm H}_2\text{O}/(\text{L/sec})^2$) representing an increase of $1.4 \text{ cm H}_2\text{O}/(\text{L/sec})$ in total airway resistance at a flow of 1 L/sec

(c) Increased small airway resistance (a positive shift of $1.4 \text{ cm H}_2\text{O}/(\text{L/sec})$ in the small airway resistance curve (Figure 3)) representing an increase of $1.4 \text{ cm H}_2\text{O}/(\text{L/sec})$ in total airway resistance (equivalent to the increase in Figure 9b)
Figure 9

4-5

LITERS

2 LITERS

4 LITERS

6 LITERS
the inverse of the absolute value of the slope of the $P_{ALV} - \dot{V}_{A0}$ curve (an increase in airway resistance produces a decrease in the absolute value of the slope), the curves indicate the volume (actually lung recoil) dependent nature of total airway resistance due mainly to increased small airway resistance (Figure 3). Hysteresis, seen in some maneuvers, is due to the parallel resistive-compliant nature of the airways. Figure 9a (the normal case) indicates the curve shape and the increase in total airway resistance with the decrease in lung volume. The small airway resistance becomes dominant at low lung volumes. Figure 9b indicates that tripled large airway resistance (approximately doubled total airway resistance) is accurately reflected at high and middle lung volumes. Again, at low lung volumes the increased small airway resistance is dominant and no discernible change is seen. Figure 9c indicates the results of the same magnitude change in airway resistance as in Figure 9b, but in the small airways. This change was accomplished by a simple upward shift in the $R_s$ curve (Figure 3) at all lung volumes. The simulation at 6 liters shows much less total airway resistance contribution than in Figure 9b. At 4 liters, the model also exhibits a small contribution to total airway resistance, but the combination of increased small airway resistance and decreased lung elastic recoil with decreased lung volume produces observable expiratory flow hysteresis, dynamic compression, and expiratory flow limitation. And, as in the other cases, at 2 liters small airway resistance dominates all other effects. These results parallel those reported

The ability of the model to demonstrate the relationship between data presented in the form of MEFV and IVPF curves is shown in Figure 10. The IVPF curves tend to plateau at low lung volumes due to dynamic compression of the collapsible airway. At high lung volumes, the expiratory flow is limited by the pleural pressures that can be generated by contraction of the respiratory muscles. As Bouhuys (1974) indicates, points on the effort independent portion of the MEFV curve correspond to plateaus of the IVPF curves below approximately 80% vital capacity in normal subjects. Figure 10 thus demonstrates that the model is capable of providing a realistic simulation of this relationship between MEFV and IVPF curves.

Figures 11a and 11b show the temporal waveforms of selected parameters during the MEFV and IVPF maneuvers. The waveforms for pleural pressure, lung volume, and flow at the mouth are consistent with patient data (Figure 7) and data reported in the literature (Milic-Emili, et al. (1964)). The waveforms for collapsible segment volume and collapsible segment resistance are included to add insight into the dynamic nature of airway compression in the model. For the MEFV maneuver, $V_C$ starts to decrease immediately, achieves its minimum value after the peak pleural pressure is attained, and increases slightly through the remainder of the maneuver due to the decrease in pleural pressure in the latter phases of the maximum expiratory maneuver. For the IVPF maneuver, $V_C$ decreases throughout. $R_C$ is inversely related to the square of $V_C$ (as
Figure 10  A simulated MEFV curve and a constructed IVPF curve for the normal case (the interrelationship of the two forms of presentation is indicated)
Figure 11 Temporal waveforms (pleural pressure ($P_{PL}$), lung volume ($V_L$), flow at the mouth ($V_{AO}$), collapsible airway volume ($V_C$), and collapsible airway resistance ($R_C$)) for model simulations for the normal case

(a) For the MEFV maneuver

(b) For the IVPF maneuver
Figure 11b
is shown in both maneuvers) and is most sensitive at low values of $V_c$.

The remaining figures demonstrate the results of parameter manipulation. Hyatt, et al. (1958) indicated and Mead et al. (1967) demonstrated that if a normal subject performed a maximum expiratory maneuver with various additional mouthpiece resistances, maximum flow is uninfluenced at lung volumes below at least 50% vital capacity. In addition, the added mouthpiece resistance increases the effective large airway resistance ($R_{LAW}$) and has the greatest effect at high lung volumes. This decreases peak flow and allows for the generation of a higher peak pleural pressure during maximum expiratory muscular effort (as shown by Mead, et al. (1967)). Airway compression and therefore limitation are unaffected so that the time duration of the maneuver remains approximately the same. The MEFV curves and pleural pressure driving waveforms for increased large airway resistance are shown in Figure 12. They show that with an increase in $R_{LAW}$ and the pleural pressure waveform, an effort independent of the portion of the MEFV curve can be maintained.

Figure 13 shows the corresponding effect of an equal increase in small airway resistance (a simple upward shift in the $R_S$ curve (Figure 3)) to approximate the results of the study by McFadden, et al. (1969). Small airway resistance can, of course, be altered while other resistance and compliance parameters are kept constant. Both total airway resistance and flow limitation are increased so that the peak
Figure 12  Simulated MEFV maneuvers for the normal case and for the case of tripled large airway resistance (associated pleural pressure waveforms are indicated in the insert)
Figure 12

Diagram showing changes in pressure (PPL) and volume (VL) over time (TIME SEC) with readings for normal and increased conditions.

Axes:
- PPL (CM H₂O) on the left
- VAO (L/SEC) on the bottom
- Normal and increased increase in RLAW on the bottom
- VL (LITERS) on the right

Graphs indicate a positive correlation between time and increase in RLAW, with a distinct peak and trough pattern for each condition.
Figure 13 Simulated MEFV maneuvers for the normal case and the case of increased small airway resistance (a positive shift of 1.4 cm H$_2$O/(L/sec) in the small airway resistance curve (Figure 3) to produce a change in total airway resistance equivalent to that seen in Figure 12). Associated pleural pressure waveforms are indicated in the insert.
pleural pressure and the time duration of the maneuver are also increased. The resulting MEFV curve demonstrates the representative effect of increased small airway resistance; peak flow is achieved early and then falls off rapidly producing a curve that is concave to the volume axis. This change in the form of the MEFV curve in simulated airway obstruction is consistent with published data (Bouhuys (1974)).

The results of changes in airway compliance are shown in Figures 14a through 14c and agree with the results of Pardaens et al. (1972). A change in the upper portion of the airway compliance curve appears to affect mainly the peak flow of the MEFV curve (Figure 14a), while a change in the lower portion of the airway compliance curve affects the slope of the MEFV curve in the flow limited region and can even produce gas trapping (Figure 14b). Gas trapping is the inability of the subject to expire to residual volume due to severe flow limitation. Figure 14c includes the combined effects of changes in upper and lower portions of the airway compliance curve.

Finally, Figure 15 shows the results of changes in lung compliance. The MEFV curves indicate simulations utilizing \( P_{EL} \) static, \( P_{EL} \) dynamic (normal), and \( P_{EL} \) dynamic (abnormal). Peak expiratory flow and rate of flow limitation are affected by changes in lung compliance as also reported by Pardaens, et al. (1972). Figure 15 demonstrates the relative importance associated with the use of dynamic rather than static lung compliance in the modeling of dynamic maneuvers.

Figures 18 through 25 indicate the ability of the model
Figure 14  Simulated MEFV maneuvers with altered airway compliance

(a) Altered upper portion of the airway compliance curve as indicated in the insert

(b) Altered lower portion of the airway compliance curve as indicated in the insert

(c) Combined changes in the upper and lower portions of the airway compliance curve as indicated in the insert
   (the arrow indicates the direction of increasing airway compliance)
Figure 14a
Figure 15 Simulated MEFV maneuvers with altered lung compliance curves as indicated in the insert (the arrow indicates changes from normal static lung compliance to normal dynamic lung compliance to abnormal dynamic lung compliance)
Figure 15

VOLUME

% TLC

PREDICTED

4-24

VAO L/SEC

Vl LITERS

PEL

CM H2O

0 2 4 6 8 10 12

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 20 25
Figure 16  Lung compliance for normal and diseased states

Emphysematic-
1- Dynamic expiratory
2- Static

Asthmatic-
3- Dynamic expiratory
4- Static

Asthmatic(PI)- 5- Dynamic expiratory
6- Static

Normal-
7- Dynamic expiratory
8- Static

Fibrotic-
9- Dynamic expiratory
10- Static
Figure 16
Figure 17  Airway compliance for normal and diseased states
to simulate MEFV curves for various diseased states. Figure 18 shows the MEFV curve for the asthmatic case. It indicates the pattern that occurs with obstructive lung disease: vital capacity is reduced, flow rates are low (especially near residual volume), and the descending portion of the MEFV curve is convex to the volume axis.

Figure 19 shows the asthmatic (post inhalation) case. The decrease in large airway resistance results in higher flow rates than for the asthmatic case throughout the maneuver, and a decrease in the degree of convexity to the volume axis. Since the lung compliance and the small airway resistance remain increased, the flows throughout the maneuver remain below normal. Figure 20 shows the MEFV curves for the asthmatic, the asthmatic (post inhalation), and the normal plotted on the volume scale relative to total lung capacity and indicates the relative differences already discussed.

Figures 21 and 23 show the MEFV curve for the emphysematic case. Since this is also considered an obstructive lung disease, the pattern that occurs parallels that for the asthmatic case: vital capacity is reduced, flow rates are low (especially near residual volume), and the descending portion on the MEFV curve is convex to the volume axis. Due to the large increase in the lung compliance, the flow rates are reduced even more than in the asthmatic case. And, due to the increase in airway compliance, the emphysematic curve is more convex to the volume axis than in the asthmatic case.

Finally, Figures 24 and 25 show the MEFV curve for the
Figure 18  Simulated MEFV curve for the asthmatic
Figure 19
Simulated MEFV curve for the asthmatic (post inhalation)
**Figure 20** Simulated MEFV curve for the asthmatic, asthmatic (post inhalation), and normal normalized to total lung capacity
Figure 21 Simulated MEFV curve for the emphysematic
Figure 22  Patient data for a typical emphysematic case showing temporal waveforms (flow at the mouth ($V_{A0}$), relative lung volume (lung volume ($V_L$) minus residual volume ($RV$)), and pleural pressure ($P_{PL}$)) for the MEFV maneuver (recorded at The Methodist Hospital, Pulmonary Function Laboratory, Houston, Texas)
Figure 22

- $\dot{V}_{A0}$
- L/SEC
- $V_{L-RV}$
- LITERS
- $P_{PL}$
- CM H$_2$O
Figure 23 Simulated MEFV curves for the emphysematic and normal, normalized to total lung capacity.
Figure 24 Simulated MEFV curve for the fibrotic
Figure 25 Simulated MEFV curves for the fibrotic and normal, normalized to total lung capacity.
fibrotic case. Since fibrosis is indicative of a restrictive function loss the curve indicates the patterns of restrictive lung disease: vital capacity is reduced even more than in the obstructive case, flow rates are high, and the descending portion of the MEFV curve is concave to the volume axis.
The mathematical model presented by Golden, et al. (1973) has been extended in this work to allow for the simulation of maximum expiratory tests as well as plethysmographic panting maneuvers. Initial conclusions having to do with the simulation of the panting maneuver verify those results reported by Golden, et al. (1973). For example, increasing large airway resistance significantly increases total airway resistance but does not affect expiratory flow limitation; increasing small airway resistance has comparatively little effect on total airway resistance but significantly affects expiratory flow hysteresis and limitation; reduced lung elastic recoil (either at lower lung volumes in the normal or in disease states such as emphysema) has little effect on total airway resistance but significantly affects expiratory flow limitation.

With regard to maximum expiratory maneuvers, the model can produce data that is in general agreement with data found in the literature. The MEFV curve represents flows that correspond to plateaus on IVPF curves at lung volumes less than approximately 80% vital capacity (Bouhuys (1974)). An increase in large airway resistance (as in Figure 12) is accompanied by corresponding increases in attainable pleural pressure during a maximum expiratory maneuver and that maximum flow is unaffected below at least 50% vital capacity (Mead, et al. (1967)). An increase in small airway resistance (Figure 13) causes a
decrease in peak flow and produces an MEFV curve that is concave to the volume axis (McFadden, et al. 1969). Also, relatively small changes in lung and airway compliance (Figure 14) have significant effects on the shape of the resulting MEFV curves (Pardaens, et al. 1972).

The model is also capable of simulating the MEFV curves for various disease states. For obstructive disease, vital capacity is decreased, flow rates are decreased (especially near residual volume), and the descending portion of the MEFV curve is convex to the volume axis. For the restrictive function loss, vital capacity is decreased, flow rates are increased, and the descending portion of the MEFV curve is concave to the volume axis.

Thus, the results shown in this study indicate that the model is capable of simulating standard breathing maneuvers associated with the clinical assessment of pulmonary function. It is structurally much simpler than the models of Fry (1968) and Pardaens, et al. (1973) and yet yields the same information in a diagnostic sense. Being of simpler form it has fewer model parameters and potentially may be used in conjunction with parameter identification techniques to obtain a set of describing parameters for individual patients. This simulation can also be seen as a teaching aid to help in the understanding of pulmonary ventilatory mechanics and is also directly extendable to a unified study of pulmonary mechanics in normal and disease states thereby providing a potentially useful tool for the interpretation of clinical pulmonary
function tests.
REFERENCES


APPENDIX A

Terminology

The following terminology is used in the text:

### PRESSURES

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>$P_{PL}$</td>
<td>Pleural pressure; the pressure in the pleural space relative to atmospheric pressure</td>
</tr>
<tr>
<td>$P_{EL}$</td>
<td>Lung elastic recoil; the transmural pressure across the wall of the alveolar space</td>
</tr>
<tr>
<td>$P_{ALV}$</td>
<td>Alveolar pressure; pressure in the alveolar space relative to atmospheric pressure</td>
</tr>
<tr>
<td>$P_{TM}$</td>
<td>Transmural pressure of the collapsible airway</td>
</tr>
</tbody>
</table>

### FLOWS

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>$V_L$</td>
<td>Airflow into the alveolar space</td>
</tr>
<tr>
<td>$V_{AO}$</td>
<td>Airflow into the mouth (inspiratory flow assumed positive)</td>
</tr>
<tr>
<td>$V_{MAX}$</td>
<td>Maximum expiratory flow</td>
</tr>
</tbody>
</table>

### VOLUMES

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>$V_L$</td>
<td>Lung volume; volume of the alveolar space</td>
</tr>
<tr>
<td>$V_C$</td>
<td>Collapsible airway volume</td>
</tr>
<tr>
<td>$V_{C\ MAX}$</td>
<td>Collapsible airway volume (maximum)</td>
</tr>
<tr>
<td>TLC</td>
<td>Total lung capacity; the maximum volume of the alveolar space</td>
</tr>
<tr>
<td>RV</td>
<td>Residual volume; the volume left in the alveolar space after maximum expiration</td>
</tr>
</tbody>
</table>
VC Vital capacity; the volume change during maximum expiration
FRC Function residual capacity; the volume of the alveolar space at resting end expiration
FVC Forced vital capacity
FEV₁ Forced expiratory volume at 1 second; the volume expired during the first second of a FVC maneuver

Resistances and Resistance Parameters

\[ R_{\text{AW}} \quad \text{Total resistance of the airways} \]
\[ R_{\text{LAW}} \quad \text{Resistance of the large airway} \]
\[ K_1 \quad \text{"Laminar" resistance term in the large airway} \]
\[ K_2 \quad \text{"Turbulent" resistance term in the large airway} \]
\[ R_C \quad \text{Collapsible airway resistance} \]
\[ K_3 \quad \text{Magnitude parameter for the collapsible airway resistance} \]
\[ K_4 \quad \text{Timing parameter for the collapsible airway resistance} \]
\[ R_S \quad \text{Small airway resistance} \]

Compliances

\[ C_L \quad \text{Lung compliance; compliance of the alveolar space} \]
\[ C_{\text{AW}} \quad \text{Airway compliance; compliance of the collapsible airway} \]
<table>
<thead>
<tr>
<th>Expressions</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>MEFV</td>
<td>Maximum expiratory flow-volume</td>
</tr>
<tr>
<td>IVPF</td>
<td>Isovolume pressure-flow</td>
</tr>
</tbody>
</table>
APPENDIX B

Analog Computer Programs

The following analog computer programs were utilized to implement the mathematical model:

<table>
<thead>
<tr>
<th>Page</th>
<th>Program</th>
</tr>
</thead>
<tbody>
<tr>
<td>B-2</td>
<td>Generation of the pleural pressure driving waveform for the MEFV maneuver</td>
</tr>
<tr>
<td>B-3</td>
<td>Generation of the pleural pressure driving waveform for the panting maneuver</td>
</tr>
<tr>
<td>B-4</td>
<td>Generation of collapsible airway volume and collapsible airway transmural pressure</td>
</tr>
<tr>
<td>B-5</td>
<td>Generation of lung volume and lung elastic recoil</td>
</tr>
<tr>
<td>B-6</td>
<td>Generation and summation of airway resistances, and generation of flow at the mouth</td>
</tr>
</tbody>
</table>