Two-compartment modelling of respiratory system mechanics at low frequencies: gas redistribution or tissue rheology?

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Two-compartment modelling of respiratory system mechanics at low frequencies: gas redistribution or tissue rheology? T. Similowski, J.H.T. Bates. ABSTRACT: The mechanical properties of the respiratory system are generally inferred from measurements of pressure and flow at the airway opening. Traditionally, these measurements have been related through a single-compartment model of the respiratory system. Recently, however, there has been considerable interest in modelling low-frequency respiratory mechanics in terms of two compartments, since this gives a much improved description of experimental data. In this paper we consider two classes of two-compartment models that are compatible with pressure-flow relationships of air measured at the airway opening. One type of model accounts for regional ventilation inhomogeneity in the lung in terms of two alveolar compartments. The other type of model considers pulmonary ventilation to be homogeneous, while the tissues of the respiratory system are modelled as being viscoelastic. In normal dogs, the appropriate two-compartment model has been shown to be the viscoelastic model. In the case of abnormal physiology, however, one must invoke a model having both viscoelastic tissues and ventilation inhomogeneities. Additional experimental data are required in order to identify such a model, and to quantify these two phenomena.


The respiratory system is comprised of a countless number of elements. Its complexity, together with the necessity to study respiratory mechanics in physiology as well as in clinics, has generated the need for relatively simple models that can mimic the mechanical behaviour of the respiratory system to some degree. The process called inverse modelling consists first of devising a model structure. The parameters of the model are then evaluated so as to make the behaviour of the model match a set of experimental data as closely as possible. The components of the model and their respective parameters should have reasonable physiological counterparts. The small number of respiratory variables that can be measured (flows, volumes and pressures, with some refinements regarding the level of their measurements) sets a limit to the sophistication of the models used and to the physiological interpretations that can be derived from them.

Although a single-compartment model has been, and still is, widely used in respiratory physiology, two-compartment models appear to be much more appropriate in various circumstances. There are two physiologically distinct classes of two-compartment models of interest for respiratory mechanics: those based on gas redistribution between different lung regions and those based on intrinsic tissue properties. However, choosing between these two families of models requires more information than is available in the relationships between the quantities that are usually measured, namely tracheal or transpulmonary pressure and tracheal flow.

The need for two-compartment models

The simplest model of the respiratory system, which is still the most commonly used, is made of two lumped elements, one representing an elastance (balloon), and the other representing a resistance (pipe) (fig. 1). This model has become so popular that the equation governing its behaviour is generally (and erroneously) referred to as the "equation of motion of the respiratory system", rather than as the "equation of motion of a single-compartment linear model of the respiratory system". This equation is [1, 2]:

\[ P(t) = RV(t) + EV(t) \]  

where \( P \) is pressure (usually airway opening pressure or transpulmonary pressure), \( R \) is the resistance of the pipe to gas flow (\( V \)), \( E \) is the elastance of the balloon, \( V \) is the volume of the balloon above its relaxed volume, and \( t \) is time. Equation 1 embodies a
number of assumptions. Important among these is that the respiratory system behaves linearly, that is that $R$ is independent of $V$ and $E$ is independent of volume. Another assumption is that inertia does not play a significant role. This postulate is probably valid within the range of physiological breathing frequencies up to 2 Hz [3] and will be accepted in the rest of this paper.

![Diagram of a single-compartment linear model of respiratory mechanics](image)

**Fig. 1.** - The single-compartment linear model of respiratory mechanics. Elastance and resistance are characterized by single parameters $E$ and $R$, respectively.

During volume cycling, values for $E$ and $R$ can be found by fitting Equation 1 to measurements of $P$, $V$ and $V$ using multiple linear regression [4, 5] or a related technique such as the electrical subtraction method [6]. However, intuition suggests that a more detailed model than the one governed by Equation 1 should provide a better description of respiratory mechanical data. There are two general approaches to increasing the complexity of a model in order to more accurately describe a set of data. One is to increase the number of mechanical degrees of freedom, that is, add more compartments. The other is to make the existing elements of the model nonlinear, such as by adding a flow-dependent term to the parameter accounting for the airway resistance. The appropriate approach depends on the data in question. For example, a manoeuvre which involves varying flow over a wide range may bring out the nonlinear effects of a flow-dependent resistance, while a manoeuvre which involves a range of different oscillation frequencies at the same tidal volume may produce behaviour of a predominantly multi-compartment nature.

There is considerable experimental evidence pointing to the necessity of more than one compartment for describing respiratory system mechanics at low frequencies. For example, Equation 1 cannot account for the frequency dependence of resistance and elastance in the range 0–2 Hz [5, 7–11]. A model of two or more compartments is required, with the compartments having different time-constants given by the ratios of the compartmental resistances to elastances [12]. It has also been observed in dogs that relaxed expiration is not well described by a single exponential function, as Equation 1 would predict, but is extremely well fitted by a double exponential function [13, 14]. Here again, one is compelled to invoke a two-compartment model with a fast and a slow compartment. Similar conclusions can be drawn from the time course of pressure (tracheal, transpulmonary or oesophageal pressure) that is observed after an end-inspiratory occlusion. If the respiratory system behaved as a single-compartment linear model, the pressure should immediately drop to its static value upon flow interruption and remain fixed thereafter. Actually, flow interruption results in a sudden drop in pressure followed by a further slow decay towards the static value. Flow interruption during expiration results in the opposite effect, with an initial rapid jump in pressure being followed by a further slow rise. Only a model including a fast and slow compartment can account for this kind of behaviour [1, 2], as depicted in figure 2.

![Diagram of the tracheal pressure signal resulting from flow interruption](image)

**Fig. 2.** - (a) A stylized representation of the tracheal pressure signal resulting from the sudden interruption of flow during constant flow inflation into a single-compartment model (dashed line) and a two-compartment model (solid line). (b) The corresponding situation for the interruption of expiratory flow, where the tracheal pressure is equal to atmospheric (i.e. zero) prior to interruption. The arrow indicates the instant of flow interruption for both plots.
Two types of two-compartment models

Linear two-compartment models of the respiratory system can be divided into two physiologically distinct types. One of these types, the gas redistribution model, ascribes the multi-compartment nature of the respiratory system to unevenness of gas distribution throughout the lungs. Two varieties of gas redistribution model have been proposed. The first, which we will call the parallel gas redistribution model, has dominated the literature since its introduction [12] and consists of a parallel arrangement of alveolar compartments connected by separate airways to the trachea (fig. 3a). The second, which we will call the series gas redistribution model, is made of two balloons connected in series [15]: the distal balloon represents the lumping of homogeneous alveoli, and is connected to the trachea via a proximal balloon representing the compliance of the airway tree (fig. 3b).

An alternative type of two-compartment model, which we call the rheologic type, does not assume the existence of an uneven distribution of ventilation. Instead, rheologic models extend the single-compartment model by incorporating a viscoelastic [16–18] or plastoelastic [19–21] structure in parallel with the components representing airway resistance and static elastance, thereby accounting for the rheological properties of the respiratory system tissues. The viscoelastic and plastoelastic rheologic two-compartment models are shown in figures 4a and 4b, respectively, and are characterized by an elastic recoil which depends not only on lung volume but also on volume history.

We should point out here that using the term "compartment" with regard to viscoelasticity extends its definition somewhat beyond that normally encountered in physiology. A compartment is normally meant to be a region within which the material of interest (gas, drug, etc.) is uniformly mixed. The dynamics of the material...
in such a region is invariably described in terms of a linear first-order differential equation. This clearly applies to each compartment of the gas redistribution models described above. Viscoelastic properties, on the other hand, are generally represented in terms of collections of springs (elastances) and dashpots (resistances) [22], such as the model shown in figure 4a. Now we apply the term compartment to any physiological entity the dynamics of which are described by a first-order equation. In the model in figure 4a, the parallel arrangement of the dashpot \( R_1 \) and the spring \( E_1 \) represents the fast compartment; whereas the series arrangement of the dashpot \( R_2 \) and the spring \( E_2 \) (which together constitute a Maxwell body) represents the slow compartment. A Maxwell body can account for the slow phase of relaxed expiration, as well as stress adaptation related phenomena such as the slow pressure changes that follow flow interruption [18, 22–25]. During ventilation, when the cycling period is close to its time constant, a Maxwell body can also predict the dissipative Lissajous pressure-volume loop [18, 22], often and inappropriately referred to as dynamic hysteresis. At significantly higher or lower frequencies, the pressure-volume loop of the Maxwell body closes to become a single straight line.

The finding of significant quasi-static pressure-volume hysteresis in isolated lungs has lead to the introduction of plastic elements in the rheologic modelling of the respiratory system [19]. The viscoelastic model (fig. 4b) differs from the viscoelastic model (fig. 4a) by the substitution of a dry friction (Coulomb) element in place of the viscous element (dashpot) in the slow compartment. The Coulomb element gives rise to hysteresis when flow is reversed quasi-statically, with an amount of energy dissipation which is only dependent on the volume reached when the direction of flow changes [26]. Recent data, however, suggest that static hysteresis in vivo, at least in normal dogs, is minimal [27, 28]. This also seems to be the case in spontaneously breathing humans at rest [29]. Thus, the viscoelastic model appears to be the most appropriate simple rheological model for describing the mechanical behaviour of the respiratory system, at least within the tidal volume range. Although the contribution of plastic elements could be more important at higher volumes, the rest of this review will be restricted to considerations of rheologic models of the viscoelastic type.

The equations which govern the behaviours of the two-compartment models considered above are as follows. The equation for the parallel gas redistribution model (fig. 3a) is obtained in an analogous manner as:

\[
\dot{P}(t) [R_j + R_j] + P(t) [E_1 + E_1] = \dot{V}(t) [R,R_1 + R,R_2 + R,E_1] + \dot{V}(t) [E_1,R_2 + R,E_1] + \dot{V}(t) [E_1,E_1] \tag{2}
\]

where the standard dot notation for time derivatives has been used (a single dot means the derivative with respect to time, while two dots means the second derivative with respect to time). \( R_1, R_2, E_1, E_2 \) and \( R, E \) are the parameters of the model shown in figure 3a.

The equation for the viscoelastic rheological model (fig. 4a) is derived in the Appendix of [18] to be:

\[
\dot{P}(t) [R_j + R_j] + P(t) [E_1 + E_1] = \dot{V}(t) [R,R_1 + R,R_2 + R,E_1] + \dot{V}(t) [E_1,R_2 + R,E_1] + \dot{V}(t) [E_1,E_1] \tag{3}
\]

The key point about Equations 2 to 4, from the point of view of deciding between them, is that they have exactly the same form. That is, there are precisely corresponding terms in \( P(t) \) and \( V(t) \) and their time-derivatives in each equation. This means that, given a set of measurements, of \( P(t) \) and \( V(t) \), it is impossible to say whether the system relating the two signals is of the gas redistribution type or of the rheologic type.

End-inspiratory interruption of flow provides a significant example of this ambiguity. If this technique is applied to the parallel gas redistribution model (fig. 3a), the initial drop in pressure that is observed immediately upon flow interruption (fig. 2a) is due to the cessation of energy dissipation within the airway tree [2]. The subsequent decay in pressure (fig. 2a) is then due to gas redistribution from the compartment with the higher pressure at the instant of interruption to the one with the lower pressure (a phenomenon often referred to as “pendelluft”). A similar explanation pertains to the series gas redistribution model (fig. 3b) [2]. When an end-inspiratory occlusion is applied to the viscoelastic rheologic model, the initial drop in pressure is again due to the immediate cessation of energy dissipation, this time in the dashport \( R_1 \) (fig. 4a). The slow pressure decay, however, is due to the relaxation of the spring \( E_1 \) against its dashpot \( R_1 \). The parameters of both gas redistribution models and the viscoelastic rheologic model can be assigned values so that all models will produce exactly the same overall behaviour, making them indistinguishable from the perspective of pressure-flow relationships observed at the airway opening. Nevertheless, the underlying physiological mechanisms giving rise to this behaviour in the models are very different. Clearly, it would be convenient to have some means of deciding which of the models was best for describing a particular situation.

Deciding between gas redistribution and rheologic models

Normal lungs

In order to decide if the respiratory system is better described in terms of a gas redistribution or a rheologic model it is necessary to make additional measurements, besides flow and pressure of air at the airway opening. This has been done recently in normal dogs in which alveolar pressures were measured directly using the alveolar capsule technique on several different lung surface sites simultaneously [21]. When an interruption was performed during expiration, the tracheal pressure
Abnormal lungs

There are many abnormalities of the lungs in which significant inhomogeneities of ventilation exist, such as during induced bronchoconstriction and in a parenchymal diseases like adult respiratory distress syndrome. A model to account for pulmonary mechanics in these situations must feature not only tissue rheologic properties, but also regional differences in mechanical properties. Such a model must therefore have at least three compartments - two for different lung regions and another for tissue rheology - and for the reasons discussed above, cannot be identified only from measurements of pressure and flow of air at the airway opening. Indeed, it has been shown in dogs treated with histamine aerosol that the relaxed expiration volume-time profile is still extremely well described by a sum of two exponentials [14], yet significant regional inhomogeneities during bronchoconstriction have been demonstrated throughout the lung [30, 31]. Thus, under such conditions both gas redistribution and tissue rheology must be important. One therefore needs to have additional experimental data in order to determine the contributions of gas redistribution and tissue rheology to the mechanical behaviour of the inhomogeneous lung.

One potential means of obtaining this information is to examine the pressure-flow relationships obtained with gases of different viscosity and density. If regional ventilation inequalities are of major importance, varying the gas density and viscosity should alter their consequences. On the other hand, the intrinsic tissue properties of the respiratory system should not be altered by changes in the characteristics of the gas used for ventilation. Such experiments done in normal rabbits have shown that the amplitude and time course of the slow phase of the post-interruption pressure changes was not modified by the use of a hydrogen-oxygen mixture, as compared to air [32]. More recently, a similar approach has given strength to the hypothesis that maldistribution of ventilation may play a more important role than viscoelasticity in smokers [33]. In acute animal experiments, it is possible to use the alveolar capsule technique to measure alveolar pressures at several lung surface sites simultaneously. Although one is left with a rather severe sampling problem given the number of alveoli in a lung, it does allow some idea of the degree of pressure inhomogeneity throughout the lung and the time-constants associated with various lung regions [31].

Conclusions

The study of respiratory system mechanics is typically characterized by a situation in which mathematical modelling is of central importance. This is because the investigator must attempt to infer the nature of the underlying system from a data set that, although usually very precise, is nevertheless taken from only a limited number of measurement sites. The particular problem considered in this paper is that of modelling respiratory mechanics in terms of more than one compartment during low-frequency manoeuvres (that is, close to the range of normal breathing frequencies). Normal physiology seems to be well characterized by a two-compartment model, and direct measurements of alveolar pressures have shown that gas redistribution is relatively unimportant during low-frequency manoeuvres. Thus, the normal lung is most appropriately represented in terms of two compartments, as a homogeneous lung surrounded by viscoelastic tissue. Abnormal physiology cannot be so simply represented, however, since significant ventilation inhomogeneities throughout the lung have been demonstrated. In such a situation one is compelled to invoke a model featuring both tissue rheology and ventilation inhomogeneity. Such a model cannot be uniquely identified from measurements of pressure and flow of air at the airway opening. Gaining the additional data necessary to assess the extent and nature of each of these two phenomena is currently an important research area.

References

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