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RESPIRATORY PARAMETER ESTIMATION USING FORCED
OSCILLATORY IMPEDANCE DATA

DISSERTATION

Presented in Partial Fulfillment of the Requirements for
the Degree Doctor of Philosophy in the Graduate
School of The Ohio State University

by

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* * * * *

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Traditionally, the respiratory mechanical system has been modeled and analyzed using linear electric circuit. The impedance of such a model can be measured using the forced oscillation technique. Based on the measured impedance data and analytical expression for impedance of the circuit model, the respiratory mechanical parameters can be determined with certain parameter estimation technique. Such an approach for determining respiratory parameters was studied in this dissertation. In this study, an extended forced oscillation technique which employs a specially designed device known as "impedance analyzer" and a least-square parameter estimation algorithm which combines several gradient methods and a uniform random search routine were utilized. Using noise-free and noisy artificial data it was found that the basic respiratory parameters in normal human beings, i.e., total resistance, inertance, and compliance of a series R-I-C model, can be accurately estimated from impedance data at 20 frequencies in the range 1 - 10 Hz even with measurement errors as high as 10%. This frequency range is

inadequate for estimating parameters from more complicated models, however, by extending the frequency range to 50 Hz and limiting the measurement errors within 5%, it may be possible to obtain reliable values for the parameters. The impedance data of supine, apneic dogs in control state and under various experimental conditions including the use of added external resistance, lighter gas, abdominal weighing, and pharmacological broncho-constriction and dilatation were actually collected at 26 frequencies in the range 1 to 16 Hz. From this data the total respiratory resistance, inertance, and compliance were determined. Our control parameter values were comparable to previously reported values. With those interventions, the alterations in parameters were consistent with predicted effects. The total resistance and compliance were also measured with the more conventional tidal breathing technique. Both parameters showed higher values than those determined by using the new approach proposed in this dissertation although the correlations were relatively high. The discrepancies may be attributed to differences in flow rates, tidal volumes, and operating frequencies used in these two techniques.

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CHAPTER I

INTRODUCTION

1.1 Respiratory Mechanics

The breathing mechanism can be characterized as a reciprocating bellows pump. The chest wall acts as the outer layer of the bellows and it is effectively coupled to the muscles which provide the source of energy. The lungs are intimately attached to this outer layer, and are specialized to disperse the gas over the gas-exchange surface. The bellows is made up of the respiratory bronchioles, alveolar ducts, alveolar sacs and the 300 million alveoli. It is connected to the atmosphere through the tracheobronchial tree and the upper airway.

The lungs are viscoelastic structures. Their elastic properties are mainly caused by the surface tension of the surfactant, a surface-active fluid lining the alveoli, and by the elastic fibers throughout the lung tissues. Likewise, the thorax has elastic properties which come from the natural elasticity of the muscles, tendons, and connective tissues of the chest. A significant part of muscular effort during breathing is simply to stretch the elastic structures of the lungs and thorax. The elasticity of the lungs is characterized by its compliance which is the ratio of lung volume to transpulmonary pressure. The static compliance is the ratio of total lung volume to total transpulmonary pressure while dynamic compliance relates an incremental volume change, for example, tidal volume, to the corresponding change in pressure. The compliance

of the thorax can be described in a similar way.

Another part of the respiratory muscular effort is utilized in overcoming frictional resistance in the airways and tissues of the lungs and thoracic cage. Airway resistance in a simplistic sense is similar to that of a fluid flowing in a tube, and it is governed by the length and diameter of the tube and by the density and viscosity of the fluid. Tissue resistance, which is similar to the frictional resistance in a solid, results from the slipping of various microscopic elements past each other as they are rearranged to accommodate the dimensional changes of the chest during ventilation.

In addition to resistance and compliance, a third mechanical factor, the inertance, is used in characterizing respiratory dynamics. This last factor accounts for inertial properties and describes the relationship between volume acceleration and its corresponding pressure. Only a very small amount of respiratory work is spent for overcoming the inertial force in normal breathing.

In view of the complex nature of the distribution of pressures and motions in the breathing mechanism, it is conceivable that the respiratory mechanical system is extremely nonlinear. In fact, this nonlinear nature has been pointed out in reports [27,49,58,59,60]. For instances, the lung compliance is highly variable and depends in a complex way on the conditions existing when the volume changes are produced [58]; under almost all conditions, the pressure-volume curve is sigmoid-shaped and shows hysteresis; values for compliance even depend on the posture of the subject; the flow resistance is also variable and depends on flow rates which produce different flow patterns in the tracheo-bronchial tree [59]; airways resistance is approximately linearly

related to the degree of inflation of the lungs [60]; either pulmonary or respiratory resistance exhibits a hyperbolic relationship with lung volumes [49,27]; hysteresis may also appear in the volume history of pulmonary [49].

Many investigators[12,23,24,34] have developed quite a few techniques to quantitatively determine the mechanical behavior of the respiratory system by regarding it as a linear system despite its nonlinear nature. This approach has been possible because in many situations, the respiratory system is restricted to operate in a very small region (e.g., 0.5 l of tidal volume and less than 0.5 l/s of flow rate) within its physically allowable capacity (e.g., 5 l of vital capacity and 5 l/s of maximum flow rate), so that the nonlinear phenomena such as hysteresis is not prominent and the nonlinear properties such as volume-dependent compliance and volume- and flow-dependent resistance can be approximated with constant linear elements without causing significant discrepancies.

1.2 Previous Work in Measuring Respiratory Mechanical Parameters

Rohrer [1], one of the earliest investigators in measuring airway resistance, anatomically measured the trachea and bronchial tree of a human lung post mortem and calculated the cumulative resistance of the entire system using Poiseuille's law and turbulence theory. Neergaard and Wirz [2] who conducted the first important in vivo experimental study of pulmonary resistance on humans in 1927, measured the intrapleural pressure through a large-bore needle with a good optical recording system and recorded the respiratory flow simultaneously with a pneumotachograph.

They were able to obtain values for pulmonary resistance by analytically separating the intrapleural pressure into two major components, the pressure to overcome the viscous resistance associated with flow and the pressure to overcome the elasticity associated with the change in lung volume.

The nonelastic pulmonary resistance is composed of airway resistance and lung tissue resistance. A number of studies [3,4,5,6,7] were devoted to separate these two quantities. Bayliss and Robertson [3] reasoned that airway resistance but not tissue resistance would vary with viscosity. By assuming that the gas flow was entirely laminar, they estimated the fraction of nonelastic pulmonary resistance attributable to airway resistance in cats by comparing the pressure-flow relationship obtained with air to those obtained with hydrogen. Fry et al. [4], comparing the pressure-flow relationships obtained in subjects breathing two different gases, air and an argon-oxygen mixture, demonstrated that tissue friction was negligible both in normal and emphysematous subjects. McIlroy et al. [5], who argued that the gas combinations which have equal kinematic viscosities should be selected, found that the tissue viscous resistance was about 30% - 40% of the pulmonary resistance. The results using this approach in separating tissue resistance from airway resistance have been inconsistent and inconclusive.

Von Neergaard and Wirz [8] first employed the airway interruption technique to measure the airway resistance of the respiratory tract with the belief that mouth pressure immediately after interruption of airflow equaled alveolar pressure. However, later studies [9,10,11] indicated that the interrupter technique overestimated alveolar pressure, and thus

airway resistance, by approximately 20% in normal subjects. Mead and Whittenberger [11] suggested that the reason is because during the time necessary for equilibration of pressure, the rate of change of lung volume becomes zero and the magnitude of change of alveolar pressure during this period is equal to the lung tissue resistive pressure that existed prior to interruption. They thus postulated that resistance determined by the interrupter technique is composed of airway resistance and lung tissue resistance. Marshall and DuBois [51] even suggested that the interrupter resistance is actually a measure of the total flow resistance throughout the entire respiratory system, i.e., the sum of airway, lung tissue and chest wall tissue resistances. Recently, Jackson et al. [52] recognizing the transient response of mouth pressure to rapid interruption is characterized by a curve composed of two distinctly different slopes, improved the correlation between resistances determined by the interrupter technique and those found by the plethysmograph in normal subjects by performing a curvilinear extrapolation back to the time of interrupt to estimate alveolar pressure just prior to the interruption.

DuBois et al. [12] first successfully used the plethysmographic method for measuring airway resistance. This method is based on Boyle's law and uses a large airtight body box. Measurements are made in two steps: first, the subject sits and pants through a pneumotachograph while box pressure and mouth flow are monitored, and then against a closed mouthpiece while monitoring box pressure and mouth pressure, which is assumed equal to alveolar pressure. Data from the former configuration provides a calibration between box pressure and alveolar

pressure which is then used with data from the first configuration to calculate the ratio of mouth flow to alveolar pressure, which is the airway resistance. In practice, airway resistance can be measured very simply and quickly using an oscilloscope and a special attachment to the scope face [38]. Although thermal effects and other features such as inhomogeneities of the lung [12-16] may introduce measurement error and variability, the plethysmographic method of measuring airway resistance has been widely employed as a research tool. Clinically its use is limited because the equipment is expensive and complicated and because confinement in the box produces problems with many subjects. Mead [39,40] modified the plethysmographic method so that it is more versatile and easier to construct, however it is still considered useful only in research and in special clinical studies.

The clinical measurement of pulmonary mechanics has been considerably facilitated since intra-esophageal pressure has been adopted as a measure of intrapleural pressure. The most commonly used method for measuring esophageal pressure employs air-containing latex balloons sealed over catheters which transmit balloon pressure to an external pressure transducer [17,18]. Previous studies have shown that volume-pressure curves for lungs based on esophageal pressure vary with the position of the balloon within the esophagus [17,19], with body posture [20,21], and with balloon volume [22]. Nevertheless, Milic-Emili et al. [22,41] suggested that esophageal pressure measured with a balloon which contains a small volume (0.5 ml) and is placed in the middle third of the esophagus closely reflects local pleural pressure variations. Most comparisons of esophageal with pleural pressure have indicated a good

agreement between changes in the two pressures measured in seated subjects, inspiring moderate volumes of air from the resting volume [41, 53]. The relationship between absolute pleural and esophageal pressure is not as precise.

From continuous records of esophageal pressure, airflow and volume signals, many methods have been developed for calculating pulmonary resistance and dynamic compliance, and all are based on the original work of Neergaard-Wirz [8]. In most of the methods, pulmonary compliance is first calculated by dividing tidal volume by the pleural pressure change between points of zero flow. By dividing the respiratory volume by this compliance, the elastic pressure is obtained. The nonelastic pressure can then be obtained by subtracting the elastic pressure from the total pleural pressure at a given flow rate. From the ratio of nonelastic pressure to flow, the pulmonary resistance is calculated.

Pulmonary resistance can also be measured directly on a cathode ray oscilloscope using the subtraction method [23], in which an appropriate amount of signal proportional to the lung volume is subtracted from the total esophageal pressure so that the pressure flow loop displayed on the oscilloscope is "closed." The slope of the resulting straight line is the pulmonary resistance. Another alternative for determining the pulmonary resistance from pressure-flow-volume recording is the method of isovolume [24], where difference in both pleural pressure (Δp) and airflow ($\Delta \dot{V}$) is measured between two instants in a steady respiratory cycle when respiratory volume is identical. Since volume is equal at these two instants, the elastic pressure is

also equal. Therefore, the measured pressure difference is attributed to flow resistance. Pulmonary resistance is calculated as $\Delta p / \Delta \dot{V}$, and a device for automatically performing these manipulations has been described [42,43].

Hilberman et al. [34] has developed a technique for automated computation of the parameters of the respiratory mechanics using digital computers. This technique assumes that the respiratory mechanical system is a second-order system and uses Fourier series analysis and phasor method of computation to determine, for the first harmonic which contains about 80% of the total energy, the magnitude of impedance, phase angle, compliance and resistance of the respiratory system. They found that this so-called phase method provided results for various groups of subjects, which did not differ significantly from the conventional method [24]. Based upon the same theory, Ostrander et al. [54] used hardware narrow band filters to extract fundamental Fourier components of esophageal and plethysmographic pressure, and flow of gas at the mouth during spontaneous breathing to determine the airway resistance, pulmonary resistance and dynamic compliance. It was found that compliance values thus obtained were statistically equivalent to conventional dynamic compliance and resistance values showed no linear trends with breathing frequency over the range of 1.2 - 3.2 Hz.

1.3 Forced Oscillation Technique

DuBois et al. [25] first employed the technique of forced oscillation for the study of respiratory mechanics. They applied sinusoidal pressure waves generated by an oscillating air pump at the mouth or around the thorax. From recording of pressure and flow they calculated

the overall impedance of the chest (Z_{rs}) over the frequency range from 2 to 15 Hz. They demonstrated that the respiratory system behaved like a second-order system similar to a resistance-inductance-capacitance (RLC) series circuit. The flow impedance of such a system is heavily dependent on total respiratory compliance (C_{rs} , analog of capacitance) at low frequencies, heavily dependent on total respiratory inertance (I_{rs} , analog of inductance) at high frequencies, and can be completely attributed to total resistance (R_{rs} , analog of electrical resistance) at a certain intermediate frequency. Impedance reaches a minimum at this frequency (resonant frequency) and the phase angle between pressure and flow is 0° . They also found that the resonance in normal subjects was at a frequency of approximately 5.8 Hz and the total respiratory resistance was 4-6 cm H₂O/l/s at a flow rate of 0.29 l/s which was not greatly different from resistance calculated from the data of Otis et al. [55], 3.9 cm H₂O/l/s at normal breathing frequency. They claimed that there was no evidence for any basic difference between resistance measurement at this forced rapid frequency and resistance measured at ordinary breathing frequency.

Hull et al. [50] in 1961 applied similar forced oscillation technique to the anesthetized, apneic dogs in a body respirator to determine their respiratory mechanics. Using an oscilloscope and the Lissajous pattern displayed by the simultaneous recording of driving pressure and flow, they could find the resonant frequency (f_o) and total respiratory resistance (R_{rs}). From the resonant frequency and independently measured total compliance (C_{rs}), they also determined the total respiratory inertance (I_{rs}) as $1/(4\pi^2 f_o^2 C_{rs})$ by analogy with a RLC second-order system.

Mead's group [26] showed that the impedance measurement could be made during spontaneous breathing by superimposing the forced oscillations on the normal respiratory patterns. This greatly facilitated the use of forced oscillation technique for measuring total respiratory resistance in conscious subjects. By tuning the frequency of forced oscillation to achieve zero phase angle between pressure and flow, Fisher et al. [27] measured total respiratory resistance and showed that it agreed well with measurements by other methods. Grimby et al. [28] simulated resonance to measure the total resistance at frequencies (3-9 Hz) other than the resonant frequency, by adding to the pressure signal ones proportional either to instantaneous volume or to volume acceleration. Total respiratory resistance in their patients with chronic obstructive diseases (COPD) was found to decrease as the frequency of oscillation was increased. In normal subjects, such frequency dependent behavior was essentially absent.

Goldman et al. [29] further simplified the forced oscillation technique by measuring the total resistance as the ratio of pressure difference to flow difference at two specific instants in the induced cycle where the components of the supplied pressure difference due to elastic and inertial impedances are both equal to zero (i.e., instants of two consecutive extremes in the observed oscillatory flow signal). This is similar to the isovolume technique described previously for tidal breathing and eliminates the need to electrically simulate resonance.

The forced oscillation technique was commonly employed to measure total respiratory resistance. But Vincent et al. [49] alternatively used this technique to determine the pulmonary resistance at

various lung volumes by utilizing esophageal pressure instead of trans-thoracic pressure. The most satisfactory procedure they adopted was that in which the subject breathed very shallowly and moderately fast (approximately 50/min) while forced oscillations at 4 Hz were applied at the mouth. Shallow breathing moved too small a volume to interfere with volume history effect, yet apparently kept the glottis wide open. They found that total pulmonary resistance and lung volume was in a hyperbolic relationship.

Using a body plethysmograph with an airtight neck seal, Peslin et al. [48] measured total respiratory impedance at FRC in normal subjects over a frequency range of 3-70 Hz, by simultaneously monitoring sinusoidal perithoracic pressure and flow at the mouth. This impedance, known as "transfer impedance" [61], is different from the input impedance which is obtained by utilizing pressure and flow both measured at the mouth. According to their data, it was suggested that the respiratory system is characterized by a fourth-order system.

Recently, Michaelson et al. [30] obtained the total respiratory impedance (Z_{rs}) from 3 to 45 Hz rapidly by employing a modification of the forced oscillation technique in which a random noise pressure containing all frequencies of interest was imposed on the respiratory system at the mouth and compared to the induced random flow using Fourier and spectral analysis. They found that Z_{rs} in COPD deviated from second-order behavior that was observed in normals in that the phase of Z_{rs} (ϕ_{rs}) remained more negative at all frequencies and the magnitude of Z_{rs} ($|Z_{rs}|$) was quite high at low frequencies and decreased to a minimum at a much higher frequency.

Another extension of the forced oscillation technique has recently been made in this laboratory [31,32]. The so-called "impedance analyzer" can generate necessary sinusoidal oscillations and electronically process pressure and induced flow signals to provide direct readouts of the magnitude and phase angle of the respiratory impedance at a certain selected frequency in the range of 1-100 Hz. With this instrument, the frequency response of the respiratory impedance in the essential frequency range can be obtained rapidly and accurately.

1.4 Models and Parameter Estimate

Physiological systems have been studied extensively and understood better by creating appropriate models for them. A large number of models have been built up in terms of electrical system because there is a well developed theory describing this system and because the electrical models are easily constructed and manipulated. Such models have been traditionally used to simulate the mechanical aspects of the respiratory system and they have provided the theoretical basis for interpreting various experimental data obtained for the study of the respiratory mechanics [44].

Earlier investigators [15,27,28,33] assumed a series arrangement of RIC elements and showed that it provided an acceptable model for many clinical and research purposes. Because the total inertance (I) has negligible effect at ordinary breathing rate (e.g., < 1 Hz) an RC circuit is usually adequate for the study of mechanics with spontaneous and even panting breathing. Many techniques [8,23,24,34] for measuring resistance and compliance are essentially based upon this

simple model. However, studies in patients with lung diseases have strongly suggested that more complex models which include series as well as parallel elements are necessary in order to explain the frequency dependence of compliance and resistance [28,45,46,47].

Although mechanical behavior of the respiratory system over a certain range of variations is basically determined by the frequency response of the forced oscillatory impedance, it is also desirable to relate this data to models with more direct physiological significances. There have been attempts to empirically manipulate parameter values in such a model to obtain the best subjective match between the model response and the experimental data [30,48]. However, there have been no attempts to apply more objective mathematical techniques for parameter estimation except the most recent work by Peslin et al. [113]. The match between an assumed realistic model for the respiratory system and the respiratory impedance data obtained experimentally by the forced oscillation technique is essentially a "parameter estimation" problem which has received a great deal of interest from system engineers and economists. Although most parameter identification techniques were developed to deal with linear dynamic systems in time-domain, they are extendible to solve this particular problem (estimation of respiratory mechanical parameters from the impedance data) in which frequency is the independent variable [35,36,56,57].

1.5 Research Objectives and Limitations

This dissertation formulates the determination of mechanical parameters in the respiratory system as a parameter estimate problem by constructing a realistic electrical model for the system. Numerical

values for these parameters will be extracted from the frequency dependence of the forced oscillatory impedance by using a parameter estimation numerical method. This approach has its advantages in that the important respiratory mechanical parameters could be determined noninvasively, simultaneously, accurately and sensitively.

Certain specific aims are pursued in this dissertation. They are the following:

1. Develop realistic electrical circuit models for the respiratory system, which may explain the impedance data obtained experimentally by using the forced oscillation technique.
2. Develop a numerical algorithm which can identify the parameters in an analog model constructed for the respiratory system, based upon the oscillatory impedance data.
3. Justify the proposed approach for determining respiratory parameters by comparing its results with those obtained by more conventional methods.
4. Validate the model by imposing known mechanical perturbations on the respiratory system and then determine whether they are reflected in the changes of values for the model parameters as predicted.

Electrical circuit models used to represent the respiratory system are usually composed of lumped, linear constant elements such as resistor, capacitor and inductor. However, the corresponding physical elements in the respiratory system are actually distributed, nonlinear, and possibly time-varying due to the phenomena such as turbulent flow, hysteresis, multi-dimensional movement of respiratory muscles, etc.

Any lumped linear electrical circuit can only approximate the complicated respiratory mechanical system to certain limited degree. It should be realized that any conclusion about the respiratory mechanics drawn from an approximate linear model only pertains to the range of variations used in developing the model.

Theoretically, the impedance of an electrical circuit is completely defined only when its frequency response characteristics are known for frequencies from 0 to ∞ . However, for the purpose of identifying an electrical system from its impedance measurement it is usually not necessary to know the entire impedance spectrum. In many cases, it is only essential to measure the impedance in a certain limited frequency range which characterizes the important behavior of the electrical system. Because of the limited frequency response of the transducers used to obtain the experimental data for the study of this dissertation, the respiratory impedance was measured without distortion at frequencies ranging from 0.9 to 16 Hz. It is believed that impedance in this frequency range is adequate to characterize the respiratory system in normal subjects, which can be represented with a second order system. Many investigations have shown that this simple second order system is inadequate to explain the physical measurements obtained in abnormal subjects [45,30,48]. There is some indication that the range of 0.6 - 16 Hz may be insufficient to characterize the respiratory system in certain diseases. If this is true, then any attempt to model such a system from its impedance measurement over the limited spectrum used in this dissertation would encounter difficulty.

1.6 Organization of the Dissertation

Chapter I is an introduction to the dissertation. It presents a brief review of various techniques which have been used to determine the mechanical parameters of the respiratory system with special attention paid to the forced oscillation technique, which serves as a basis for the research reported in this dissertation. The problem to be investigated, and the scopes and objectives of the research are then defined. Finally, a summary of the contents of each chapter is given.

In Chapter II, realistic electrical circuit models for the respiratory mechanical system are developed and the physiological significance associated with parameters in the models are discussed. The frequency response characteristics of these models in terms of pole-zero configurations, Bode diagrams and Nyquist plots are then analyzed. These models are useful in Chapter V for estimating the respiratory parameters from the measured respiratory impedance data.

A brief discussion of the basic ideas and features of several numerical methods applicable for the parameter estimation problems are first discussed in Chapter III. Next, a universal parameter estimation algorithm which combines random searching with gradient methods to handle the particular identification problem in this dissertation is described. The results of studies to verify the correctness of the program and the usefulness of this algorithm are then summarized.

In the next chapter, the configuration of the overall experimental system, the calibration of various devices including the specially designed impedance analyzer, the experimental procedures in collecting respiratory impedance data in different conditions, and the correction

of this data for the impedance of the endotracheal tube are described. Basically, the whole chapter is an extended and detailed description of the forced oscillation technique which provides the necessary data for the estimation of respiratory mechanical parameters as will be discussed in Chapter V.

In Chapter V, Respiratory impedance data obtained by using the forced oscillation technique in normal dogs, dogs under pharmacological and mechanical interventions, and dogs with respiratory diseases is first presented. In the next section, the total respiratory resistance, compliance and inertance (parameters in the series R-I-C model) are estimated from the impedance data obtained in various experimental conditions by using the parameter estimate algorithm developed in Chapter III. The resulting values for the total resistance and compliance are compared respectively with those reported by other investigators and with those obtained in the same study by using more conventional methods. The statistical significances of the variations in parameter values due to different experimental conditions are tested and justified with predicted results.

Chapter VI summarizes the specific results, makes a conclusion, indicates certain problems, and suggests the possible improvements and further works for the approach presented in this dissertation.

CHAPTER II

ELECTRICAL ANALOG MODELS FOR THE RESPIRATORY MECHANICAL SYSTEM

2.1 Dynamic Analogy

Since all physical systems must obey the laws of thermodynamics, it is not surprising to find considerable similarities in the models and equations describing these systems. This natural analogy between different systems facilitates the transfer of analytical techniques and provides insights into the behavior of these systems. Analogies are particularly useful when comparing an unfamiliar system with one that is better understood.

Mathematical and structural analyses have been established between many engineering systems such as electrical, mechanical, acoustical, and magnetic systems[62]. Understanding and analytical techniques accumulated for one system have benefitted the study of other systems. At the present time, linear electrical circuit theory has been developed to a more sophisticated level than the corresponding theory of other systems; it is common to apply this knowledge in solving problems in other fields. The mechanical behavior of the respiratory system is in nature a mechanical system and provides an excellent example of where electrical analog models have been successfully applied.

Generally speaking, the properties of a dynamic system can be separated into two general categories, depending on whether they dissipate or conserve energy. Resistive properties describe the loss

of energy while storage properties describe the conservation of energy and can be further separated into storage of potential energy and kinetic energy. Both resistive and storage properties are always present in real dynamic systems, although they may be more or less important in specific systems. The particular distribution of these properties in a dynamic system is responsible for its inherent behavior.

Although the nature of the system property (resistive or storage) is exactly the same in all dynamic systems, they may be defined by different physical quantities in different fields. Nevertheless, a general definition of these system properties that is independent of a particular system can be given in terms of a pair of characterizing variables: across (or relative) variable and through (or transfer) variable. Voltage or pressure drop across an element are illustrations of across or relative variables; voltage or pressure at one terminal is measured relative to that at the other terminal. Electrical current and fluid flow are obvious examples of through variables. In a less clear sense, force and velocity in the mechanical rectilinear system may be conceived respectively as across and through variables. The resistive property of a dynamic system can be defined by the ratio of an across-variable to a through-variable; the potential storage property is defined by the ratio of the across-variable to the integral of a through-variable, and the kinetic storage property is defined by the ratio of an across-variable to the derivative of a through variable. These properties can also be defined by the reciprocal of the ratios and this is commonly done with the potential storage property. A more

generalized definition for these system properties can be found in the book by Blesser [63].

Table I lists comparative variables and parameters in three different types of second-order dynamic systems as shown in Figure 1. Note that the elements in each system are defined in the way described above. The structures and describing equations for a system can be obtained by simply interchanging each quantity of this system with its counterpart in the analogous system.

Table 1 Analogies between three second-order dynamic systems

System Quantity	Mechanical	Pressure-Volume	Electrical
Across Quantity	Force f	Pressure p	Voltage v
Through Quantity	Velocity $\dot{x}$	Flow $\dot{v}$	Current i
Integral	Displacement x	Volume v	Charge q
Derivative	Acceleration $\ddot{x}$	Volume Acceleration $\ddot{v}$	Charge Acceleration $\ddot{q}$
Resistive Element	Friction $B = f/\dot{x}$	Flow Resistance $R = p/\dot{v}$	Ohm's Resistance $R = v/i$
Potential Storage Element	Elasticity $\frac{1}{k} = \frac{x}{f}$	Compliance $C = v/p$	Capacitance $C = q/v$
Kinetic Storage Element	Mass .. $M = f/\ddot{x}$	Inertance $I = p/\ddot{v}$	Inductance $L = v/\ddot{q}$

Figure 1 Three analog second-order systems: (A) Mechanical rectilinear system, (B) Pressure-volume system, and (C) electrical system.

Figure 1-A shows a mechanism consisting of an inertial element (mass), a viscous element (dashpot), and an elastic element (spring). Motion in this system is measured in terms of the distance $x(t)$ that the mass M moves relative to the point where M is in the equilibrium state with no force $f(t)$ exerted from outside. If the three elements are all linear, the equation of motion can be obtained from Newton's laws and is shown in Eq.(2.1) in which B is the viscosity of the dashpot and K is the elastic constant of the spring.

$$M \ddot{x}(t) + B \dot{x}(t) + K x(t) = f(t) \quad (2.1)$$

Figure 1-B shows a pressure-volume system, a rigid conducting tube connected to an elastic balloon. In this case, motion is expressed as volume $v(t)$ and force as pressure $p(t)$. Three properties are distributed throughout this system; however, for many purposes these distributed effects can be lumped into the compliance of the balloon (C), the flow resistance in the tube (R) and the combined inertia of the fluid and balloon (I). By analog to the mechanical system without actual

derivation, the equation of motion of this pressure-volume system is easily obtained and is given in Eq. (2.2).

$$I \dot{v}(t) + R v(t) + \frac{1}{C} v(t) = p(t) \quad (2.2)$$

Similarly, by analogy, the R-L-C in series circuit (Fig. 1-C) is described by Eq. (2.3a, b).

$$L \ddot{q}(t) + R \dot{q}(t) + \frac{1}{C} q(t) = v(t) \quad (2.3a)$$

or

$$L \dot{i}(t) + R i(t) + \frac{1}{C} \int i(t) dt = v(t) \quad (2.3b)$$

As shown in Table 1, the system property is defined as the ratio of two physical quantities. For instance, fluid resistance is defined as the ratio of pressure to flow in the pressure-volume system. This ratio is known as the "static" value of the associated element. This definition is only meaningful when the element is linear and its static value is constant, independent of particular values of the corresponding physical quantities. Frequently the relationship between the two physical quantities which define a system property is nonlinear, i.e., the characteristic curve of the concerned element cannot be represented with a straight line. In such instance, the static value of the element changes from point to point on the nonlinear characteristic curve and hence no single numerical value can be used to represent the nonlinear property. Graphical techniques often offer the best way for describing and analyzing the behavior of such nonlinear elements and the system containing them.

However, if relatively small signals are involved, then only a small section of the nonlinear characteristic curve must be considered. In this case, a single "dynamic" value can be used to approximate the property of the element without causing significant discrepancy. By

doing so, nonlinear elements can be replaced with linear ones and a dynamic system containing nonlinear elements can thus be linearized. The dynamic value of a system element may be defined as the slope of the tangent line at a particular point of the associated characteristic curve. Once a nonlinear system is linearized, the system analysis becomes much easier. Many well developed analytical methods for linear systems can be employed to yield rather precise results. These results, however, only pertain to the particular operating range in which the nonlinear system is actually linearized.

As will be seen later, the study in this dissertation does not consider the static response of the respiratory mechanical system and only concerns itself with the dynamic behavior of this system in response to a small externally applied sinusoidal pressure disturbance. The applied disturbance is so small that the system only operates in a relatively small portion of the entire physical admissible region. Therefore, the respiratory system under study can be well approximated with a linear dynamic system in which each element is assigned a dynamic value at the actual operating point (e.g., FRC) regardless of the inherent nonlinearities of the system.

2.2 Review of Respiratory Mechanics

Before the electrical analog models for the respiratory mechanical system can be developed, it is desirable to review certain aspects of respiratory mechanics. Detailed discussion on this subject can be found in many texts [64,65,66].

Figure 2 summarizes events which occur during normal respiration. Just before the inspiration, the respiratory muscles are relaxed and no

Figure 2 Variations in pressures and volume during a normal respiration cycle.

air is flowing. The intrapleural pressure is subatmospheric and intra-alveolar pressure is exactly atmospheric. Inspiration is initiated by the contraction of intercostal muscles and the diaphragm. When the diaphragm contracts, its dome moves downward into the abdomen, thus enlarging the volume of the thoracic cage. Meanwhile the inspiratory intercostal muscles contract, leading to an upward and outward movement of the ribs and further increase in thoracic cage size. As the thoracic cage begins to expand, the intrapleural pressure decreases. This increases the difference between the intra-alveolar and intrapleural pressure, and the lungs are forced to enlarge. As the lungs enlarge, the air pressure within the alveoli drops to less than atmospheric causing bulk flow of air from the atmosphere through the airways into the alveoli until their pressure again equals atmospheric. The expansion of thorax and lungs produced during inspiration by active muscular contraction stretches both lungs and thoracic wall elastic tissues. When inspiratory muscles begin relaxing, the stretched tissues recoil to their original length since there is no force left to maintain their expansion. The thorax and lungs return to their original sizes, alveolar air becomes temporarily compressed so that its pressure exceeds atmosphere. Thus normal expiration appears to be completely passive, depending only upon the cessation of inspiratory muscular activity and the relaxation of these muscles. In actuality, the inspiratory muscles relax gradually to eliminate the large flows that would result with rapid relaxation. Under certain conditions, however, expiration can be enhanced by the contraction of expiratory muscles including abdominal muscles, which actively decreases thoracic cage size. The abdo-

minal muscles help by increasing intra-abdominal pressure and passing the diaphragm up higher into the thorax.

The forces developed by various respiratory muscles are the energy source that powers the pulmonary machine. The forces are opposed by the sum of a number of different forces. These force components may be divided into three general categories. The first is the force used to overcome the elastic properties of the lung and chest wall. This represents the potential energy of the system, since the work done on the elastic elements during inspiration is returned during expiration. A typical relationship between pressure and volume is shown in Figure 3, and it can be seen that the relationship is nearly linear for small volume variations around FRC.

The second component of the opposing force is that required to overcome the frictional resistance, which exists only when the system is in motion; unlike the elastic force, resistive force includes two significant components: that due to gas flow through the trachealbronchial tree and that due to movement of the lung and thoracic tissues. In considering flow resistance in the respiratory tree, three types of fluid flow may be involved: laminar, transitional disturbed, or true turbulent flow. When flow is laminar, the associated pressure is proportional to the flow rate and depends on the viscosity of the gas. The pressure associated with turbulent flow is considerably greater than laminar flow. For turbulent flow, the density of the gas becomes important and viscosity unimportant, and the pressure is approximately proportional to the square of the flow. For transitional flow, the pressure-flow relationship lies somewhere between these two. Flow changes from laminar to turbulent when the Reynolds number exceeds 2000.

Figure 3 Static volume-pressure curve of the total respiratory system during relaxation in the upright posture. The volume at zero pressure corresponds to FRC.

Figure 4 Equation and graph of alveolar pressure and air flow.

(This is a dimensionless number equal to $(\text{density} \times \text{velocity} \times \text{diameter}) / \text{viscosity}$). In smooth straight tubes, turbulent flow occurs at high velocity and in the respiratory system this essentially occurs only in the larger airways, such as the main bronchi and trachea. The flow rate in the smaller airways is very low. However, entrance region effects are found at each branching of the tracheobronchial tree, and the pressure required for the disturbed flow in these regions is difficult to determine. Figure 4 shows the relationship between flow and the pressure due to the airway resistance, and it can be seen that this relationship is approximately linear for flows below 0.5 l/s. The airway resistance varies with lung volume but this effect is negligible for small volume changes (0.5l) around the FRC.

The third component is the force required to accelerate various elements of the respiratory system including the mass of the lung and chest wall and the gas in the airways. This has been shown to be negligible when compared to other force components at normal breathing rates, however, it does become the limiting factor at unphysiological rates as with the application of forced oscillations. Relatively little is known about the inertial effects but they are generally thought to be constant for small variations around FRC.

2.3 Electrical Analog Models

Figure 5 shows a simplified analogous electrical network of the total respiratory system [44]. The entire system is divided into three major parts: airways, lungs and chest wall. The compliance of the cheeks, gas compressibility and small airway distensibility are represented with shunt capacitors. The motion of the chest wall is concen-

Figure 5 An electrical analog of the total respiratory system during spontaneous breathing.

Figure 6 An electrical analog of the total respiratory system in an anesthetized and paralyzed subject under forced oscillations.

Figure 7 Series R-I-C circuit representing the total respiratory mechanical system.

trated in three pathways; rib cage, diaphragm and abdomen. The lungs and chest wall are approximated with a series arrangement of resistance, compliance and inertance. The atmosphere is analogous to electrical ground (terminal 2). Terminal 1 is actually grounded during normal breathing when air passes through either nose or mouth.

However, when forced oscillations are applied at the mouth, it is equivalent to inserting an external voltage source between terminal 1 and 2. The system is thus driven by both the applied external and natural internal pressure sources. According to the superposition principle in linear system theory [67], both types of sources contribute to the total response of the system independently. In the application of forced oscillation technique [28,29], it is usually desired to obtain the response only due to the forced oscillations. This component can be separated from that due to natural breathing if their operating frequencies are distinct from each other. Usually, the forced oscillations are at a much higher frequency than the spontaneous breathing patterns.

In the experiments designed for this dissertation, the forced oscillation technique is applied to dogs which are intubated, anesthetized and paralyzed. In this case, the voltage sources in the analogous network (Figure 5) corresponding to the muscular pressure sources should be removed and the external sinusoidal voltage is the one to drive the system. Meanwhile the portion of circuit representing the upper airway (mouth or nose, nasopharynx, glottis, and larynx) should be replaced with a series resistor and inductor for the endotracheal tube used in the experiments. The electrical analog of such a system is shown in Figure 6 in which the myriads of individual components are added so that

each major area is represented as having one resistance, one compliance, and one inertance. Various pressures at different sites in the system are noted. For example, the pressure in the airways is the difference between alveolar pressure (P_{alv}) and pressure at the mouth (P_{ao}). The pressure across the lung tissue is the difference between alveolar and pleural pressure (P_{pl}) and pleural pressure relative to the atmospheric pressure equals pressure across the chest wall. C_g represents the compressibility of air and thus is represented as connected to ground since its degree depends on the difference between atmospheric and airway pressure.

A two-terminal linear network like that in Figure 6 made up of basic passive elements (i.e., resistor, capacitor, and inductor) shows a particular relationship between voltage and current as measured at the two input terminals. When the input voltage is sinusoidal, this relationship is known as input impedance. In Figure 6, C_g is normally very small compared to C_l or C_{cw} so that when it is removed the input impedance is not significantly altered. After moving C_g and then combining the same type of elements into a single one, the electrical analog in Figure 6 is reduced into a series R-I-C circuit as shown in Figure 7. Although this is a greatly simplified model for the actual respiratory system, it is adequate for interpreting much of the experimental data obtained in studying the respiratory mechanics in normal subjects [25,30,44,50].

In patients with chronic obstructive pulmonary disease (COPD), many investigators [28,30,45,46,68] have recognized that the measured pulmonary compliance and resistance are frequency-dependent. This

observation is obviously inconsistent with the simple R-I-C model and several alternate models have been proposed to explain this frequency-dependent behavior. In the model of Otis et al. [45], the lungs are considered to be made up of a number of parallel air pathways, each consisting of a resistance and a compliance (the inertance is ignored). According to their theory, the frequency-dependency of compliance or resistance is caused by the discrepancies in time constant between separated pathways of the lungs. (Time constant of a pathway is the product of its associated flow resistance and compliance. It is a convenient expression for the speed of filling air into the pathway). This model could be interpreted with an electrical analog circuit as shown in Figure 8-A, where only two pathways are used to approximate the air passage in the lungs. These two pathways share the other three elements C_{cw} , I (an approximate of total inertance), and R (sum of extrathoracic airway resistance and tissue resistance of chest wall).

Mead [46] considered the airways as a compliant structure in parallel with the air spaces, and using a two-compartment model, demonstrated that time constant discrepancies between the airway and the parenchyma could explain the decreasing of compliance and resistance with increase of frequency. This frequency-dependence in normal subjects is too small to be detected in the frequency range for practical measurements. As peripheral airway resistance is increased, the time-constant inequality becomes greater, and can account for most of the frequency-dependent behavior in patients with COPD. This model can be represented with the electrical circuit as shown in Figure 8-B as suggested by Pimmel [37]. A feature of this representation is the separation of the airway resis-

A

B

C

Figure 8 Three different two-pathway models for the respiratory system: (A) Otis' model, (B) Mead's model, and (C) Hogg's model.

tance into a central component (R_{ca}) and a peripheral component (R_{pa}) by inserting an element (C_{aw}) standing for the airway compliance between the junction of R_{ca} and R_{pa} and the point corresponding to the pleural pressure. The resistance of the airway compartment is so small that it is practically omitted from the model. It should be noticed that the circuit shown in Fig. 8-A will have the same input impedance as the one shown in Fig. 8-B if $R = R_{ca} + R_{cw}$, $R_1 = 0$, $C_1 = C_{aw}$ and $R_2 = R_l$.

Another model proposed by Hogg et al. [68] considers the resistance of channels for collateral ventilation to be too high (compared to resistance of normal ventilatory pathway) to result in frequency-dependent behavior in normal lungs. But collateral channels become important for air ventilation with obstruction of peripheral airway, causing time-constant difference between collateral and normal ventilated areas, accounting for frequency-dependent compliance in emphysematous lungs. The appropriate electrical analogue of this situation is shown in Figure 8-C in which the resistor R_C accounts for the collateral channels. In severe emphysema, airway resistance in the obstructed area (e.g., the pathway of $R_B - C_B$) is much greater than the collateral flow resistance and can be practically removed from the analog circuit. Two parallel pathways, $R_C - C_B$ and C_A , are thus formed and their time constants will be unequal. This electrical analog circuit can also be transformed into the one as shown in Figure 8-A without altering the input impedance by setting $R = R_D + R_A$, $R_1 = 0$, $C_1 = C_A$, $R_2 = R_C$ and $C_2 = C_B$.

2.4 Frequency Analysis of Electrical Analog Models

One of the major aims of this dissertation is to estimate the

parameters of the respiratory system, which cannot be measured directly. Mouth pressure and airflow are the only easily measurable physical quantities by using forced oscillations. Thus, the mechanical parameters must be estimated from these measurements. When the system is represented by any one of the models developed in the last section, estimating the electrical parameters in the model can be done from the input voltage and current, which are analog to the mouth pressure and airflow in the respiratory system subjected to forced oscillations. The input impedance is a very convenient method for characterizing this relationship and it is extremely useful in relating the measured quantities to the system parameters. As will be seen in the next chapter, the conventional forced oscillation technique is extended to directly provide the input impedance of the respiratory system at a specific frequency by electronically processing the measured pressure and flow signals. The impedance data thus obtained in a certain frequency range will be the basis upon which the respiratory mechanical parameters can be determined.

At any given frequency, the input impedance Z of a two-terminal linear network is generally a complex quantity. Its absolute value or magnitude $|Z|$ is defined as the ratio of the amplitude of the input voltage to the amplitude of the input current and its argument or phase angle ϕ is defined as the phase shift between the current and the voltage with the current as a reference. The real part of the impedance is referred to as its resistance R and the imaginary part as its reactance X . The reciprocal of the impedance is called admittance. The impedances of the three passive two-terminal elements, resistor (R), capacitor (C), and inductor (L), are respectively known as R , $1/j\omega C$ and $j\omega L$ or

R , $1/(Cs)$, and Ls , where $s = j\omega$. The impedance of a series circuit consisting of several circuit elements is the sum of the impedances of the individual circuit elements. The impedance of a circuit made up of parallel elements can be obtained by taking the reciprocal of the corresponding admittance which is the sum of the admittances of the individual elements.

The input impedance of a two-terminal linear circuit is a function of frequency except when the circuit contains only resistors, in which case the input impedance is a real number, and is independent of frequency. Many important characteristics of a two-terminal linear circuit can be obtained by examining the frequency response of its input impedance. The frequency response of a system is generally presented in certain standard graphical forms such as Nyquist and Bode diagrams. The latter is extensively employed in the following paragraphs. More detailed discussions of input impedance of a two-terminal linear network are available in standard texts on linear circuit theory [61,67,69].

Applying these techniques to the electrical analog model shown in Figure 7 leads to an expression for the input impedance of the circuit as shown in Eq. (2.4) and (2.5).

$$\begin{aligned} Z_{rs} &= R_{rs} + I_{rs}S + \frac{1}{C_{rs}S} \\ &= \frac{I_{rs}}{S} \left(S^2 + \frac{R_{rs}}{I_{rs}}S + \frac{1}{I_{rs}C_{rs}} \right) \end{aligned} \quad (2.4a)$$

$$Z_{rs} = \frac{I_{rs}}{S} (S-S_1)(S-S_2) \quad (2.4b)$$

$$S_1, S_2 = \frac{1}{2} \left(-\frac{R_{rs}}{I_{rs}} \pm \sqrt{\left(\frac{R_{rs}}{I_{rs}}\right)^2 - \frac{4}{I_{rs}C_{rs}}} \right) \quad (2.5)$$

If two new parameters, ω_n , the undamped natural frequency, and ξ , the damping ratio, defined as

$$\omega_n^2 = \frac{1}{I_{rs} C_{rs}} \quad \text{and} \quad \xi = \frac{R_{rs}}{2} \sqrt{\frac{C_{rs}}{I_{rs}}}$$

are introduced, then Eq. (2.5) may be rewritten as shown below:

$$s_1, s_2 = -\xi \omega_n \pm \omega_n \sqrt{\xi^2 - 1} \quad (2.6)$$

The two zeros of Z_{rs} (s_1 and s_2) are a complex conjugate pair if $\xi < 1$, two equal real numbers if $\xi = 1$, and two unequal real numbers if $\xi > 1$.

Substitution of $s = j\omega$ into Eq. (2.4a) yields the equation

$$Z_{rs} = R_{rs} + j\left(\omega I_{rs} - \frac{1}{\omega C_{rs}}\right) = R_{rs} + jX_{rs} \quad (2.7)$$

It is obvious that the real part R_{rs} of the impedance is independent of frequency but the imaginary part X_{rs} is frequency-dependent. At low frequencies, X_{rs} is dominated by the compliant component $X_c = -\frac{1}{\omega C_{rs}}$ but it is dominated by the inertial component $X_m = \omega I_{rs}$ at high frequency. When $\omega = \omega_n = \frac{1}{\sqrt{I_{rs} C_{rs}}}$, X_m and X_c cancel each other and X_{rs} becomes zero. Consequently, at this frequency, the phase angle $\phi_{rs} = 0$ and the magnitude $|Z_{rs}|$ is minimal. In general, this condition is called resonance, and ω_n is called the resonant frequency of the series R-I-C circuit.

Typical values for the mechanical parameters in normal adult humans are $R_{rs} = 2.7 \text{ cmH}_2\text{O}/1/\text{s}$, $C_{rs} = 0.1 \text{ l}/\text{cmH}_2\text{O}$, and $I_{rs} = 0.01 \text{ cm H}_2\text{O}/1/\text{s}^2$ [44]. The corresponding respiratory impedance, from Eq. (2.4), is shown in Eq. (2.8).

$$Z_{rs} = \left(\frac{0.01}{\omega}\right) (j\omega + 3.765) (j\omega + 266.24) \quad (2.8)$$

This system has a resonant frequency at $\omega = 31.62 \text{ rad/sec}$ or $f = 5 \text{ Hz}$. One pole at origin and two zeros at -3.756 and -266.24 . Its Bode diagram representation is given in Figure 9, in which the two corner fre-

quencies are at $\omega = 3.756$ and 266.24 rad/sec or $f = 0.6$ and 42.37 Hz.

Note that at the resonant frequency phase angle crosses over zero degree and the magnitude reaches a minimum. Figure 10 shows the relative contribution of X_m and X_c to the total reactance X_{rs} as functions of frequency.

Figure 10 Relative contribution of inertance and compliance reactances (X_m and X_c) to the total respiratory reactance (X_{rs}) in normal adult humans.

Applying this approach to the electrical analog model shown in Figure 6 results in the expression for the input impedance shown in Eq. (2.9) in which $R_{l\omega} = R_l + R_{cw}$, $I_{l\omega} = I_l + I_{cw}$ and $1/C_{l\omega} = 1/C_l + 1/C_{cw}$.

$$Z_{rs} = \frac{P(s)}{Q(s)} \quad (2.9a)$$

$$P(s) = 1 \cdot C_g \cdot C_{l\omega} \cdot I_{l\omega} \cdot s^4 + (R_{aw} I_{l\omega} + I_{aw} R_{l\omega}) C_g \cdot C_{l\omega} s^3 \\ + [R_{aw} C_g \cdot R_{l\omega} C_{l\omega} + I_{aw} (C_g + C_{l\omega}) + I_{l\omega} C_{l\omega}] s^2$$

Figure 9 Frequency response of a RIC model with nominal parameter values

Figure 11 Frequency response of the input impedance of the model as shown in Fig. 6 with nominal values for the parameters.

$$+ R_{aw}(C_g + C_{l\omega}) + R_{l\omega} C_{l\omega}] S + 1 \quad (2.9b)$$

$$Q(s) = C_{l\omega} I_{l\omega} C_{aw} s^3 + C_g R_{l\omega} C_{l\omega} s^2 + (C_g + C_{l\omega}) s \quad (2.9c)$$

By letting $s = j\omega$ and collecting terms, the impedance may be written in rectangular coordinates as shown in Eq. (2.10).

$$Z_{rs} = RE + jIM \quad (2.10a)$$

$$RE = R_{aw} + \frac{R_{l\omega}^2 C_{l\omega}^2}{\omega^2 R_{l\omega}^2 C_{l\omega}^2 C_g^2 + [C_{l\omega} + C_g (1 - \omega^2 I_{l\omega} C_{l\omega})]^2} \quad (2.10b)$$

$$IM = \omega I_{aw} - \frac{(1 - \omega^2 I_{l\omega} C_{l\omega}) [C_{l\omega} + C_g (1 - \omega^2 I_{l\omega} C_{l\omega})] + \omega^2 C_g^2 C_{l\omega}^2 R_{l\omega}^2}{\omega [C_{l\omega} + C_g (1 - \omega^2 I_{l\omega} C_{l\omega})]^2 + \omega^2 R_{l\omega}^2 C_{l\omega}^2 C_g^2} \quad (2.10c)$$

It can also be written in polar coordinates as shown in Eq. (2.11)

$$|Z_{rs}| = (RE^2 + IM^2)^{1/2} \quad (2.11a)$$

$$\phi_{rs} = \tan^{-1} (IM/RE) \quad (2.11b)$$

In the two limiting cases where ω is equal to 0 and ∞ , it is obvious that ϕ_{rs} approaches -90° and $+90^\circ$ respectively.

Typical values for elements in this model are $R_{aw} = 1.5$, $R_l = 0.2$, $R_{cw} = 1.0$ in cmH₂O/LPS; $C_g = 0.003$, $C_l = 0.2$, $C_{cw} = 0.2$ in L/cmH₂O; and $I_{aw} = 0.01$, $I_l = I_{cw} \approx 0$, in cmH₂O/LPS² [44] and their use results in Eq. (2.12).

$$Z_{rs} = \frac{3.6 \times 10^{-6} s^3 + 1.57 \times 10^{-3} s^2 + 0.27 s + 1}{3.6 \times 10^{-4} s^2 + 1.03 \times 10^{-1} s} \quad (2.12a)$$

$$Z_{rs} = 0.01 \times \frac{(s+3.72)(s+216.2+j167)(s+216.2-j167)}{s(s+286.11)} \quad (2.12b)$$

This impedance has three zeros which are located at -3.72 and $-216.2 \pm j167$

and two poles which are located at origin and -286.11. For the pair of complex conjugate zeros, the damping ratio is equal to 1.57 and the undamped natural frequency is 137.7 Hz. The frequency response is shown in Figure 11. A comparison between Figures 9 and 11 points out that the frequency responses of the respiratory impedance in both cases are almost identical except when angular frequency is greater than 100 rad/sec (or 16 Hz). This implies that the shunt capacitor C_g in Figure 6 has little effect on total respiratory impedance at frequencies less than 16 Hz in normal subjects and consequently the respiratory mechanical system can be well represented by the simple RIC in series circuit.

Since the three different models described in the previous section for explaining the frequency-dependent behavior can be interpreted within the framework of a single electrical analog circuit, although each element in this circuit has a different anatomical counterpart in each of the three models, it is not necessary to treat them separately in order to analyze the frequency response of these models.

Using the model in Figure 8-A which also represents the other two models since they can be transformed into it, the equations (13 and 14) of Otis et al. [45] can be adopted directly to obtain the impedance between points a and b. The results are shown in Eqs. (2.13) through (2.15) in which $T_1 = R_1 C_1$ and $T_2 = R_2 C_2$.

$$Z_{ab} = R_{ab} - j \frac{1}{\omega C_{ab}} \quad (2.13)$$

$$R_{ab} = \frac{\omega^2 T_1 T_2 (T_2 C_1 + T_1 C_2) + T_1 C_1 + T_2 C_2}{\omega^2 (T_2 C_1 + T_1 C_2)^2 + (C_1 + C_2)^2} \quad (2.14)$$

$$C_{ab} = \frac{\omega^2(T_1C_2+T_2C_1)^2+(C_1+C_2)^2}{\omega^2(T_2^2C_1+T_1^2C_2)+(C_1+C_2)} \quad (2.15)$$

The impedance Z_{ab} can be combined with that of the shared compliance $C_{c\omega}$, to find the impedance between points a and c which is given by Eq. (2.16) or (2.17).

$$Z_{ac} = Z_{ab} + \frac{1}{j\omega C_{c\omega}} \quad (2.16)$$

$$Z_{ac} = R_{ab} - \frac{j}{\omega} \left(\frac{1}{C_{ab}} + \frac{1}{C_{c\omega}} \right) \quad (2.17)$$

Z_{ac} can also be represented by an equivalent circuit made up of a single frequency-dependent resistor R_e and capacitor C_e in series. These can be found by comparing Eq. (2.17) with (2.18), and the results are shown in Eqs. (2.19) and (2.20).

$$Z_{ac} = R_e - j \frac{1}{\omega C_e} \quad (2.18)$$

$$R_e = R_{ab} = \frac{\omega^2 T_1 T_2 (T_2 C_1 + T_1 C_2) + T_1 C_1 + T_2 C_2}{\omega^2 (T_2 C_1 + T_1 C_2)^2 + (C_1 + C_2)^2} \quad (2.19)$$

$$C_e = \frac{C_{ab} C_{c\omega}}{C_{ab} + C_{c\omega}} = \frac{\omega^2 C_{c\omega} (T_1 C_2 + T_2 C_1)^2 + C_{c\omega} (C_1 + C_2)^2}{C_{c\omega} [\omega^2 (T_2^2 C_1 + T_1^2 C_2) + (C_1 + C_2)] + \omega^2 (T_1 C_2 + T_2 C_1)^2 + (C_1 + C_2)^2} \quad (2.20)$$

When the time constants of the two separate pathways are equal, i.e., $T_1 = T_2$, these expressions can be simplified as shown in Eqs. (2.21) and (2.22). It is noteworthy that for this case ($T_1 = T_2$), the desired parameters R_e and C_e are independent of frequency.

$$R_e = \frac{R_1 R_2}{R_1 + R_2} \quad (2.21)$$

$$C_e = \frac{C_{c\omega} (C_1 + C_2)}{C_1 + C_2 + C_{c\omega}} \quad (2.22)$$

The total input impedance may be expressed as shown in Fig. (2.23) in which total respiratory resistance (R_{rs}) is equal to $R+R_e$ and the total effective compliance C_{rs} is equal to C_e .

$$Z_{rs} = R + R_e + j \left(\omega I - \frac{1}{\omega C_e} \right) \quad (2.23)$$

Both R_{rs} and C_{rs} are frequently-dependent except when the time constants of the two parallel pathways are equal ($T_1=T_2$).

In order to illustrate the frequency-dependent behavior, Mead's model (Fig. 8-B) [46] and his parameter values for normal humans are employed. These parameters are:

$$\begin{array}{lll} R = 2.5; & I = 0.01; & C_{cw} = 0.2; \\ R_1 = 0; & C_1 = 0.0005; & T_1 = 0; \\ R_2 = 0.5; & C_2 = 0.2; & T_2 = 0.01 \end{array}$$

The effective respiratory compliance and resistance for this case are shown in Figure 12, (curve A), together with those for increasing peripheral airway resistance (curves B-C) and compliance as in COPD (curve D). The values of compliance and resistance in the two pathways are identical to those used by Mead [46]. The corresponding total respiratory impedances for these four cases are shown in Figure 13. It can be seen that no detectable changes in effective compliance and resistance occur in the frequency range for practical measurements (0-1.5 Hz for compliance, 10 BPM - 10 Hz for resistance) in normal lungs. However, when the peripheral airway resistance is raised, the frequency-dependency becomes more prominent. In COPD (curve D), drastic decreases in both compliance and resistance with frequency are very obvious. The total dynamic compliance falls by 65% at 1 Hz and 80%

Figure 12 Total effective compliance and resistance in Mead's model in four different conditions (see text).

Figure 13 Magnitude (a) and phase (b) of total respiratory impedance in Mead's model in various conditions (see text)

at 2 Hz; total resistance falls by 45% at 5 Hz and 65% at 10 Hz.

Figure 14 shows the pole-zero configurations of the respiratory impedances in the four cases mentioned above. It is found that as the peripheral airway resistance increases both zeros and poles of the respiratory impedance move toward the origin. This implies that the respiratory impedance becomes more sensitive to the change of frequency in the region near the origin as the peripheral airway resistance increases. In other words, a frequency change in the lower frequency range can cause more prominent change in respiratory impedance if the peripheral airway resistance is raised. This may explain why the frequency-dependence behavior of effective compliance and resistance in COPD is detectable in the practical measurement frequency range which is relatively low.

Figure 14 Pole (solid symbol) and zero (empty symbol) configurations of the input impedance in Mead's model with four different conditions: normal (O), increasing peripheral resistance (Δ), increasing peripheral resistance ($\square$), and COPD ($\circ$).

In previous sections, all discussions about the analog linear electrical models representing the respiratory mechanical system were directed toward human subjects. However as will be noticed in Chapter 4, dogs were the experimental animals used for the study described in this dissertation. One may wonder if those models for human lungs are also applicable to dogs?

The anatomical studies reported by Tyler et al [75] indicated significant structural differences in lungs of man and mammals commonly used in experimental studies. For example, interlobular air drifts are nearly nonexistent in cow and pig; occur more frequently in the horse and man; and are present to a relatively greater degree on a segmental basis in the dog. Tyler also suggested that these specimens might be grouped into three distinct morphological groups with the cow and pig designated as type 1, the dog as type 2, and the horse and man as type 3. Since anatomical features certainly have some influence on function, lung mechanics in dog might be different from that in man. Certain differences between dog and man have been shown in several comparative studies [76,77,78]. On the other hand, the same studies have also established the basic mechanical behaviors in dog and man are identical.

Emilio et al [76] found that the relationships between dynamic respiratory pressure and flow in both dog and man follow Rohrer's equation and that the relaxation pressure-volume curves in both species were nearly identical. Hull et al [50] suggested that the gross behavior of the respiratory system in dogs can be modeled by a constant series R-L-C circuit. The frequency-dependent behavior of compliance

and resistance caused by inequality in the time constants of various pathways in the lungs was also demonstrated in dogs [79].

All these facts strongly suggest that the linear electrical circuit models developed in previous sections to represent the respiratory mechanical system for man also is appropriate for dogs.

2.6 Summary

Although the breathing mechanism is very complicated, its mechanics are basically analogous to other dynamic systems such as mechanical and electrical circuit systems. The well developed theories for electrical circuit systems can greatly facilitate studies of the respiratory mechanical system by applying dynamic analogy between these two systems. The use of two-terminal linear electrical circuits for modeling the respiratory mechanical system in order to explain the impedance data obtained from forced oscillations is fully justified. The mechanical behavior of a normal respiratory system can be represented by a simple second order R-I-C model. But, models containing two pathways are necessary in accounting for the frequency-dependent behavior of compliance and resistance. The frequency analysis of the input impedance of a particular model can provide valuable information on the inherent nature of the associated respiratory system. The discussions in this chapter have provided theoretical bases for those in the next chapter which deals with the estimation of respiratory parameters from the impedance data.

CHAPTER III

PARAMETER ESTIMATE BY NONLINEAR REGRESSION ANALYSIS

3.1 Parameter Estimate Problem

In the studies of various systems such as automatic control systems, physiological systems, economic systems, etc., two types of problems are generally encountered. The first one is to find the response of a given system to specific inputs or excitations. The other problem is to find a mathematical description (model) of an unknown system based on a certain set of inputs and corresponding outputs. This type of problems is known as the modeling or identification problem [35].

Modeling problems can be separated into two broad categories, depending on the degree of a priori knowledge of the system. If the nature of the system is completely unknown, the problem may be termed as a "Black Box" identification problem. In many cases, a great deal of knowledge concerning the basic equations describing the system, often from a knowledge of its structure or from the available mathematical models or similar system, may exist, but the specific values of the system parameters may be unknown. Some authors have termed this the "Grey Box" problem [35]. The problem addressed in this dissertation is essentially a modeling problem, and belongs to the second category.

Modeling problems usually encompass four sub-problems: representation, measurement, estimation, and validation [88]. The representation

problem deals with how a system should be modeled. It is necessary to know whether the model should be static or dynamic, linear or nonlinear, deterministic or random, continuous or discrete, and so on. In order to verify a model, physical quantities must be measured, and the measurement problem consists of defining which physical quantities should be measured and how they should be measured. Usually, a certain number of non-measurable parameters are involved in the model, and the estimation problem deals with the determination of these parameters from the measured quantities. After a model has been completely specified, through choice of an appropriate mathematical representation, measurement of signals and estimation of parameters, the model must be verified. The validation problem deals with demonstrating confidence in the model and this is often achieved by a statistical test involving confidence limits, and physical justification of the model. These four sub-problems as applied to respiratory mechanics are considered in various chapters of this dissertation: the representation, measurement and validation problems are respectively dealt in Chapter II, IV, and V; the remaining problem, parameter estimation, is discussed in this chapter.

A general structure for considering this type of problem has been discussed by Bekey [35]. In these discussions the system is represented as shown in Figure 15. The k input variables to the system are designated as $x_1, x_2, \dots, x_k$ and the single output variable of the system is y_o . If a priori knowledge can be used to develop a mathematical representation of the system that contains a certain number of unspecified parameters, $\theta_{o1}, \theta_{o2}, \dots, \theta_{op}$, then the system can be characterized by Eq. (3.1a).

$$y_o = f(x_1, \dots, x_k; \theta_{o1}, \dots, \theta_{op}) \quad (3.1a)$$

Figure 15 A dynamic system with multiple inputs and single output

By defining two vectors,

$$X = (x_1, \dots, x_k)'$$

and $\theta_o = (\theta_{o1}, \dots, \theta_{op})'$,

where the prime symbol represents the transpose of a vector, then

Eq. (3.1a) can be rewritten as Eq. (3.1b).

$$y_o = f(X; \theta_o) \quad (3.1b)$$

Suppose n observations of the form; $y_{ou}, x_{1u}, \dots, x_{ku}$; $u = 1, 2, \dots, n$, are available by direct measurements of the input and output variables. Regardless of how $X_u = (x_{1u}, \dots, x_{ku})'$ and y_{ou} for $u = 1, 2, \dots, n$ are actually obtained, two distinct situations are possible. These measurements can be without any error or there can be a certain amount of random error in the measurement. In the first case, Eq.(3.1b) for the n observations can be written as shown in Eq.(3.2a) or in vector form as in Eq.(3.2b).

$$y_{ou} = f(X_u; \theta_o) \quad u=1, 2, \dots, n \quad (3.2a)$$

$$Y_o = \begin{bmatrix} y_{o1} \\ \vdots \\ y_{on} \end{bmatrix} = \begin{bmatrix} f(X_1; \theta_o) \\ \vdots \\ f(X_n; \theta_o) \end{bmatrix} \quad (3.2b)$$

In the second case, only noisy measurements are available and these are represented by R_u and y_{eu} which are the measured values of X_u and y_{ou} as defined in Eq.(3.3) where N_u and v_u are two random sequences.

$$R_u = X_u + N_u \quad u = 1, 2, \dots, n \quad (3.3a)$$

$$y_{eu} = y_{ou} + v_u \quad (3.3b)$$

Eq.(3.3) can be abbreviated using matrix notation as shown in Eq.(3.4) in which R , X , and N are $k \times n$ matrices and Y_e , Y_o , and V are n dimensional vectors.

$$R = X + N \quad (3.4a)$$

$$Y_e = Y_o + V \quad (3.4b)$$

where

$$R = (R_1, \dots, R_n)'$$

$$X = (X_1, \dots, X_n)'$$

$$N = (N_1, \dots, N_n)'$$

$$Y_e = (y_{e1}, \dots, y_{en})'$$

$$Y_o = (y_{o1}, \dots, y_{on})'$$

$$V = (v_1, \dots, v_n)'$$

Eq.(3.4) is referred to as stochastic measurement equation[88].

There is a third important situation in which the input variables can be measured perfectly but the measurement of the output variable is noisy. The stochastic measurement equation for this case is expressed as shown in Eq.(3.5).

$$R = X \quad (3.5a)$$

$$Y_e = Y_o + V \quad (3.5b)$$

The estimation of parameters in such a system may be accomplished by

following the scheme as shown in Figure 16 [88]. The measured output variable, Y_e , is approximated by Y_m as defined by Eq.(3.6).

$$Y_m = \begin{bmatrix} y_{m1} \\ \vdots \\ y_{mn} \end{bmatrix} = \begin{bmatrix} f(x_1; \theta) \\ \vdots \\ f(X_n; \theta) \end{bmatrix} \quad (3.6)$$

Y_m is a structural model of Y_o , in which $\theta = (\theta_1, \dots, \theta_p)'$ denotes an estimated value of θ_o . The stochastic error between the measured output Y_e and model output Y_m is symbolized by $\tilde{Y}$ and is defined in Eq.(3.7).

$$\tilde{Y} = Y_e - Y_m \quad (3.7)$$

Figure 16 A parameter identification system

This error, $\tilde{Y}$, which is computable, is used along with the measured noise-free input variables, X , to obtain an estimate for θ_o from a parameter estimation algorithm. This algorithm is usually an iterative process in which values for θ and Y_m are changed iteratively until the final values for θ and Y_m are obtained.

The problems described in this dissertation as well as in many other engineering problems fit into this third category. Many algorithms have been developed for solving this type of problems [35,36], and the more important ones are discussed briefly in the following sections.

3.2 Numerical Methods for Parameter Estimation

3.2.1 Regression Analysis Method

Consider the system as shown in Figure 15. Suppose the input variables of the system can be measured without any errors, but the measurement of the output variable is noisy as expressed by Eq.(3.8) in which v_u , $u = 1, 2, \dots, n$, is a random sequence.

$$y_{eu} = f(X_u; \theta_o) + v_u \quad u=1, 2, \dots, n \quad (3.8)$$

This is a system of n equations with p unknown parameters. If $n < p$, there are fewer equations than unknowns. Such an underdetermined system of equations does not lead to unique or meaningful values for $\theta_o = (\theta_{o1}, \dots, \theta_{op})$ [83]. If $n = p$, there are exactly as many equations as unknowns, and if measurement errors are not present, θ_o could be obtained exactly by solving the set of equations although the solution may not be unique. In this case, nothing can be done about the measurement errors. The characteristics of the errors will greatly affect the solution for θ_o . If

$n > p$, there more equations than unknowns, and within this overdetermined structure, the effect of measurement errors could be offset. This is the case of real interest in this dissertation, and in classical statistics, this type of problems is studied under the subject of "Regression Analysis" [84].

Generally speaking, the objective of regression analysis is to determine a vector $\hat{\theta}$ which serves as an estimate of the true parameter vector θ_0 , by making use of the theoretical response function of the system. This estimation may be accomplished by minimizing a specific measure of the error $\tilde{Y}$ (Eq. 3.7) and this measure is usually referred to as criterion or error function. The estimate vector $\hat{\theta}$ is usually chosen so as to minimize a weighted sum of squares of the components of $\tilde{Y}$, J , as defined in Eq.(3.8a) or in matrix form in Eq.(3.8b), in which

$$J(\theta) = w_1 \tilde{y}_1^2 + w_2 \tilde{y}_2^2 + \dots + w_n \tilde{y}_n^2 \quad (3.8a)$$

$$J(\theta) = \tilde{Y}' W \tilde{Y} \quad (3.8b)$$

the matrix W is given by Eq.(3.9).

$$W = \begin{bmatrix} w_1 & & 0 \\ & w_2 & \\ 0 & & \ddots \\ & & & w_n \end{bmatrix} \quad (3.9)$$

In other words, the estimate vector $\hat{\theta}$ is determined according to Eq.(3.10).

$$\min_{\theta} J(\theta) = J(\hat{\theta}) \quad (3.10)$$

This technique for choosing $\hat{\theta}$ is known as the generalized least squares or weighted least squares method. When each component of $\tilde{Y}$ is weighted equally, the weighting matrix is reduced to as shown in Eq.(3.11)

in which I is the $n \times n$ identity matrix and w is a constant, and this equation is referred to as the least squares method.

$$W = w I \quad (3.11)$$

Linear Regression Analysis

When the theoretical response function $f(X_u; \theta)$ is a linear function of the parameter vector θ , the minimization of the sum squares is particularly simple. For this case, Eqs.(3.2b), (3.6), (3.5b), and (3.7) can be expressed as Eqs.(3.12), (3.13), (3.14), and (3.15) respectively.

$$Y_o = H \theta_o \quad (3.12)$$

$$Y_m = H \theta \quad (3.13)$$

$$Y_e = H \theta_o + V \quad (3.14)$$

$$\tilde{Y} = H (\theta_o - \theta) + V \quad (3.15)$$

In these equations H is an $n \times p$ matrix whose components can be computed from elements of the input matrix X . The criterion function J given by Eq.(3.8) may be written in a quadratic form in θ as shown in Eq.(3.16).

$$J(\theta) = Y_e' W Y_e - 2 Y_e' W H \theta + \theta' H' W H \theta \quad (3.16)$$

If W is a symmetrical and positive definitive matrix, the criterion function J in Eq.(3.16) is also positive definitive and has a minimum at $\theta = \hat{\theta}$ which may be found by equating to zero the gradient of J with respect to θ . The resulting $\hat{\theta}$ is given implicitly by Eq.(3.17).

$$(H' W H) \hat{\theta} = H' W Y_e \quad (3.17)$$

This equation is usually called the "Normal Equation" by statisticians [84]. If the matrix H is of full rank, $\hat{\theta}$ can be expressed explicitly by Eq.(3.18).

$$\hat{\theta} = (H' W H)^{-1} H' W Y_e \quad (3.18)$$

The parameter vector provided by Eq.(3.18) is usually known as the linear generalized least-square estimator of the true parameter vector θ_0 . In the case where $W = wI$, the least-square estimator of θ_0 is given by Eq.(3.19).

$$\hat{\theta} = (H' H)^{-1} H' Y_e \quad (3.19)$$

Nonlinear Regression Analysis

When the theoretical response function $f(X_u; \theta)$ is nonlinear in the parameter vector the parameter estimate problem usually becomes much more difficult. For this situation the criterion function defined by Eq.(3.8) may be expressed as shown in Eq.(3.20).

$$J(\theta) = \sum_{u=1}^n w_u [y_{eu} - f(X_u; \theta)]^2 \quad (3.20)$$

In order to find the generalized least-square estimate of θ_0 , the normal equations should be obtained by differentiating Eq.(3.20) with respect to θ . The equations are found to take the form as shown in Eq.(3.21) in which $i=1,2,\dots,p$, and the quantity denoted by the second pair of brackets is the first partial derivative of $f(X_u; \theta)$ with respect to θ_i with all θ 's replaced by the corresponding $\hat{\theta}$'s, which has the same subscript.

$$\sum_{u=1}^n w_u [y_{eu} - f(X_u; \theta)] \left[\frac{\partial f(X_u; \theta)}{\partial \theta_i} \right]_{\theta = \hat{\theta}} = 0 \quad i=1, \dots, p \quad (3.21)$$

Eq.(3.21) must be solved for $\hat{\theta}$, and since no general formula can be obtained each problem must be treated individually. Draper and Smith [84] have pointed out that even with one unknown parameter and a relatively simple nonlinear function, finding $\hat{\theta}$ by solving the normal equations is not easy. When more parameters are involved and the nonlinear function is more complicated, the solution of normal equations can be extremely difficult to obtain, and iterative methods must be employed in nearly all cases. The difficulties in obtaining $\hat{\theta}$ may be compounded by the fact that multiple solutions may exist, corresponding to multiple stationary values of the criterion function.

In many nonlinear cases, since it is difficult to find $\hat{\theta}$ directly from the normal equations, estimation of parameters is frequently achieved by utilizing certain optimum seeking methods with the aid of high speed digital computers. These computing techniques fall into two general categories: gradient methods and search techniques [35], which are briefly discussed in the following paragraphs.

3.2.2 Gradient Methods

Gradient methods are based on finding the values of θ for which the gradient vector of the criterion function, J , with respect to the parameter vector equals zero, since the condition satisfies a necessary condition for the existence of a local minimum of J . The corresponding computer algorithms are based upon computing the $i+1^{\text{th}}$ parameter estimate using Eqs.(3.22) and (3.23).

$$\theta^{i+1} = \theta^i + \Delta\theta^i \quad (3.22)$$

$$\Delta\theta^i = -K \nabla J(\theta^i) \quad (3.23)$$

In this last equation K is a $p \times p$ matrix whose choice in each iteration leads to several variations of the gradient method and some of the important ones are discussed in the following sections.

Gauss-Newton Method

The Gauss-Newton method [86,87] is based on the linearization of the nonlinear response function $f(X_u; \theta)$ in a succession of stages. At each stage a matrix of partial derivative which is defined in Eq.(3.24) is computed.

$$Q = \begin{bmatrix} \frac{\partial f(X_1; \theta)}{\partial \theta_1} & \dots & \frac{\partial f(X_1; \theta)}{\partial \theta_p} \\ \vdots & & \vdots \\ \frac{\partial f(X_u; \theta)}{\partial \theta_1} & \dots & \frac{\partial f(X_u; \theta)}{\partial \theta_p} \end{bmatrix}_{\theta=\theta^i} \quad (3.24)$$

From this an approximation to the model response vector $Y_m(\theta^i + \Delta\theta)$ can be constructed by truncating the Taylor's series for Y_m as shown in Eq.(3.25).

$$Y_m(\theta^i + \Delta\theta) \approx Y_m(\theta^i) + Q \Delta\theta \quad (3.25)$$

Associated with this approximation to Y_m is an approximate error vector and an approximate criterion function, given by Eqs.(3.26) and (3.27) respectively.

$$\tilde{Y}(\theta^i + \Delta\theta) = \tilde{Y}(\theta^i) - Q \Delta\theta \quad (3.26)$$

$$J(\theta^i + \Delta\theta) = \tilde{Y}(\theta^i)' W \tilde{Y}(\theta^i) - 2\tilde{Y}(\theta^i)' W Q \Delta\theta + \Delta\theta' Q' W Q \Delta\theta \quad (3.27)$$

The parameter change vector $\Delta\theta$ can be obtained by minimizing $J(\theta^1 + \Delta\theta)$. Since the expression in Eq.(3.27) is analog to that in Eq.(3.16), the minimizing value of $\Delta\theta$ can be obtained by simply comparing to Eq.(3.18). It is given by Eq.(3.28).

$$\Delta\theta^1 = (Q'W Q)^{-1} Q' W \tilde{Y}(\theta^1) \quad (3.28)$$

This result can be written in a more meaningful form as shown in Eq.(3.30) by using the relationship described by Eq.(3.29).

$$\begin{aligned} \nabla J(\theta^1) &= \frac{\partial J}{\partial \theta} \bigg|_{\theta=\theta^1} \\ &= \frac{\partial (\tilde{Y}' W \tilde{Y})}{\partial \theta} \bigg|_{\theta=\theta^1} \\ &= -2 Q' W \tilde{Y}(\theta^1) \end{aligned} \quad (3.29)$$

$$\Delta\theta^1 = -\frac{1}{2} (Q' W Q)^{-1} \nabla J(\theta^1) \quad (3.30)$$

The value for $\Delta\theta$ at the i^{th} iteration provided by Eq.(3.30) is then used to obtain a new value of θ according to Eq.(3.22) for further iteration. It is clear that the term, $-\frac{1}{2}(Q'W Q)^{-1}$, in Eq.(3.30) corresponds to the K matrix in Eq.(3.23). This procedure, which is called the Gauss-Newton method, has possible drawbacks in certain applications since it may converge very slowly, oscillate widely, or even not converge at all.

Steepest Descent Method

The steepest descent method is based on adjusting parameters along a line parallel the local gradient vector, i.e., K in Eq.(3.23) is a constant diagonal matrix. For this method, the parameter change vector

given by Eq.(3.23) can be written as Eq.(3.31) in which k is a scalar constant.

$$\Delta\theta^1 = -k \nabla J(\theta^1) \quad (3.31)$$

Since the gradient vector is normal to the corresponding contour lines, the movement of the parameter vector in each step is in a direction perpendicular to the contour at the starting point. The scalar constant k determines the step size of each movement. It can be chosen in each step in such a way that it leads to the largest possible decrease in $J(\theta)$ along the gradient direction from the starting point. Since at the minimum of the criterion function, $\nabla J(\theta)=0$, the step size becomes very small near the minimum for any finite value of k . Consequently the steepest descent method is expected to be inefficient at the terminal iterations.

Newton-Raphson Method

The Newton-Raphson method [89] uses linear extrapolation of $J(\theta)$ to zero for obtaining the quantity K in Eq.(3.23), while $J(\theta)$ is approximated with the first two terms of its Taylor's series expansion. For the scalar case, $J(\theta)$ is expressed as Eq.(3.32).

$$J(\theta) \approx J(\theta^1) + \left. \frac{\partial J}{\partial \theta} \right|_{\theta=\theta^1} (\theta - \theta^1) \quad (3.32)$$

If $\theta = \theta^{1+1}$ is selected so that $J(\theta)=0$, then $\Delta\theta^1$ is given by Eq.(3.33).

$$\Delta\theta^1 = -\frac{J(\theta^1)}{\nabla J(\theta^1)} \quad (3.33)$$

For the vector case, the parameter change vector can be analogously obtained as shown in Eq.(3.34).

$$\begin{aligned}\Delta\theta^1 &= -\left[\frac{J(\theta^1)}{|\nabla J(\theta^1)|^2}\right] \nabla J(\theta^1) \\ &= -k^0 \nabla J(\theta^1)\end{aligned}\tag{3.34}$$

The K matrix in Eq.(3.23) is found by multiplying the identity matrix by the term in brackets which is denoted as k^0 . The parameter change vector, like the steepest descent method, is in the direction normal to the contour of $J(\theta)$ at the starting point.

This method usually works successfully in early stages of the iterative process, but produces very large steps near the minimum where $|\nabla J| \rightarrow 0$, unless $J(\theta) \rightarrow 0$. Since it is unreasonable to expect $J(\theta) \rightarrow 0$ when real physical data is involved, another way of obtaining the scale factor k in terminal stages is necessary.

Gradient Searching Method

The steepest descent method may be inefficient near the minimum because of very small step adjustments of the parameter vector. On the other hand, the Newton-Raphson method may fail in accurately locating the minimum because of the large parameter changes near the minimum. The gradient searching method [90] represents a compromise between these two methods for obtaining the scale factor k . Since the criterion function, J , is bounded from below by the value zero, it follows that in any region where J is continuous, there exists at least one value for k in each step, k^* , so that Eq.(3.35) is satisfied.

$$\min_{k>0} J[\theta^i - k \nabla J(\theta^i)] = J[\theta^i - k^* \nabla J(\theta^i)] \quad (3.35)$$

So long as $\nabla J=0$, then $J(\theta^{i+1}) < J(\theta^i)$ where $\theta^{i+1} = \theta^i - k^* \nabla J(\theta^i)$, and thus the sequence of values for J converges. Ordinarily, the convergence is toward a minimum of J and the sequence in J is accompanied by a related convergent sequence of parameter vectors.

A particular searching routine for k^* can be obtained by starting with the value of k^0 given by Eq.(3.34) and then halving it if $J(\theta^{i+1}) > J(\theta^i)$ or doubling it if $J(\theta^{i+1}) < J(\theta^i)$. This adjusting process is continued until three points between θ^i and θ^{i+1} are found which include a local minimum of $J(\theta)$. A quadratic interpolation is then used to find k^* which leads to this local minimum of $J(\theta)$. Using this value of k^* , a parameter change vector and a new parameter vector can be obtained and the iteration cycle may begin again.

Gradient Projection Method

In the estimation of parameters of a nonlinear system, it may quite often be possible that all feasible values of the parameter vector lie within certain closed and bounded convex region in the parameter space because of certain constraints imposed on the parameters. For this case, the search for optimum parameters which minimize a specified criterion function J can be carried out only in the admissible region. A very general approach to these constrained parameter estimation problems, called gradient projection method, was developed by Rosen [91-93]. In his scheme, the parameter vector is changed in the direction of steepest descent with optimal step size until a minimum of J is found. (It is essentially a gradient searching method.) If moving in the

direction of steepest descent causes any of the constraints to be violated, the parameter vector is changed along the projection of the negative gradient onto the boundary of the admissible region.

The computation for the gradient projection involved in Rosen's approach is quite complicated because of its applicability to a broad category of parameter constraints. If the constraints on parameters take the form shown in Eq.(3.36), then the admissible region becomes a hypercube and the projection of the gradient is greatly simplified [95].

$$a_j \geq \theta_j \geq b_j \quad j= 1,2, \dots ,p \quad (3.36)$$

This particular type of constraints, is frequently encountered in many parameter estimation problems including the one encountered in this dissertation. For this type of problem, the iteration procedure to obtain a solution would be as follows:

1. Calculate the gradient vector with the current parameter vector, θ^1 .
2. For each component of θ^1 , determine whether it is interior to the admissible region or at the upper or lower extreme of the region.
3. For each of these components lying on the boundary, determine whether or not its corresponding gradient component points into the region. If it does, set that gradient component to zero. Otherwise, leave the gradient component unchanged.
4. For those components interior to the admissible region, leave their gradient components unaltered. The gradient vector thus

obtained, denoted as ∇J_p^i , is the desired gradient projection.

5. Compute the maximum allowable step size k_p^0 which is the minimum positive value of k_j found by evaluating Eq.(3.37).

$$k_j = \begin{cases} \frac{\theta_j^i - a_j}{\partial J / \partial \theta_j} & \text{if } \frac{\partial J(\theta^i)}{\partial \theta_j} < 0 \\ \frac{\theta_j^i - b_j}{\partial J / \partial \theta_j} & \text{if } \frac{\partial J(\theta^i)}{\partial \theta_j} > 0 \end{cases} \quad j=1,2,\dots,p \quad (3.37)$$

6. Execute the gradient searching routine to find an optimum constrained step size k_p^* , starting with k_p^0 obtained in Step 5.
7. Set $\Delta \theta^i = -k_p^* \nabla J_p^i$ and $\theta^{i+1} = \theta^i + \Delta \theta^i$, and return to Step 1 for another iteration.

3.2.3 An Algorithm for Constrained Parameter Estimation

In the last sections, several different methods for nonlinear regression analysis of parameter estimation problems have been briefly discussed. Each method has certain advantages and drawbacks. Although one particular method might work best in one type of problem, it may be considerably inferior to the other methods with a different type of problem. Actually, for each method there are problems which are ineffectively handled, and thus no method can be called "best" for all nonlinear regression problems. Nevertheless, an algorithm which can effectively solve a large number of problems may be constructed by combining the best features of various methods while avoiding their most serious

limitations. For example, an excellent method developed by Marquardt [94] represents a compromise between the Gauss-Newton method and the steepest descent method which almost always converges and does not "slow down" like the steepest descent method often does. McGhee [57] also devised such an algorithm which is a combination of basic Gauss-Newton method, the optimum gradient searching method and the gradient projection method. This algorithm is universally convergent for problems with parameters subject to range constraints. The computational strategy employed in this algorithm may be summarized as follows:

1. At i^{th} iteration, compute $\Delta\theta^i$ according to Eq.(3.30) using the basic Gauss-Newton method.
2. If the resulting θ^{i+1} from Step 1 satisfies the constraints and reduces the value of J , use it for next iteration.
3. Otherwise, compute $\Delta\theta^i$ by Newton-Raphson method (Eq.(3.34)). If the resulting θ^{i+1} satisfies all constraints, find the optimum step and associated new parameter vector for next iteration, using the gradient searching method.
4. If the constraints are not satisfied by the Newton-Raphson method, compute ∇J_p and maximum allowable step size by gradient projection method and then carry out a search for the optimum $\Delta\theta^i$ and associated θ^{i+1} for further iteration.

Figure 17 presents a flow chart which implements the above strategy. The programming of this flow chart has been implemented by McGhee [57] as a Fortran subroutine and given the title LOCMIN. After certain modifications, the routine is executable on the IBM 370/165 system. A listing of the modified program is included in Appendix A. As shown in

Figure 17 Flow chart for a minimization algorithm

the flow chart, three subroutines, REGRES, GRPREX, and GRASER, are called in LOCMIN. They respectively implement the basic Gauss-Newton method, gradient projection method and gradient searching method. Although not shown in the flow chart, three another subroutines, SUMSQ, MODEL, and MINV, are also called in this program. SUMSQ and MODEL are two user's supplied subroutines which are used for computing the value of the criterion function and the response of the mathematical model respectively. MINV is a subroutine in the system library for matrix inversion. Since the criterion function and the model are dependent on particular problems, subroutines MODEL and REGRES would have to be modified if applied to different problems.

As indicated in the flow chart, the program terminates when one of the following criteria is satisfied:

1. The change in J is less than a specified value (EPHI).
2. The change in any parameter is less than a specified value (EC).
3. The number of iterations is more than a specified value (NLOOP).
4. $|VJ|^2$ is less than a specified value (EGRAD).
5. The gradient projection attains a constrained minimum.
6. The absolute value of the model response is greater than a specified value (ZSTOP).

Since the nature of various parameter estimation problems is different, the criteria for terminating the program in order to save computation time or to achieve high accuracy will depend on the particular problem. The stop criteria provide the users more flexible control over the iteration process and the most efficient use of this algorithm may be obtained by selecting appropriate stop criteria. The last three

criteria described above also help to avoid computational problems arising from round-off and overflow of the arithmetic registers.

3.2.4 Uniform Random Search Method

All methods described this far in the chapter are limited to the determination of local minimums. They can be used for the location of global (or absolute) minimums only when the criterion function is unimodal over the constrained parameter space. Unfortunately, the sum squared error function displays multiple minimums in many parameter estimation problems including the one presented in this dissertation. In dealing with this situation, gradient methods must be combined with certain random search methods [97]. The pure random search method originally proposed by Brooks [95] and discussed by others [89,96] may be used. The method consists of measuring the sum of squared errors, $J(\theta)$, at N random points selected from a probability distribution uniform over the entire admissible parameter space and taking the point with the smallest value of J as an approximation for the minimum. According to Korn [96], the probability of locating a point lying within 10% of the optimum for each parameter in N trials is given by Eq.(3.38) in which p is the number of parameters.

$$P_r = 1 - (1 - 10^{-p})^N \approx N 10^{-p} \quad \text{for } 10^p \gg N \quad (3.38)$$

Conversely, the number required to have a probability of 0.9 of locating such a point is $N \approx 2.3 \times 10^p$ [89]. When p is large, the number of trials needed to insure a sufficiently high probability of obtaining a value near the true minimum may be extremely large.

Nevertheless, this method may be useful in choosing a starting point for the subsequent gradient methods in the absence of any information regarding the location of the optimum.

3.2.5 A Complete Algorithm for Constrained Parameter Estimation

By combining gradient methods and random search methods, it is possible to construct an algorithm for finding the global minimum of the sum squared error function in most parameter estimation problems. A flow chart for the combination described by McGhee [57] is shown in Figure 18. The strategy is as follows:

1. Start the estimation procedure by locating the minimum associated with an initial guess for the parameter vector provided by the human experimenter (LOCMIN subroutine).
2. Carry out a uniform random search within the admissible parameter space and select the best parameter vector in a specified number of trials (RANSER subroutine).
3. Locate the minimum using the best parameter vector obtained in Step 2 as the starting vector.
4. Go to Step 2, repeat for a preset number of times (NTRIAL) and choose a best estimation.

The RANSER routine which searches for a "promising" starting vector provides that the overall algorithm will converge to the global minimum of the criterion function with probability arbitrary close to one. The LOCMIN subroutine efficiently refines the rough parameter estimate provided by random searching. By repeatedly exercising the outermost loop, the algorithm can provide a specified number of

Figure 18 Flow chart for a complete algorithm for constrained parameter estimation

independent estimates. In the situations where the human experimenter can provide a promising initial guess for the parameter vector, this loop may be not necessary. When the loop is essential, the specification of the optimum number of trials depends on the nature of the special problems and usually requires an empirical judgement.

The whole algorithm was coded in Fortran [57] and the program which is ready for running in IBM 370/165 system is attached in Appendix A. In addition to those subroutines mentioned previously, this program uses two additional subroutines, RANDU and INPUT. RANDU which is contained in the library and called by RANSER, is an uniformly distributed random number generator. The subroutine INPUT is used to read input data based on which the parameter estimation is conducted.

As has been pointed out, several subroutines in the program are problem-oriented. In Appendix A those subroutines are written for the purpose of estimating respiratory mechanical parameters from impedance data. For other applications, these subroutines must be modified.

3.3 Application of the Algorithm in Estimating Respiratory Parameters from Artificial Impedance Data

It is clear from the discussions in Chapter II, that under certain conditions the respiratory mechanical system can be represented by analog electrical circuits in which each element is associated with certain physiological effects. A modification of the forced oscillation technique may serve as a relatively easy experimental means for obtaining data for use in estimating the parameters in the model. This technique which has been described previously [18] and is reviewed in detail in Chapter I, allows measurement of the respiratory input

impedance over a certain frequency range. Based upon this experimental impedance data and an assumed theoretical electrical model, it is possible to invoke the parameter estimation technique described above to estimate the significant mechanical parameters of the respiratory system.

This particular parameter estimation problem can be clearly described by using the configuration as shown in Figure 19 which is actually identical to Figure 16 except the symbols used for various variables have been changed. The input impedance of the electrical model, z_m , may be expressed as a function of frequency and system parameters as shown in Eq.(3.39) in which ω is the angular frequency and $\theta = (\theta_1, \dots, \theta_p)$ is an p -vector of unknown parameters, each representing one element (resistance, capacitance, or inductance) in the model.

$$z_m = f(\omega; \theta) \quad (3.39)$$

The angular frequency is the only input variable which is assumed to be measurable without any error. The output variable is the respiratory impedance and random noise is present in its measurement. The measured noisy output, z_e , is written in Eq.(3.40) in which v is a random variable and z_o is defined by Eq.(3.41) with θ_o being the true parameter vector.

$$z_e = z_o + v \quad (3.40)$$

$$z_o = f(\omega; \theta_o) \quad (3.41)$$

The measured impedance z_e is approximated by z_m , and the optimum estimate $\hat{\theta}$ is obtained using the algorithm developed in the last section with ω as the input variable and the error defined by Eq.(3.42).

Figure 19 A scheme for estimating respiratory parameters from impedance data

$$\tilde{z} = z_e - z_m \quad (3.42)$$

Note that since impedance is a complex variable, z_e , z_m , z_o , and $\tilde{z}$ are all complex-valued.

Suppose (ω_1, z_{e1}) , (ω_2, z_{e2}) , ..., (ω_n, z_{en}) are n available observations. A criterion function may be defined as shown in Eq.(3.43) in which the subscript i denotes the sequence of observations, each corresponding to a particular frequency.

$$\begin{aligned} J(\theta) &= \sum_{i=1}^n |\tilde{z}_i|^2 \\ &= \sum_{i=1}^n |z_{ei} - z_{mi}|^2 \end{aligned} \quad (3.43)$$

The complex impedances can be expressed in rectangular form as shown in Eqs.(3.44) and (3.45) and Eq.(3.43) can be rewritten as Eq.(3.46).

$$z_{ei} = \mu_{ei} + j v_{ei} \quad (3.44)$$

$$z_{mi} = \mu_{mi} + j v_{mi} \quad (3.45)$$

$$J(\theta) = \sum_{i=1}^n [(\mu_{ei} - \mu_{mi})^2 + (v_{ei} - v_{mi})^2] \quad (3.46)$$

Using the relationship expressed in Eqs.(3.47) and (3.48), the criterion function J in Eq.(3.46) can be modified as shown in Eq.(3.49) where each element in the summation is a real number.

$$y_{ei} = \begin{cases} \mu_{ei} & 1 < i < n \\ v_{e(i-n)} & (n+1) < i < 2n \end{cases} \quad (3.47)$$

$$y_{mi} = \begin{cases} \mu_{mi} & 1 < i < n \\ v_{m(i-n)} & (n+1) < i < 2n \end{cases} \quad (3.48)$$

$$J(\theta) = \sum_{i=1}^{2n} (y_{ei} - y_{mi})^2 \quad (3.49)$$

It is known that the parameter estimation algorithm employed here is an iteration process. At each iteration, the gradient of the criterion function with respect to the parameter vector, $\nabla J(\theta)$, must be computed according to Eq.(3.29) with the weighting matrix $W = I$ as shown in Eq.(3.50).

$$J(\theta) = -2 Q' \tilde{Z} \quad (3.50)$$

For the particular criterion function given in Eq.(3.49), the error vector $\tilde{Z}$ is defined in Eq.(3.51) and the derivative matrix in Eq.(3.52).

$$\tilde{Z} = \begin{bmatrix} y_{e1} - y_{m1} \\ \vdots \\ y_{e2n} - y_{m2n} \end{bmatrix} \quad (3.51)$$

$$Q = \begin{bmatrix} \frac{\partial \mu_m(\omega_1)}{\partial \theta_1} & \dots & \frac{\partial \mu_m(\omega_1)}{\partial \theta_p} \\ \vdots & & \vdots \\ \frac{\partial \mu_m(\omega_n)}{\partial \theta_1} & \dots & \frac{\partial \mu_m(\omega_n)}{\partial \theta_p} \\ \frac{\partial v_m(\omega_1)}{\partial \theta_1} & \dots & \frac{\partial v_m(\omega_1)}{\partial \theta_p} \\ \vdots & & \vdots \\ \frac{\partial v_m(\omega_n)}{\partial \theta_1} & \dots & \frac{\partial v_m(\omega_n)}{\partial \theta_p} \end{bmatrix} \quad (3.52)$$

3.3.2 Estimations Based on Artificial Noisy Impedance Data

In this section the application of the parameter estimation algorithm developed in this chapter is tested with artificially generated impedance data. A specific linear electrical circuit model of the respiratory mechanical system is assumed and its input impedance is computed at various frequencies over the range of interest. Elements in a sequence of gaussian random noise are added to the computed impedance values to simulate experimental errors. With either noisy or noise-free data, the parameters in the model are estimated using the same algorithm. The ability of this algorithm to accurately estimate parameters in this particular problem is verified by comparing the estimated parameter vector with the true one.

To be more specific, the noisy impedance data, z_{eu} , $u=1, \dots, n$, is produced in the following way. A random sample of size m , $\chi_1, \chi_2, \dots, \chi_m$, from an uniform distribution is first generated by the computer, using an appropriate subroutine. For each sample, the mean is equal to $1/2$ and variance $1/12$. According to the central limit theorem [85], the statistic given in Eq.(3.53) approaches a standard normally distributed variable with the distribution, $n(0,1)$. Then, from $n(0,1)$ a random sample of size $2n$, $S_1, S_2, \dots, S_{2n}$, can be produced by the computer.

$$S = \frac{m}{12} \left(\sum_{j=1}^n \chi_j - \frac{m}{2} \right) \quad (3.53)$$

In practice, the impedance at each frequency, z_{eu} , is measured in terms of amplitude ρ_{eu} and phase ϕ_{eu} to which the random noise are actually introduced. Expressions for the polar forms of z_{eu} and z_{ou} (noise-free impedance) are shown in Eqs.(3.54) and (3.55).

$$z_{ou} = \rho_{ou} e^{j\phi_{ou}} \quad (3.54)$$

$$u = 1, 2, \dots, n$$

$$z_{eu} = \rho_{eu} e^{j\phi_{eu}} \quad (3.55)$$

Then the artificial impedance data are defined by Eqs.(3.56) and (3.57) in which σ_1 and σ_2 specify the level of noise on the measurement of the amplitude and phase angle.

$$\rho_{eu} = \rho_{ou} + \sigma_1 \rho_{ou} S_{2u-1} \quad (3.56)$$

$$\phi_{eu} = \phi_{ou} + \sigma_2 \phi_{ou} S_{2u} \quad (3.57)$$

$$u = 1, 2, \dots, n$$

The Simple Series R-I-C Model

The first model considered was the simple series R-I-C model as shown in Figure 7. The input impedance of this model is given in Eq.(2.7) and is repeated here as Eq.(3.58).

$$z_m = R + j (\omega I - 1/(\omega C)) \quad (3.58)$$

The artificial data was generated according to typical values as given in the following [44]:

$$R = 2.7, \quad I = 0.01, \quad C = 0.1$$

Let $\theta = (\theta_1, \theta_2, \theta_3) = (R, I, C)$. Then the elements in the criterion function defined by Eq.(3.49) is now given by Eq.(3.59) for this model and the $2n \times p$ derivative matrix Q in Eq.(3.52) is given by Eq.(3.60) in which ω_i , $i=1, 2, \dots, n$, is the i^{th} angular frequency component. Values for θ_i , $i=1, 2, 3$, are constrained to be between 0 and ten times the nominal value for each parameter.

$$Y_{mi} = \begin{cases} \theta_1 & 1 \leq i \leq n \\ \omega_i \theta_2 - 1/(\omega_i \theta_3) & (n+1) \leq i \leq 2n \end{cases} \quad (3.59)$$

$$Q = \begin{bmatrix} 1 & 0 & 0 \\ 1 & 0 & 0 \\ \vdots & \vdots & \vdots \\ 1 & 0 & 0 \\ 0 & 0 & 1/(\omega_1 \theta_3^2) \\ 0 & 0 & 1/(\omega_2 \theta_3^2) \\ \vdots & \vdots & \vdots \\ 0 & 0 & 1/(\omega_2 \theta_3^2) \end{bmatrix} \leftarrow \text{nth row} \quad (3.60)$$

The results of estimations in six separate cases are summarized in Table 2. Artificial impedance data with no noise (cases 1 and 4), 5% noise, i.e., $\sigma_1 = \sigma_2 = 0.05$, (cases 2 and 5), and 10% noise, i.e., $\sigma_1 = \sigma_2 = 0.1$, (cases 3 and 6) were utilized. In the first three cases ten observations at frequencies, $f_i = i$, $i=1,2, \dots, 10$ were used and in the other three cases, twenty observations at frequencies $f_i = i/2$, $i=1,2, \dots, 20$ were used. For all cases, the stop criterions used are as follows:

$$ZSTOP=10^{10}, \text{EPHI}=10^{-16}, \text{EC}=10^{-16}, \text{EGRAD}=10^{-11}, \text{NLOOP}=200$$

For each case, ten independent estimations were obtained with ten different initial guesses each of which was provided by the RANSER subroutine from 1000 random selections.

In the ten independent trials for each of the six cases the estimated values for the three parameters were identical to fifth significant digit. In the two cases with no noise (cases 1 and 4), the estimated parameter vectors were identical to the true one within the

Table 2 Summary of parameter estimate for the R-I-C model based on artificial impedance data.

case no	no. of observations	freq. range	noise level	estimated values		
				θ_1	θ_2	θ_3
1	10	1-10Hz	0%	.275E01 (0%)	.1 E-1 (0%)	.1 E+0 (0%)
2	10	1-10	5%	.277E01 (0.8%)	.108E-1 (0.1%)	.940E-1 (-6%)
3	10	1-10	10%	.278E01 (1.1%)	.115E-1 (15%)	.885E-1 (-12%)
4	20	0.5-10	0%	.275E01 (0%)	.1E-1 (0%)	.1 E+0 (0%)
5	20	0.5-10	5%	.276E01 (0.4%)	.102E-1 (2%)	.955E-1 (-4.5%)
6	20	0.5-10	10%	.277E01 (0.7%)	.104E-1 (4.2%)	.913E-1 (-8.7%)
true value				2.75	.01	.1
upper bound				25.	.1	1.
lower bound				0.	0.	0.

1. Value in parentheses is the % difference of the estimated parameter from the true one.

2. $(\theta_1, \theta_2, \theta_3) = (R_{rs}, I_{rs}, C_{rs})$

precision of the computer. When noise was present, the estimated parameter vector was slightly different than the true one, and the deviation was more prominent with higher level of noise. For example, in case 3 10% noise resulted in 1%, 15%, and 12% errors in the estimated values for R, I, and C respectively. Comparing the % errors in case 2 to those in case 5 (or case 3 to case 6), it seems that a larger number of observations offset the effect of random noise.

Based on this study it seems that the respiratory mechanical parameters in normal humanbeings can be accurately estimated from the impedance data at 20 frequencies in the range from 1 to 10 Hz even with measurement error as high as 10%.

The Airway and Lung-Chest Model

A second model which separates the airways and lung-chest combination with a shunt compliance as shown in Figure 6 was then investigated. The input impedance of this model has been given in Eq.(2.10). Let $\theta = (\theta_1, \theta_2, \theta_3, \theta_4, \theta_5, \theta_6) = (R_{aw}, R_{lw}, I_{aw}, I_{lw}, C_g, C_{lw})$. The model response can be expressed as shown in Eq.(3.61). The corresponding derivative matrix $Q = (q_{ij})$ can be then computed according to Eq.(3.62).

The artificial impedance data was generated by using typical values for parameters in normal adult humans as shown in the following:

$$\theta_{o1} = 1.5, \theta_{o2} = 1.2, \theta_{o3} = 0.01, \theta_{o4} = 0., \theta_{o5} = 0.003, \theta_{o6} = 0.1.$$

The program stop criterions used in this case were the same as those used for the R-I-C model.

With $f_i = i$, $i = 1, 2, \dots, n$ and $n = 20, 30$, or 40 , it was found that there was considerable disagreement between independent estimates

$$y_{mi} = \begin{cases} \theta_1 + k_1/k_2 & 1 \leq i \leq n \\ \omega_1 \theta_3 + k_3/k_4 & (n+1) \leq i \leq 2n \end{cases} \quad (3.61)$$

$$(q_{ij}) = \begin{cases} 1 & j=1 \\ (k^2 \theta_6^2 - \omega_1^2 \theta_2^2 \theta_5 \theta_6^4)/k_2^2 & j=2 \\ 0 & j=3 \\ 2\omega_1^2 k k_1 \theta_5 \theta_6 / k_2^2 & j=4 \\ 2k_1(-\omega_1^2 \theta_2^2 \theta_5 \theta_6^2 + 2k k_1)/k_2^2 & j=5 \\ [2k_2 \theta_2 \theta_6 - 2k_1(\omega_1^2 \theta_2^2 \theta_5^2 \theta_6 + k k_6)]/k_2^2 & j=6 \\ 0 & j=1 \\ 2\omega_1^2 \theta_2 \theta_5 \theta_6^2 (k_4 + \omega_1 k_3 \theta_5)/k_4^2 & j=2 \\ \omega_1 & j=3 \\ [k_4(-\omega_1^2 k \theta_6 - k_5 \omega_1^2 \theta_5 \theta_6) - 2\omega_1^3 k k_3 \theta_5 \theta_6]/k_4^2 & j=4 \\ [k_4(\omega_1^2 \theta_2^2 \theta_6^2 + k_5^2) + 2k_3(\omega_1^3 \theta_2^2 \theta_5 \theta_6^2 + \omega_1 k k_5)]/k_4^2 & j=5 \\ [k_4(-\omega_1^2 k \theta_4 + 2\omega_1^2 \theta_2^2 \theta_5 \theta_6 + k_5 k_6) + 2k_3(\omega_1^3 \theta_2^2 \theta_5^2 \theta_6 + \omega_1 k k_6)]/k_4^2 & j=6 \end{cases} \quad \begin{matrix} 1 \leq i \leq n \\ (n+1) \leq i \leq 2n \end{matrix} \quad (3.62)$$

with $k_1 = \theta_2 \theta_6^2$

$$k_2 = k^2 + \omega_1^2 \theta_2^2 \theta_6^2 \theta_5^2$$

$$k_3 = k k_5 + \omega_1^2 \theta_5 \theta_2^2 \theta_6^2$$

$$k_4 = -\omega_1 k^2 - \omega_1^3 \theta_2^2 \theta_5^2 \theta_6^2$$

$$k_5 = 1 - \omega_1^2 \theta_4 \theta_6$$

$$k_6 = 1 - \omega_1^2 \theta_4 \theta_5$$

$$k = \theta_6 + \theta_5 k_5$$

obtained with different starting vectors and that there were significant discrepancies between these values and the true parameter values. This probably results from the fact that the above frequency ranges are not adequate for defining the characteristics of the respiratory impedance of this particular model.

When $n=50$, i.e., 50 observations are obtained at frequencies, 1, 2, ..., 50 Hz, the estimation becomes more accurate. The results of 11 independent successful estimations based on impedance data with no noise, 1%, 3%, and 5% random measurement errors are listed in Table 3. For each estimation, the number of iterations required and the mean residual sum squared errors, J_m , are tabulated. Values for the true parameters and their lower and upper bounds are also included in the table. The initial parameter vector in each case was selected by the RANSER subroutine from 3000 random trials. For all cases presented in Table 3, the associated iteration processes were terminated by the parameter change criterion. However, about 50% of other trials which are not listed in the table, the program was terminated by the loop count criterion. In these situations, the estimations were terminated prematurely or were converging to local, non-global minimums. This seems to suggest that if the estimation is terminated by the parameter change criterion, the estimated parameter values would more likely be reliable.

From Table 3, it can be seen that for each parameter, the discrepancy between the estimated and true values and the mean residual sum of squared errors become larger when the noise level is increased. It was found that with measurement errors up to 5%, there were good agreements between estimated and true values for θ_3 (I_{aw}) and θ_6 (C_{lw}); the

Table 3 Summary of parameter estimate for the airway and lung-chest model based on artificial data

case no	noise level	θ_1	θ_2	θ_3	θ_4	θ_5	θ_6	no. of iterations	J_m
1	0%	.130E+1	.155E+1	.954E-2	.507E-3	.260E-2	.766E-1	56	.95E-12
		.150E+1	.120E+1	.100E-1	.933E-5	.301E-2	.100E-1		
2		.155E+1	.918E+0	.964E-2	.402E-3	.540E-2	.870E-1	10	.43E-10
		.150E+1	.120E+1	.100E-1	.643E-4	.305E-2	.100E+0		
3		.177E+1	.743E+0	.906E-2	.860E-3	.420E-2	.836E-1	12	.35E-8
		.135E+1	.118E+1	.999E-2	.622E-3	.361E-2	.994E-1		
4	1%	.195E+1	.102E+1	.923E-2	.540E-4	.531E-2	.991E-1	18	.10E-2
		.163E+1	.109E+1	.986E-2	.916E-3	.451E-2	.987E-1		
5		.153E+1	.140E+1	.108E-1	.807E-4	.434E-2	.105E+0	19	.10E-2
		.163E+1	.108E+1	.979E-2	.293E-3	.400E-2	.989E-1		
6		.189E+1	.939E+0	.105E-1	.442E-3	.611E-2	.121E+0	30	.10E-2
		.159E+1	.113E+1	.991E-2	.715E-3	.405E-2	.988E-1		
7	3%	.212E+1	.254E+0	.707E-2	.862E-4	.196E-2	.138E+0	33	.92E-2
		.174E+1	.986E+0	.962E-2	.784E-3	.552E-2	.978E-1		
8		.188E+1	.915E+0	.961E-2	.407E-3	.568E-2	.120E+0	15	.91E-2
		.168E+1	.103E+1	.970E-2	.207E-3	.440E-2	.990E-1		
9		.189E+1	.939E+0	.105E-1	.442E-3	.611E-2	.121E+0	194	.93E-2
		.176E+1	.961E+0	.960E-2	.999E-3	.593E-2	.940E-1		
10	5%	.192E+1	.964E+0	.906E-2	.196E-3	.437E-2	.103E+0	17	.24E-3
		.177E+1	.972E+0	.965E-2	.573E-3	.547E-2	.917E-1		
11		.130E+1	.155E+1	.954E-2	.507E-3	.260E-2	.766E-1	9	.24E-3
		.171E+1	.103E+1	.977E-2	.188E-3	.450E-2	.941E-1		
True parameter		1.5	1.2	.01	0.	.003	.1		
upper bound		.3	.3	.05	.001	.008	.2		
lower bound		0.	0.	0.	0.	0.	0.		

There are two rows of data in each case. The first row represents the initial parameter vector and the second row represents the final estimate of parameters.

discrepancies for $\theta_1 (R_{aw})$ and $\theta_2 (R_{lw})$ were larger but in all cases they were within 20% of the true values; estimated values for $\theta_4 (I_{lw})$ were in the order of 10^{-3} which was very close to its true value; estimates for $\theta_5 (C_g)$ were not as good as those for the other parameters, but the estimated values still had the same order of magnitude as the true one.

The difficulties in estimating parameters for this model arise mainly from the small value of the shunt compliance, C_g , whose effect on the total respiratory impedance is shadowed by C_{lw} at lower frequencies and by I_{aw} at higher frequencies. As a consequence, its precise determination from the impedance data over practical frequency range is quite limited. Nevertheless, the estimation of parameters in this model can still be accomplished if more data which contain less noise and spread over a wider frequency range can be collected.

Since the element I_{lw} included in this model has a value nearly equal to zero, and shows little contribution to the total impedance from which the six parameters are estimated, it is not necessary to include it in the model. Its inclusion may have compromised the model and caused some of the difficulties encountered in parameter estimation. If I_{lw} is removed from the model, these difficulties are expected to be reduced.

The parallel Compartments Model

The parallel compartment model shown in Figure 8A may be used to represent the lungs' mechanics in patients with COPD. This model has seven parameters in it, i.e., $\theta = (\theta_1, \theta_2, \theta_3, \theta_4, \theta_5, \theta_6, \theta_7) = (R, R_1, R_2, I, C_1, C_2, C_{cw})$. According to Eqs. (2.19), (2.20), and (2.23) the theoretical model

$$\begin{aligned}
 y_{mi} &= \theta_1 + k_1/k_2 & 1 \leq i \leq n \\
 \omega_1 \theta_4 &= k_3/k_4 & (n+1) \leq i \leq 2n
 \end{aligned} \tag{3.63}$$

$$\begin{aligned}
 q_{1i} &= \begin{cases} 1 & j=1 \\ \{k_2[\omega_1^2(T_1 T_2 \theta_5 \theta_6 + k T_2 \theta_5) + \theta_5^2] - 2k_1 \omega_1^2 k \theta_5 \theta_6\} / k_2^2 & j=2 \\ \{k_2[\omega_1^2(T_1 T_2 \theta_5 \theta_6 + k T_1 \theta_6) + \theta_6^2] - 2k_1 \omega_1^2 k \theta_6 \theta_5\} / k_2^2 & j=3 \\ 0 & j=4 \\ \{k_2[\omega_1^2(T_1 T_2^2 + T_1 T_2 \theta_2 \theta_6 + k T_2 \theta_2) + 2\theta_2 \theta_5] - 2k_1[\omega_1^2 k(T_2 + \theta_2 \theta_6) + \theta_5 + \theta_6]\} / k_2^2 & j=5 \\ \{k_2[\omega_1^2(T_2 T_1^2 + T_2 T_1 \theta_3 \theta_5 + k T_1 \theta_3) + 2\theta_3 \theta_6] - 2k_1[\omega_1^2 k(T_1 + \theta_3 \theta_5) + \theta_6 + \theta_5]\} / k_2^2 & j=6 \\ 0 & j=7 \end{cases} & 1 \leq i \leq n \\
 &= \begin{cases} 0 & j=1 \\ -[2k_4 \omega_1^2 \theta_5 \theta_6 (T_1 \theta_7 + k) - 2k_3 \omega_1^3 k \theta_5 \theta_6 \theta_7] / k_4^2 & j=2 \\ -[2k_4 \omega_1^2 \theta_6 \theta_5 (T_2 \theta_7 + k) - 2k_3 \omega_1^3 k \theta_6 \theta_5 \theta_7] / k_4^2 & j=3 \\ \omega_1 & j=4 \\ -\{k_4[\omega_1^2 \theta_7 (T_2^2 + 2T_1 \theta_2 \theta_6) + \theta_7 + 2\omega_1^2 k(T_2 + \theta_2 \theta_6) + 2(\theta_5 + \theta_6)] - 2k_3[\omega_1^3 \theta_7 k(T_2 + \theta_2 \theta_6) + \omega_1 \theta_7 (\theta_5 + \theta_6)]\} / k_4^2 & j=5 \\ -\{k_4[\omega_1^2 \theta_7 (T_1^2 + 2T_2 \theta_3 \theta_5) + \theta_7 + 2\omega_1^2 k(T_1 + \theta_3 \theta_5) + 2(\theta_6 + \theta_5)] - 2k_3[\omega_1^3 \theta_7 k(T_1 + \theta_3 \theta_5) + \omega_1 \theta_7 (\theta_5 + \theta_6)]\} / k_4^2 & j=6 \\ -\{k_4[\omega_1^2 (T_2^2 \theta_5 + T_1^2 \theta_6) + \theta_5 + \theta_6] - k_3[\omega_1^3 k^2 + \omega_1 (\theta_5 + \theta_6)^2]\} / k_4^2 & j=7 \end{cases} & (n+1) \leq i \leq 2n
 \end{aligned} \tag{3.64}$$

where

$$k_1 = \omega_1^2 T_1 T_2 k + (T_1 \theta_5 + T_2 \theta_6)$$

$$k_2 = \omega_1^2 k^2 + (\theta_5 + \theta_6)^2$$

$$k_3 = \theta_7 [\omega_1^2 (T_2^2 \theta_5 + T_1^2 \theta_6) + \theta_5 + \theta_6] + \omega_1^2 k^2 + (\theta_5 + \theta_6)^2$$

$$k_4 = \omega_1 \theta_7 [\omega_1^2 k^2 + (\theta_5 + \theta_6)^2]$$

$$k = T_2 \theta_5 + T_1 \theta_6$$

$$T_1 = \theta_2 \theta_5$$

$$T_2 = \theta_3 \theta_6$$

response in this case is given as shown in Eq.(3.63). Meanwhile the $2n \times 7$ derivative matrix Q is given in Eq.(3.64). Since the exact expression for Q is rather complicated, it may be worthwhile to approximate the first derivatives by finite differences as shown in Eq.(3.65).

$$q_{ij} = \left. \frac{\partial y_m}{\partial \theta_j} \right|_{\omega_1} = \frac{y_m(\theta_1, \dots, \theta_j + \Delta\theta_j, \dots, \theta_p) - y_m(\theta_1, \dots, \theta_j, \dots, \theta_p)}{\Delta\theta_j} \Big|_{\omega_1} \quad (3.65)$$

The choice of $\Delta\theta_j$ is a compromise between arithmetic round-off errors and approximation accuracy. Usually $\Delta\theta_j$ can be chosen as small as possible if the corresponding difference in y_m does not vanish due to round-off error. If the derivative matrix is computed in this manner, the subroutine REGRES incorporate in the complete program for parameter estimation can be made independent of any particular problem.

A set of artificial data was generated at 50 frequencies, 1, 2, ..., 50 Hz, according to the following nominal values for the seven parameters:

$$R=2.5, R_1=0., R_2=0.2, I=0.01, C_1=0.005, C_2=0.2, C_w=0.2.$$

From this set of impedance data, the seven parameters were in turn estimated by using the parameter estimation algorithm. The program stop criterions used in this case were as those used for the previous models. The lower bound was zero for each parameter and the upper bound was 5 times the nominal value for each of the three resistors, 10 times for the inductor, and 5 times for each the three capacitors. Each initial guess was selected from 3000 trials.

It was found that a relatively accurate estimation could be obtained only when the resistive components of the initial parameter vector, R, R_1 , and R_2 , were quite close to the true values. The

parameter C_1 could not be identified exactly but its estimated value, like the true value, was always smaller than those for C_2 and C_w . The parameter I , however, had a good recovery in most cases. As in the airway and lung-chest model, the solutions were more reliable when the program was terminated due to the satisfaction of the parameter change criterion. When the data is noisy, the chance for an accurate estimation became much less. With 1% of random noise, only about 20% of independent trials provided "good" estimates. This probably results from the multiple extremums of the criterion surface and its distortion due to measurement noise.

3.4 Summary

This chapter shows that the parameter estimation problem can be solved by using a nonlinear regression analysis technique. With this technique, the effect of random measurement error on the parameter estimation can be offset since the problem is overspecified. Each individual algorithm for nonlinear regression analysis has certain advantages and disadvantages with regard to converging speed and accuracy. A superior method may be obtained by combining several algorithms so that the best features of each can be utilized while avoiding the drawbacks. A universally convergent algorithm which is applicable in the situations where the parameters are subject to certain range constraints and the criterion function has multiple minimums in the constrained parameter space, has been developed. It combines the Gauss-Newton, Newton-Raphson, gradient searching, gradient projection and uniform random searching methods.

This algorithm is applied to the problem of estimating mechanical parameters of the respiratory system from impedance data provided by the forced oscillation technique. By using artificially generated impedance data from certain assumed electrical circuit models of the respiratory system, it is found that parameters in a series R-I-C model can be identified easily and accurately even with experimental random errors as high as 10%. When the respiratory system is represented by other more sophisticated models such as those shown in Figures 6 and 8, the parameter estimation problem becomes more difficult. To accomplish an accurate estimation with these models, it may be necessary to utilize more impedance data over a wider frequency range with less experimental error and more computer time to pick a more promising initial parameter vector and to allow more convergence to a local minimum.

CHAPTER IV

PROCEDURES AND METHODS

The forced oscillation technique, which is used in this study to obtain experimental data, is a modification of the approach first used by DuBois et al. [25]. In their study, the impedance of the total respiratory system at frequencies from 2 to 15 Hz was determined. Fisher et al. [27], Grimby et al. [28], and Goldman et al. [29] used the same technique to measure the respiratory resistance in normal subjects and in subjects with lung diseases. Recently, Peslin et al. [48] measured total respiratory impedance in normal subjects over a frequency range of 3 - 70 Hz by applying perithoracic pressure oscillations. Michaelson et al. [30] used forced random noise to obtain the total respiratory impedance from 3 to 45 Hz with the aid of computer in analyzing experimental data. For the same purpose, a relatively simple and direct method was developed by Pimmel et al. [32] and is essentially employed for this dissertation.

4.1 Overall System

A block diagram for the overall experimental system is shown in Figure 20, in which the impedance analyzer is a specially designed instrument [31]. This unit is mainly composed of five blocks of circuits (Figure 21): 1) an oscillator in the frequency range of 1 to 100 Hz, which is used to drive an acoustic suspension speaker (AR 3-A, Acoustic Research) to produce sinusoidal pressure waveforms which are

Figure 20 Block diagram for the overall experimental system

Figure 21 Block diagram for the Impedance Analyzer

applied to the airway of the subject; 2) two matched narrow bandpass filters which are mechanically latched to the oscillator frequency control; 3) two identical peak detectors, each of which samples the filtered signal (pressure or flow) and holds at its peak value for meter display; 4) a phase detector for sensing the phase difference between the two sinusoidal signals; 5) a frequency detector for measuring the frequency of preset oscillation.

In performing the experiments, a volume-controlled respirator (Model 607, Howard Apparatus) was connected to the endotracheal tube of the paralyzed dog through a three-way valve whose the other opening was connected to the loudspeaker. A heated pneumotachograph (Model 3700, Hans Rudolph Co.) in conjunction with a high quality differential pressure transducer (Model MP-45, Valadyne) was used to monitor the flow signal. An identical differential pressure transducer was connected to the mouth side of the pneumotachograph with the reference open to the atmosphere, and it was used to measure mouth pressure. All connecting tubes were matched in length and made as short as physically possible, in order to minimize the artifactual phase lags introduced by these tubes [71].

Pressure and flow signals from the transducer carrier-amplifiers were processed by the impedance analyzer. Peak values for both signals, the phase angle between them, and the frequency of the forced oscillation were recorded from the panel of the impedance analyzer. A graphical recording of the pressure and flow signals, both with forced oscillations and with tidal breathing can be displayed on a chart recorder (Series 200, Brush Instrumentation). A respiratory integrator (Series 200, Brush Instrumentation) provided a volume signal.

4.2 System Calibration

Calibration of Pressure Channel

The peak amplitude of the sinusoidal pressure signal at a particular frequency is indicated by one of the two galvanometers on the panel of the impedance analyzer. The magnitude of the meter deflection depends on the gain of the pressure transducer and its associated carrier-amplifier, and on the gain of the filter, peak detector and galvanometer in the impedance analyzer. The calibration of the entire channel using a water manometer as a standard must be performed in two steps since the impedance analyzer responds only to relatively high frequency oscillation which is too rapid for the water manometer to follow.

In the first step, various intensities of static pressure were measured by the water manometer and applied to the pressure transducer and recorded with the span control of the carrier-amplifier set to 0.1 and sensitivity of the DC amplifier set to 5 mv/div. The setup is as shown in Figure 22. The two sets of readings in the range of interest are listed in Table 4. This data indicates that the pressure transducer plus its carrier-amplifier had a linear response to static pressure up to 6 cm H₂O and the conversion factor between pressure and chart deflection is simply:

$$\begin{aligned} 1 \text{ cm H}_2\text{O} &\sim 4 \text{ divisions of deflection} \\ \text{or} \quad 1 \text{ division of deflection} &\sim 0.25 \text{ cm H}_2\text{O} \end{aligned} \tag{4.1}$$

A push button was mounted on the carrier-amplifier for the convenience of daily calibration. Its output was found to correspond to 4.45 cm H₂O of pressure and would cause 21.8 divisions of deflection on the chart

recording if control settings were the same as mentioned before.

Figure 22 Set-up for pressure calibration

Table 4 Correspondence between Readings from Water Manometer and Chart Recorder in Calibrating Pressure Measurements.

Pressure cm H ₂ O	0	1	2	3	4	5	5.45	6
Divisions of deflections	0	4	8	12	16	20	21.8	23.5

* output of the pressure calibration button

In the second step, the setup as shown in Figure 1 was modified so that the subject end of the tubing was blocked and sinusoidal pressures generated by the impedance analyzer and speaker at various intensities and frequencies were applied. Pressure variations were recorded on the chart recorder and the values displayed on the pressure panel meter on the impedance analyzer were compared to the magnitudes of the signal displayed by the chart recorder. Data are given in

Table 5. Note that the strip chart recorder had a flat frequency response from DC to at least 20 Hz. This means that the chart recorder caused no distortion in measuring the sinusoidal pressures in the range of interest.

Table 5 Correspondence between Readings from Chart Recorder and Impedance Analyzer in Calibrating Pressure Measurements.

Meter Reading	Peak to Peak Deflection in Divisions		
	1 Hz	10.1 Hz	20.1 Hz
0	0	0	0
0.5	2.1	2.1	2.0
1.0	4.2	4.1	3.6
1.5	6.3	6.3	5.6
2.0	8.4	8.3	7.6
2.5	10.5	10.4	9.2
3.0	11.8	12.0	11.2
3.5	15.3	14.2	13.2
4.0	17.5	16.2	15.0
4.5	20.0	18.5	17.0

By applying linear regression analysis [72,75], a relationship between the observed deflections on the strip chart and the meter readings at certain frequencies may be expressed as shown in Eq. 4.2 in which P_{def} is the number of divisions of deflection from peak to peak, R_p is the meter reading for pressure, and F is the frequency in Hz.

$$P_{\text{def}} = 0.74 + 3.82 R_p - 0.06 F \quad (4.2)$$

By incorporating the conversion factor as given in Eq. 4.1, the observed deflection (Eq. 4.2) can be converted into actual physical quantity as expressed in Eq. 4.3 where P is the peak value of mouth pressure in cm H_2O .

$$P = 9.2 \times 10^{-2} + 0.48 R_p - 7.7 \times 10^{-3} F \quad (4.3)$$

Calibration of Flow Channel

The flow recording channel includes the pneumotachograph, its associated pressure transducer and carrier-amplifier, and the filter, detector and panel meter in the impedance analyzer. The magnitude of the flow signal is indicated by the other galvanometer on the front panel of the analyzer. It can also be monitored and displayed on the strip chart recorder. For calibration, the span control of the carrier-amplifier was set to 1.2 and the sensitivity of the DC amplifier was set to 2 mv/div. The volume-controlled respirator which supplied the necessary flow was arranged so that the gas (air or He-O₂ mixture) flowed in and out of the cylinder of the respirator through the pneumotachograph. The ratio control was set to 50%. An almost sinusoidal flow waveform was recorded on the strip chart. The exact frequency was obtained from the time-marker available on the chart.

Suppose the stroke volume of the respirator was adjusted to x cc. and the revolving speed y Hz. Peak value of the flow signal was measured as z divisions of deflection. Then the conversion factor between the chart recording and the actual flow quantity was simply

$$1 \text{ division of deflection} \sim \left(\frac{2\pi y x}{z} \right) \text{ cc/s.} \quad (4.4)$$

It was found that for any combination of x and y , the conversion factor was almost identical. It was 33.3 cc/div for air and 29.8 cc/div for He-O₂ mixture. The flow recording system was slightly less sensitive to He-O₂ mixture than to air. In addition, the calibration button for flow was found to correspond to 380 cc/s and 340 cc/s for air and He-O₂ respectively.

The calibration of the flow panel meter on the analyzer must also be done in two steps, similar to the method used for pressure calibration. The only difference was that the subject end of the tubing was open. Table 6 the observations and Eq. 4.5 describes the linear regression relationship between the peak-to-peak deflection of the flow signal and the panel meter readings.

$$\dot{V}_{\text{def}} = 8.88 \times 10^{-2} + 11.56 R_f - 0.27 R_f^2 \quad (4.5)$$

In this equation, $\dot{V}_{\text{def}}$ is the number of divisions of the peak-to-peak deflection and R_f is the panel meter reading for flow.

Table 6 Correspondence between Readings from Chart Recorder and Impedance Analyzer in Calibrating Flow Measurements

Meter Reading	Peak-to-Peak Deflection (divisions)						
	0.9	1.01	1.12	1.80	4.94	10.1	20.1 Hz
0	0	0	0	0	0	0	0
0.5	6	5.9	5.9	5.9	6.1	6.1	5.8
1.0	11	11.2	11.0	10.9	12.0	12.0	11.0
1.5	17	16.0	16.5	16.0	17.0	17.0	16.8
2.0	23	22.0	22.0	21.0	21.2	22.1	22.0
2.5	30	29.0	28.0	26.0	27.3	27.5	27.0
3.0				31.0	32.3	32.2	32.1
3.5					37.2	37.2	37.0
4.0					42.0	42.0	42.0

The actual peak flow in cc/s is given by Eq. 4.6 for air ($\dot{V}_{\text{air}}$) and by Eq. 4.7 for He-O₂ mixture ($\dot{V}_{\text{He-O}_2}$).

$$\dot{V}_{\text{air}} = 0.15 \times 10^{-2} + 0.19 R_f - 0.45 \times 10^{-2} R_f^2 \quad (4.6)$$

$$\dot{V}_{\text{He-O}_2} = 0.13 \times 10^{-2} + 0.17 R_f - 0.4 \times 10^{-2} R_f^2 \quad (4.7)$$

In summary, the actual physical quantities of pressure and flow can be obtained from the two galvanometer readings on the impedance analyzer by employing Eqs. 4.3 and 4.6 or 4.7.

Correction of Phase Measurement

A five gallon glass bottle was connected to the subject end of the system as shown in Fig. 20 [31] in order to test the phase measurement. This element approximates a pure compliance which has an impedance of $(1/j\omega c)$. Thus, the phase shift between pressure and flow should be -90° at all frequencies. Table 7 shows the difference between the phase angles measured (by the impedance analyzer) and theoretical values. This variation probably arises from the following sources: 1) the differences in characteristics between pressure and flow transducers, 2) the differences in phase lags of the two associated

Table 7 Errors in Phase Measurements

Freq. (Hz)	Phase Diff. (degree)	Freq. (Hz)	Phase Diff. (degree)
0.9	-5	4.0	0
1.01	-4	4.43	-2
1.12	-4	5.0	-1
1.27	-2	5.6	-1
1.42	-5	6.28	0
1.60	-4	7.15	-2
1.80	-2	8.0	-2
2.01	-2	9.0	-3
2.25	-2	10.1	-3
2.54	0	11.2	-3
2.83	0	12.7	-3
3.19	0	14.2	-4
3.58	0	16.0	-5

carrier-amplifiers, and 3) the distortion in waveforms. It was found that in this particular loading condition, pressure and flow waveforms deviate from pure sine-waves at frequencies below 1.8 Hz and at frequencies above 12.7 Hz. However, since the variations in the phase measurements are within 5° , no phase corrections will be made in the subsequent animal experiments.

Correction for the Impedance of the Endotracheal Tube

A cuffed tracheal tube (37 cm in length and 1.1 cm in diameter) was always inserted into the trachea of the subject animals during the experiments. The actual measured impedance should include the impedance of the tube in addition to the respiratory impedance of the subject. The latter can be obtained by simply subtracting the impedance of the endotracheal tube from the measured impedance.

The impedance of the endotracheal tube was measured with the same equipment setup used in measuring the respiratory impedance except that the tube was open to the atmosphere instead of being inserted into the lower airway of the subject.

Figure 23 is the Bode plot of the measured impedance of the endotracheal tube at the flow rate of about 0.25 l/s, with air. Examining the Bode plot indicates that it can be approximated by a transfer function with a single zero. This fact suggests that the endotracheal tube can be represented by a series R-L electrical circuit which has a single zero at $\omega = R/L$. Practically, the compliance effect of the endotracheal tube can be neglected because of its rigidity. By using the parameter estimation algorithm (as described in the previous chapter), the optimum parameters in the R-L circuit were found to be

Figure 23 Impedance of endotracheal tube in air

Figure 24 Impedance of endotracheal tube in He+O₂

$R = 1.11 \text{ cm H}_2\text{O}/\ell/\text{s}$ and $L = 0.063 \text{ cm H}_2\text{O}/\ell/\text{s}^2$.

For the He-O₂ mixture, the same analysis can be applied. The Bode plot of the impedance of the endotracheal tube for this gas at a flow rate of 0.3 ℓ/s is given in Figure 24. The optimum parameters are $R = 1.0 \text{ cm H}_2\text{O}/\ell/\text{s}$ and $L = 0.025 \text{ cm H}_2\text{O}/\ell/\text{s}^2$.

4.3 Experimental Procedures

At the beginning of each experiment, before the system was activated, it was checked to insure that the transducers and amplifiers were connected properly, that the pneumotachograph was clean, and that no leaks existed in the tubing. After the system was turned on, and allowed to warm up, the control switches in various electronic units were set to the normal operating positions. There are as follows:

1. Pneumotachograph heater was set to 105°F.
2. In pressure recording channel, span control of the carrier-amplifier was set to 0.1 and sensitivity of the DC amplifier was set to 5 mv/div.
3. In flow recording channel, span control of the carrier amplifier was set to 1.2 and sensitivity of the DC amplifier was set to 2 mv/div.
4. Ventilation rate of the respirator was set to 20 BPM, duration ratio 50% and stroke volume 350 cc.

All dogs were weighed and apparent abnormalities such as ocular and nasal discharge were observed and recorded. The dog was anesthetized with intravenous injections of fentanyl, 0.035 mg/kg, droperidol, 1.8 mg/kg, (Innovar, 0.05 cc/kg) and sodium pentobarbital, 6 mg/kg.

Intubation was accomplished while in a ventral supine recumbency and the cuff of the endotracheal tube was inflated with 8-12 cc of air depending on the size of the dog. After placing the dog in a dorsal supine recumbency, it was secured to insure uniformity of the pulmonary testing. Succinyl choline, 1 mg/kg, was then used to effect respiratory arrest and respiration was maintained by using a volume-controlled respirator at the rate of 20 BPM and a tidal volume of 8 cc/lb. After approximately 15 minutes of artificial ventilation, the experiment began. Maintenance doses were used as necessary during the experiment.

Data from two distinct sets of experiments were utilized in this dissertation. One, collected by Robinson [74], involved the use of bronchoconstricting and dilating drugs. The second series of experiments constitutes a part of this dissertation research and was concerned with the effects of various physical interventions on the measured and computed respiratory parameters. The procedures for the second set of experiments are described as follows.

Ten mongrel dogs (20 - 25 kg in weight) were used and four different experimental conditions were usually studied. These included a control study and while ventilating with an external resistor, abdominal weighting and He-O₂ mixture. In each experimental condition, three kinds of data were obtained consistently on most of the dogs.

Forced oscillations were applied intermittently at 26 logarithmically-spaced frequencies in the range from 0.91 Hz to 16 Hz. At each frequency, the magnitudes of the mouth pressure and airflow and the phase angle between them were recorded from the panel meters on the impedance analyzer. Before each reading, the dog's lungs were first

ventilated several times and then inflated to near total lung capacity (TLC) three times to produce a constant lung history. The lungs were always assured to be at functional residual capacity (FRC) after inflations and while forced oscillations were applied. Peak oscillatory flow was maintained between 0.2 l/s and 0.5 l/s during all experiments. Collecting of an entire set of impedance data took approximately 15 minutes.

The second Set of data was obtained while the dog was ventilated from a closed air circuit at about 20 cycles/min and a stroke volume of 8 cc/lb of body weight. This circuit was formed by connecting the air inlet and outlet of the respirator to the two openings of the associated cylinder with two pieces of tubes. Mouth pressure, flow and volume were recorded on the strip chart for at least five consecutive respiratory cycles. Volume was obtained by integrating flow with an electronic integrator. An inflation to near TLC was performed just prior to obtaining this data.

Next, after inflating the lungs to near TLC three times, a graduated large plastic syringe was used to inflate the lungs with 1200 cc of room air (or of the He-O₂ mixture) and then deflate them in 100 cc increments back to FRC. At each point, a pause of 3-4 seconds was adequate to produce a plateau in the transthoracic (mouth) pressure tracing. The lungs were then re-inflated in 100 cc increments to the 1200 cc maximum.

These three sets of data requiring about 45 minutes were obtained with each of four variations in experimental conditions. Between each experimental variation, the dog was ventilated for 5 minutes or so.

After obtaining a set of control data, the abdominal region of the dog was weighted using approximately 10 lbs and the three types of data were collected. In Dog # 9, 20 lbs of weight was used. The third set of data were obtained while an external resistor was connected in series with the endotracheal tube. The resistor consisted of an orifice (18 mm in length and 6 mm in ID) placed in the middle of two identical tubes (65 mm in length and 125 mm in ID). The resistance was measured using a technique identical to that described for measuring the impedance of the endotracheal tube and found to be $1.37 \text{ cm H}_2\text{O}/\ell/\text{s}$. In the final experimental variation, a 80% He - 20% O_2 gas mixture was used in ventilating the lungs. To insure that all N_2 was eliminated, a 5 minute washout of the lungs before collecting data was performed. The experiment was facilitated with the use of a 60 liter gas bag filled with the He- O_2 mixture.

4.4 Data Analysis

During forced oscillation, peak values for pressure and flow, phase angle and frequency of oscillation were obtained directly from the penal meters on the impedance analyzer. Meter readings for pressure and flow were converted into physical quantities using Eqs. 4.3, 4.6, and 4.7 and the magnitude of the impedance was calculated from these quantities. This data described the frequency dependence of the complex flow impedance, and was used to estimate the mechanical parameters of the respiratory system. Parameter estimation was accomplished by using the estimation algorithm developed in Chapter 3, in which the criterion function J was defined in Eq. 4.8 in which Z_E represented the

experimental impedance data at various frequencies, and Z_M was the theoretical impedance of an assumed electrical circuit model.

$$J = \sum_{i=1}^n |Z_M(f_i) - Z_E(f_i)|^2 \quad (4.8)$$

In general, n was 26, however in some studies less data was collected. This methodology was applied with the simple R-I-C model and with the other more complicated models as developed in Chapter 2. The mean residual sum of squared errors was used as an indicator of the goodness of the agreement between the experimental data and the optimal model response. All data were analyzed on the IBM 370/165 digital computer.

Figure 25 illustrates a mouth pressure tracing during the static deflations. During inflations, the tracing was similar except the change of pressure was reversed. Data for pressure and volume were used to construct the pressure-volume curves. Respiratory static compliance was calculated from the pressure-volume curve at FRC in the range of tidal volume.

While using artificial ventilation in a closed air circuit, the recorded pressure, flow and volume signals were almost sinusoidal. Figure 26 shows a segment of such recording from which respiratory resistance and dynamic compliance may be calculated. Total dynamic compliance was calculated by dividing tidal volume by the total pressure change between points of zero flow (e.g., a and b). The isovolume technique [24] was employed in calculating total respiratory resistance. Two points (e.g., c and d) were selected on the volume curve where respiratory volume was identical and flow rate was approximately 0.4 l/s. Difference in both

Figure 25 Transthoracic pressure tracing during lung deflation

Figure 26 Pressure, flow, and volume recordings during artificial ventilation in anesthetized and paralyzed dog

pressure and flow rate occurred between these two points was measured. Since volume was identical at these two points, elastic forces should also have been identical. Therefore, the entire pressure difference was attributed to flow resistance which can be calculated from the ratio $\Delta p / \Delta \dot{v}$. The resistance and dynamic compliance were defined as the average of the values computed from at least 5 consecutive breaths.

Total respiratory resistance and compliance obtained from the forced oscillation technique were compared with values obtained by the more conventional method and the correlation was obtained. In each experimental condition, data was collected on at least four dogs. Differences among mean values for total respiratory resistance, inertance, and compliance in various conditions were tested for statistical significance using the Student t-distribution [73].

CHAPTER V

RESULTS AND DISCUSSIONS

As mentioned in Chapter VI, data from 18 dogs was included in this study. Data for Dogs #1-10 were obtained by the author while the data for Dogs #11-18 was obtained by others [71,74]. Among the first 10 dogs, six were considered to be in normal healthy conditions based on a rather limited physical examination. Data obtained from these 6 dogs can be regarded as a representation for the class of normal dogs. Among the second 8 dogs (Dogs #11-18), six were normal, one had a narrowed trachea, and the remaining one had "small airways disease" induced by smoking cigarettes for 6 years. Both sets of dogs were studied under the same experimental conditions except that different pneumotachographs were used. It is believed that less distortions and thus less experimental errors were present in the data from Dogs #1-10.

5.1 Frequency Response of Respiratory Impedance in Dogs

Figure 27 is a Bode diagram, illustrating typical reproducibility of impedance data when multiple sets of data were collected on a single dog during one experiment. The flow rates for these three different runs were 0.15, 0.22, and 0.28 ℓ/s in average over all the frequency components. Although there were some small variations at certain frequencies, no consistent differences in the overall responses were observed. The mean value of these three sets of data, tabulated in Table 8 and

plotted in Figure 28, represented a typical frequency response of the respiratory impedance in a normal dog. Impedance data from all dogs are attached in Appendix B. The impedance data for each dog as listed in the appendix includes the impedance of the endotracheal tube used in the experiments in addition to the respiratory impedance of the dog.

Table 8 Typical frequency response of the respiratory impedance in a normal dog

Freq.	Impedance	
	Mag.	Phase
0.90	6.67	-54.3
1.01	5.17	-51.0
1.12	4.96	-51.3
1.25	4.34	-49.3
1.41	4.06	-43.7
1.57	3.59	-40.0
1.80	3.16	-36.3
2.01	3.13	-32.0
2.24	2.84	-26.0
2.51	2.59	-22.7
2.82	2.39	-14.0
3.17	2.40	-5.7
3.54	2.36	1.7
3.97	2.28	10.0
4.42	2.28	23.0
4.96	2.56	34.3
5.58	2.75	42.0
6.24	2.97	46.7
7.14	3.33	57.0
7.95	3.81	59.3
9.03	4.17	64.0
10.10	4.87	68.3
11.17	5.30	70.0
12.60	5.89	72.3
14.13	6.51	75.3
15.90	7.68	77.3

Figure 29 shows the frequency variations in the magnitudes ($|Z_{rs}|$), phases (ϕ_{rs}), real parts (R_{rs}), and imaginary parts (X_{rs}) of the respiratory impedances (Z_{rs}) of the six healthy dogs in the first group of subjects (Dogs #1, 2, 4, 5, 6, 8). Each curve in the figure was drawn by connecting consecutive points with a straight line. Some variations among dogs can be seen in each of the four diagrams of the figure, but these differences are quite small and reflect small individual variations in the mechanical properties of the respiratory systems in different dogs.

It can be seen from the magnitude and the phase curves of Figure 29 that the frequency response of the respiratory impedance in a normal dog has a pattern consistent with a series R-I-C electrical circuit. The resonance frequency of the system (f_o) identified by the frequency where the magnitude is a minimum and where the phase angle equals 0° is about 3.5 Hz. If the measured impedance is corrected for the impedance of the endotracheal tube, the resonance frequency will be higher.

As shown in Fig. 29, R_{rs} decreased with increasing frequency in the range 0.9 - 3.5 Hz and remained relatively constant at higher frequencies, 3.5 - 16 Hz. This phenomenon suggests that the series R-I-C model is not adequate to explain the experimental impedance data at frequencies below 3.5 Hz since R_{rs} in the R-I-C model should be independent of frequency. This higher frequency behavior of R_{rs} in normal dogs is consistent with the result obtained in healthy individuals by Grimby et al. [28] which showed no significant change in R_{rs} at frequencies from 3 to 9 Hz. As to the frequency-dependent R_{rs} at frequencies below 3.5 Hz, there are no similar data in the literature for comparison.

Figures 30, 31, and 32 illustrate variations in respiratory impedances as three different mechanical interventions were introduced. These included breathing with mass loading of the abdomen, an external resistor, and a lighter gas mixture (80% He - 20% O₂). With ten pounds of abdominal weight the phase curve shifted downward (Fig. 30B) and the lower frequency portion of the magnitude curve moved upward (Fig. 30A). The external resistor significantly increased the magnitude of the impedance at all frequencies (Fig. 31A). While breathing the gas mixture, the phase curve shifted to the right (Fig. 32A) and the higher frequency portion of the magnitude curve moved downward (Fig. 32B).

Figure 33 illustrates the effects of two drugs, physostigmine and atropine, on the respiratory impedance of a single dog (Dog # 12). Physostigmine, a powerful broncho-constrictor, raised the magnitude of the impedance significantly at all frequencies (Fig. 33A) and atropine, a broncho-dilator, which was administered 60 minutes after the first drug, reversed the effect of physostigmine and brought the impedance back to control values. No significant change in phase data was observed with these two drugs (Fig. 33B).

Figure 34 shows $|Z_{rs}|$, ϕ_{rs} , R_{rs} and X_{rs} of the respiratory impedance of the two dogs with respiratory diseases and the average response of the six normal dogs in the same study. When compared to normals, the dog with narrowed trachea, Dog # 14 (denoted by '2'), showed a large increase in $|Z_{rs}|$ and no variations in ϕ_{rs} . The dog with obstructive disease, Dog # 13 (denoted by '1') showed a smaller increase in $|Z_{rs}|$ and a small change in the phase curve. Both of the increases in Z_{rs} were associated with increases in R_{rs} as indicated in Fig. 34C.

Figure 27 Reproducibility of impedance data obtained in a single dog (Dog # 1) during one experiment.

Figure 28 Typical frequency response of the respiratory impedance of a paralyzed apneic dog (Dog # 1).

Figure 29 Frequency responses of the magnitudes (A), phases (B), real parts (C), and imaginary parts (D) of the respiratory impedances in 6 normal dogs (#1,2,4,5,6, and 8) in control states.

Figure 30 An example of variation in respiratory impedance due to mass loading in the abdominal region of a paralyzed apneic dog.

Figure 31 An example of variation in respiratory impedance due to an added external resistor.

Figure 32 An example of variation in respiratory impedance due to breathing a He - O₂ gas mixture.

Figure 33 Variations in the respiratory impedance of Dog # 12 due to a bronchoconstrictor , physostigmine, and a bronchodilator, atropine.

Figure 34 Frequency responses in magnitudes (A), phase (B), real parts (C), and imaginary parts (D) of the respiratory impedances in the dog with narrowed trachea ('2'), the dog with obstructive small airways ('1') and 6 normal dogs in average (solid lines).

Fig. 34D demonstrates that X_{rs} for Dog # 14 was much different from those for normal dogs. This fact implies that the inertial and elastic properties of the lungs in this dog were greatly different than those in normal dogs since X_{rs} is determined by these energy storage properties.

5.2 Estimated Values for R_{rs} , I_{rs} , and C_{rs} from Impedance Data

The variations in impedances due to either mechanical or pharmacological interventions are resulted from changes in the mechanical properties of the respiratory systems. As mentioned in the previous chapter, the mechanism of the respiratory system can be studied using electrical analog circuits whose elements have physiological significances. Therefore it is entirely possible to link induced variations in impedance of the respiratory system to alterations in the values of analogous elements in the corresponding electrical circuits.

Using the series R-I-C electrical circuit, values for these three elements, the total resistance (R_{rs}), inertance (I_{rs}), and compliance (C_{rs}) of the respiratory system, can be estimated from the measured frequency response of the respiratory impedance by employing the parameter estimate technique described in Chapter III. The results for the ten dogs (Dogs # 1-10) in various experimental conditions are summarized in Table 9. Note that those values for R_{rs} , I_{rs} , and C_{rs} includes the effects of the endotracheal tube. Values for C_{rs} thus obtained represent the dynamic total compliances at FRC.

Also included in Table 9 is the mean residual sum of squared errors (J_m) for each estimation, which is a gross indication of how good the model is in explaining the experimental data. Figure 35 shows the

Table 9 Estimated values for R_{rs} , I_{rs} , and C_{rs} for all 10 dogs used in the studies of effects of three mechanical interventions

Dog #	Wt. kg	Control				Mass Loading				External Resistor				80% He-20% O ₂			
		R_{rs}	I_{rs}	C_{rs}	J_m	R_{rs}	I_{rs}	C_{rs}	J_m	R_{rs}	I_{rs}	C_{rs}	J_m	R_{rs}	I_{rs}	C_{rs}	J_m
1*	20	2.324	.0763	.0325	.31												
2*	20	2.578	.0739	.0276	.346									2.407	.0293	.0292	.423
3	20	3.042	.0786	.0229	.481					4.155	.0915	.0233	.692				
4*	20	2.460	.07	.0319	.365					3.639	.0938	.0299	.396	2.151	.0325	.0298	.315
5*	22	2.094	.0736	.0332	.154					3.778	.0975	.0304	.269	1.926	.0292	.0339	.238
6*	25	2.792	.084	.0279	.419	2.874	.0799	.0212	.554	4.145	.0978	.0325	.527	2.673	.0375	.0315	.319
7	20	2.943	.0871	.0274	.454	2.801	.0834	.0224	.481	3.935	.1033	.0319	.362	2.591	.0393	.0339	.185
8*	23	2.201	.0686	.0317	.242	2.308	.0642	.0215	.354	3.411	.0866	.0355	.246	2.074	.0335	.0351	.181
9	25	2.386	.0654	.0352	.219	2.67	.065	.018**	.527	3.558	.0863	.0373	.238	2.173	.0304	.0359	.242
10	20	3.057	.0768	.0261	.446	3.407	.0751	.0175	.75	4.385	.0976	.028	.354	3.04	.0393	.0291	.173
$\bar{x}$		2.583	.0754	.0296	.344	2.848	.0766	.0207	.535	3.876	.0943	.0311	.386	2.379	.0339	.0323	.260
SE		0.109	.0021	.0012	.035	0.225	.004	.0011	.083	0.119	.002	.0015	.063	0.131	.004	.0010	.031

$\bar{x}$ = mean; SE = standard error; J_m = mean residual sum of squared errors

units: R_{rs} , cm H₂O/l/s; I_{rs} , cm H₂O/l/s²; C_{rs} , l/cm H₂O

* denotes dogs with a normal (superficial) examination.

** indicates that 20 lbs of weight was used in this particular dog.

Figure 35 An example of agreement between experimental and theoretical (R-I-C model) impedances.

experimental measurements and the response with the optimum parameters for Dog # 1 and indicates the typical agreement that was achieved in these ten dogs. The mean residual error J_m is, in this case, equal to 0.3. This number represents the mean square of the distance in complex plane between experimental and theoretical impedances at a particular frequency.

Control Measurement

Values for R_{rs} , I_{rs} , and C_{rs} from control measurements obtained in six dogs which were judged to be normal are given in Table 10 after correcting for resistance (1.11 cm H₂O/l/s) and inertance (0.063 cm H₂O/l/s²) of the endotracheal tube. Mean values $\pm$ SE for all six dogs were R_{rs} : 1.298 ± 0.104 cm H₂O/l/s; I_{rs} : 0.0114 ± 0.0022 cm H₂O/l/s²; C_{rs} : 30.6 ± 0.9 ml/cm H₂O; and FRC: 718.2 ± 28 ml. FRC values were predicted by using the formula for anesthetized, supine dogs as shown in Eq. (5.1) [98].

$$\text{FRC (ml)} = (\text{body weight in kg}) \times 34$$

Using the analysis in Chapter II for the R-I-C circuit and the mean parameter values from the six normal dogs, the respiratory system is characterized by a pole at $p = 0$ and two zeros at $z_1 = -5.97$ and $z_2 = -12.1$; resonant frequency is 8.5 Hz; and the system is slightly overdamped with a damping ratio of 1.06. According to the same model and parameter values, Figure 36 illustrates the relative contribution of compliance reactance X_c and inertance reactance X_m to total respiratory impedance.

Table 10 Corrected values for R_{rs} , I_{rs} , and C_{rs} in 6 normal dogs

Dog #	Body wt. kg	FRC ml	Corrected R_{rs} cm H ₂ O/l/s	Corrected I_{rs} cm H ₂ O/l/s ²	Corrected C_{rs} ml/cm H ₂ O		C_{rs}/FRC cm H ₂ O ⁻¹
					Abs.	per kg	
1	20	663	1.214	0.0133	32.4	1.62	0.0489
2	20	663	1.468	0.0109	27.6	1.38	0.0416
4	20	663	1.35	0.007	31.9	1.6	0.0481
5	22	729	0.984	0.0106	33.2	1.51	0.0455
6	25	829	1.682	0.021	27.9	1.12	0.0337
8	23	762	1.091	0.0056	31.7	1.38	0.0416
$\bar{x}$	21.7	718	1.298	0.0114	30.6	1.435	0.0432
SE	0.84	28	0.104	0.0022	0.9	0.076	0.0056

$\bar{x}$: mean; SE: standard error.

Figure 36 Relative contributions of compliance reactance (X_c) and inertance reactance (X_m) to the total reactance (X) and total impedance ($|Z|$) based on the mean values for R_{rs} , I_{rs} , and C_{rs} given in Table 10.

Effect of Loading in Abdomen

Five dogs (Dogs # 6,7,8,9,10) were used to study the effect of mass loading of the abdomen. Values for R_{rs} , I_{rs} , and C_{rs} for all five dogs in this experimental condition can be found in Table 9. Table 11 shows the mean values of the control and mass loaded parameters for four dogs (Dogs # 6, 7, 8, and 10) in which ten pounds of weight were used. (twenty pounds of weight were used in Dog # 9.) Student t-value for comparing the two means for each parameter are also given in the table.

No significant difference was detected in the value for R_{rs} or I_{rs} . However, the abdominal loading produced a very significant decrease in compliance ($p < 0.01$). Twenty pounds of abdominal weight (Dog # 9) produced a change in compliance which was about twice that produced by ten pounds.

Effect of External Resistor

Respiratory impedances in 8 dogs (Dogs # 3-10) were measured with and without an additional external resistor connected in series to the endotracheal tube. The external resistor was made of an orifice (length 18 mm, diameter 6 mm). placed in the middle of two identical short tubes (length 65 mm, diameter 12.5 mm). Its resistance was independently determined as $1.37 \text{ cm H}_2\text{O/l/s}$ at flow rates in the range used for impedance measurements at various frequencies.

Values for R_{rs} , I_{rs} , and C_{rs} in the 8 dogs are given in Table 9. Mean values $\pm$ SE for control parameters and for those obtained with external resistor are shown in Table 12. The t-values for comparing the

Table 11 Variations in R_{rs} , I_{rs} , and C_{rs} due to mass loading of the abdomen.

	Control	Mass Loading	t-value
R_{rs} (cm H ₂ O/l/s)	2.748±0.19	2.848±0.225	0.34
I_{rs} (cm H ₂ O/l/s ²)	0.079±0.004	0.076±0.004	0.59
C_{rs} (ml/cm H ₂ O)	28.27±1.2	20.65±1.08	4.71

Values are means ± SE.

Table 12 Variations in R_{rs} , I_{rs} , and C_{rs} due to an external resistor

	Control	External Resistor	t-value
R_{rs} (cm H ₂ O/l/s)	2.622±0.136	3.876±0.119	6.93
I_{rs} (cm H ₂ O/l/s ²)	0.076±0.003	0.094±0.002	5.53
C_{rs} (ml/cm H ₂ O)	29.54±1.46	31.1±1.5	0.73

Values are means ± SE.

Table 13 Variations in R_{rs} , I_{rs} , and C_{rs} due to breathing He-O₂ mixture

	Control	He-O ₂	t-value
R_{rs} (cm H ₂ O/l/s)	2.564±0.122	2.379±0.131	1.03
I_{rs} (cm H ₂ O/l/s ²)	0.075±0.003	0.034±0.004	13.46
C_{rs} (ml/cm H ₂ O)	29.7±1.4	32.3±0.97	1.51

Values are means ± SE..

means are also included.

These statistics indicate that the added external resistor did not change compliance. However inertance and resistance were significantly increased ($p < 0.001$). Increased inertance may be attributed to the more turbulent flow in the neighborhood of the orifice because of its small diameter. The difference in the two mean values for R_{rs} was 1.254 cm H₂O/l/s which is within 10% of the independently measured value of the external resistance. This result suggests that this technique may be successful in detecting alteration of respiratory resistance.

Effect of Different Gas

The gas mixture containing 80% He - 20% O₂ was used in ventilating 8 dogs (Dogs # 2, 4 - 10). Mean values for R_{rs} , I_{rs} , and C_{rs} in both the control and the experimental condition are tabulated in Table 13.

Although there was a slight decrease in R_{rs} and slight increase in C_{rs} the mean differences for both of them were not statistically significant ($p > 0.1$). However, the total respiratory inertance, I_{rs} , was greatly reduced ($p < 0.001$). The ratio of the observed inertances was 0.45 and this corresponds to a predicted ratio based on the densities of the two gas mixtures of 0.33.

Effect of Drugs

Six dogs (Dogs # 11, 12, 15 - 18) were used in studying the effect of two drugs that effect bronchomotor tone. After the administration of physostigmine, a general and progressive increase in the

magnitude of the impedance at every frequency was observed, and a maximum effect was reached after 1 to 1.5 hours [74]. Atropine was administered intravenously one hour after physostigmine. Estimated values for R_{rs} , I_{rs} , and C_{rs} from impedance data for each dog in control state and under the influence of these two drugs are given in Table 14. Note that the impedance data for atropine was taken 45 minutes after its administration.

R_{rs} increased to 135% of control value after physostigmine and this increase was associated with a significant increase in I_{rs} and a slight decrease in C_{rs} . In all but two dogs (Dogs # 16 and 18), atropine almost completely reversed the increases in R_{rs} and I_{rs} induced by physostigmine. Physostigmine, a acetylcholinesterase inhibitor, can cause bronchoconstriction by stimulation of the parasympathetic receptors and atropine acts as a bronchodilator by inhibiting the bronchoconstrictive effects of parasympathetic mediators. One possible reason for the failure of atropine in Dogs #16 and 18 is that during the period when the impedance data was collected after the administration of atropine the effect of atropine might not strong enough to counteract the physostigmine which might reach its maximum effect during that period.

Two Diseased Cases

Data from two diseased dogs (Dogs # 13 and 14) were also analyzed. In the obstructed dog (Dog # 13), the respiratory resistance ($3.7 \text{ cm H}_2\text{O}/\ell/\text{s}$) and inertance ($0.068 \text{ cm H}_2\text{O}/\ell/\text{s}^2$) were found to be higher than those for normal dogs in the same study (Table 14) by 50% and 24% respectively while the total compliance ($0.019 \ell/\text{cm H}_2\text{O}$) was 24% lower. The value for

Table 14 Estimated values for R_{rs} , I_{rs} , and C_{rs} for the 6 normal dogs used in the drug study

Dog #	Wt. kg	Control				Physostigmine				Atropine			
		R_{rs}	I_{rs}	C_{rs}	J_m	R_{rs}	I_{rs}	C_{rs}	J_m	R_{rs}	I_{rs}	C_{rs}	J_m
11	17.3	1.93	.059	.028	.23	3.38	.075	.020	.80	2.48	.059	.023	1.1
12	17.3	2.03	.060	.023	.50	2.61	.076	.018	.67	2.01	.062	.023	.55
15	15	2.04	.060	.023	.49	2.58	.077	.019	.65	2.02	.063	.023	.59
17	22.7	3.16	.053	.018	1.8	3.64	.070	.014	2.2	3.15	.051	.018	1.8
16	21.8	2.75	.051	.030	.48	3.96	.058	.028	.75	4.86	.051	.029	.86
18	17.3	2.81	.049	.029	.63	3.84	.055	.023	.43	5.27	.05	.027	.82
$\bar{x}$	18.6	2.46	.055	.025	.69	3.33	.069	.020	.92	2.41*	.059*	.022*	.95
SE	.12	.21	.002	.002	.23	.25	.004	.002	.26	.27	.003	.001	.19

$\bar{x}$ = mean; SE = standard error; J_m = mean residual sum of squared errors

units: R_{rs} , cm H₂O/l/s; I_{rs} , cm H₂O/l/s²; C_{rs} , 1/cm H₂O

* Mean value is taken over the first four entries in the corresponding column.

J_m was 0.6 which was comparable to those for normal dogs in this study. This relatively small value of J_m indicates that the respiratory system of this dog can be also modeled with the second order R-I-C circuit. This indication becomes more obvious when noting the similarities in the frequency dependence of impedance for this dog and for the normal dogs in this study as shown in Figure 34. The same finding was also described by Michaelson et al. [30] in the study of pulmonary mechanics by spectral analysis of forced random noise.

In Dog # 14 which had a congenitally narrowed trachea as diagnosed by an X-ray, a greatly increased airway resistance would be expected. Indeed, this dog was found to have $R_{rs} = 9.78 \text{ cm H}_2\text{O/l/s}$ which was four times the control value. The total inertance ($0.21 \text{ cm H}_2\text{O/l/s}^2$) was also greatly increased. Value for J_m in this case, 7.0, was much higher than in other cases (Table 14), and this implies that the simple R-I-C model may be inadequate for representing the respiratory mechanical system in this particular dog.

5.3 A Comparison of Forced Oscillation and Other Conventional Techniques for Measuring R_{rs} and C_{rs}

In Dogs # 6 - 10, total respiratory resistance, R_{rs} , and compliance, C_{rs} , were measured both by the forced oscillation and a tidal breathing method as described in Section 4.3. Values for R_{rs} and C_{rs} determined by using these two methods are compared in Figures 37 A and B in which the subscripts "dyn" and "fo" are used respectively to denote the results from tidal breathing and forced oscillation techniques.

As made clear in the last section, the forced oscillation technique in combination with a parameter estimate algorithm is sensitive

for detecting changes in mechanical parameters induced by various mechanical interventions. It was found that these changes were also detectable by using the tidal breathing method. From Fig. 37 it can be seen that dogs with external resistor had the highest values for R_{dyn} or R_{fo} and the same compliance measurements (C_{dyn} or C_{fo}) as in the control state; Dogs with abdominal mass loading had the lowest values for C_{dyn} or C_{fo} and a slightly increased R_{dyn} or R_{fo} ; Dogs breathing He-O₂ mixture showed no prominent differences in resistance and compliance from the control measurements.

Undoubtedly, values for R_{rs} and C_{rs} obtained from these two different techniques should be highly correlated. In fact, it was found that the sample correlation coefficients were respectively $r=0.87$ between R_{dyn} and R_{fo} and $r=0.80$ between C_{dyn} and C_{fo} . Furthermore a linear model was found to be adequate in explaining the relationship between R_{dyn} and R_{fo} or between C_{dyn} and C_{fo} . By the method of least squares, linear regression lines for C_{dyn} vs C_{fo} and R_{dyn} vs R_{fo} are given in Eqs. 5.2 and 5.3.

$$C_{dyn} = -3.2 \times 10^{-4} + 1.38 C_{fo} \quad (5.2)$$

$$R_{dyn} = -8.9 \times 10^{-3} + 1.44 R_{fo} \quad (5.3)$$

The coefficients in these two equations are all highly significant.

There two possible reasons for explaining the discrepancy between R_{dyn} and R_{fo} . Airflow rates employed in the tidal breathing method were approximately 1.5 times higher than in the forced oscillation technique, and these higher flow rates could produce an increase in measured R_{rs} . The operating frequencies employed in both methods were

also different. With the forced oscillation technique, impedance data was collected at 26 frequencies between 0.9 and 16 Hz. The resonance frequency where the respiratory impedance (including the apparatus impedance) is pure resistive was about 3.5 Hz, which was approximately 10 times the rate of artificial ventilation used in tidal breathing. The resistance at resonance frequency was usually only slightly less than the estimated R_{rs} from the whole impedance data. As pointed out in the first section of this chapter, the total resistance (real part of the impedance) decreased with increasing frequency in every dog studied. This frequency-dependent tendency was particularly strong for frequencies between 0.9-4 Hz. Therefore, by extrapolation, R_{dyn} which was determined at 0.35 Hz is expected to have value higher than that obtained with the forced oscillation technique.

Figure 38 presents static pressure-volume (p-v) curves of the total respiratory systems during deflations in each of the four experimental conditions: control, external resistor, mass loading and breathing He-O₂, for Dogs #6,7,8,9 and 10. The relative positions or shapes (or both) of the curves showed slight individual-to-individual variations. The mass loading curves tended to be to the right of the other curves. The other interventions, external resistor and breathing He-O₂, had little effects on the position and shape of the p-v curve.

Figure 39 presents a typical p-v curves (Dog #8) in the control and the mass loaded state. Hysteresis was present, and the static respiratory compliance (C_{st}) calculated from the inflation p-v curve was $20\% \pm 1.4\%$ less than that measured from the deflation curve. Values for average C_{st} are given in Table 9. Values for C_{st} were not significantly influenced by the introductions of external resistor and breathing of

Figure 37 Comparison of the forced oscillation technique (fo) with the tidal breathing method (dyn) in measuring R_{RS} (A) and C_{RS} (B).

Figure 38 Static deflation pressure-volume curves in 5 paralyzed apneic dogs.

Figure 39 Hysteresis phenomena in p-v curves.

He-O₂. Mean values for C_{st} were 64±4 (control), 67±3 (external resistor), and 65±3 (He-O₂) ml/cm H₂O. However with 10 lbs of abdominal loading, mean values for C_{st} (44±3 ml/cm H₂O) were significantly decreased. In addition, the 20 lbs of weight placed on Dog #9 caused a more marked decrease in C_{st}.

A comparison of C_{st} with C_{fo} obviously showed that values for C_{st} greatly exceeded those for C_{fo} although their correlation was high (r=0.85). The author cannot explain this discrepancy. It is suspected that certain systematic experimental error was introduced during collecting the static pressure and volume data.

Table 15 Static respiratory compliance measured in 5 dogs

Dog no.	Control	External Resistor	Mass Loading	He-O ₂
6	74	67	51	67
7	62	69	46	72
8	65	67	41	57
9	70	76	42	71
10	48	55	38	56
$\bar{x}$	64	67	44 ✓	65
SE	4	3	3	3

unit: ml/cm H₂O

10 lbs of weight was used for Dog #6,7,8 and 10, but 20 lbs for Dog #9.

5.4 Correlations with Works of Others

Hull and Long [50] used the forced oscillation technique similar to that described in this study except the oscillations were applied to the body surface and the data analysis was based on a manually manipulated electrical subtraction technique. They reported the following values for 7 normal, anesthetized, apneic (induced by hyperventilation) dogs:

$R_{rs}=4.3\pm0.9$ cm H₂O/l/s, $C_{rs}=0.022\pm0.004$ l/cm H₂O, $I_{rs}=0.041\pm0.008$ cm H₂O/l/s², $f_o=5.4\pm0.5$ Hz, and a damping ratio of 1.57 ± 0.14 .

The author is unaware of any other studies using forced oscillation technique in dogs, however there are considerable data on resistance and compliance as measured by other techniques. Dain and Gold [99] using an electrical subtraction technique (Mead and Wittenberger) found that the average pulmonary resistance for three conscious, standing dogs (wt. 19-22 kg) was 1.33 cm H₂O/l/s and the total respiratory resistance was 1.26 ± 0.09 (SE) while they were anesthetized, supine and paralyzed, and artificially ventilated. These values agree reasonably with our value for R_{rs} obtained from the forced oscillation technique. Our values for R_{rs} are also similar to those for pulmonary resistance reported by others in dogs anesthetized with various anesthetic agents [100,101,78]. The values of C_{rs} measured in this study compare favorably with values reported in the literature as shown in Table 16. Absolute values for our C_{rs} were slightly higher than others, but this is attributed to the larger sizes of our dogs. Mean values for specific compliance (C_{rs}/FRC) or compliance per kg of body weight in our dogs were slightly lower.

Sharp et al. [104] have reported that mass loading of the abdomen reduces the slope of the linear portion of the thoracic p-v curve both in conscious subjects and in anesthetized paralyzed subjects. Ting [105] reported the reduction in total respiratory compliance for thoracoabdominal loading. These findings together with those of others [106,107] are consistent with the changes in the total compliance that were observed in this study.

Table 16 Values for C_{rs} reported in the literature

no. of dogs	By.wt. kg	Anesthesia	Body Position	C_{rs}		C_{rs}/FRC	Para- lyzed	Ref
				Abs.	Per kg			
15	12.6	Pentobarbital	Supine	17.78	1.41	0.0415	No	78
17	17.7	Thiopental	Supine	30.1	1.7	0.05	Yes	102
6	8-20.6	Pentobarbital	Supine	-	1.6	0.0471	Yes	103
7	12	Diallylbarbituric	Lateral	22	1.83	0.0538	Yes	50
6	21.7	Pentobarbital	Supine	30.6	1.435	0.0432	Yes	*

units: C_{rs} , ml/cm H_2O , C_{rs}/FRC , cm H_2O^{-1}
 FRC is predicted value.

* present study

The mixture of 80% He - 20% O_2 (with a density of 1/3 and viscosity 1.11 times those of air) was proposed as physiological therapy for patients with obstructive lung diseases [108]. Barach [109] reported that less respiratory effort was required for human-beings and dogs breathing the He- O_2 mixture. McIlory et al. [5] and Maio et al. [110] reported large decreases in airway resistance during spontaneous breathing of He- O_2 mixture in normal subjects and subjects with asthma.

The flow rates used in the experiments of this study (approximately 0.3 l/s for air and 0.4 l/s for He- O_2) were relatively low compared to those in other studies using He- O_2 mixtures. In fact, it is believed that in most areas of the airways the flow pattern was nearly laminar [111] for both gases. For laminar flow, flow resistance does not depend on flow rate but instead, depends upon the viscosity of gas, which is slightly higher for the He- O_2 mixture. This may explain the insignificant reduction in total respiratory resistance that was observed in this study when the He- O_2 mixture was used. An additional factor is the fact that the airway resistance accounts for about 60% of the total respiratory resistance [112] and thus small changes in airway resistance would have

an even smaller effect on the total resistance.

Most of the pressure associated with inertial effects is attributed to accelerating the lightest element in the respiratory system, the gas in the airways. This results since the gas must be accelerated to high velocities whereas the low velocities associated with lung and chest wall motion require little acceleration. The density of the gas is therefore the most important factor in determining the total respiratory inertance. Consequently, the 55% reduction in inertance for the He-O₂ mixture (Table 13) is fairly consistent with the fact that this mixture has a density which is one third that of air.

5.5 Discussions on the Experimental Conditions

During forced oscillations, the pressure and flow measurements at a frequency around 1.2 Hz were not as stable as at other frequencies. This was probably caused by cardiac pulsations and could be suppressed by increasing the intensity of the forced oscillation at this particular frequency. However it was sometimes necessary to repeat the same measurement several times at this frequency and use averaged readings.

While the dog was breathing the He-O₂ mixture from a close system, CO₂ concentration in the gas bag increased during the period of forced oscillations. However, since the maximum concentration of CO₂ was about 5%, its effect on diluting the He-O₂ mixture was ignored.

Since the slowest time constant of the respiratory system including the endotracheal tube was on the order of one tenth of a second, a couple of seconds was adequate to reach a steady state condition. In practice, the impedance data at each frequency was obtained several seconds after forced oscillations were initiated. Transient effect should

not interfere with obtaining the true frequency response of the respiratory impedance. During static lung inflation and deflation, a pause of 3-4 seconds at each step was definitely enough to obtain a steady trans-thoracic pressure tracing.

As mentioned in Section 3.1, the use of linear electrical circuit model to represent the respiratory system is valid only when the system operates in a relatively small region around a particular operating point so that the inherent nonlinearities of the system can be validly linearized. This constraint was satisfied during forced oscillations, since forced oscillatory mouth pressure, flow, and volume were almost sinusoidal waveforms oscillating about the FRC of the paralyzed apneic dog. Table 17 gives an example of peak values of forced oscillatory mouth pressure and flow and calculated values of volume obtained by dividing peak flow by the angular frequency. It is evident that the dynamic operating area of the respiratory system during forced oscillations was so restricted in comparison to the physically admissible region that linear approximate to the nonlinear respiratory system was acceptable.

As also shown in Table 17, the flow rates varied with the frequencies of the forced oscillations. This variation might result in different flow patterns and flow resistance in the tracheobronchial tree at different frequencies. Actually this was probably not the case, since all flow rates were very small, laminar flow dominated in all cases and hence the flow resistances at all frequencies were basically independent of the flow rates employed. Nevertheless, it is still desirable to keep flow rates constant at all frequencies of interest. This can be achieved by either adding certain feedback circuit in the present impedance analyzer [71] or increasing internal impedance of the

air pressure generator [28].

In obtaining the static pressure-volume curve, volume readings were taken directly from the graduations on the syringe. The pressure and temperature differences between lungs and the syringe were not taken into account. Actually the apparent readings for lung volume were different from the true values. But, since in any state of the inflation and deflation process, this difference was very small so that no correction was necessary.

Table 17 Measured values for mouth pressure, flow and volume during forced oscillations

Frequency (Hz)	Pressure (cm H ₂ O)	flow (l/s)	volume (ml)
0.9	1.23	0.19	33.6
1.01	1.18	0.19	29.9
1.12	1.32	0.23	32.7
1.26	1.23	0.24	30.3
1.41	1.18	0.26	29.3
1.59	1.22	0.30	30.0
1.8	1.08	0.28	24.8
2.01	0.93	0.26	20.6
2.24	1.03	0.32	22.7
2.53	0.88	0.30	18.9
2.82	0.93	0.33	18.6
3.18	0.83	0.32	16.0
3.51	0.88	0.33	15.0
3.99	0.78	0.32	12.8
4.42	0.77	0.33	11.9
4.94	0.82	0.33	10.6
5.58	0.86	0.33	9.4
6.27	0.85	0.30	7.6
7.14	0.90	0.28	6.2
7.98	1.18	0.30	6.0
9.0	1.07	0.28	5.0
10.1	1.16	0.26	4.1
11.2	1.01	0.21	3.0
12.6	1.19	0.21	2.7
14.2	0.84	0.12	1.3
15.9	1.02	0.13	1.3

5.6 Summary

By using the forced oscillation technique respiratory impedance (Z_{rs}) at 26 frequencies between 0.9 and 16 Hz were determined in 18 dogs during two separate periods. The 10 dogs (Dogs #1-10) used during the second period were subject to various mechanical interventions; on the other hand, during the first period, 6 dogs were subject to pharmacological interventions and the remaining two were diseased dogs. It was found that alteration in respiratory mechanics due to these interventions and abnormal conditions were significantly reflected in the response of Z_{rs} to different frequencies.

By using a parameter estimation algorithm, the total respiratory resistance (R_{rs}), inertance (I_{rs}), and compliance (C_{rs}) were estimated from the impedance data, based on a R-I-C second order model. For normal dogs, $R_{rs}=1.3\pm0.1$ (SE) cm H₂O, $I_{rs}=0.0114\pm0.0022$ cm H₂O/l/s², and $C_{rs}=1.435\pm0.076$ ml/cm H₂O per kg, which are all in the normal ranges for these parameters. The variations of R_{rs} , I_{rs} , and C_{rs} from control values due to various interventions and respiratory diseases were consistent with the predicted effects and justified by works of other investigators.

R_{rs} and C_{rs} were also determined by using the tidal breathing technique. Although this more conventional method produced higher values of R_{rs} and C_{rs} than the forced oscillation technique, the discrepancies were not exceeding large and their correlation was very high.

In a word, the forced oscillation technique combined with the parameter estimation algorithm has been demonstrated to be sensitive in detecting changes in respiratory mechanical parameters caused by a wide scope of different situations.

CHAPTER VI

SUMMARY AND SUGGESTIONS

6.1 Summary and Conclusion

The study of the respiratory mechanical system can be facilitated by using its dynamic analogies. The analogous electrical circuits are most convenient for this purpose because of the extensive theory that has been developed for these systems.

Many investigators have established that the respiratory compliance and resistance are almost independent of frequency in the practical range of measurement in normal subjects, but they are frequency-dependent in patients with chronic obstructive lung diseases. Also it is generally accepted that the respiratory mechanical system in normals can be represented by a second order RLC circuit model, but more complex models (e.g. two-compartment parallel models) are necessary to account for the respiratory mechanics in patients with lung diseases.

Respiratory impedance (Z_{RS}) is a convenient method in characterizing the mechanical properties of the respiratory system. Any significant physiological alterations in the respiratory system should be reflected by the changes in the frequency response of Z_{RS} . The magnitude and phase angle of Z_{RS} at 26 frequencies between 0.9 and 16 Hz were obtained by employing the forced oscillation technique with the use of a specially designed device, the "Impedance Analyzer". Under the experimental conditions in which the impedance data was collected, the

physical signals (pressure, flow, and volume) were restricted to operate in a sufficiently small portion of the physically admissible region so that the inherently nonlinear respiratory mechanical system could be approximated with a linear system.

The analogous electrical circuit model provides the theoretical basis for interpreting the impedance data obtained from the forced oscillation technique. Based on a realistic model, certain physiologically significant parameters in the respiratory system were estimated simultaneously from the impedance data by employing a parameter estimation technique. The estimation algorithm used in this study is a combination of several gradient methods and a random searching routine. It is universally convergent and applicable in cases where the parameters are subject to range constraints and the criterion surface contains multiple minimums.

This new approach was used to study the respiratory mechanics in dogs. It was found that Z_{RS} in normal dogs behaved approximately like a second order system. The following values of the respiratory resistance (R_{RS}), inertance (I_{RS}), and compliance (C_{RS}) were obtained in normal dogs: $R_{RS} = 1.298 \pm 0.104$ (SE) cm H₂O/l/s, $I_{RS} = 0.0114 \pm 0.0022$ cm H₂O/l/s², and $C_{RS} = 30.6 \pm 0.9$ ml/cm H₂O, which are all in the normal ranges for these parameters. The variations of R_{RS} , I_{RS} , and C_{RS} from control values due to mechanical (mass loading in the abdominal region, adding an external resistor, and breathing a He-O₂ mixture) and pharmacological (physostigmine and atropine) interventions were consistent with the predicted effects. R_{RS} in a dog with narrowed trachea was markedly increased. R_{RS} was also raised in dog with obstructive lung

disease but to a less degree. Good correlation existed between values for R_{rs} or C_{rs} obtained with forced oscillations and with tidal breathing.

All these findings have led to the conclusion that the approach proposed in this dissertation provides an alternate technique for studying the mechanics of the respiratory system. This approach is accurate in determining the respiratory mechanical parameters and it is sensitive to variations caused by a wide varieties of perturbations.

6.2 Applications

Since the parameter estimation algorithm used in this research is for the most part independent of the particulars of this problem, only slight modifications are necessary to allow its application to other parameter estimation problems in the fields of economics, engineering, and biology. One of the most immediate applications of this algorithm may be the fitting of data with a nonlinear algebraic equation with certain unknown parameters. In addition to the respiratory parameter estimation problem described in this dissertation, this algorithm has also been used to study the recoverability of ventilation-perfusion ratios from inert gas retention measurements [80].

Since the general methodology and techniques (circuit theory, frequency response analysis, parameter optimization) used in developing and evaluating the respiratory mechanical models have been successful, it may provide an approach for studying other biological or physiological problems. The extension to studies of the cardiovascular system are apparent and additional promising areas include the study of muscle mechanics and ion transport across cell membranes.

6.3 Extensions and Suggestions

The parameter estimation algorithm employed in this study is a combination of several gradient methods and a uniform random search routine. The several gradient methods together are responsible for locating the relative minimum of the criterion surface. Although this algorithm has proved to be universally convergent, it may converge slowly if the criterion surface exhibits narrow valleys [35]. In its application to the parameter estimation problems in this study, it was found that the algorithm converged very slowly and showed difficulty in reaching the minimum within a practical computing time when the model used to represent the respiratory system contained two parallel pathways. There are several techniques for improving the performance of gradient methods. Among them are the "method of parallel tangent" due to Shah, Buehler and Kempthorne [81] and the "deflected gradient" method of Fletcher, Powell and Davidon [82]. It will be interesting to investigate whether these alternatives are more powerful in handling the same estimation problems as dealt in this study, particularly when the models become more complicated.

The impedance data available for the study of this dissertation were taken at 26 frequency components logarithmically spaced between 0.9 and 16 Hz. This data was sufficient for determining the three parameters in the second order R-I-C model by using the parameter estimation algorithm. However, as pointed out in Chapter 3, more impedance data over a wider frequency range is necessary for successful estimation of parameters which appear in a more complex model. This model may include certain important parameters of the respiratory function which have previously been difficult to assess. These includes the contribution

of small airways to airways resistance and the compliance of airways at various lung volume [37]. It is of considerable physiological interest to identify those parameters using the approach employed in this study. Therefore it is worthwhile to extend the experimental design to provide more impedance data over a wider frequency range (e.g. 1 - 50 Hz).

In the present study, the mechanical properties of the respiratory system in dogs were investigated by using a new approach which is actually a combination of forced oscillation technique and parameter estimation method. Using this approach, it is possible and valuable to conduct similar investigations on other animals whose lungs according to Tyler's classification belong to the other two types of mammalian lung structure (Dog lungs belong to the second type) [75]. Since, within certain limits, anatomy dictates function, it is expected to find differences in mechanical behavior between the three distinct subgross lung types.

Experiences accumulated on experimental design and data analysis during animal studies can greatly facilitate a similar study in man. By imposing forced oscillations on spontaneously breathing patterns, the respiratory parameters in conscious subjects can be determined by using the same approach. The possible subjects include normals, patients with various lung's diseases, and cigarette smokers. The physiological abnormalities in human respiratory system can be investigated by this approach.

In addition, the approach leads itself to rapid testing using random oscillation which contains all frequencies of interest [30]. The respiratory impedance data over a wider frequency range can be made available much more rapidly with random forced oscillations than by

"deterministic approach" described in this dissertation and it would be particularly valuable with children and with critically ill patients. The one limitation of the random forced oscillation approach is the increased complexity of the data analysis.

APPENDIX A

COMPUTER PROGRAMS

This appendix is composed of a listing of the Fortran program for the estimation of respiratory parameters from the forced oscillatory impedance data. The complete program as listed applies only to the estimation of parameters in the series R-I-C model. However, it can be used to estimate parameters in other models just by changing two subroutines, MODEL and REGRES. This program can also be applied to other parameter estimate problems after rewriting three problem-oriented subroutines, INPUT, MODEL and REGRES.

This program is directly executable in IBM 360/165 system. It is also executable in other comparable computer systems without requiring any modifications except the possible changes of system library subroutine names, which are called in the program.

A brief description of this program is contained in the following paragraphs. Detailed discussions can be found in Chapter 3 of this dissertation and in Reference 57 where the original version of this program was developed.

The main program is simply a proper collection of various subroutines. It implements the flow chart shown in Figure 18 in Chapter 3. The necessary parameters for the entire program are first set up. They are as follows:

NP = number of parameters to be estimated
 NPOINT = number of elements in the data vector, Y0.
 NTRIAL = total number of independent parameter determinations desired.
 MRAND = number of independent parameter vectors to be generated in random search (RANSER subroutine)
 NLOOP = maximum number of iterations in an independent parameter determination.
 IRPAT = an odd integer less than 9 digits for RANDU subroutine used in random searching.
 CE = initial guess for the unknown parameter vector provided by the human experimenter.
 A = vector of lower limits for parameters.
 B = vector of upper limits for parameters.
 EBDRY = constant used in GRPREX subroutine to prevent division by zero.
 ZSTOP, EPHI, EC, EGRAD = values for the stop criteria (see § 3.2.3)

The INPUT subroutine accepts the experimental impedance data including magnitude and phase at each frequency and then set up two arrays for the dependent variable (Y0) and independent variable (FREQ). Based on a given parameter vector (C) and the frequency sequence (FREQ), the MODEL subroutine computes the model response (Y). The SUMSQR subroutine simply computes the value of the criterion function (PHI) at a given parameter vector (C).

The REGRES subroutine provides the gradient vector (GRADP) of the criterion function with respect to the parameter vector and the parameter change vector (BETA) of the basic Gauss-Newton method from a specified parameter vector (C). Note that the two dimensional array X which contains the derivative matrix Q as defined in Eq. (3.24) is

the only variable to be changed in this subroutine if the entire program is to be applied to the other models or problems.

The LOCMIN subroutine implements the flow chart as shown in Figure 17 in Chapter 3. It can determine a local minimum of the criterion function by calling three subroutines, REGRES, GRASER, and GRPREX, which respectively implement the basic Gauss-Newton, Optimum gradient searching and Gradient projection methods. The optimum parameter vector is found with a given starting vector and within the range specified by the lower and upper bounds of the parameters (A and B). After computation the optimum parameter vector is returned in the array C1. The iteration process is terminated by one of the four stop criteria (EPHI, EGRAD, EBDY, and NLOOP). Intermediate results of the estimation process can be selectively obtained by specifying the argument INTRVL.

The RANSER subroutine implements the uniform random search to provide a starting parameter vector for the LOCMIN subroutine. This vector, C1, is selected within a specified number of independent trials (MRAND). A library subroutine (RANDU) is called by this subroutine, which is used to generate a sequence of uniformly distributed random number.

Finally, it should be noticed that in this program all arrays except the one, S, used in the REGRES subroutine have sizes large enough to allow the problem to be used in any situation where the number of parameters and number of data points are not greater than 20 and 100 respectively. The array S must have a dimension exactly equal to $NP \times NP$. Additionally, it is worthwhile to know that most messages

which are prohibited in this listed program because they are only related to the execution process of the algorithm and do not effect the final result can be made available by removing the first character "C" in the statement which contains the "PRINT" instruction.

C
C
C
C

INPUT

```

SUBROUTINE INPUT(FREQ,YO)
  DIMENSION YO(100),FREQ(50),AMP(50),ANG(50)
  COMMON NPOINT,NP,ZSTOP
  PRINT 11
  FORMAT(//,' ENTER INPUT SUBROUTINE. '/')
  NH=NPOINT/2
  READ(5,1) (FREQ(I),AMP(I),ANG(I),I=1,NH)
  1  FORMAT(F7.2,F7.3,F7.1)
  DO 10 I=1,NH
    YO(I)=AMP(I)*COS(ANG(I)*3.1416/180.)
    YO(I+NH)=AMP(I)*SIN(ANG(I)*3.1416/180.)
  10  PRINT 12
  12  FORMAT(5X,'RESPIRATORY IMPEDANCE DATA:')
  PRINT 15
  15  FORMAT(/14X,'I',7X,'AMP',11X,'ANG',10X,'REAL',9X,'IMAG',12X,
    *FREQ,')
  PRINT 14, (I,AMP(I),ANG(I),YO(I),YO(I+NH),FREQ(I),I=1,NH)
  14  FORMAT(115,5E15.7)
  PRINT 13
  13  FORMAT(/,' EXIT INPUT SUBROUTINE. ')
  RETURN
END

```

C
C
C
C

MODEL

```

SUBROUTINE MODEL(C,FREQ,Y,NP,NPOINT)
  R-I-C MODEL
  IMPLICIT COMPLEX(J,Z)
  DIMENSION Y(100),C(20),FREQ(50)
  J=(0.,1.)
  NH=NPOINT/2
  DO 10 I=1,NH
    W=2.*3.1416*FREQ(I)
    ZC=1./(J*W+C(3))
    ZL=J*W*C(2)
    Z=C(1)+ZC+ZL
    Y(I)=REAL(Z)
    Y(I+NH)=AIMAG(Z)
  10  CONTINUE
  RETURN
END

```

C
C
C
C

REGRES

```

SUBROUTINE REGRES(C,GRADP,BETA,PHI)
  DIMENSION E(100),X(100,20),S(3,3),GRADP(20),C(20),Y(100),
    *LM(20),KM(20),YO(100),BETA(20),FREQ(50)
  COMMON NPOINT,NP,ZSTOP,YO,FREQ
  PRINT 19
  19  FORMAT(//5X,24HENTER REGRES SUBROUTINE.)
  CALL MODEL(C,FREQ,Y,NP,NPOINT)
  DO 1 I=1,NPOINT
    E(I)=YO(I)-Y(I)
  1  NH=NPOINT/2
  DO 21 I=1,NH
    X(I,1)=1.
    X(I,2)=0.
    X(I,3)=0.
  21  CONTINUE
  NH1=NH+1
  DO 22 J=NH1,NPOINT
    W=2.*3.1416*FREQ(J-NH)
    X(J,1)=0.
    X(J,2)=W
    X(J,3)=1./(W*C(3)**2)
  22  CONTINUE
  DO 6 J=1,NP
    DO 6 I=1,NP
      S(I,J)=0.
    DO 7 I=1,NP
      DO 7 J=1,NP
        DO 7 K=1,NPOINT
          S(I,J)=S(I,J)+X(K,I)*X(K,J)
        CALL MTNV (S,NP,C,LM,KH)
      DO 10 I=1,NP
        GRADP(I)=0.
    10

```

O.C.

```

      DO 11 I = 1, NP
      DO 11 J = 1, NPPOINT
      GRADP(I) = GRADP(I) - 2.*X(J,I)*F(J)
      DO 14 I = 1, NP
      BETA(I) = 0.
      DO 14 K = 1, NP
      BETA(I) = BETA(I) - (1./2.)*(S(I,K)*GRADP(K))
      PHI = 0.
      DO 15 K = 1, NPPOINT
      PHI = E(K)*E(K) + PHI
      PRINT 17, PHI
      C17 FORMAT(7X, 'PHI = ', E16.8)
      C18 PRINT 18
      C18 FORMAT('      EXIT REGRES SUBROUTINE. ')
      RETURN
      END

      CCCCCC
      ***SUMSQR***

      SUBROUTINE SUMSQR(C, PHI, KX)
      DIMENSION YO(100), C1(20), Y(100), E(100)
      COMMON NPPOINT, NP, ZSTOP, YO, FREQ
      PHI = 0.
      KX = 0
      CALL MODEL(C, FREQ, Y, NP, NPPOINT)
      DO 1 I = 1, NPPOINT
      IF (ABS(Y(I)) - ZSTOP) 11, 12, 12
      KX = 1
      PRINT 13
      C13 FORMAT(7X, 'UNSTABLE SYSTEM. SUM-SQUARED ERROR WILL NOT EVALUATED. ')
      *1 GO TO 14
      11 E(I) = YO(I) - Y(I)
      PHI = PHI + E(I)*E(I)
      14 RETURN
      END

      CCCCCC
      ***LOCMIN***

      SUBROUTINE LOCMIN(C1, PHI, A, B, FPHI, EC, EGRAD, EBDY, NLOOP, NP, INTRVL)
      DIMENSION C(20), C1(20), GRADP(20), A(20), B(20), DELTAC(20), BETA(20)
      PRINT 1
      C1 FORMAT(////24H ENTER LOCMIN SUBROUTINE)
      ND = 0
      NS = 0
      NLOOP = 0
      12 NLOOP = NLOOP + 1
      CALL REGRES(C1, GRADP, BETA, PHI)
      PHID = PHI
      ABSVC = 0.
      DO 14 I = 1, NP
      ABSVC = ABSVC + C1(I)*C1(I)
      SCALEF = 0.
      DO 15 I = 1, NP
      SCALEF = SCALEF + GRADP(I)*GRADP(I)
      IF (SCALEF - EGRAD) 26, 43, 43
      26 CONTINUE
      PRINT 27, SCALEF
      C27 FORMAT(61H GRADIENT CONDITION SATISFIED. GRADIENT MAGNITUDE SQUA
      *RED = E15.8)
      GO TO 9
      43 DO 37 I = 1, NP
      C(I) = C1(I) + BETA(I)
      DO 38 I = 1, NP
      IF (C(I) - A(I)) 3, 3, 40
      IF (C(I) - B(I)) 38, 3, 3
      38 CONTINUE
      CALL SUMSQR(C, PHIT, KX, NSMSQ)
      IF (KX) 39, 39, 25
      IF (PHIT - PHID) 41, 25, 25
      39 PHI = PHIT
      DO 42 I = 1, NP
      C1(I) = C(I)
      DELTAC(I) = BETA(I)
      GO TO 17
      3 CONTINUE
      PRINT 4
      C4 FORMAT(112H THE GAUSS-NEWTON PARAMETER CHANGE VECTOR VIOLATES TH
      *E RANGE CONSTRAINTS. A NEWTON-RAPHSON STEP WILL BE TRIED.)
      25 DO 16 I = 1, NP
      DELTAC(I) = -(PHID*GRADP(I))/SCALEF

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DO 4 I = 1, NP
  DELTAC(I) = DELTAC(I)/2.
  C(I) = C(I) + DELTAC(I)
  CALL SUMSOR(C, PHI1, KX)
  IF(KX) 32, 32, 48
CONTINUE
PRINT 49
FORMAT(5X, 'THE STABLE REGION IN PARAMETER SPACE IS NOT CONVEX. EXIT GRASER SUBROUTINE.')
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      N = N + 1
      CALL SUMSQ(C,PHI0,KX)
      IF(KX)43,43,48
      IF(PHI1 - PHI0)11,11,10
      43 PHI2 = PHI1
      PHI1 = PHI0
      GO TO 6
      11 IF(PHI1 - PHI1)12,12,10
      12 DO 13 I = 1,NP
      13 DELTAC(I) = 2.*DELTAC(I)
      GO TO 14
      8 IF(N)16,16,15
      15 DO 17 I = 1,NP
      17 DELTAC(I) = 4.*DELTAC(I)
      18 C(I) = C(I) + DELTAC(I)
      N = N - 1
      PHI0 = PHI1
      PHI1 = PHI2
      CALL SUMSQ(C,PHI2,KX)
      IF(KX)37,37,52
      52 CONTINUE
      PRINT 53
      53 FORMAT(5X, 'DECREASING N HAS CAUSED THE SEARCH TO ENTER AN UNSTABLE
      * REGION. EXIT GRASER SUBROUTINE.')
      GO TO 26
      37 IF(PHI1-PHI2)19,20,20
      20 IF(N)1,1,21
      1 PHI = PHI2
      PRINT 36
      36 FORMAT(7X, 'DECREASING N HAS REDUCED N TO ZERO. EXIT GRASER SUBRO
      * UTINE.')
      DO 25 I = 1,NP
      25 C(I) = C(I) + DELTAC(I)
      GO TO 26
      21 DO 23 I = 1,NP
      23 DELTAC(I) = 2.*DELTAC(I)
      C(I) = C(I) + DELTAC(I)
      GO TO 18
      19 DO 24 I = 1,NP
      24 DELTAC(I) = DELTAC(I)/2.
      N=N+1
      GO TO 14
      16 CONTINUE
      PRINT 34
      34 FORMAT(5X, 'THE STEP FOR N = 0 IS LOCALLY MINIMIZING. EXIT GRASER
      * SUBROUTINE.')
      DO 27 I = 1,NP
      27 C(I) = C(I) + 2.*DELTAC(I)
      PHI = PHI2
      GO TO 26
      14 IF((PHI2-3.*PHI1+2.*PHI0).NE.0.)GO TO 62
      PRINT 63
      63 FORMAT(5X, 'THE QUADRATIC FIT FORMULA COULD NOT BE USED. THE BINARY
      * MINIMUM IS TAKEN')
      GO TO 42
      62 QUADFT = (3.*(PHI2 - 5.*PHI1 + 4.*PHI0))/(4.*(PHI2 - 3.*PHI1 + 2.*
      * PHI0))
      DO 28 I = 1,NP
      28 DELCMN(I) = QUADFT*DELTAC(I)
      C(I) = C(I) + DELCMN(I)
      CALL SUMSQ(C,PHIMIN,KX)
      IF(KX)40,40,48
      40 IF(PHIMIN - PHI1)29,42,42
      42 PHI = PHI1
      PRINT 39,N
      39 FORMAT(5X, 'THE BINARY MINIMUM IS LOWER THAN THE QUADRATIC MINIMU
      * M. EXIT GRASER SUBROUTINE. N=',I3)
      GO TO 22
      29 DO 30 I = 1,NP
      30 C(I) = C(I) + DELCMN(I)
      PHI = PHIMIN
      PRINT 41,N
      41 FORMAT(5X, 'THE QUADRATIC FIT FORMULA WAS USED TO COMPUTE DELTAC.
      * EXIT GRASER SUBROUTINE. N=',I3)
      26 RETURN
      END

      ***GRPREX***

      SUBROUTINE GRPREX(C,DELTAC,NP,A,B,GRADP,KEXIT,FDDRY)
      DIMENSION C(20),DELTAC(20),A(20),B(20),GRADP(20),NOK(20)
      PRINT 31
      31 FORMAT(5X, 'ENTER GRPREX SUBROUTINE')

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APPENDIX B

EXPERIMENTAL DATA

All forced oscillatory impedance data used in this dissertation are listed in this appendix. Totally, 18 mongrel dogs were used for collecting this data. In each of the first 10 dogs (# 1-10), data was collected in control condition and conditions in which part or all of the three mechanical interventions (mass loading in the abdominal region, inserting an external resistor, and breathing 80% He-20% O₂ gas mixture) were respectively introduced. Data for Dogs #11-18 were collected by D.J. Robinson in this laboratory (see references 71 and 74). Six of these eight dogs were subject to the perturbations of two drugs, physostigmine and atropine, which can effect the bronchomotor tone. One of the remaining two dogs, #14, had narrowed trachea and the other, #13, had obstructive airways due to smoking cigarettes for six years.

Each set of data in the listing contains the impedances measured at 26 different frequencies between 0.9 and 16 Hz. The magnitude of the impedance is in the unit of cm H₂O/l/s and the phase angle is in degree.

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Dog 1 control #1			#2			#3			average		
FREQ	MAG.	PHASE	FREQ	MAG.	PHASE	FREQ	MAG.	PHASE	FREQ	MAG.	PHASE
0.90	4.93	-55.0	0.90	5.73	-54.0	0.90	5.81	-54.0	0.90	6.16	-54.3
1.01	5.25	-52.0	1.01	5.22	-50.0	1.01	5.04	-49.0	1.01	5.17	-51.0
1.12	4.76	-53.0	1.12	4.76	-50.0	1.12	4.89	-49.0	1.12	4.96	-51.3
1.26	4.27	-53.0	1.26	4.52	-49.0	1.26	4.20	-46.0	1.26	4.34	-49.3
1.41	3.94	-46.0	1.41	3.94	-44.0	1.41	3.95	-41.0	1.41	4.06	-43.7
1.59	3.53	-44.0	1.59	3.72	-40.0	1.59	3.52	-36.0	1.59	3.59	-40.0
1.80	3.24	-40.0	1.80	3.30	-35.0	1.80	3.04	-34.0	1.80	3.16	-36.3
2.01	3.31	-39.0	2.01	3.13	-34.0	2.01	2.96	-30.0	2.01	3.13	-32.0
2.24	3.01	-32.0	2.24	2.83	-25.0	2.24	2.70	-25.0	2.24	2.84	-26.0
2.52	2.65	-24.0	2.52	2.64	-23.0	2.52	2.48	-21.0	2.52	2.59	-22.7
2.82	2.35	-13.0	2.82	2.45	-15.0	2.82	2.33	-14.0	2.82	2.39	-14.0
3.15	2.45	-1.0	3.15	2.42	-4.0	3.15	2.30	-6.0	3.15	2.40	-5.7
3.50	2.35	-1.0	3.50	2.43	-4.0	3.50	2.32	-4.0	3.50	2.36	-1.7
3.88	2.45	-1.0	3.88	2.23	10.0	3.88	2.13	10.0	3.88	2.28	10.0
4.28	2.31	24.0	4.28	2.22	23.0	4.28	2.50	22.0	4.28	2.28	23.0
4.69	2.56	34.0	4.69	2.56	34.0	4.69	2.58	33.0	4.69	2.56	34.3
5.13	2.70	44.0	5.13	2.74	42.0	5.13	2.72	40.0	5.13	2.75	42.0
5.58	3.10	51.0	5.58	2.93	42.0	5.58	2.88	47.0	5.58	2.97	46.7
6.04	3.26	59.0	6.04	3.39	57.0	6.04	3.23	55.0	6.04	3.33	57.0
6.51	3.78	62.0	6.51	3.93	60.0	6.51	3.72	56.0	6.51	3.81	59.3
6.99	4.21	65.0	6.99	4.31	64.0	6.99	3.99	63.0	6.99	4.17	64.0
7.48	5.44	70.0	7.48	4.70	68.0	7.48	4.47	67.0	7.48	4.87	68.3
7.98	5.42	71.0	7.98	5.61	71.0	7.98	4.87	68.0	7.98	5.30	70.0
8.48	6.15	73.0	8.48	5.76	73.0	8.48	5.77	71.0	8.48	5.89	72.3
8.98	6.51	75.0	8.98	6.88	74.0	8.98	6.13	75.0	8.98	6.51	75.3
9.48	6.19	77.0	9.48	7.24	78.0	9.48	7.60	77.0	9.48	7.68	77.3

Dog 2 control			He-02		
FREQ	MAG.	PHASE	FREQ	MAG.	PHASE
0.90	4.48	-55.0	0.90	7.02	-56.0
1.01	4.73	-54.0	1.01	6.06	-55.0
1.12	5.85	-55.0	1.12	5.64	-53.0
1.26	4.02	-52.0	1.26	5.22	-52.0
1.41	4.49	-48.0	1.41	4.69	-50.0
1.59	4.10	-44.0	1.59	4.33	-45.0
1.80	3.85	-43.0	1.80	4.04	-44.0
2.01	3.56	-38.0	2.01	3.92	-42.0
2.24	3.25	-33.0	2.24	3.44	-40.0
2.52	2.96	-25.0	2.52	3.12	-37.0
2.82	2.78	-23.0	2.82	3.05	-33.0
3.15	2.43	-12.0	3.15	2.74	-30.0
3.50	2.62	-5.0	3.50	2.43	-23.0
3.88	2.46	-3.0	3.88	2.32	-21.0
4.28	2.32	10.0	4.28	2.10	-14.0
4.69	2.45	20.0	4.69	1.95	-5.0
5.13	2.57	30.0	5.13	1.94	-3.0
5.58	2.56	30.0	5.58	2.01	12.0
6.04	3.10	41.0	6.04	2.09	22.0
6.51	3.44	55.0	6.51	2.18	24.0
6.99	3.82	58.0	6.99	2.31	33.0
7.48	4.41	63.0	7.48	2.44	40.0
7.98	4.84	65.0	7.98	2.33	42.0
8.48	5.71	68.0	8.48	2.63	45.0
8.98	7.21	72.0	8.98	2.59	54.0
9.48	7.62	75.0	9.48	2.93	58.0

Dog 3 control ex. R

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FREQ	MAG.	PHASE	FREQ	MAG.	PHASE
0.00	7.00	-59.0	0.90	8.24	0.0
1.01	7.20	-57.0	1.01	8.24	-50.0
1.12	6.80	-55.0	1.12	7.73	-47.0
1.23	6.50	-53.0	1.23	6.05	-34.0
1.34	6.20	-51.0	1.34	5.70	-32.0
1.45	5.90	-49.0	1.45	5.41	-30.0
1.56	5.60	-47.0	1.56	5.11	-28.0
1.67	5.30	-45.0	1.67	4.82	-26.0
1.78	5.00	-43.0	1.78	4.52	-24.0
1.89	4.70	-41.0	1.89	4.22	-22.0
1.90	4.40	-39.0	1.90	3.92	-20.0
2.01	4.10	-37.0	2.01	3.62	-18.0
2.12	3.80	-35.0	2.12	3.32	-16.0
2.23	3.50	-33.0	2.23	3.02	-14.0
2.34	3.20	-31.0	2.34	2.72	-12.0
2.45	2.90	-29.0	2.45	2.42	-10.0
2.56	2.60	-27.0	2.56	2.12	-8.0
2.67	2.30	-25.0	2.67	1.82	-6.0
2.78	2.00	-23.0	2.78	1.52	-4.0
2.89	1.70	-21.0	2.89	1.22	-2.0
2.90	1.40	-19.0	2.90	0.92	0.0
3.01	1.10	-17.0	3.01	0.62	2.0
3.12	0.80	-15.0	3.12	0.32	4.0
3.23	0.50	-13.0	3.23	0.02	6.0
3.34	0.20	-11.0	3.34	-0.28	8.0
3.45	-0.10	-9.0	3.45	-0.58	10.0
3.56	-0.40	-7.0	3.56	-0.88	12.0
3.67	-0.70	-5.0	3.67	-1.18	14.0
3.78	-1.00	-3.0	3.78	-1.48	16.0
3.89	-1.30	-1.0	3.89	-1.78	18.0
3.90	-1.60	1.0	3.90	-2.08	20.0
4.01	-1.90	3.0	4.01	-2.38	22.0
4.12	-2.20	5.0	4.12	-2.68	24.0
4.23	-2.50	7.0	4.23	-2.98	26.0
4.34	-2.80	9.0	4.34	-3.28	28.0
4.45	-3.10	11.0	4.45	-3.58	30.0
4.56	-3.40	13.0	4.56	-3.88	32.0
4.67	-3.70	15.0	4.67	-4.18	34.0
4.78	-4.00	17.0	4.78	-4.48	36.0
4.89	-4.30	19.0	4.89	-4.78	38.0
4.90	-4.60	21.0	4.90	-5.08	40.0
5.01	-4.90	23.0	5.01	-5.38	42.0
5.12	-5.20	25.0	5.12	-5.68	44.0
5.23	-5.50	27.0	5.23	-5.98	46.0
5.34	-5.80	29.0	5.34	-6.28	48.0
5.45	-6.10	31.0	5.45	-6.58	50.0
5.56	-6.40	33.0	5.56	-6.88	52.0
5.67	-6.70	35.0	5.67	-7.18	54.0
5.78	-7.00	37.0	5.78	-7.48	56.0
5.89	-7.30	39.0	5.89	-7.78	58.0
5.90	-7.60	41.0	5.90	-8.08	60.0
6.01	-7.90	43.0	6.01	-8.38	62.0
6.12	-8.20	45.0	6.12	-8.68	64.0
6.23	-8.50	47.0	6.23	-8.98	66.0
6.34	-8.80	49.0	6.34	-9.28	68.0
6.45	-9.10	51.0	6.45	-9.58	70.0
6.56	-9.40	53.0	6.56	-9.88	72.0
6.67	-9.70	55.0	6.67	-10.18	74.0
6.78	-10.00	57.0	6.78	-10.48	76.0
6.89	-10.30	59.0	6.89	-10.78	78.0
6.90	-10.60	61.0	6.90	-11.08	80.0
7.01	-10.90	63.0	7.01	-11.38	82.0
7.12	-11.20	65.0	7.12	-11.68	84.0
7.23	-11.50	67.0	7.23	-11.98	86.0
7.34	-11.80	69.0	7.34	-12.28	88.0
7.45	-12.10	71.0	7.45	-12.58	90.0
7.56	-12.40	73.0	7.56	-12.88	92.0
7.67	-12.70	75.0	7.67	-13.18	94.0
7.78	-13.00	77.0	7.78	-13.48	96.0
7.89	-13.30	79.0	7.89	-13.78	98.0
7.90	-13.60	81.0	7.90	-14.08	100.0
8.01	-13.90	83.0	8.01	-14.38	102.0
8.12	-14.20	85.0	8.12	-14.68	104.0
8.23	-14.50	87.0	8.23	-14.98	106.0
8.34	-14.80	89.0	8.34	-15.28	108.0
8.45	-15.10	91.0	8.45	-15.58	110.0
8.56	-15.40	93.0	8.56	-15.88	112.0
8.67	-15.70	95.0	8.67	-16.18	114.0
8.78	-16.00	97.0	8.78	-16.48	116.0
8.89	-16.30	99.0	8.89	-16.78	118.0
8.90	-16.60	101.0	8.90	-17.08	120.0
9.01	-16.90	103.0	9.01	-17.38	122.0
9.12	-17.20	105.0	9.12	-17.68	124.0
9.23	-17.50	107.0	9.23	-17.98	126.0
9.34	-17.80	109.0	9.34	-18.28	128.0
9.45	-18.10	111.0	9.45	-18.58	130.0
9.56	-18.40	113.0	9.56	-18.88	132.0
9.67	-18.70	115.0	9.67	-19.18	134.0
9.78	-19.00	117.0	9.78	-19.48	136.0
9.89	-19.30	119.0	9.89	-19.78	138.0
9.90	-19.60	121.0	9.90	-20.08	140.0
10.01	-19.90	123.0	10.01	-20.38	142.0
10.12	-20.20	125.0	10.12	-20.68	144.0
10.23	-20.50	127.0	10.23	-20.98	146.0
10.34	-20.80	129.0	10.34	-21.28	148.0
10.45	-21.10	131.0	10.45	-21.58	150.0
10.56	-21.40	133.0	10.56	-21.88	152.0
10.67	-21.70	135.0	10.67	-22.18	154.0
10.78	-22.00	137.0	10.78	-22.48	156.0
10.89	-22.30	139.0	10.89	-22.78	158.0
10.90	-22.60	141.0	10.90	-23.08	160.0
11.01	-22.90	143.0	11.01	-23.38	162.0
11.12	-23.20	145.0	11.12	-23.68	164.0
11.23	-23.50	147.0	11.23	-23.98	166.0
11.34	-23.80	149.0	11.34	-24.28	168.0
11.45	-24.10	151.0	11.45	-24.58	170.0
11.56	-24.40	153.0	11.56	-24.88	172.0
11.67	-24.70	155.0	11.67	-25.18	174.0
11.78	-25.00	157.0	11.78	-25.48	176.0
11.89	-25.30	159.0	11.89	-25.78	178.0
11.90	-25.60	161.0	11.90	-26.08	180.0
12.01	-25.90	163.0	12.01	-26.38	182.0
12.12	-26.20	165.0	12.12	-26.68	184.0
12.23	-26.50	167.0	12.23	-26.98	186.0
12.34	-26.80	169.0	12.34	-27.28	188.0
12.45	-27.10	171.0	12.45	-27.58	190.0
12.56	-27.40	173.0	12.56	-27.88	192.0
12.67	-27.70	175.0	12.67	-28.18	194.0
12.78	-28.00	177.0	12.78	-28.48	196.0
12.89	-28.30	179.0	12.89	-28.78	198.0
12.90	-28.60	181.0	12.90	-29.08	200.0
13.01	-28.90	183.0	13.01	-29.38	202.0
13.12	-29.20	185.0	13.12	-29.68	204.0
13.23	-29.50	187.0	13.23	-29.98	206.0
13.34	-29.80	189.0	13.34	-30.28	208.0
13.45	-30.10	191.0	13.45	-30.58	210.0
13.56	-30.40	193.0	13.56	-30.88	212.0
13.67	-30.70	195.0	13.67	-31.18	214.0
13.78	-31.00	197.0	13.78	-31.48	216.0
13.89	-31.30	199.0	13.89	-31.78	218.0
13.90	-31.60	201.0	13.90	-32.08	220.0
14.01	-31.90	203.0	14.01	-32.38	222.0
14.12	-32.20	205.0	14.12	-32.68	224.0
14.23	-32.50	207.0	14.23	-32.98	226.0
14.34	-32.80	209.0	14.34	-33.28	228.0
14.45	-33.10	211.0	14.45	-33.58	230.0
14.56	-33.40	213.0	14.56	-33.88	232.0
14.67	-33.70	215.0	14.67	-34.18	234.0
14.78	-34.00	217.0	14.78	-34.48	236.0
14.89	-34.30	219.0	14.89	-34.78	238.0
14.90	-34.60	221.0	14.90	-35.08	240.0
15.01	-34.90	223.0	15.01	-35.38	242.0
15.12	-35.20	225.0	15.12	-35.68	244.0
15.23	-35.50	227.0	15.23	-35.98	246.0
15.34	-35.80	229.0	15.34	-36.28	248.0
15.45	-36.10	231.0	15.45	-36.58	250.0
15.56	-36.40	233.0	15.56	-36.88	252.0
15.67	-36.70	235.0	15.67	-37.18	254.0
15.78	-37.00	237.0	15.78	-37.48	256.0
15.89	-37.30	239.0	15.89	-37.78	258.0
15.90	-37.60	241.0	15.90	-38.08	260.0
16.01	-37.90	243.0	16.01	-38.38	262.0
16.12	-38.20	245.0	16.12	-38.68	264.0
16.23	-38.50	247.0	16.23	-38.98	266.0
16.34	-38.80	249.0	16.34	-39.28	268.0
16.45	-39.10	251.0	16.45	-39.58	270.0
16.56	-39.40	253.0	16.56	-39.88	272.0
16.67	-39.70	255.0	16.67	-40.18	274.0
16.78	-40.00	257.0	16.78	-40.48	276.0
16.89	-40.30	259.0	16.89	-40.78	278.0
16.90	-40.60	261.0	16.90	-41.08	280.0
17.01	-40.90	263.0	17.01	-41.38	282.0
17.12	-41.20	265.0	17.12	-41.68	284.0
17.23	-41.50	267.0	17.23	-41.98	286.0
17.34	-41.80	269.0	17.34	-42.28	288.0
17.45	-42.10	271.0	17.45	-42.58	290.0
17.56	-42.40	273.0	17.56	-42.88	292.0
17.67	-42.70	275.0	17.67	-43.18	294.0
17.78	-43.00	277.0	17.78	-43.48	296.0
17.89	-43.30	279.0	17.89	-43.78	298.0
17.90	-43.60	281.0	17.90	-44.08	300.0
18.01	-43.90	283.0	18.01	-44.38	302.0
18.12	-44.20	285.0	18.12	-44.68	304.0
18.23	-44.50	287.0	18.23	-44.98	306.0
18.34	-44.80	289.0	18.34	-45.28	308.0
18.45	-45.10	291.0	18.45	-45.58	310.0
18.56	-45.40	293.0	18.56	-45.88	312.0
18.67	-45.70	295.0	18.67	-46.18	314.0
18.78	-46.00	297.0	18.78	-46.48	316.0
18.89	-46.30	299.0	18.89	-46.78	318.0
18.90	-46.60	301.0	18.90	-47.08	320.0
19.01	-46.90	303.0	19.01	-47.38	322.0
19.12	-47.20	305.0	19.12	-47.68	324.0
19.23	-47.50	307.0	19.23	-47.98	326.0
19.34	-47.80	309.0	19.34	-48.28	328.0
19.45	-48.10	311.0	19.45	-48.58	330.0
19.56	-48.40	313.0	19.56	-48.88	332.0
19.67	-48.70	315.0	19.67	-49.18	334.0
19.78	-49.00	317.0	19.78	-49.48	336.0
19.89	-49.30	319.0	19.89	-49.78	338.0
19.90	-49.60	321.0	19.90	-50.08	340.0
20.01	-49.90	323.0	20.01	-50.38	342.0
20.12	-50.20	325.0	20.12	-50.68	344.0
20.23	-50.50	327.0	20.23	-50.98	346.0
20.34	-50.80	329.0	20.34	-51.28	348.0

[illegible]

Dog 6	control	weight	ex. R	He-02
FREQ	MAG.	PHASE	FREQ	MAG.
0.00	0.00	0.00	0.00	0.00
0.01	0.01	0.00	0.01	0.01
0.02	0.02	0.00	0.02	0.02
0.03	0.03	0.00	0.03	0.03
0.04	0.04	0.00	0.04	0.04
0.05	0.05	0.00	0.05	0.05
0.06	0.06	0.00	0.06	0.06
0.07	0.07	0.00	0.07	0.07
0.08	0.08	0.00	0.08	0.08
0.09	0.09	0.00	0.09	0.09
0.10	0.10	0.00	0.10	0.10
0.11	0.11	0.00	0.11	0.11
0.12	0.12	0.00	0.12	0.12
0.13	0.13	0.00	0.13	0.13
0.14	0.14	0.00	0.14	0.14
0.15	0.15	0.00	0.15	0.15
0.16	0.16	0.00	0.16	0.16
0.17	0.17	0.00	0.17	0.17
0.18	0.18	0.00	0.18	0.18
0.19	0.19	0.00	0.19	0.19
0.20	0.20	0.00	0.20	0.20
0.21	0.21	0.00	0.21	0.21
0.22	0.22	0.00	0.22	0.22
0.23	0.23	0.00	0.23	0.23
0.24	0.24	0.00	0.24	0.24
0.25	0.25	0.00	0.25	0.25
0.26	0.26	0.00	0.26	0.26
0.27	0.27	0.00	0.27	0.27
0.28	0.28	0.00	0.28	0.28
0.29	0.29	0.00	0.29	0.29
0.30	0.30	0.00	0.30	0.30
0.31	0.31	0.00	0.31	0.31
0.32	0.32	0.00	0.32	0.32
0.33	0.33	0.00	0.33	0.33
0.34	0.34	0.00	0.34	0.34
0.35	0.35	0.00	0.35	0.35
0.36	0.36	0.00	0.36	0.36
0.37	0.37	0.00	0.37	0.37
0.38	0.38	0.00	0.38	0.38
0.39	0.39	0.00	0.39	0.39
0.40	0.40	0.00	0.40	0.40
0.41	0.41	0.00	0.41	0.41
0.42	0.42	0.00	0.42	0.42
0.43	0.43	0.00	0.43	0.43
0.44	0.44	0.00	0.44	0.44
0.45	0.45	0.00	0.45	0.45
0.46	0.46	0.00	0.46	0.46
0.47	0.47	0.00	0.47	0.47
0.48	0.48	0.00	0.48	0.48
0.49	0.49	0.00	0.49	0.49
0.50	0.50	0.00	0.50	0.50
0.51	0.51	0.00	0.51	0.51
0.52	0.52	0.00	0.52	0.52
0.53	0.53	0.00	0.53	0.53
0.54	0.54	0.00	0.54	0.54
0.55	0.55	0.00	0.55	0.55
0.56	0.56	0.00	0.56	0.56
0.57	0.57	0.00	0.57	0.57
0.58	0.58	0.00	0.58	0.58
0.59	0.59	0.00	0.59	0.59
0.60	0.60	0.00	0.60	0.60
0.61	0.61	0.00	0.61	0.61
0.62	0.62	0.00	0.62	0.62
0.63	0.63	0.00	0.63	0.63
0.64	0.64	0.00	0.64	0.64
0.65	0.65	0.00	0.65	0.65
0.66	0.66	0.00	0.66	0.66
0.67	0.67	0.00	0.67	0.67
0.68	0.68	0.00	0.68	0.68
0.69	0.69	0.00	0.69	0.69
0.70	0.70	0.00	0.70	0.70
0.71	0.71	0.00	0.71	0.71
0.72	0.72	0.00	0.72	0.72
0.73	0.73	0.00	0.73	0.73
0.74	0.74	0.00	0.74	0.74
0.75	0.75	0.00	0.75	0.75
0.76	0.76	0.00	0.76	0.76
0.77	0.77	0.00	0.77	0.77
0.78	0.78	0.00	0.78	0.78
0.79	0.79	0.00	0.79	0.79
0.80	0.80	0.00	0.80	0.80
0.81	0.81	0.00	0.81	0.81
0.82	0.82	0.00	0.82	0.82
0.83	0.83	0.00	0.83	0.83
0.84	0.84	0.00	0.84	0.84
0.85	0.85	0.00	0.85	0.85
0.86	0.86	0.00	0.86	0.86
0.87	0.87	0.00	0.87	0.87
0.88	0.88	0.00	0.88	0.88
0.89	0.89	0.00	0.89	0.89
0.90	0.90	0.00	0.90	0.90

Dog 7 control				ex. R				He-02			
FREQ	MAG.	PHASE	weight	FREQ	MAG.	PHASE		FREQ	MAG.	PHASE	
0.01	6.91	0.00	7.33	0.01	6.70	-43.00		0.01	5.48	0.00	
0.02	6.90	0.00	7.12	0.02	6.57	-43.00		0.02	5.07	0.00	
0.03	6.89	0.00	6.91	0.03	6.44	-43.00		0.03	4.66	0.00	
0.04	6.88	0.00	6.70	0.04	6.31	-43.00		0.04	4.25	0.00	
0.05	6.87	0.00	6.49	0.05	6.18	-43.00		0.05	3.84	0.00	
0.06	6.86	0.00	6.28	0.06	6.05	-43.00		0.06	3.43	0.00	
0.07	6.85	0.00	6.07	0.07	5.92	-43.00		0.07	3.02	0.00	
0.08	6.84	0.00	5.86	0.08	5.79	-43.00		0.08	2.61	0.00	
0.09	6.83	0.00	5.65	0.09	5.66	-43.00		0.09	2.20	0.00	
0.10	6.82	0.00	5.44	0.10	5.53	-43.00		0.10	1.79	0.00	
0.11	6.81	0.00	5.23	0.11	5.40	-43.00		0.11	1.38	0.00	
0.12	6.80	0.00	5.02	0.12	5.27	-43.00		0.12	0.97	0.00	
0.13	6.79	0.00	4.81	0.13	5.14	-43.00		0.13	0.56	0.00	
0.14	6.78	0.00	4.60	0.14	5.01	-43.00		0.14	0.15	0.00	
0.15	6.77	0.00	4.39	0.15	4.88	-43.00		0.15	0.00	0.00	
0.16	6.76	0.00	4.18	0.16	4.75	-43.00		0.16	0.00	0.00	
0.17	6.75	0.00	3.97	0.17	4.62	-43.00		0.17	0.00	0.00	
0.18	6.74	0.00	3.76	0.18	4.49	-43.00		0.18	0.00	0.00	
0.19	6.73	0.00	3.55	0.19	4.36	-43.00		0.19	0.00	0.00	
0.20	6.72	0.00	3.34	0.20	4.23	-43.00		0.20	0.00	0.00	
0.21	6.71	0.00	3.13	0.21	4.10	-43.00		0.21	0.00	0.00	
0.22	6.70	0.00	2.92	0.22	3.97	-43.00		0.22	0.00	0.00	
0.23	6.69	0.00	2.71	0.23	3.84	-43.00		0.23	0.00	0.00	
0.24	6.68	0.00	2.50	0.24	3.71	-43.00		0.24	0.00	0.00	
0.25	6.67	0.00	2.29	0.25	3.58	-43.00		0.25	0.00	0.00	
0.26	6.66	0.00	2.08	0.26	3.45	-43.00		0.26	0.00	0.00	
0.27	6.65	0.00	1.87	0.27	3.32	-43.00		0.27	0.00	0.00	
0.28	6.64	0.00	1.66	0.28	3.19	-43.00		0.28	0.00	0.00	
0.29	6.63	0.00	1.45	0.29	3.06	-43.00		0.29	0.00	0.00	
0.30	6.62	0.00	1.24	0.30	2.93	-43.00		0.30	0.00	0.00	
0.31	6.61	0.00	1.03	0.31	2.80	-43.00		0.31	0.00	0.00	
0.32	6.60	0.00	0.82	0.32	2.67	-43.00		0.32	0.00	0.00	
0.33	6.59	0.00	0.61	0.33	2.54	-43.00		0.33	0.00	0.00	
0.34	6.58	0.00	0.40	0.34	2.41	-43.00		0.34	0.00	0.00	
0.35	6.57	0.00	0.19	0.35	2.28	-43.00		0.35	0.00	0.00	
0.36	6.56	0.00	0.00	0.36	2.15	-43.00		0.36	0.00	0.00	
0.37	6.55	0.00	0.00	0.37	2.02	-43.00		0.37	0.00	0.00	
0.38	6.54	0.00	0.00	0.38	1.89	-43.00		0.38	0.00	0.00	
0.39	6.53	0.00	0.00	0.39	1.76	-43.00		0.39	0.00	0.00	
0.40	6.52	0.00	0.00	0.40	1.63	-43.00		0.40	0.00	0.00	
0.41	6.51	0.00	0.00	0.41	1.50	-43.00		0.41	0.00	0.00	
0.42	6.50	0.00	0.00	0.42	1.37	-43.00		0.42	0.00	0.00	
0.43	6.49	0.00	0.00	0.43	1.24	-43.00		0.43	0.00	0.00	
0.44	6.48	0.00	0.00	0.44	1.11	-43.00		0.44	0.00	0.00	
0.45	6.47	0.00	0.00	0.45	0.98	-43.00		0.45	0.00	0.00	
0.46	6.46	0.00	0.00	0.46	0.85	-43.00		0.46	0.00	0.00	
0.47	6.45	0.00	0.00	0.47	0.72	-43.00		0.47	0.00	0.00	
0.48	6.44	0.00	0.00	0.48	0.59	-43.00		0.48	0.00	0.00	
0.49	6.43	0.00	0.00	0.49	0.46	-43.00		0.49	0.00	0.00	
0.50	6.42	0.00	0.00	0.50	0.33	-43.00		0.50	0.00	0.00	
0.51	6.41	0.00	0.00	0.51	0.20	-43.00		0.51	0.00	0.00	
0.52	6.40	0.00	0.00	0.52	0.07	-43.00		0.52	0.00	0.00	
0.53	6.39	0.00	0.00	0.53	0.00	-43.00		0.53	0.00	0.00	
0.54	6.38	0.00	0.00	0.54	0.00	-43.00		0.54	0.00	0.00	
0.55	6.37	0.00	0.00	0.55	0.00	-43.00		0.55	0.00	0.00	
0.56	6.36	0.00	0.00	0.56	0.00	-43.00		0.56	0.00	0.00	
0.57	6.35	0.00	0.00	0.57	0.00	-43.00		0.57	0.00	0.00	
0.58	6.34	0.00	0.00	0.58	0.00	-43.00		0.58	0.00	0.00	
0.59	6.33	0.00	0.00	0.59	0.00	-43.00		0.59	0.00	0.00	
0.60	6.32	0.00	0.00	0.60	0.00	-43.00		0.60	0.00	0.00	
0.61	6.31	0.00	0.00	0.61	0.00	-43.00		0.61	0.00	0.00	
0.62	6.30	0.00	0.00	0.62	0.00	-43.00		0.62	0.00	0.00	
0.63	6.29	0.00	0.00	0.63	0.00	-43.00		0.63	0.00	0.00	
0.64	6.28	0.00	0.00	0.64	0.00	-43.00		0.64	0.00	0.00	
0.65	6.27	0.00	0.00	0.65	0.00	-43.00		0.65	0.00	0.00	
0.66	6.26	0.00	0.00	0.66	0.00	-43.00		0.66	0.00	0.00	
0.67	6.25	0.00	0.00	0.67	0.00	-43.00		0.67	0.00	0.00	
0.68	6.24	0.00	0.00	0.68	0.00	-43.00		0.68	0.00	0.00	
0.69	6.23	0.00	0.00	0.69	0.00	-43.00		0.69	0.00	0.00	
0.70	6.22	0.00	0.00	0.70	0.00	-43.00		0.70	0.00	0.00	
0.71	6.21	0.00	0.00	0.71	0.00	-43.00		0.71	0.00	0.00	
0.72	6.20	0.00	0.00	0.72	0.00	-43.00		0.72	0.00	0.00	
0.73	6.19	0.00	0.00	0.73	0.00	-43.00		0.73	0.00	0.00	
0.74	6.18	0.00	0.00	0.74	0.00	-43.00		0.74	0.00	0.00	
0.75	6.17	0.00	0.00	0.75	0.00	-43.00		0.75	0.00	0.00	
0.76	6.16	0.00	0.00	0.76	0.00	-43.00		0.76	0.00	0.00	
0.77	6.15	0.00	0.00	0.77	0.00	-43.00		0.77	0.00	0.00	
0.78	6.14	0.00	0.00	0.78	0.00	-43.00		0.78	0.00	0.00	
0.79	6.13	0.00	0.00	0.79	0.00	-43.00		0.79	0.00	0.00	
0.80	6.12	0.00	0.00	0.80	0.00	-43.00		0.80	0.00	0.00	
0.81	6.11	0.00	0.00	0.81	0.00	-43.00		0.81	0.00	0.00	
0.82	6.10	0.00	0.00	0.82	0.00	-43.00		0.82	0.00	0.00	
0.83	6.09	0.00	0.00	0.83	0.00	-43.00		0.83	0.00	0.00	
0.84	6.08	0.00	0.00	0.84	0.00	-43.00		0.84	0.00	0.00	
0.85	6.07	0.00	0.00	0.85	0.00	-43.00		0.85	0.00	0.00	
0.86	6.06	0.00	0.00	0.86	0.00	-43.00		0.86	0.00	0.00	
0.87	6.05	0.00	0.00	0.87	0.00	-43.00		0.87	0.00	0.00	
0.88	6.04	0.00	0.00	0.88	0.00	-43.00		0.88	0.00	0.00	
0.89	6.03	0.00	0.00	0.89	0.00	-43.00		0.89	0.00	0.00	
0.90	6.02	0.00	0.00	0.90	0.00	-43.00		0.90	0.00	0.00	
0.91	6.01	0.00	0.00	0.91	0.00	-43.00		0.91	0.00	0.00	
0.92	6.00	0.00	0.00	0.92	0.00	-43.00		0.92	0.00	0.00	
0.93	5.99	0.00	0.00	0.93	0.00	-43.00		0.93	0.00	0.00	
0.94	5.98	0.00	0.00	0.94	0.00	-43.00		0.94	0.00	0.00	
0.95	5.97	0.00	0.00	0.95	0.00	-43.00		0.95	0.00	0.00	
0.96	5.96	0.00	0.00	0.96	0.00	-43.00		0.96	0.00	0.00	
0.97	5.95	0.00	0.00	0.97	0.00	-43.00		0.97	0.00	0.00	
0.98	5.94	0.00	0.00	0.98	0.00	-43.00		0.98	0.00	0.00	
0.99	5.93	0.00	0.00	0.99	0.00	-43.00		0.99	0.00	0.00	
1.00	5.92	0.00	0.00	1.00	0.00	-43.00		1.00	0.00	0.00	

Dog 8 control				ex. R				He-02			
FREQ	MAG.	PHASE	weight	FREQ	MAG.	PHASE		FREQ	MAG.	PHASE	
0.01	8.74	0.00	7.96	0.01	7.70	0.00	00				

Dog 11

FREQ	MAG.	PHASE	FREQ	MAG.	PHASE	FREQ	MAG.	PHASE	FREQ	MAG.	PHASE
0.90	5.86	-69.0	0.90	9.67	-58.0	0.90	9.52	-58.0	0.90	9.52	-58.0
1.02	4.94	-66.0	1.02	7.10	-56.0	1.02	5.14	-57.0	1.02	5.14	-57.0
1.21	4.22	-65.0	1.21	7.10	-60.0	1.21	5.97	-62.0	1.21	5.97	-62.0
1.43	4.22	-60.0	1.43	6.35	-51.0	1.43	7.40	-60.0	1.43	7.40	-60.0
1.61	3.33	-55.0	1.61	5.04	-48.0	1.61	4.24	-55.0	1.61	4.24	-55.0
1.82	3.19	-52.0	1.82	4.42	-45.0	1.82	4.53	-50.0	1.82	4.53	-50.0
2.03	2.15	-51.0	2.03	4.49	-41.0	2.03	3.12	-49.0	2.03	3.12	-49.0
2.25	2.15	-45.0	2.25	4.73	-39.0	2.25	2.78	-38.0	2.25	2.78	-38.0
2.47	1.66	-26.0	2.47	3.80	-23.0	2.47	2.26	-28.0	2.47	2.26	-28.0
2.69	1.81	-16.0	2.69	3.30	-19.0	2.69	2.26	-13.0	2.69	2.26	-13.0
2.91	1.96	0.0	2.91	3.30	-4.0	2.91	2.26	0.0	2.91	2.26	0.0
3.13	1.81	12.0	3.13	3.30	13.0	3.13	2.26	17.0	3.13	2.26	17.0
3.35	1.90	23.0	3.35	3.30	29.0	3.35	2.26	32.0	3.35	2.26	32.0
3.57	1.83	31.0	3.57	3.30	46.0	3.57	2.26	43.0	3.57	2.26	43.0
3.79	1.90	45.0	3.79	3.30	51.0	3.79	2.26	58.0	3.79	2.26	58.0
4.01	2.23	58.0	4.01	3.30	60.0	4.01	2.26	62.0	4.01	2.26	62.0
4.23	2.23	61.0	4.23	3.30	67.0	4.23	2.26	64.0	4.23	2.26	64.0
4.45	2.23	67.0	4.45	3.30	71.0	4.45	2.26	69.0	4.45	2.26	69.0
4.67	2.23	71.0	4.67	3.30	71.0	4.67	2.26	69.0	4.67	2.26	69.0

Dog 12

FREQ	MAG.	PHASE	FREQ	MAG.	PHASE	FREQ	MAG.	PHASE	FREQ	MAG.	PHASE
0.90	7.20	-64.0	0.90	9.36	-65.0	0.90	7.41	-62.0	0.90	7.41	-62.0
1.02	6.45	-62.0	1.02	9.59	-60.0	1.02	6.59	-60.0	1.02	6.59	-60.0
1.21	5.45	-60.0	1.21	6.17	-60.0	1.21	5.15	-77.0	1.21	5.15	-77.0
1.43	6.43	-55.0	1.43	6.55	-56.0	1.43	4.63	-63.0	1.43	4.63	-63.0
1.61	3.33	-50.0	1.61	4.22	-57.0	1.61	4.01	-51.0	1.61	4.01	-51.0
1.82	3.19	-46.0	1.82	3.66	-60.0	1.82	3.40	-53.0	1.82	3.40	-53.0
2.03	2.15	-44.0	2.03	3.76	-44.0	2.03	3.19	-55.0	2.03	3.19	-55.0
2.25	2.15	-43.0	2.25	3.47	-33.0	2.25	2.26	-41.0	2.25	2.26	-41.0
2.47	1.66	-33.0	2.47	2.26	-22.0	2.47	1.54	-36.0	2.47	1.54	-36.0
2.69	1.81	-18.0	2.69	2.26	-10.0	2.69	1.11	-20.0	2.69	1.11	-20.0
2.91	1.96	0.0	2.91	2.26	0.0	2.91	1.11	0.0	2.91	1.11	0.0
3.13	1.81	19.0	3.13	2.26	20.0	3.13	1.11	16.0	3.13	1.11	16.0
3.35	1.90	48.0	3.35	2.26	40.0	3.35	1.11	30.0	3.35	1.11	30.0
3.57	1.83	54.0	3.57	2.26	43.0	3.57	1.11	43.0	3.57	1.11	43.0
3.79	1.90	58.0	3.79	2.26	50.0	3.79	1.11	50.0	3.79	1.11	50.0
4.01	2.23	64.0	4.01	2.26	55.0	4.01	1.11	53.0	4.01	1.11	53.0
4.23	2.23	69.0	4.23	2.26	65.0	4.23	1.11	61.0	4.23	1.11	61.0
4.45	2.23	70.0	4.45	2.26	70.0	4.45	1.11	65.0	4.45	1.11	65.0
4.67	2.23	70.0	4.67	2.26	70.0	4.67	1.11	70.0	4.67	1.11	70.0

Dog 13

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FREQ	MAG.	PHASE
0.90	10.60	-62.0
1.02	9.20	-58.0
1.21	7.60	-56.0
1.37	6.80	-55.0
1.43	6.50	-50.0
1.61	5.10	-47.0
1.82	5.20	-41.0
2.03	4.70	-30.0
2.41	4.10	-36.0
2.72	3.60	-33.0
2.85	3.90	-28.0
3.20	3.50	-20.0
3.60	3.60	-10.0
4.02	3.40	0.0
4.77	3.20	3.0
5.39	3.20	8.0
5.64	3.40	17.0
6.34	3.80	22.0
7.20	3.60	27.0
8.05	4.20	34.0
9.00	4.70	41.0
10.20	5.50	48.0
12.00	5.90	51.0
13.60	6.10	54.0
14.20	9.20	58.0

Dog 14

FREQ	MAG.	PHASE
0.90	35.30	-59.0
1.02	25.00	-59.0
1.21	25.10	-61.0
1.37	21.60	-58.0
1.43	18.00	-56.0
1.61	18.80	-54.0
1.82	17.40	-51.0
2.03	14.40	-45.0
2.41	10.50	-40.0
2.72	19.10	-39.0
2.85	10.50	-37.0
3.20	9.20	-30.0
3.60	8.50	-20.0
4.02	8.00	-15.0
4.77	7.60	-10.0
5.39	7.90	0.0
5.64	9.10	2.0
6.34	9.70	23.0
7.20	9.90	30.0
8.05	10.20	40.0
9.00	12.20	45.0
10.20	14.20	51.0
12.00	17.40	55.0
14.20	23.70	60.0

Dog 15

o.c.

FREQ	MAG.	PHASE	FREQ	MAG.	PHASE	FREQ	MAG.	PHASE	FREQ	MAG.	PHASE
0.90	7.21	-64.0	0.90	9.37	-65.0	0.90	7.42	-62.0	0.90	7.42	-62.0
1.01	6.49	-62.0	1.01	6.27	-60.0	1.01	6.59	-63.0	1.01	6.59	-63.0
1.20	5.46	-66.0	1.20	6.59	-68.0	1.20	5.25	-60.0	1.20	5.25	-60.0
1.36	5.46	-60.0	1.36	6.18	-60.0	1.36	5.15	-77.0	1.36	5.15	-77.0
1.42	6.08	-55.0	1.42	5.25	-55.0	1.42	4.94	-63.0	1.42	4.94	-63.0
1.60	4.64	-59.0	1.60	5.84	-57.0	1.60	4.02	-51.0	1.60	4.02	-51.0
1.80	3.81	-52.0	1.80	4.22	-60.0	1.80	3.40	-53.0	1.80	3.40	-53.0
2.01	3.31	-56.0	2.01	3.09	-44.0	2.01	3.27	-51.0	2.01	3.27	-51.0
2.20	2.78	-46.0	2.20	3.78	-33.0	2.20	3.19	-41.0	2.20	3.19	-41.0
2.36	1.96	-33.0	2.36	2.47	-30.0	2.36	1.96	-36.0	2.36	1.96	-36.0
2.57	1.65	-18.0	2.57	2.26	-11.0	2.57	1.55	-26.0	2.57	1.55	-26.0
3.00	1.47	0.0	3.00	2.21	10.0	3.00	1.75	0.0	3.00	1.75	0.0
3.36	1.44	19.0	3.36	2.06	21.0	3.36	1.55	4.0	3.36	1.55	4.0
3.61	1.65	30.0	3.61	2.47	32.0	3.61	1.65	16.0	3.61	1.65	16.0
4.00	1.85	43.0	4.00	2.88	40.0	4.00	1.85	30.0	4.00	1.85	30.0
4.30	2.16	48.0	4.30	3.19	45.0	4.30	2.16	43.0	4.30	2.16	43.0
4.75	2.47	54.0	4.75	3.50	53.0	4.75	2.47	50.0	4.75	2.47	50.0
5.00	2.78	58.0	5.00	4.12	55.0	5.00	2.78	58.0	5.00	2.78	58.0
5.36	3.50	60.0	5.36	5.72	65.0	5.36	3.50	61.0	5.36	3.50	61.0
6.00	4.56	64.0	6.00	7.52	65.0	6.00	4.56	65.0	6.00	4.56	65.0
6.30	5.66	69.0	6.30	8.43	70.0	6.30	5.66	70.0	6.30	5.66	70.0
7.00	6.90	70.0	7.00	8.43	70.0	7.00	6.90	71.0	7.00	6.90	71.0

Dog 16

FREQ	MAG.	PHASE	FREQ	MAG.	PHASE	FREQ	MAG.	PHASE	FREQ	MAG.	PHASE
0.90	6.08	-61.0	0.90	7.31	-50.0	0.90	7.83	-40.0	0.90	7.83	-40.0
1.01	5.47	-59.0	1.01	7.21	-46.0	1.01	7.42	-36.0	1.01	7.42	-36.0
1.20	4.74	-51.0	1.20	6.49	-41.0	1.20	7.21	-33.0	1.20	7.21	-33.0
1.36	4.53	-40.0	1.36	5.87	-29.0	1.36	6.70	-30.0	1.36	6.70	-30.0
1.42	4.53	-34.0	1.42	5.56	-23.0	1.42	6.39	-28.0	1.42	6.39	-28.0
1.60	3.91	-32.0	1.60	5.15	-30.0	1.60	6.02	-20.0	1.60	6.02	-20.0
1.80	3.27	-31.0	1.80	4.53	-36.0	1.80	5.61	-25.0	1.80	5.61	-25.0
2.01	2.78	-21.0	2.01	3.99	-12.0	2.01	5.09	-18.0	2.01	5.09	-18.0
2.20	2.47	-15.0	2.20	3.40	-17.0	2.20	4.53	-14.0	2.20	4.53	-14.0
2.36	2.16	-5.0	2.36	3.01	-5.0	2.36	4.22	-6.0	2.36	4.22	-6.0
2.57	1.85	2.0	2.57	2.40	5.0	2.57	4.22	-2.0	2.57	4.22	-2.0
3.00	1.75	9.0	3.00	2.40	5.0	3.00	4.22	-2.0	3.00	4.22	-2.0
3.36	1.75	16.0	3.36	2.81	7.0	3.36	4.22	-2.0	3.36	4.22	-2.0
3.61	1.85	16.0	3.61	3.09	12.0	3.61	4.22	-2.0	3.61	4.22	-2.0
4.00	2.16	16.0	4.00	3.40	12.0	4.00	4.22	-2.0	4.00	4.22	-2.0
4.30	2.47	16.0	4.30	3.78	12.0	4.30	4.22	-2.0	4.30	4.22	-2.0
4.75	2.78	16.0	4.75	4.12	12.0	4.75	4.22	-2.0	4.75	4.22	-2.0
5.00	3.50	16.0	5.00	4.75	12.0	5.00	4.22	-2.0	5.00	4.22	-2.0
5.36	4.56	16.0	5.36	5.09	12.0	5.36	4.22	-2.0	5.36	4.22	-2.0
6.00	5.66	16.0	6.00	5.72	12.0	6.00	4.22	-2.0	6.00	4.22	-2.0
6.30	6.90	16.0	6.30	5.72	12.0	6.30	4.22	-2.0	6.30	4.22	-2.0
7.00	8.43	16.0	7.00	5.72	12.0	7.00	4.22	-2.0	7.00	4.22	-2.0
7.30	8.43	16.0	7.30	5.72	12.0	7.30	4.22	-2.0	7.30	4.22	-2.0
7.60	8.43	16.0	7.60	5.72	12.0	7.60	4.22	-2.0	7.60	4.22	-2.0
8.00	8.43	16.0	8.00	5.72	12.0	8.00	4.22	-2.0	8.00	4.22	-2.0
8.30	8.43	16.0	8.30	5.72	12.0	8.30	4.22	-2.0	8.30	4.22	-2.0
8.60	8.43	16.0	8.60	5.72	12.0	8.60	4.22	-2.0	8.60	4.22	-2.0
9.00	8.43	16.0	9.00	5.72	12.0	9.00	4.22	-2.0	9.00	4.22	-2.0
9.30	8.43	16.0	9.30	5.72	12.0	9.30	4.22	-2.0	9.30	4.22	-2.0
9.60	8.43	16.0	9.60	5.72	12.0	9.60	4.22	-2.0	9.60	4.22	-2.0
10.00	8.43	16.0	10.00	5.72	12.0	10.00	4.22	-2.0	10.00	4.22	-2.0
10.30	8.43	16.0	10.30	5.72	12.0	10.30	4.22	-2.0	10.30	4.22	-2.0
10.60	8.43	16.0	10.60	5.72	12.0	10.60	4.22	-2.0	10.60	4.22	-2.0
11.00	8.43	16.0	11.00	5.72	12.0	11.00	4.22	-2.0	11.00	4.22	-2.0
11.30	8.43	16.0	11.30	5.72	12.0	11.30	4.22	-2.0	11.30	4.22	-2.0
11.60	8.43	16.0	11.60	5.72	12.0	11.60	4.22	-2.0	11.60	4.22	-2.0
12.00	8.43	16.0	12.00	5.72	12.0	12.00	4.22	-2.0	12.00	4.22	-2.0
12.30	8.43	16.0	12.30	5.72	12.0	12.30	4.22	-2.0	12.30	4.22	-2.0
12.60	8.43	16.0	12.60	5.72	12.0	12.60	4.22	-2.0	12.60	4.22	-2.0
13.00	8.43	16.0	13.00	5.72	12.0	13.00	4.22	-2.0	13.00	4.22	-2.0
13.30	8.43	16.0	13.30	5.72	12.0	13.30	4.22	-2.0	13.30	4.22	-2.0
13.60	8.43	16.0	13.60	5.72	12.0	13.60	4.22	-2.0	13.60	4.22	-2.0
14.00	8.43	16.0	14.00	5.72	12.0	14.00	4.22	-2.0	14.00	4.22	-2.0
14.30	8.43	16.0	14.30	5.72	12.0	14.30	4.22	-2.0	14.30	4.22	-2.0
14.60	8.43	16.0	14.60	5.72	12.0	14.60	4.22	-2.0	14.60	4.22	-2.0
15.00	8.43	16.0	15.00	5.72	12.0	15.00	4.22	-2.0	15.00	4.22	-2.0
15.30	8.43	16.0	15.30	5.72	12.0	15.30	4.22	-2.0	15.30	4.22	-2.0
15.60	8.43	16.0	15.60	5.72	12.0	15.60	4.22	-2.0	15.60	4.22	-2.0
16.00	8.43	16.0	16.00	5.72	12.0	16.00	4.22	-2.0	16.00	4.22	-2.0

o.c. Dog 17

FREQ	MAG.	PHASE	FREQ	MAG.	PHASE	FREQ	MAG.	PHASE
1.21	10.30	-57.0	1.21	12.10	-62.0	1.21	10.30	-61.0
1.37	8.03	-49.0	1.37	10.30	-50.0	1.37	8.03	-50.0
1.43	7.82	-45.0	1.43	8.76	-49.0	1.43	7.82	-45.0
1.61	6.90	-43.0	1.61	8.24	-46.0	1.61	6.90	-41.0
1.82	6.09	-37.0	1.82	7.01	-43.0	1.82	6.09	-39.0
2.03	5.25	-38.0	2.03	5.49	-46.0	2.03	5.25	-37.0
2.41	4.64	-38.0	2.41	5.67	-42.0	2.41	4.64	-35.0
2.72	4.22	-26.0	2.72	4.94	-33.0	2.72	4.22	-26.0
2.85	3.61	-25.0	2.85	4.22	-28.0	2.85	3.61	-19.0
3.20	3.30	-16.0	3.20	3.61	-20.0	3.20	3.33	-14.0
3.60	2.99	-13.0	3.60	3.81	-17.0	3.60	3.04	-10.0
4.02	2.80	-7.0	4.02	3.19	-13.0	4.02	2.43	-7.0
4.77	1.85	0.0	4.77	2.47	0.0	4.77	1.75	0.0
5.39	1.75	4.0	5.39	2.06	3.0	5.39	1.85	4.0
5.64	1.85	12.0	5.64	2.01	14.0	5.64	1.75	11.0
6.34	1.85	23.0	6.34	2.06	21.0	6.34	1.85	17.0
7.20	1.96	29.0	7.20	2.37	26.0	7.20	2.08	23.0
8.03	2.01	33.0	8.03	2.88	34.0	8.03	2.10	28.0
9.00	2.06	34.0	9.00	3.09	41.0	9.00	2.06	33.0
10.20	3.58	41.0	10.20	3.71	49.0	10.20	2.51	39.0
12.00	3.71	46.0	12.00	5.36	55.0	12.00	3.67	45.0
13.60	4.53	53.0	13.60	6.18	58.0	13.60	4.53	51.0
14.20	5.25	60.0	14.20	6.70	59.0	14.20	5.30	53.0
16.00	6.18	62.0	16.00	7.62	60.0	16.00	6.07	60.0

Dog 18

FREQ	MAG.	PHASE	FREQ	MAG.	PHASE	FREQ	MAG.	PHASE
0.90	6.14	-61.0	0.90	7.51	-61.0	0.90	7.72	-60.0
1.01	6.09	-59.0	1.01	7.32	-59.0	1.01	7.59	-36.0
1.21	5.90	-54.0	1.21	7.24	-56.0	1.21	7.45	-32.0
1.37	5.51	-51.0	1.37	6.71	-51.0	1.37	7.28	-33.0
1.42	4.76	-42.0	1.42	6.00	-40.0	1.42	7.01	-21.0
1.60	4.57	-36.0	1.60	5.72	-38.0	1.60	6.73	-22.0
1.80	4.42	-20.0	1.80	5.61	-39.0	1.80	6.71	-28.0
2.01	3.96	-23.0	2.01	5.20	-32.0	2.01	6.50	-28.0
2.40	3.83	-20.0	2.40	4.63	-32.0	2.40	6.23	-20.0
2.71	3.00	-26.0	2.71	3.72	-31.0	2.71	5.33	-25.0
2.83	2.01	-12.0	2.83	3.20	-23.0	2.83	6.28	-18.0
3.19	2.01	-10.0	3.19	2.89	-15.0	3.19	5.01	-14.0
3.57	2.20	-7.0	3.57	3.43	-9.0	3.57	4.53	-8.0
4.00	1.98	-5.0	4.00	3.47	-5.0	4.00	4.62	-4.0
4.75	1.83	0.0	4.75	3.52	0.0	4.75	4.74	0.0
5.26	1.85	4.0	5.26	3.41	2.0	5.26	4.83	2.0
5.61	1.81	7.0	5.61	3.83	4.0	5.61	4.98	6.0
6.30	2.37	12.0	6.30	3.77	6.0	6.30	5.02	11.0
7.14	2.69	26.0	7.14	3.98	16.0	7.14	5.18	18.0
8.00	2.91	28.0	8.00	4.01	28.0	8.00	5.32	23.0
9.00	3.01	36.0	9.00	4.23	33.0	9.00	5.75	24.0
10.10	3.84	41.0	10.10	4.82	34.0	10.10	5.91	29.0
12.00	4.20	47.0	12.00	5.43	39.0	12.00	6.28	34.0
13.60	4.81	51.0	13.60	6.18	42.0	13.60	6.59	39.0
14.20	5.48	54.0	14.20	6.92	47.0	14.20	7.20	44.0
16.00	6.32	60.0	16.00	7.68	56.0	16.00	7.81	52.0

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