

CHAPTER 4

Lung ventilation modeling and assessment

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Abstract

We have developed a lung-ventilation model by modeling the lung-volume response to mouth minus pleural driving pressure (by means of first- and second-order differential equations) in terms of resistance to airflow (R) and the lung compliance (C). The lung-volume solution of the differential equation is matched with the clinical-volume data, to evaluate the parameters, R and C . These parameter values can help us to distinguish an obstructive lung and a lung with stiffened parenchyma from a normal lung, and hence diagnose lung diseases such as asthma and emphysema. We have also formulated a nonlinear compliance lung model, and demonstrated decreased lung compliance with filling volume. We then formulated a nondimensional lung-ventilatory index (VTI), incorporating the parameters R and C as well as the lung-breathing rate. When the VTI is evaluated for various lung diseases, it will conveniently enable us to diagnose lung diseases in terms of just one VTI number. Finally, we have shown how to model a two-lobe lung, and differentiate between normal and diseased lobes.

1 Introduction

1.1 Role of lung ventilation

Lung ventilation constitutes inhalation of an appropriate air volume under driving pressure (=mouth pressure – pleural pressure), so as to: (i) provide an adequate alveolar O_2 amount at an appropriate partial pressure, (ii) oxygenate the pulmonary blood, and (iii) thereby provide adequate metabolic oxygen to the cells.



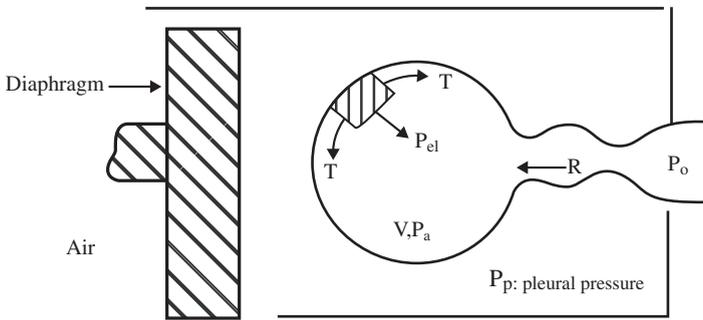


Figure 1: Alveolar model.

Hence, ventilatory function and performance assessment entails determining how much air volume is provided to the alveoli, to make available adequate alveolar oxygen for blood oxygenation and cellular respiration.

Based on Fig. 1, we get:

- (i) $(P_a - P_p) - P_{el} = 0$
- (ii) $P_{el} = (2ah)/Rr = 2T/r = V/C + P_{el0}$
- (iii) $(P_m - P_a) = R(dV/dt)$
- (iv) $P_L = P_m - P_p$
- (v) $R(dV/dt) + VIC = P_L - P_{el0}$ (lung elastic recoil pressure at end of expiration)

2 Lung-ventilation performance using a linear first-order model

We first analyze the lung-ventilation function by means of a very simple model represented by a first-order differential equation (De_q) in lung-volume (V) dynamics in response to the driving pressure ($P_1 = \text{atmospheric pressure} - \text{pleural pressure}$), as displayed in Fig. 1. The clinical pressure-volume data is in Fig. 2.

The model-governing equation (shown derived in Fig. 1) is as follows:

$$R\dot{V} + \frac{V}{C} = P_L(t) - P_{el0} = P_N(t), \quad (1a)$$

wherein:

- (i) the values of pressure are obtained from the given $P_L (= P_m - P_p)$ data
- (ii) the parameters of this governing De_q are lung compliance (C) and airflow resistance (R); in the equation both R and C are instantaneous values
- (iii) $V = V(t) - V_0$ (the lung volume at the end of expiration)
- (iv) P_{el0} is the lung elastic-recoil pressure at the end of expiration, and

$$P_{el0} = P_{el} - \frac{V}{C}. \quad (1b)$$

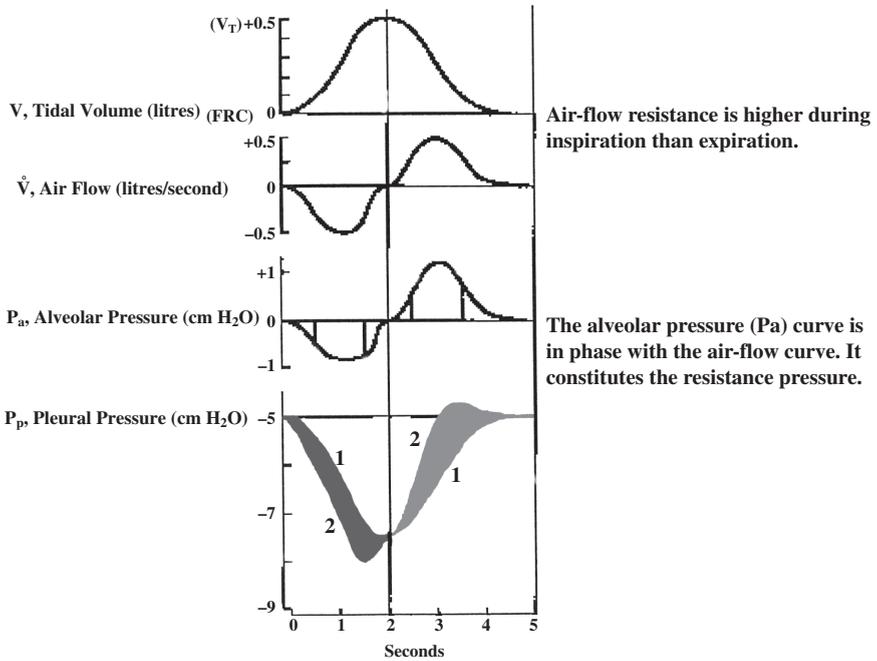


Figure 2: Lung-ventilatory model and lung-volume and pleural-pressure data. Curve 1 on the curve represents P_{el} , the pressure required to overcome lung elastance ($=V/C$). Curve 2 curve represents P_p , the summation of P_{el} and P_a . The pressure $P_N(t)$ in eqn. (1a) equals P_p minus P_{el} at end of expiration.

At the end of expiration when $\omega t = \omega T, P_L = P_{el0} = P_N(t)$, which is represented by

$$P_N(t) = \sum_{i=1}^3 P_i \sin(\omega_i t + c_i),$$

and the governing eqn. (1a) becomes:

$$R\dot{V} + \frac{V}{C} = P_N(t) = \sum_{i=1}^3 P_i \sin(\omega_i t + c_i), \tag{2a}$$

where the right-hand side represents the net driving pressure minus pleural pressure. $P_N = (P_m - P_p) - P_{el0}$. This P_N is, in fact, the driving pressure $(P_m - P_p)$ normalized with respect to its value at end of expiration. Equation (2a) can be rewritten as follows:

$$\dot{V} + \frac{V}{RC} = \frac{1}{R} \sum_{i=1}^3 P_i \sin(\omega_i t + c_i), \tag{2b}$$



wherein the $P(t)$ clinical data (displayed in Fig. 2) is assumed to be represented by:

$$P(t) = \sum_{i=1}^3 P_i \sin(\omega_i t + c_i), \quad (3)$$

$$\begin{array}{lll} P_1 = 1.581 \text{ cmH}_2\text{O} & P_2 = -5.534 \text{ cmH}_2\text{O} & P_3 = 0.5523 \text{ cmH}_2\text{O} \\ \omega_1 = 1.214 \text{ rad/s} & \omega_2 = 0.001414 \text{ rad/s} & \omega_3 = 2.401 \text{ rad/s} \\ c_1 = -0.3132 \text{ rad} & c_2 = 3.297 \text{ rad} & c_3 = -2.381 \text{ rad}. \end{array}$$

The pressure curve (in Fig. 3A) represented by the above eqn. (3) closely matches the pressure data of Fig. 2. If, in eqn. (1), we designate R_a and C_a as the average values (R and C) for the ventilatory cycle, then the solution of eqn. (1) is given by:

$$V(t) = \sum_{i=1}^3 \frac{P_i C_a [\sin(\omega_i t + c_i) - b_i R_a C_a \cos(\omega_i t + c_i)]}{(1 + \omega_i^2 (R_a C_a)^2)} - H e^{-\frac{t}{R_a C_a}}, \quad (4)$$

wherein the term $(R_a C_a)$ is denoted by τ_a . We need to have $V = 0$ at $t = 0$. Hence, putting V (at $t = 0$) = 0, gives us:

$$H = \sum_{i=1}^3 \frac{P_i C_a [\sin(\omega_i t + c_i) - b_i R_a C_a \cos(\omega_i t + c_i)]}{(1 + \omega_i^2 (R_a C_a)^2)}. \quad (5)$$

Then from eqns. (4) and (5), the overall expressions for $V(t)$ becomes

$$\begin{aligned} V(t) &= \sum_{i=1}^3 \frac{P_i C_a [\sin(\omega_i t + c_i) - \omega_i \tau_a^2 \cos(\omega_i t + c_i)]}{(1 + \omega_i^2 \tau_a^2)} \\ &\quad - \sum_{i=1}^3 \frac{P_i C_a [\sin(\omega_i t + c_i) - \omega_i \tau_a^2 \cos(\omega_i t + c_i)]}{(1 + \omega_i^2 \tau_a^2)} e^{-\frac{t}{\tau_a}} \\ &= \sum_{i=1}^3 \frac{P_i C_a [\sin(\omega_i t + c_i) - \omega_i \tau_a^2 \cos(\omega_i t + c_i)]}{(1 + \omega_i^2 \tau_a^2)} \left[1 - e^{-\frac{t}{\tau_a}} \right]. \end{aligned} \quad (6)$$

We also want that $dV/dt = 0$ at $t = 0$, implying no air-flow at the start of inspiration. So, by differentiating eqn. (6), we get:

$$\begin{aligned} \dot{V} &= \sum_{i=1}^3 \frac{P_i C_a [\omega_i \cos(\omega_i t + c_i) + \omega_i^2 \tau_a \sin(\omega_i t + c_i)]}{(1 + \omega_i^2 \tau_a^2)} \left[1 - e^{-\frac{t}{\tau_a}} \right] \\ &\quad + \sum_{i=1}^3 \frac{P_i C_a [\sin(\omega_i t + c_i) - \omega_i \tau_a \cos(\omega_i t + c_i)]}{(1 + \omega_i^2 \tau_a^2) \tau_a} e^{-\frac{t}{\tau_a}}. \end{aligned} \quad (7)$$

From eqn. (7), we get $\dot{V} \neq 0$ at $t = 0$, thereby also satisfying this initial condition.



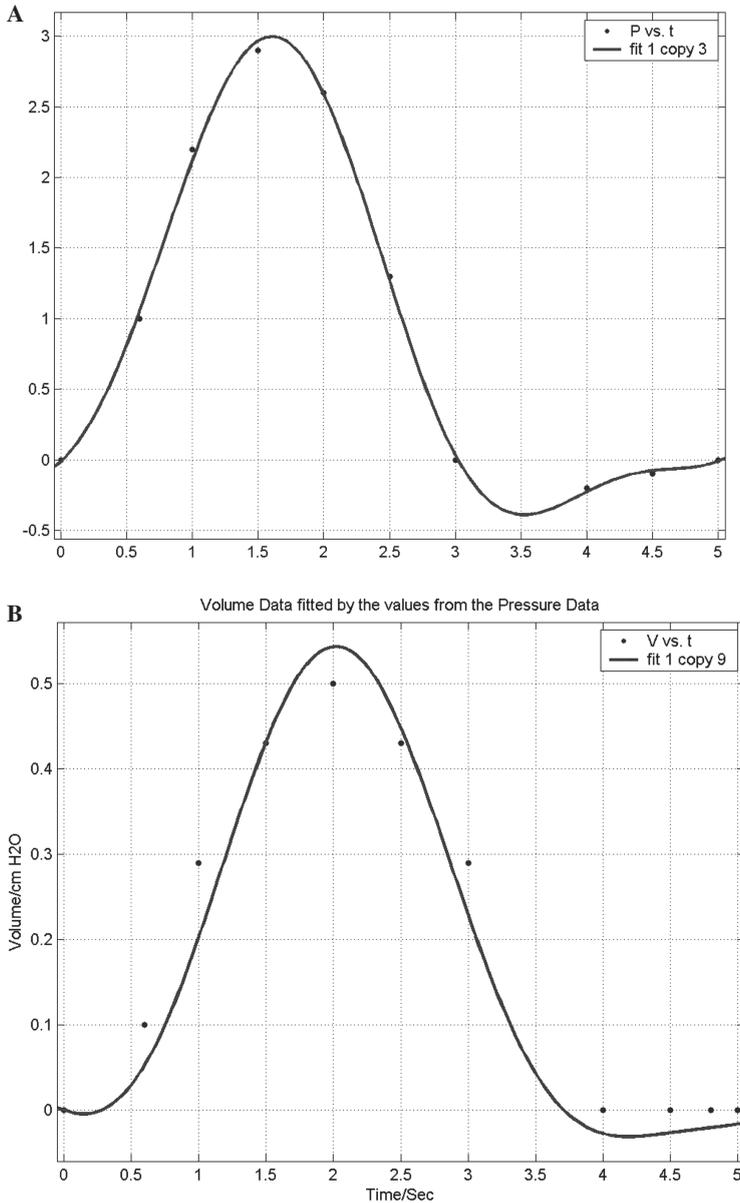


Figure 3: **A** The pressure curve represented by eqn. (3) matched against the pressure data (represented by dots). **B** The volume curve represented by eqn. (6), for from $C_a = 0.2132 \text{ (cmH}_2\text{O)}^{-1}$ and $R_a = 2.275 \text{ cmH}_2\text{Osl}^{-1}$ pp. 3 matched against the volume data represented by dots.

Now, by matching the above $V(t)$ expression (6) with the given $V(t)$ data in Fig. 2, and carrying out parameter identification, we can determine the in vivo values of R_a and C_a , to be

$$C_a = 0.2132 \text{ (cmH}_2\text{O)}^{-1}, \quad R_a = 2.275 \text{ cmH}_2\text{Osl}^{-1}$$

The computed $V(t)$ curve, represented by eqn. (6) for the above values of C_a and R_a , is shown in Fig. 3B. We can however analytically evaluate R_a and C_a by satisfying some conditions. For this purpose, we first note that V is maximum (= tidal volume, TV) at about $t = t_V = 2.02$ s. At $t = t_V$, the exponential term $e^{-\frac{t}{\tau_a}}$ in (6) becomes of the order of e^{-10} , and hence negligible. Then by putting $\dot{V}(t = 2.02) = 0$ in eqn. (7), without the exponential term we obtain:

$$\dot{V}|_{t=2.02} = \sum_{i=1}^3 \frac{P_i C_a [\omega_i \cos(\omega_i \times 2.02 + c_i) + \omega_i^2 \tau_a \sin(\omega_i \times 2.02 + c_i)]}{(1 + \omega_i^2 \tau_a^2)} = 0, \quad (8)$$

in which the values of P_i , ω_i , and c_i are given by eqn. (3). Then by solving eqn. (8), we get $\tau_a = 0.522$ s. We can also put $\dot{V} = 0$ at $t \cong 1.81/2.87$ s and obtain a similar value for τ .

Then, we also note that at $t_V = 2.02$ s (at which $dV/dt = 0$) and $V = 0.55$ l. Hence upon substituting into eqn. (6), and neglecting the exponential term, we get the following algebraic equation:

$$V(t)|_{t=2.02} = \sum_{i=1}^3 \frac{P_i C_a [\sin(\omega_i t + c_i) - \omega_i \tau_a^2 \cos(\omega_i t + c_i)]}{(1 + \omega_i^2 \tau_a^2)} = 2.55 C_a, \quad (9)$$

by employing the values of P_i , ω_i and c_i from eqn. (3). Now since $V(t = 2.02 \text{ s}) = 0.55$ l, we get

$$2.55 C_a = 0.55$$

$$C_a = 0.221 \text{ (cmH}_2\text{O)}^{-1}. \quad (10)$$

We can substitute, therein, the values of P_1 and P_2 from eqn. (3), and obtain the value of C_a as: $C_a = 0.221 \text{ (cmH}_2\text{O)}^{-1}$. Since we have computed $\tau_a = 0.485$ s, therefore $R_a = 2.275 \text{ (cmH}_2\text{O)} \text{sl}^{-1}$. These are the average values of resistance to airflow and lung compliance during the ventilatory cycle shown in Fig. 2.

Since lung disease will influence the values of R and C , these parameters can be employed to diagnose lung diseases. For instance in the case of emphysema, the destruction of lung tissue between the alveoli produces a more compliant lung, and hence results in a larger value of C . In asthma, there is increased airway resistance (R) due to contraction of the smooth muscle around the airways. In fibrosis of the lung, the membranes between the alveoli thicken and hence lung compliance (C) decreases. Thus, by determining the normal and diseased ranges of the parameters R and C , we can employ this simple lung-ventilation model for differential diagnosis.

3 Ventilatory index

Let us, however, formulate just one non dimensional number to serve as a ventilatory-performance index VTI_1 (to characterize ventilatory function), as:

$$VTI_1 = [(R_a C_a)(\text{Ventilatory rate in } s^{-1}) 60]^2 = \tau_a^2 (BR)^2 60^2, \quad (11)$$

where BR is the breathing rate.

Now, let us obtain its order of magnitude by adopting representative values of R_a and C_a in normal and disease states. Let us take the above computed values of $R_a = 2.275 \text{ (cmH}_2\text{O)sl}^{-1}$ and $C_a = 0.21321 \text{ (cmH}_2\text{O)}^{-1}$ and $BR = 12 \text{ m}^{-1}$ or 0.2 s^{-1} , computed for the data of Fig. 2 and eqn. (3). Then, in a supposed normal situation, the value of VTI_1 is of the order of 33.88. In the case of obstructive lung disease, (with increased R_a), let us take $R_a = 5 \text{ (cmH}_2\text{O)sl}^{-1}$, $C_a = 0.121 \text{ (cmH}_2\text{O)}^{-1}$ and $BR = 0.3 \text{ s}^{-1}$; then we get $VTI_1 = 116.6$. For the case of emphysema (with enhanced C_a), let us take $R_a = 2.0 \text{ cmH}_2\text{Osl}^{-1}$, $C_a = 0.51 \text{ (cmH}_2\text{O)}^{-1}$ and $BR = 0.2 \text{ s}^{-1}$; then we obtain $VTI_1 = 144$. In the case of lung fibrosis (with decreased C_a), we take $R_a = 2.0 \text{ cmH}_2\text{Osl}^{-1}$, $C_a = 0.081 \text{ (cmH}_2\text{O)}^{-1}$ and $BR = 0.2 \text{ s}^{-1}$; then we obtain $VTI_1 = 3.7$. We can hence summarize that VTI_1 would be in the range of 2–5 in the case of fibrotic lung disease, 5–50 in normal persons, 50–150 in the case of obstructive lung disease and 150–200 for the case of emphysema. This would of course need verification by analyzing a big patient population.

Now, all of this analysis requites pleural-pressure data, for which the patient has to be intubated. If now we evaluate the patient in an outpatient clinic, in which we can only monitor lung volume and not the pleural pressure, then can we develop a non invasively obtainable ventilatory index?

3.1 Noninvasively determinable ventilatory index

In order to formulate a non-invasively determinable ventilatory index from eqn. (1), we need to recognize that in this case $P_N(t)$ (and hence P_i , ω and c_i) will be unknown and we need to redesignate the model parameters and indicate their identification procedure. So we make use of the following features from the volume–time data to facilitate evaluation of the following three parameters:

(P_i, C_a) , ω_i , c_i , and τ_a .

At $t = t_v = 2.02 \text{ s}$, V is max and $dV/dt = 0$; hence we rewrite eqn. (9) as:

$$\dot{V}|_{t=2.02} = \sum_{i=1}^3 \frac{(P_i C_a) [\omega_i \cos(2.02 \times \omega_i + c_i) + \omega_i^2 \tau_a \sin(2.02 \times \omega_i + c_i)]}{(1 + \omega_i^2 \tau_a^2)} = 0. \quad (12)$$



Also, at $t = t_m = 1.82/2.87$ s, $\dot{V} = 0$. Hence by differentiating eqn. (7), without the exponential term, we obtain:

$$\begin{aligned} \dot{V}^\infty(t) = & \sum_{i=1}^3 \frac{(P_i C_a) [-\sin(\omega_i t_m + c_i) \omega_i^2 + \omega_i^3 \tau_a^2 \cos(\omega_i t_m + c_i)]}{(1 + \omega_i^2 \tau_a^2)} \left[1 - e^{-\frac{t_m}{\tau_a}} \right] \\ & + 2 \sum_{i=1}^3 \frac{(P_i C_a) [\omega_i \cos(\omega_i t_m + c_i) - \omega_i^2 \tau_a \sin(\omega_i t_m + c_i)]}{\tau_a (1 + \omega_i^2 \tau_a^2)} e^{-\frac{t_m}{\tau_a}} \\ & - \sum_{i=1}^3 \frac{(P_i C_a) [\sin(\omega_i t_m + c_i) - \omega_i \tau_a^2 \cos(\omega_i t_m + c_i)]}{\tau_a^2 (1 + \omega_i^2 \tau_a^2)} e^{-\frac{t_m}{\tau_a}} = 0. \end{aligned} \quad (13)$$

Then, at $t = 1$ s, $V_1 = 2.02$ l. From eqn. (6), without the exponential term, this condition yields:

$$V_1 = \sum_{i=1}^3 \frac{(P_i C_a) [-\sin(\omega_i + c_i) \omega_i^2 + \omega_i^3 \tau_a^2 \cos(\omega_i + c_i)]}{(1 + \omega_i^2 \tau_a^2)} = 2.02.$$

In addition, we can utilize data information concerning V_j at t_j ($j = 1$ to 8), and put down:

$$V_j = \sum_{i=1}^3 \frac{(P_i C_a) [-\sin(\omega_i t_j + c_i) \omega_i^2 + \omega_i^3 \tau_a^2 \cos(\omega_i t_j + c_i)]}{(1 + \omega_i^2 \tau_a^2)}; \quad j = 1 \quad \text{to} \quad 8. \quad (14)$$

From eqns. (12)–(14), we can obtain the values of $P_i C_a$ (but not of P_1, P_2 and P_3 by themselves), ω_i, c_i and τ_a . On the other hand, by also fitting eqn. (6), (without the exponential term) to the $V(t)$ data, we obtain:

$$P_1 C = 0.3223 \quad P_2 C = 0.3143 \quad P_3 C = -0.02269 \quad (15)$$

$$\omega_1 = -1.178 \quad \omega_2 = 0.5067 \quad \omega_3 = 1.855 \quad (16)$$

$$c_1 = 90223 \quad c_2 = 0.2242 \quad c_3 = -3.961$$

$$\tau_a = 0.5535. \quad (17)$$

We can now also formulate another noninvasively determinable nondimensional ventilatory index (VTI_2) in terms of these parameters as follows:

$$VTI_2 = \frac{(BR)\tau[TV]^2}{|P_1 C||P_2 C||P_3 C|} = \frac{(BR)R[TV]^2}{|P_1 P_2 P_3 C^2|}. \quad (18)$$

It is seen that VTI_2 can in fact be expressed in terms of P_1, P_2, P_3 and R, C . This VTI_2 index can be evaluated by computing the values of (BR) and τ , along with $(P_i C)$, as given by eqn. (17). Then, after evaluating VTI_2 for a number of patients, its distribution can enable us to categorize and differentially diagnose patients with various lung disorders and diseases.



4 Variations in R and C during a respiratory cycle (towards nonlinear)

Thus far, we have adopted the average cyclic values C_a and R_a for our DE_q model parameters. However, we expect that C will vary with lung volume (V), and that R will perhaps vary with the airflow rate or (\dot{V}) or even ω . Hence, for a true representation of the lung properties C and R , let us determine their values for different times during the ventilatory cycle, and compare them with their average values C_a and R_a , so as to make a case for a nonlinear ventilatory-function model.

Let us hence compute the instantaneous value of compliance (C) at time ($t = t_m$), when $\dot{V} = 0$. Let us differentiate eqn. (2a), giving:

$$R\dot{V} + \frac{\dot{V}}{C} = \sum_{i=1}^3 P_i C \omega_i \cos(\omega_i t + c_i). \quad (19)$$

Now at about mid-inspiration, when $t = t_m = 1.18$ and $\dot{V} = 0.48$ l/s, $\ddot{V} = 0$ l/s and $V = 0.291$ (based on Fig. 2). By substituting for \ddot{V} , \dot{V} and V in eqn. (19), we obtain, $C = 0.486$ l/cmH₂O (compared to its C_a value of 0.21). Now, in order to compute R , we utilize the data information that at $t_V = 2.02$ s we substitute $\dot{V} = 0$ l/s, $\ddot{V} = -0.89$ l/s and $V = 0.541$ (from the Fig. 2 data) into eqn. (2a), to obtain:

$$R\ddot{V} = \sum_{i=1}^3 P_i \omega_i \cos(\omega_i t + c_i)$$

$$R = \frac{\sum_{i=1}^3 P_i \omega_i \cos(\omega_i t + c_i)}{\ddot{V}}. \quad (20)$$

Substitute C (at $t_m = 1.18$ s) = 0.486 l/cmH₂O in either eqns. (6) or (2b), and obtain $R = 1.122$ (cmH₂O)sl⁻¹. This gives us some idea of the order of magnitude of R and C , in comparison to their average values C_a and R_a . We could naturally expect C at $t = t_m$ (which is about mid-inspiration) to be higher than its value at the end of inspiration, when the lung is fully inflated. Also, we could expect the flow resistance to be minimum at the peak of inspiration, when $\dot{V} = 0$.

Because C and R are not constant, but a function of V and \dot{V} , we can hence represent lung compliance (C) and resistance (R) as follows:

$$C = C_0 e^{-k_C V} \quad \text{or} \quad E = \frac{1}{C} = E_0 e^{k_e V} \quad (21a)$$

$$R = R_0 e^{k_R \dot{V}}, \quad (21b)$$

wherein \dot{V} can also be varied by having the subjects breathe at different ventilation frequencies (ω).



4.1 Nonlinear compliance

We note as per the conventional formulation of compliance, given by eqn. (2) in Fig. 1 as:

$$P_{el} = \frac{V}{C} + P_{el0} = VE + P_{el0}. \quad (22)$$

In the above formulation, we assume that C and $E(=1/C)$ remains constant throughout the ventilation cycle. However, at the start of inspiration, $C = C_0$ at $t = 0$, and it decreases as the lung volume increases, based on the lung (static) volume vs pressure curve. So let us improve upon this (22) model, by making P_{el} a nonlinear function of volume, as follows:

$$P_{el} = P_{el0} + VE_0e^{kV}. \quad (23a)$$

We can alternatively write eqn. (23) as:

$$P_{el} = P_{el0} + V(E_0 + E_1t + E_3t^2). \quad (23b)$$

Employing the above format of compliance, the governing DE_q (1) becomes

$$R\dot{V} + VE_0e^{kV} = P_L(t) - P_{el0} = P_N(t) = \sum_{i=1}^3 P_i \sin(\omega_i t + c_i). \quad (24)$$

Again at the end of expiration, $P_{el0} =$ intrapulmonary pressure $= (P_0 + P_1)$. Hence eqn. (24) becomes:

$$R\dot{V} + VE_0e^{kV} = \sum_{i=1}^3 P_i \sin(\omega_i t + c_i) \quad (25a)$$

whose RHS is similar to that of eqn. (2a), and the values of P_1, P_2 , and P_3 are given by eqn. (3) for the Fig. 2 data.

Solving eqn. (25a):

$$R\dot{V} + VE_0e^{kV} = \sum_{i=1}^3 P_i \sin(\omega_i t + c_i),$$

$$\text{or, } \dot{V} + \frac{VE_0}{R}e^{kV} = \sum_{i=1}^3 \frac{P_i}{R} \sin(\omega_i t + c_i),$$

or, based on eqn. (23b),

$$\dot{V} + \frac{V}{R}[E_0 + E_1t + E_2t^2] = \sum_{i=1}^3 \frac{P_i}{R} \sin(\omega_i t + c_i).$$



This yields:

$$V(t) = e^{\frac{t(6E_0+3E_1t+2E_2t^2)}{6k}} \int_0^t e^{\frac{u(6E_0+3E_1u+2E_2u^2)}{6k}} \sum_{i=1}^3 \frac{P_i}{R} \sin(\omega_i u + c_i) du. \quad (25b)$$

We could employ this expression for $V(t)$ to fit the clinical $V(t)$ data. However, let us try a simpler approach to evaluate these parameters k and E_0 . For this purpose, we again bring to bear the situation that at the end of inspiration, for $t = t_v = 2.02$ s, we have $\dot{V} = 0$ and $V = V_{\max} = TV = 0.55$ l. Hence, from Fig. 2 data, and eqns. (3) and (25a), we obtain:

$$0.55E_0e^{0.55k} = 2.55. \quad (26)$$

Let us now employ the volume data point at which $\ddot{V} = 0$. For this purpose, we differentiate eqn. (25a), to obtain:

$$\begin{aligned} \ddot{V} + \frac{E_0}{R} e^{kV} (1 + kV) &= \sum_{i=1}^3 \frac{P_i C_a \omega_i}{R} \cos(\omega_i t + c_i) \\ \ddot{V} + \frac{(1 + kV)}{R} [E_0 + E_1 t + E_2 t^2] &= \sum_{i=1}^3 \frac{P_i C_a \omega_i}{R} \cos(\omega_i t + c_i). \end{aligned} \quad (27)$$

From the Fig. 2 data at about mid-inspiration, for which at $t = t_m = 1.18$ s, $\ddot{V} = 0$, $V = 0.29$ and $P = 2.53$, from Fig. 2 data. Substituting these values into eqn. (27), we get:

$$(1 + 0.29k)(E_0 + 1.18E_1 + 1.39E_2) = 2.53. \quad (28)$$

Now, in eqns. (26) and (28), we have four unknowns to be identified: k, E_0, E_1 , and E_2 . Hence we need two more equations, corresponding to two additional time instants. From the values in the following table,

t	V	\dot{V}	\ddot{V}	P	Using eqn.
1.18	0.29	0.48	0	2.53	26
2.02	0.55	0	-0.89	2.55	26
2.87	0.29	-0.47	0	0.29	28
4.19	-0.03	0	0.16	-0.15	26
4.76	-0.02	0.02	0	-0.06	28

we can determine the unknowns:

$$k = -0.13, E_0 = 4.98, E_1 = -2.24 \text{ and } E_2 = 0.21. \quad (29)$$

Hence, by employing the nonlinear formulation,

$$P_{el} = P_{el0} + E_0 e^{-kV}, \quad (30)$$



we obtain the following expression for nonlinear lung compliance (or elastance):

$$\frac{dP_{el}}{dV} = E = \frac{1}{C} = E_0 k e^{kV} = 0.65e^{0.13V}. \quad (31)$$

Based on this expression, we obtain , for $t = t_m$ and $V = 0.291$:

$$E = \frac{1}{C} = 0.67 \text{ cmH}_2\text{O/l and } C = 1.48 \text{ l/cm H}_2\text{O}. \quad (32)$$

Equation (31) can now provide us a more realistic characterization of lung compliance as follows:

$$\left. \begin{array}{l} \text{At } t = 0 \text{ and } V = 0, \text{ we compute } E = \frac{1}{C} = 0.65 \text{ and } C = 1.53 \text{ cmH}_2\text{O/l} \\ \text{At } t = t_m = 1.18 \text{ s and } V = 0.291, E = \frac{1}{C} = 0.67 \text{ and } C = 1.48 \text{ cmH}_2\text{O/l} \\ \text{At } t = t_v = 2.02 \text{ s and } V = 0.551 \text{ and } E = \frac{1}{C} = 0.70 \text{ and } C = 1.43 \text{ cmH}_2\text{O/l} \end{array} \right\} \quad (33)$$

which corresponds to the value of C_a .

Our nonlinear formulation of lung compliance, as depicted by eqns. (31) and (33), indicates that compliance decreases from 1.53 cm H₂O/l at the start of inspiration to 1.48 cmH₂O/l at about mid-inspiration, and then to 1.43 cmH₂O/l at the end of inspiration. What this also tells us is that the ventilatory model (1) gives the correct reading of the compliance at V_{max} , i.e. at the end of inspiration. At other times of inspiration and expiration, the C_a parameter underestimates the instantaneous value of lung compliance. Now, we could also obtain an analytical solution of eqn. (25) for $V(t)$, and fit the expression for $V(t)$ to the lung-volume data, to evaluate the parameters

- (i) R, E_0 and k for an intubated patient
- (ii) R, E_0, k and P_1, P_2 and P_3 for a non-intubated patient in the out-patient clinic.

However, this is outside the scope of this chapter.

5 Work of breathing (WOB)

This is an important diagnostic index, especially if it can be obtained without intubating the patient and even without using the ventilator. The premise for determining WOB is that the respiratory muscles expand the chest wall during inspiration, thereby lowering the pleural pressure (i.e., making it more negative) below the atmospheric pressure to create a pressure differential from the mouth to the alveoli during inspiration. Then, during expiration, the lung recoils passively.

Hence, the work done during a respiratory life cycle, is given by the area of the loop generated by plotting lung volume (V) versus net driving pressure (P_p).



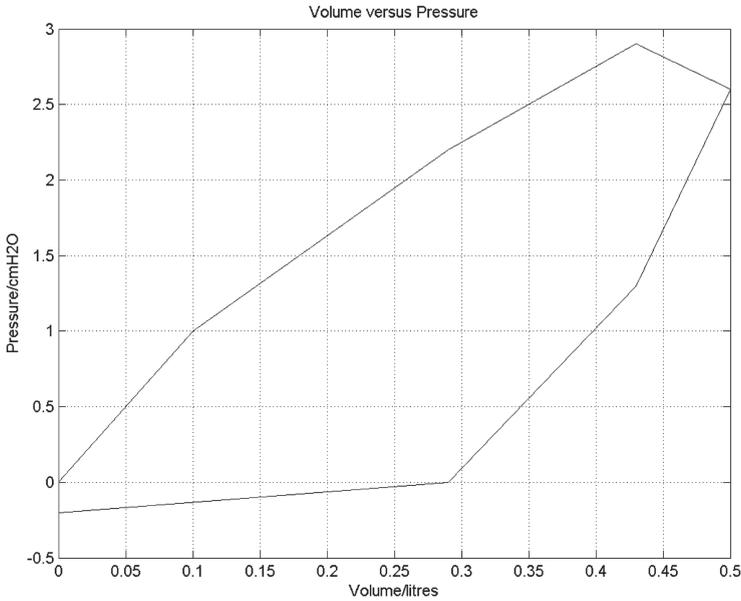


Figure 4: Plot of pressure versus volume. The area under the curve provides the work done.

This plot is shown in Fig. 4. Its area can be obtained graphically, as well as analytically as shown below:

$$\begin{aligned}
 WOB &= \int_0^{t=T} V dP_p(t) = \int_0^T V \frac{dP_p(t)}{dt} dt \quad (34) \\
 &= \int_0^{t=T} \left(\sum_{i=1}^3 \frac{P_i C_a [\sin(\omega_i t + c_i) - \omega_i \tau_a^2 \cos(\omega_i t + c_i)]}{(1 + \omega_i^2 \tau_a^2)} \right) \\
 &\quad \sum_{i=1}^3 P_i \omega_i \cos(\omega_i t + c_i) dt \\
 &= \sum_{i=1}^3 \frac{-P_i C_a [\cos(\omega_i T + c_i) + \omega_i \tau_a \sin(\omega_i T + c_i) - \cos c_i - \omega_i \tau_a \sin c_i]}{\omega_i (1 + \omega_i^2 \tau_a^2)}. \quad (35)
 \end{aligned}$$

The above expression for WOB can be evaluated, once the values of C_i and τ (or $\omega\tau$) and P_1, P_2 and P_3 and have been computed (as shown in the previous section). So let us substitute into this equation, the following values associated with eqn. (3).

$$\begin{array}{lll}
 P_1 = 1.581 \text{ cmH}_2\text{O} & P_2 = -5.534 \text{ cmH}_2\text{O} & P_3 = 0.5523 \text{ cmH}_2\text{O} \\
 \omega_1 = 1.214 \text{ rad/s} & \omega_2 = 0.001414 \text{ rad/s} & \omega_3 = 2.401 \text{ rad/s} \\
 c_1 = -0.3132 \text{ rad} & c_2 = 3.297 \text{ rad} & c_3 = -2.381 \text{ rad}.
 \end{array}$$



We compute the value of WOB to be 0.9446 (cmH₂O l) in 5 s, or 0.19 cmH₂O l s⁻¹ or 0.14 mmHg l s⁻¹ or 0.02 W, which is equivalent to an oxygen consumption of about 0.51 ml/min or about 0.18% of the resting \dot{V}_{O_2} of 28.87 ml/min. This value can be verified by calculating the value of the area of the pressure-volume loop in Fig. 4 which is equal to 0.8 cmH₂O l.

6 Second-order model for single-compartment lung model

Let us now consider the dynamic (instead of static) equilibrium of a spherical segment of the lung model in Fig. 1, obtained as (by dividing throughout by the elemental lung area):

$$m_s \ddot{u} + (P_p - P_a) + P_{\text{elas}} = 0, \quad (36a)$$

wherein: P_a and P_p are the alveolar and pleural pressures, u is the alveolar-wall displacement, $m_s = \text{lung mass } (M) \text{ per unit surface area} = M/4\pi R^2$, (1b) and

$$P_{\text{elas}} = \frac{2\sigma h}{R} = \frac{V}{C} + P_{\text{el0}}, \quad (36b)$$

where:

- (i) C is in l (cmH₂O)⁻¹
- (ii) m_s (wall mass per unit surface area or surface density) = ρh , ρ is the density (mass per unit volume)
- (iii) σ is the wall stress
- (iv) h and R are the wall thickness and radius of the equivalent-lung model.

Now, the displaced alveolar volume, $V = \frac{4}{3}\pi(R + u)^3$,

$$\text{from which we get} \quad \ddot{V} \approx 4\pi R^2 \ddot{u}. \quad (37)$$

Now, from eqn. (1), by putting

$$\begin{aligned} \text{(i)} \quad P_p - P_a &= (P_o - P_a) + (P_p - P_o) \quad \text{and} \quad P_L = P_o - P_p, \\ \text{so that } P_p - P_a &= P_o - P_a - P_L = R\dot{V} - P_L, \end{aligned} \quad (38)$$

$$\begin{aligned} \text{(ii)} \quad m_s \ddot{u} &= \left(\frac{M}{4\pi R^2} \right) \left(\frac{\ddot{V}}{4\pi R^2} \right) = \frac{M \ddot{V}}{16\pi^2 R^4} = M^* \dot{V}; \quad M^* = \frac{M}{16\pi^2 R^4} \\ &= \frac{m_s}{4\pi R^2}, \end{aligned} \quad (39)$$



we obtain, from eqns. (1), (2) and (3):

$$M^* \ddot{V} + (P_o - P_a) + \frac{V}{C} = P_L - P_{el,o}; \quad M^* = \frac{M}{16\pi^2 R^4} \left(= \frac{m_s}{4\pi R^2} \right). \quad (40)$$

Now, putting $P_o - P_a = R\dot{V}$, we obtain:

$$\begin{aligned} M^* \ddot{V} + R\dot{V} + \frac{V}{C} &= P_L - P_{el0} = \sum_{i=1}^3 P_i \sin(\omega_i t + c_i) - P_{el0} \\ &= P_N. \end{aligned} \quad (41)$$

Since at the end of expiration when $\omega_i t = \omega_i T$ for $i = 1$ to 3 and $P_L = P_{el0}$ so that $P_{el0} = 0$. In eqn. (6), we have: wherein:

- (i) $M^* = m_s/4\pi R^2 = \rho_s h$; ρ_s is the lung volume-density per unit surface area (in Kgm^{-5}) and M^* is in Kgm^{-4} ;
- (ii) the clinical data in Fig. 2 is assumed to be represented by

$$P_N(t) = \sum_{i=1}^3 P_i \sin(\omega_i t + c_i) \quad \text{with} \quad (42)$$

$P_1 = 1.581 \text{ cmH}_2\text{O}$	$P_2 = -5.534 \text{ cmH}_2\text{O}$	$P_3 = 0.5523 \text{ cmH}_2\text{O}$
$\omega_1 = 1.214 \text{ rad/s}$	$\omega_2 = 0.001414 \text{ rad/s}$	$\omega_3 = 2.401 \text{ rad/s}$
$c_1 = -0.3132 \text{ rad}$	$c_2 = 3.297 \text{ rad}$	$c_3 = -2.381 \text{ rad.}$

Then we can rewrite eqn. (6) as:

$$\ddot{V} + \left(\frac{R}{M^*} \right) \dot{V} + \frac{V}{CM^*} = \sum_{i=1}^3 \frac{P_i}{M^*} \sin(\omega_i t + c_i), \quad (43a)$$

or as:

$$\ddot{V} + 2n\dot{V} + p^2 V = \sum_{i=1}^3 Q_i \sin(\omega_i t + c_i). \quad (43b)$$

In the above equation:

- (i) the damping coefficient, $2n = R/M^*$
- (ii) the natural frequency of the lung-ventilatory cycle, $p^2 = 1/CM^*$
- (iii) $Q_i = P_i/M^*$. (43c)

So the governing eqn. (8) of the lung-ventilatory response to the inhalation pressure has three parameters: M^* , R and C (if the lung pressure is also monitored by



intubating the patient). The solution of this equation is given by:

$$\begin{aligned}
 V(t) = \sum_{i=1}^3 \left\{ \left[\frac{Q_i(-2\omega_i \cos(\omega_i t + c_i)n + \sin(\omega_i t + c_i)p^2 - \sin(\omega_i t + c_i)\omega_i^2)}{4n^2\omega^2 + p^4 - 2p^2\omega^2} \right. \right. \\
 - 1/2Q_i \left[-(n^2 - p^2)^{\frac{1}{2}} c_i \sin \omega_i^2 + p^2(n^2 - p^2)^{\frac{1}{2}} \sin c_i - 2\omega_i n^2 \cos c_i \right. \\
 + p^2 n \sin c_i - 2\omega_i n(n^2 - p^2)^{\frac{1}{2}} \cos c_i - \omega_i^3 \cos c_i + \omega_i^2 n \sin c_i \\
 \left. \left. + \omega_i p^2 \cos c_i \right] e^{-(n - (-p-n)(p+n)^{\frac{1}{2}})t} \right. \\
 \left. \left. \left/ (n^2 - p^2)^{\frac{1}{2}} (4n^2\omega_i^2 + p^4 - 2p^2\omega_i^2 + \omega_i^4) \right] \right\} \\
 + \sum_{i=1}^3 1/2 \left\{ \left[-p^2(n^2 - p^2)^{\frac{1}{2}} \sin c_i + np^2 \sin c_i + \omega_i \cos c_i p^2 \right. \right. \\
 + \omega_i^2 n \sin c_i - 2\omega_i n^2 \cos c_i + 2\omega_i n(n^2 - p^2)^{\frac{1}{2}} \cos c_i \\
 \left. \left. + \omega_i^2(n^2 - p^2)^{\frac{1}{2}} \sin c_i - \omega_i^3 \cos c_i \right] e^{-(n - (-p-n)(p+n)^{\frac{1}{2}})t} \right. \\
 \left. \left. \left/ (n^2 - p^2)^{\frac{1}{2}} (4n^2\omega_i^2 + p^4 - 2p^2\omega_i^2 + \omega_i^4) \right] \right\}. \tag{44}
 \end{aligned}$$

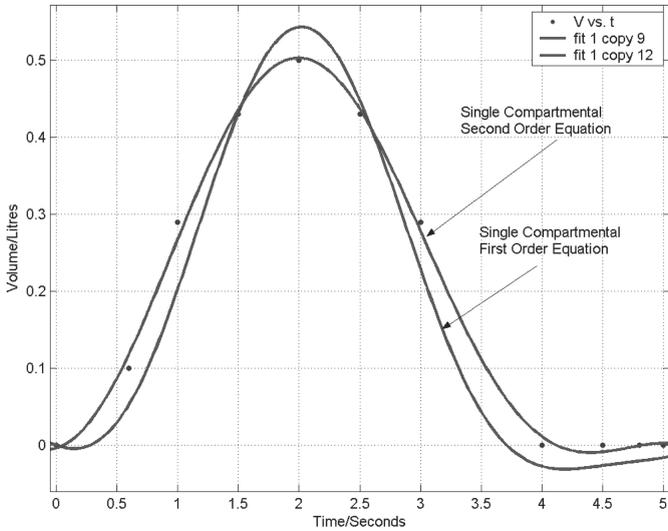
We will ignore the exponential terms and perform parameters identification by matching the above expression for $V(t)$ to the clinical data, shown in Fig. 2. The matching is illustrated in Fig. 5, wherein the first- and second-order differential equation solutions for $V(t)$ are depicted. The computed values of the model parameters are also shown in the table below the figure. Further, the first- and second-order model values of R and C are compared in the table.

Let us compare these values with those obtained by simulating the first-order model to the clinical data.

7 Two-compartment linear model

Now, it is possible that only one of the two lungs (or lung lobes) may be diseased. So, let us develop a procedure to distinguish between the normal lung and the pathological lung? We hence employ the 2-compartment model (based on our first-order differential equation of lung ventilatory function) to solve the problem of a two-lung model (schematized in Fig. 6).

For this purpose we make the subject breath at different values of frequency (ω), and monitor the total lung pressure $P_1^T(t)$ (i.e., P_{1i} and P_{2i}) and total lung volume $V_i(t)$. Correspondingly, we have $P_i^L(t)$, and $V_i^L(t)$ and $P_i^R(t)$ and $V_i^R(t)$ for the left and right lungs, respectively. The governing equations will be as follows



	First order model	Second order model
R [cmH ₂ O l ⁻¹ s]	2.28	3.44
C [l/cmH ₂ O]	0.21	0.85
M^* [cmH ₂ O l ⁻¹ s ²]		3.02
$n \left(= \frac{R}{M^*} \right)$ [s ⁻¹]		1.14
$p^2 \left(= \frac{1}{CM^*} \right)$ [s ⁻²]		0.39

Figure 5: Results of single compartmental model based on differentiate equation formulation, compared with the first-order differential equation model.

(refer to Fig. 3)

$$P^T = P^l = P^R, \quad \text{i.e. } P_1^T = P_1^l = P_1^R \quad \& \quad P_2^T = P_2^l = P_2^R \quad (45)$$

$$V^T = V^l + V^r \quad (46)$$

corresponding to ω_i ; wherein

$$(i) \quad V^l(t) = f(\omega, R^l, C^l, P^T(t)) \quad (47)$$

$$(ii) \quad V^R(t) = f(\omega, R^r, C^r, P^T(t)). \quad (48)$$

In these equations (20),

- (i) the variables $\omega, P^T(t), V^T(t)$ are deemed to be known, i.e. monitored.
- (ii) the parameters $R^l, C^l,$ and R^r, C^r are to be evaluated.



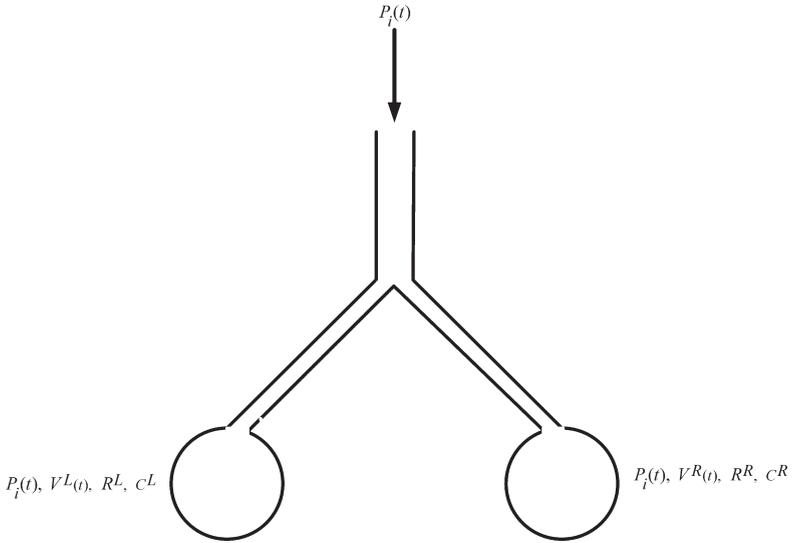


Figure 6: Schematic of two-compartment first-order lung-ventilation model.

Using the first-order differential equation model, (presented in sect. 2, as given by eqn. (6) or (14):

$$V(t) = \sum_{i=1}^3 \frac{(P_i C_a) [-\sin(\omega_i t + c_i) \omega_i^2 + \omega_i^3 \tau_a^2 \cos(\omega_i t + c_i)]}{(1 + \omega_i^2 \tau^2)}. \quad (49)$$

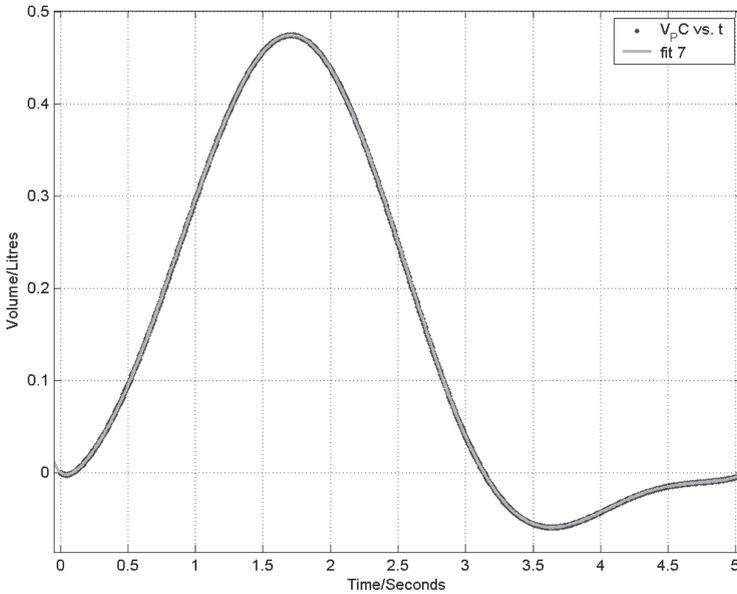
We put down the expression for $V^T(t) = V^L(C_L, \tau_L) + V^R(C_R, \tau_R)$, match it with the volume data (using a parameter-identification technique (software), to obtain the values of (C_L, τ_L) and (C_R, τ_R) by means of which we can differentially diagnose left and right lung lobes' ventilatory capacities and associated disorders (or diseases).

7.1 Two compartmental model using first-order ventilatory model

Using eqn. (6) without the exponential term, we put down the expression for the total lung volume equal to the sum of left and right lung volumes, as follows:

$$V(t) = \sum_{i=1}^3 \frac{P_i C_L [\sin(\omega_i t + c_i) - \omega_i \tau_L^2 \cos(\omega_i t + c_i)]}{(1 + \omega_i^2 \tau_L^2)} + \sum_{i=1}^3 \frac{P_i C_R [\sin(\omega_i t + c_i) - \omega_i \tau_R^2 \cos(\omega_i t + c_i)]}{(1 + \omega_i^2 \tau_R^2)}, \quad (50)$$





Two compartmental model

First order model

	Left lung	Right lung
R [cmH ₂ O l ⁻¹ s]	1.137	1.137
C [l/cmH ₂ O]	0.1066	0.0533
VTL_1	2.115	0.5289
VTL_2	0.2198	1.0320

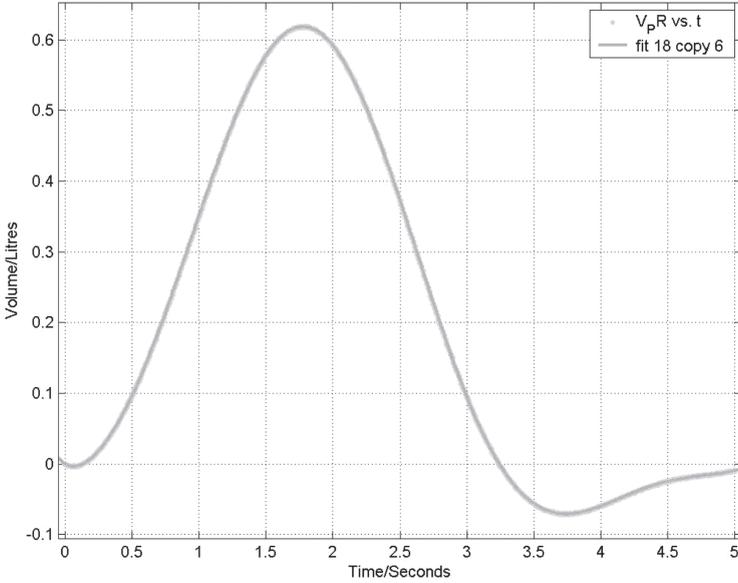
Figure 7: Results of the two-compartment model, based on the first-order differential equation model. Based on our assumption of $TV^L/TV^R = 0.92$ we have $TV^L = 0.48 \times 0.48 = 0.23041$ and $TV^R = 0.52 \times 0.48 = 0.24961$.

wherein, for the clinical data, we have:

$$\begin{array}{lll}
 P_1 = 1.581 \text{ cmH}_2\text{O} & P_2 = -5.534 \text{ cmH}_2\text{O} & P_3 = 0.5523 \text{ cmH}_2\text{O} \\
 \omega_1 = 1.214 \text{ rad/s} & \omega_2 = 0.001414 \text{ rad/s} & \omega_3 = 2.401 \text{ rad/s} \\
 c_1 = -0.3132 \text{ rad} & c_2 = 3.297 \text{ rad} & c_3 = -2.381 \text{ rad.}
 \end{array}$$

We further assume that the ratio of TV of the left lung to that of the right lung is 0.92.

Now, in order to develop a measure of confidence in our analysis, we first generate the total lung-volume data by assuming different values of C and R for left



Two compartmental model

First order model

	Left lung	Right lung
R [cmH ₂ O l ⁻¹ s]	1.138	2.276
C [l/cmH ₂ O]	0.1066	0.1066
VTL_1	2.1192	8.4766
VTL_2	0.3553	0.8341

Figure 8: Results of the two-compartment model, based on the first-order differential equation model. Based on our assumption of $TV^L/TV^R = 0.92$ we have $TV^L = 0.48 \times 0.61 = 0.29281$ and $TV^R = 0.52 \times 0.61 = 0.31721$.

and right lung lobes. We then use eqn. (50) along with the above data on pressure and frequency, to generate the total lung-volume data. We adopt this generated lung volume data as the clinical-volume data.

We now make our volume-solution expression (eqn. (50)) match this generated clinical-volume data, by means of the parameter-identification procedures, to evaluate C and R for the left and right lung-lobes and hence VTL_1 and VTL_2 (eqns. (11) and (18)) for these lobes. Based on the values of VTL_1 and VTL_2 , we can differentially diagnose the left and right lung lobes.



7.1.1 Stiff right lung (with compliance problems)

We now simulate a normal left lung and stiff right lung, represented by:

$$R^L = R^R = 1.14 \text{ cmH}_2\text{O l}^{-1} \text{ s and } C^L = 0.11, C^R = 0.05 \text{ l/cmH}_2\text{O.} \quad (51)$$

Substituting these parametric values into eqn. (50), we generate the total lung-volume data, as illustrated in Fig. 7.

Now our clinical data for this two-compartment model comprises of the pressure data of Fig. 2 and the generated volume data of Fig. 6. For this clinical data, we match the volume solution given by eqn. (50) with the generated volume data, illustrated in Fig. 7, and carry our parameter identification. The computed values of R and C , listed in the table of Fig. 7, are in close agreement with the initially assumed parametric values of eqn. (51). This lends credibility to our model and to our use of parameter-identification method.

Now for differential diagnosis, we compute the lung-ventilatory indices, as shown in the table in Fig. 7.

7.1.2 Right lung with R problems

Now, we simulate a lung with an obstructive right lung, as represented by:

$$R^L = 1.14 \text{ and } R^R = 2.28 \text{ cmH}_2\text{O l}^{-1} \text{ s and } C_L = C_R = 0.11 \text{ l/cmH}_2\text{O.} \quad (52)$$

As in the case of the stiff right lung, we first generate the lung-volume data for the above values of compliance and resistances. We then match the total lung-volume solution given by eqn. (50) with the generated lung-volume data, and compute the compliance and flow resistance values of the right and left lung. These are tabulated in Fig. 8, and found to have good correspondence with the assumed values of eqn. (52).

