

Time dependence of recruitment and derecruitment in the lung: a theoretical model

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Received 2 January 2002; accepted in final form 30 April 2002

Bates, Jason H. T., and Charles G. Irvin. Time dependence of recruitment and derecruitment in the lung: a theoretical model. *J Appl Physiol* 93: 705–713, 2002. First published May 3, 2002; 10.1152/jappphysiol.01274.2001.— Recruitment and derecruitment (R/D) of air spaces within the lung is greatly enhanced in lung injury and is thought to be responsible for exacerbating injury during mechanical ventilation. There is evidence to suggest that R/D is a time-dependent phenomenon. We have developed a computer model of the lung consisting of a parallel arrangement of airways and alveolar units. Each airway has a critical pressure (P_{crit}) above which it tends to open and below which it tends to close but at a rate determined by how far pressure is from P_{crit} . With an appropriate distribution of P_{crit} and R/D velocity characteristics, the model able to produce realistic first and second pressure-volume curves of a lung inflated from an initially degassed state. The model also predicts that lung elastance will increase transiently after a deep inflation to a degree that increases as lung volume decreases and as the lung becomes injured. We conclude that our model captures the time-dependent mechanical behavior of the lung due to gradual R/D of lung units.

lung injury; atelectasis; mechanical ventilation; pressure-volume loop; lung elastance

THERE ARE THOUGHT TO BE two principle mechanisms by which lung volume may change during inspiration and expiration: 1) changes in the volumes of individual alveoli and 2) recruitment and derecruitment (R/D) of air spaces (which can occur at the level of both the airways and the alveoli). Although there is still controversy about which is the dominant mechanism (5), it is well established that R/D can increase substantially in lung injury (6, 14, 24, 34). Although R/D plays a significant role when the volume of a normal lung is changed over the vital capacity range (12), R/D is thought by some to be a major phenomenon in normal lungs even during tidal ventilation (5).

R/D is generally thought to be governed by critical opening and closing pressures. This view holds that recruitment of a closed lung unit occurs when the pressure acting to distend the unit reaches a critical value, at which point the subtended unit suddenly pops open and joins other open units in receiving any additionally administered volume. During deflation, it is

similarly thought that the unit suddenly closes when its distending pressure drops below another critical value, which is less than the critical opening pressure for that unit (36). Consequently, current mathematical or computer models of R/D in the lung assume a given airway opens and closes as a function of transmural pressure (6, 15, 36, 39–41). However, these models are unable to account for long-term transient effects of a change in lung volume, such as the gradual decrease in lung compliance that has been shown to occur over a period of several minutes after a sigh (8, 18, 23, 45). These long-term transients may correspond to the periods of improved gas exchange that have been reported after sighs in injured lungs (33). The genesis of such transients is not entirely clear. The earlier literature tended to explain them as being due to the dynamics of surfactant at the air-liquid interface (45), although Horie and Hildebrandt (18) acknowledged that derecruitment could play a role in low lung volumes. Recent work on optimal ventilation of injured lungs has suggested that R/D may take place throughout much of the breath (7, 14). We further consider here that R/D is not instantaneous but rather has a time scale associated with it that may extend from seconds to minutes. This implies that airway R/D should be determined by time as well as by pressure. This notion is further supported by both in vitro and theoretical models (11, 29) that show that opening and closing of flexible fluid-lined conduits is not instantaneous once a critical pressure (P_{crit}) threshold is reached. Instead, these events occur progressively over the time required for a liquid bridge across the lumen first to break and then reform.

The above considerations led us to hypothesize that the time dependence of R/D in the lung should have a significant impact on its dynamic behavior, particularly in situations of lung injury or disease. This should, in turn, have implications for the optimal ventilation of injured lungs and, in particular, the use of recruitment maneuvers (sighs) that serve to improve gas exchange. In the present study, we developed a mathematical/computer model of the mechanically ventilated lung that incorporated a time-dependent behavior of airway opening and closing. We showed

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that this model can account for certain mechanical phenomena in the lung that cannot be explained simply in terms of critical opening and closing pressures. Data simulated with the model further demonstrate that, during mechanical ventilation of an injured lung, the efficacy of periodic recruitment maneuvers may be critically dependent on how the maneuvers are timed.

METHODS

We begin by constructing a model of a single lung unit consisting of a single alveolar compartment served by a collapsible airway. The model is driven by an applied pressure waveform (P). If we limit our attention to relatively slow inflations and deflations of this model lung, we can consider that P is effectively the pressure applied to inflate the alveolar compartment. To be complete, we could assign the airway a resistance and keep track of the pressure drop across it, but this does little to change our conclusions, so we will neglect it. Provided the airway remains open, the alveolar compartment will expand and contract with P , according to the Salazar-Knowles relationship (35)

$$V = A - Be^{-KP} \quad (1)$$

where A , B , and K are constants, and V is the volume of the alveolar compartment. If the airway closes, compartment volume will remain fixed until the airway reopens, when it will immediately assume the V appropriate to the value of P at that time according to Eq. 1.

The key to the model, and also its innovative aspect, is how airway opening and closure are determined. The airway can exist in either of two states (open or closed) and has a single P_{crit} above which opening occurs and below which closure occurs. However, opening and closure do not occur instantaneously once P passes to either side of P_{crit} . Instead, it takes a certain amount of time for a closed airway to open or for an open airway to close. This time is a function of how far P is from P_{crit} . Thus, for example, if the airway starts in the closed position and P is set to be only slightly above P_{crit} , then the airway will take a long time to open. However, if P is set much greater than P_{crit} , the airway will open quickly. Similarly, an open airway will close in progressively less time as P descends below P_{crit} .

We formalize this concept by associating with the airway a virtual trajectory (x) confined between the limits of 0 and 1 (Fig. 1). This trajectory may correspond, for example, to the configurational changes within an airway leading from a fully open conduit ($x = 1$) to one that is completely closed ($x = 0$) by a liquid bridge (11, 29). Correspondingly, intermediate values of x ($0 < x < 1$) represent the continuous states of progressive narrowing due to fluid accumulation at the eventual site of the liquid bridge. If $(P - P_{crit})$ is positive, the velocity along x (dx/dt) is positive until x reaches the upper limit of 1, where it remains until dx/dt reverses sign. Similarly, if $(P - P_{crit})$ is negative, x decreases until it reaches 0, where again it stays until dx/dt becomes positive again. The

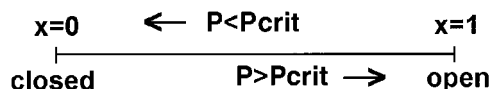


Fig. 1. Virtual trajectory (x) associated with each lung unit. The unit moves along the trajectory to the right if pressure (P) is greater than the critical pressure (P_{crit}) and to the left if P is less than P_{crit} . If the unit reaches $x = 1$, the unit opens unless it was already open, and if it reaches $x = 0$, it closes unless it was already closed.

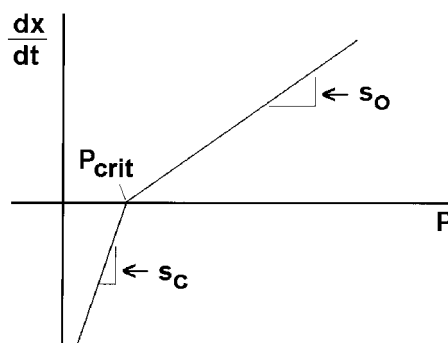


Fig. 2. Velocity along x (dx/dt) is linearly related to the difference between P and P_{crit} . The slope of this relationship is the rate at which opening velocities increase (s_o) when $P > P_{crit}$ and the rate at which closing velocities increase (s_c) when $P < P_{crit}$.

state of the airway (i.e., either open or closed) is determined by the most recent of the two limits of x that was visited. That is, if the most recent limit was 0, then the airway is closed, and it remains closed until x reaches 1. On reaching 1, the airway immediately opens and remains so until x next reaches 0, where it closes again.

It remains to be determined how dx/dt should depend on $(P - P_{crit})$. The simplest dependence we could reasonably assume is a linear one, and in fact there is *in vitro* experimental evidence to support such a choice for the case of airway opening (11). However, there is no reason we know of to suggest that the dependence of dx/dt on $(P - P_{crit})$ should be the same for opening and closure. Thus we choose the model equations

$$\begin{aligned} \frac{dx}{dt} &= s_o (P - P_{crit}), P > P_{crit} \\ &= s_c (P - P_{crit}), P < P_{crit} \end{aligned} \quad (2)$$

with the proviso that $0 \leq x \leq 1$. The parameters s_o and s_c are, respectively, the rates at which opening and closing velocities increase as P moves away from P_{crit} (Fig. 2).

This model was implemented on computer by integrating Eq. 2 with respect to time by using first-order (Euler) integration. If x reaches either 0 or 1 (Fig. 1), the state of the airway is adjusted accordingly (closed for 0 and open for 1), unless it is already in the appropriate state, in which case it simply remains in that state. Having reached 0 or 1, x remains there until dx/dt changes sign. The state dynamics of an airway are thus characterized by the three parameters in Eq. 2, namely s_o , s_c , and P_{crit} (Fig. 2).

Figure 3 shows the pressure-volume (P - V) loop obtained by subjecting a single airway-alveolar unit to a sinusoidal perturbation in P with an amplitude of 30 cmH₂O and a period of 100 s. The perturbation began at 0 cmH₂O, with $x = 0$. The values of the parameters in Eq. 1 were $A = B =$ arbitrary units, and $K = 0.14$ cmH₂O⁻¹. This gives the model a half-inflation pressure of 5 cmH₂O, similar to that employed by Hickling (15). The values of the parameters in Eq. 2 were $s_o = 0.05$ s⁻¹·cmH₂O⁻¹, $s_c = 0.05$ s⁻¹·cmH₂O⁻¹, and $P_{crit} = 5$ cmH₂O. The P - V loop shows hysteresis because opening and closing of the airway do not occur as soon as P passes through P_{crit} due to the time it takes for the virtual position x of the airway to move from 0 to 1 or vice versa.

Of course, a real lung does not have a single airway that is either open or closed but, rather, has a great many airways connected in series and parallel, each of which may open or close independently of the others. To simulate this situation,

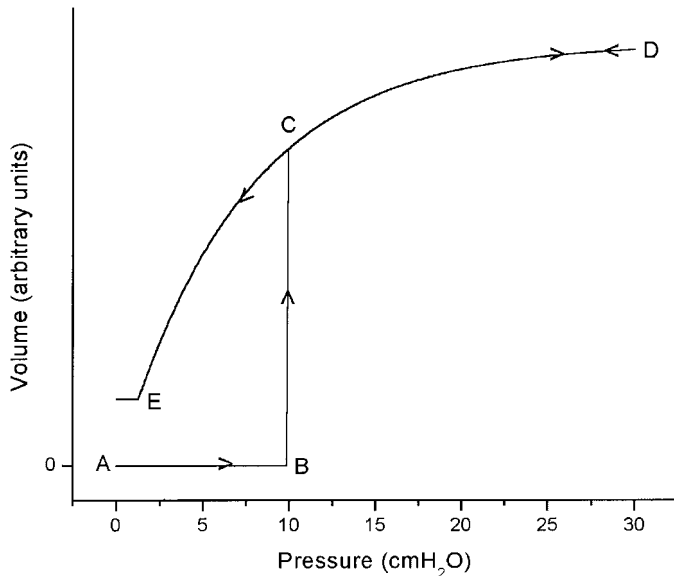


Fig. 3. Pressure-volume (P-V) curve of a single lung unit during inflation and deflation over its total volume range. The unit begins at a pressure of zero (point A) in the closed state and at position 0 on its x . As pressure increases from 0 and passes through 5 cmH₂O, the unit begins to move along x until, at ~9 cmH₂O, it reaches $x = 1$ (point B). At this point, the unit pops open and assumes a volume commensurate with the P-V relationship of the unit (point C). The rest of the inflation then proceeds along the open P-V curve of the unit until the maximum inflation pressure is reached at point D. During the subsequent deflation, the curve retraces its steps but continues through point C until it passes 5 cmH₂O. At this point, it starts to move back along its x until $x = 0$ again at point E, where the unit closes and the remainder of the expiration proceeds at fixed volume.

we connected a number of the airway-alveolar units in parallel. The units each had identical volumes, which combined to give the total lung volume. Each unit had its own value of s_o , s_c , and P_{crit} . These values are distributed randomly to represent spatially heterogeneous variation in mechanical properties throughout the lung. The probability distributions for s_o , s_c , and P_{crit} determine the overall behavior of the model and, in the present study, were chosen according to the following considerations. First, Pelosi et al. (31) and Crotti et al. (7) presented data suggesting that the critical opening and closing pressures in the lung are normally distributed. We therefore let the distribution of P_{crit} be Gaussian with mean (μ_P) and standard deviation (σ_P). Second, we consider it likely that most units of the lung will have a relatively slow rate of closure and opening because the lung is, at least normally, quite stable. Only a small number will have rapid closure and opening rates. Thus we let s_o and s_c be distributed quasihyperbolically, according to the probability distributions S_o/ξ and S_c/ξ , respectively, where ξ is a uniformly distributed random variable on the interval [0,1] and S_o and S_c are scale factors. These choices of distributions for s_o and s_c are also motivated by the fact that many processes in nature are distributed in a hyperbolic fashion, reflecting an inherently fractal character (2, 41, 44). The detailed steady-state behavior of the multicompartment model is thus determined by the values of μ_P and σ_P that specify the distribution of P_{crit} and by the values of S_o and S_c that determine the distributions of s_o and s_c . The transient behavior of the model is also determined by the initial conditions of which lung units start off open, which start off closed, and the initial value of x for each compartment.

RESULTS

Quasi-static P-V characteristics. To decide how μ_P , σ_P , S_o , and S_c should be chosen, we first set out to reproduce the quasi-static P-V curve of the normal isolated lung during the first and second vital capacity inflations from the degassed state. We performed a simulation with a model containing 5,000 parallel lung units by using an integration time step of 100 ms. We found, through a process of trial and error, that values of $\mu_P = 5$ cmH₂O, $\sigma_P = 3$ cmH₂O, and $S_o = S_c = 0.005$ s⁻¹·cmH₂O⁻¹ gave the P-V loops shown in Fig. 4. The simulation was started with all lung units closed and all the x set to zero. P was then cycled between 0 and 30 cmH₂O sinusoidally with a period of 100 s for two complete cycles. The first loop thus shows a great deal of hysteresis as the units must all open on the inspiratory limb whereas only some reclose on the expiratory limb. The inspiratory limb of the second loop thus is very different from that of the first loop and, as a result, shows less hysteresis. The expiratory limbs of the two loops are virtually identical. These curves are similar to the P-V loops obtained during first and second inflations of degassed mammalian lungs (40).

The P-V characteristics of this model vary with the cycling rate. Figure 5A shows first and second P-V loops obtained under the same conditions as in Fig. 4, except with cycling periods of 50 and 200 s. The hysteresis is more pronounced at the faster cycling rate, but the qualitative loop features are similar to those in Fig. 4. Figure 5B shows loops obtained under identical conditions, except this time s_o and s_c were both distributed uniformly between 0 and 0.05.

An injured lung has a greater tendency to experience air space closure than a normal lung. Increased closure can be produced in the model in three ways: 1) increasing P_{crit} , 2) decreasing s_o , and 3) increasing s_c . Figure 6

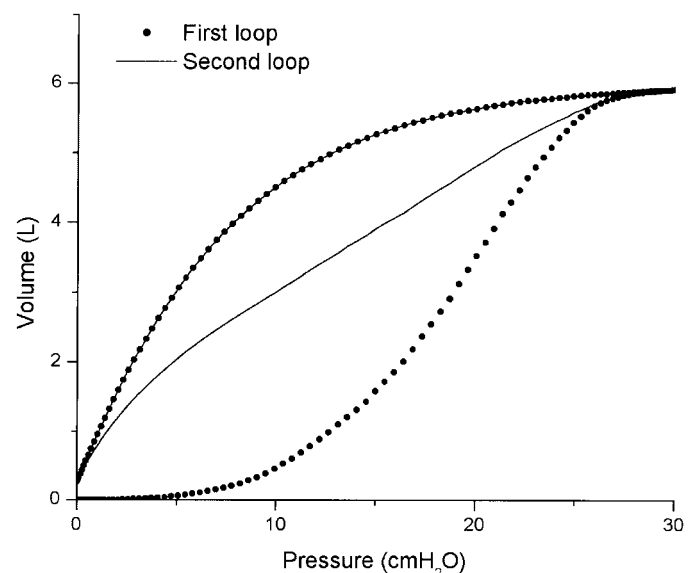


Fig. 4. First (dotted line) and second (solid line) P-V loops of a degassed lung cycled over the total lung capacity range. Each pressure cycle was sinusoidal with a period of 100 s.

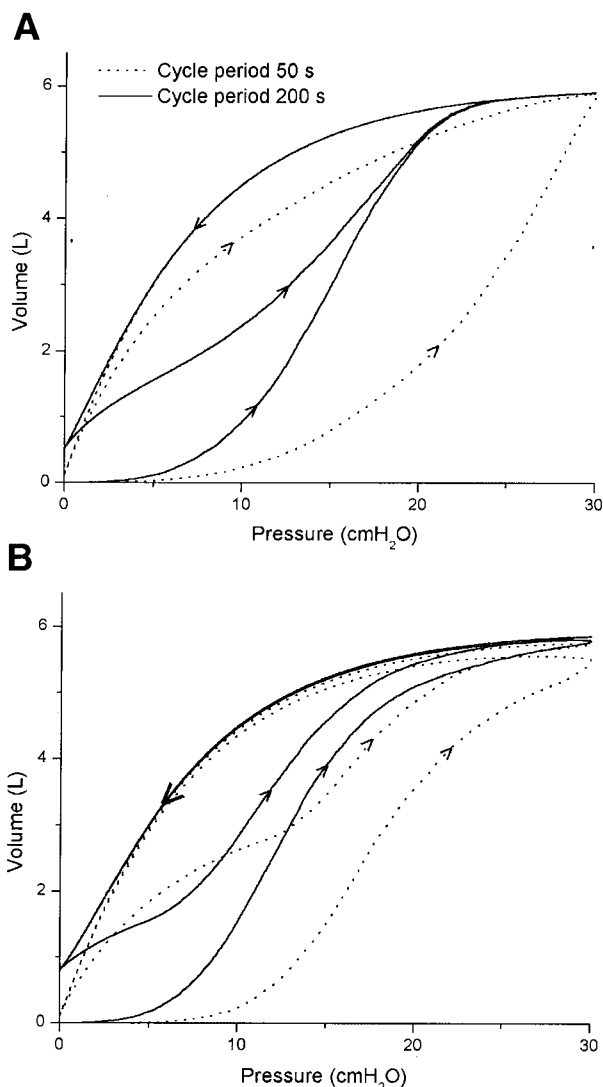


Fig. 5. A: first and second P-V loops corresponding to the loops shown in Fig. 4 when the model was cycled with a period of 200 (solid line) and 50 s (dotted line). B: P-V loops obtained under identical conditions, except this time s_o and s_c were both distributed uniformly between 0 and 0.05. Arrows on the loops show direction of cycling around the loops.

shows example P-V loops obtained in all three cases. Figure 6A shows that doubling both P_{crit} and σ_P causes a widening of the P-V loop and an increase in lung volume at the end of the cycle as a result of increased air trapping. Figure 6B shows that halving s_o produces a rightward shift in the inflation limb of the curve with no change in the deflation limb. Figure 6C shows that doubling s_c has relatively little effect on the curve apart from a slight increase in trapped volume. When all three changes are implemented simultaneously, the P-V curve is considerably wider than control (Fig. 6D) with incomplete inflation of all lung units at the apex of the curve and substantial air trapping at the end of deflation.

Time dependence of compliance. It has been demonstrated that the compliance of the lung decreases gradually during regular ventilation after a deep inflation

(8, 18, 26). Although this phenomenon has been ascribed by some to dynamics of surfactant at the air-liquid interface, we focus on the possibility that it is due to the gradual and progressive closure of airspaces (atelectasis) that are initially recruited by the deep inflation. We reproduced this phenomenon by subjecting the model to a sinusoidally oscillating P at a frequency of 0.2 Hz, a peak-to-peak amplitude of 5 cmH₂O, and a positive end-expiratory pressure (PEEP) level of 5 cmH₂O. The model ventilated for 10 min, starting from an initial configuration in which all units were open and all x were set to 1, such as might pertain to the situation immediately after a deep lung inflation. The model parameters were the same as those used to produce Fig. 4. Figure 7 shows the elastance (E) of the model calculated by fitting the equation

$$P(t) = EV(t) + P_o \quad (3)$$

to the 600-s-simulated signals of $P(t)$ and $V(t)$ by using recursive linear regression with a memory time-constant of 5 s (20), where P_o is a pressure offset term corresponding to the PEEP and t is time. Figure 7 also shows E obtained when the simulation was repeated with PEEP levels of 3 and 1 cmH₂O. These plots show that E increases progressively as lung units are derecruited with time. The rate of derecruitment increases as PEEP decreases. Figure 7 (bottom) shows the fraction of lung units that are open as a function of time throughout the simulations. All units are open initially, but a progressively increasing fraction is unable to remain open as ventilation continues. This fraction is substantially larger when PEEP is reduced from 5 to 1 cmH₂O.

These simulations were repeated with the injured lung model employed to generate Fig. 6D. The increase in E with time (Fig. 8, top) is much more pronounced than in the normal lung simulation (Fig. 7, top), and the fraction of lung units closing with time is commensurately greater (Fig. 8, bottom). The injured lung thus closes much more precipitously than the normal lung and to a much greater degree. Also, the PEEP dependence of closure is more pronounced in the injured lung.

DISCUSSION

It has long been known that the mechanical properties of the lungs are not static. Rather, there is a substantial dynamic aspect to lung mechanics that is manifest in such phenomena as stress adaptation after sudden changes in volume (16) and the dependence of lung resistance and compliance on the frequency at which flow is driven into and out of the lungs (32). Accordingly, lung mechanics depend not only on the volume of gas in the lungs or the flow into it at any instant in time but also on how lung volume has changed during the immediate past, i.e., volume history. These phenomena have mostly been accounted for thus far in terms of mathematical models embodying mechanisms representing tissue viscoelasticity and regional mechanical heterogeneities (16, 27, 28, 37), both

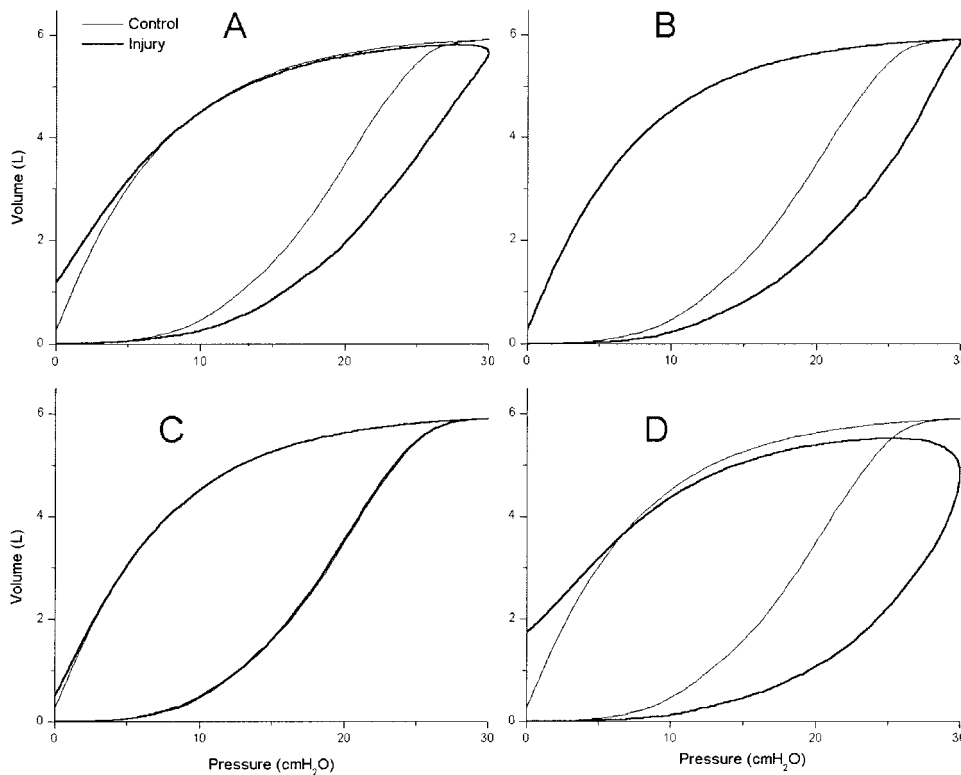


Fig. 6. First P-V loops from the degassed state obtained under various conditions. Thin lines in A–D is the first loop shown in Fig. 4. Thick lines show the P-V loops obtained when P_{crit} and its standard deviation were doubled (A), when s_0 was halved (B), when s_c was doubled (C), and when all parameter changes were implemented together (D).

of which give rise to qualitatively identical influences on the relationships between transpulmonary pressure and flow. In normal lungs, there are quantitative differences between the effects of complex tissue rheology and regional heterogeneity: rheological effects occur over a time scale typically of seconds (4, 16), whereas gas redistribution resulting from regional time con-

stant inequalities occurs much more rapidly (3, 25). In diseased or injured lungs, however, gas redistribution becomes both slower and more pronounced, making its effects on transpulmonary P-V relationships indistinguishable from those due to tissue rheology (22).

In this study, we consider a third possible mechanism to account for the effects of lung volume history

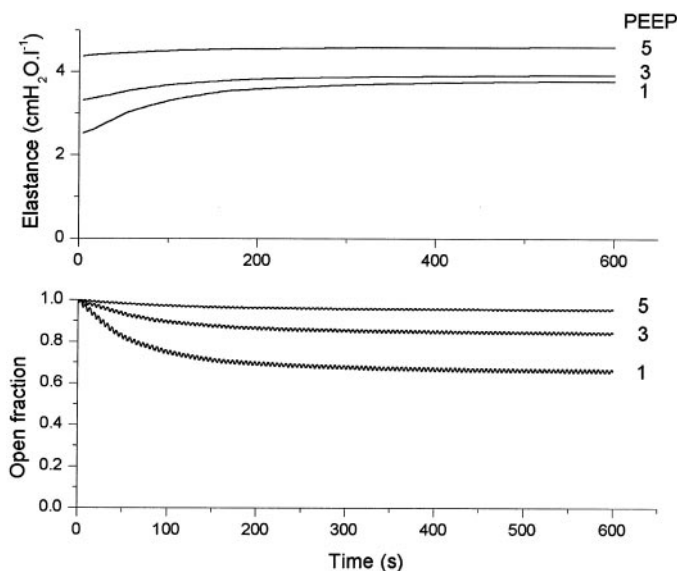


Fig. 7. Derecruitment in a normal lung simulation. Model parameters were the same as for Fig. 4. *Top*: time course of elastance starting from a fully open lung ventilated for 10 min at 5, 3, and 1 cmH₂O positive end-expiratory pressure (PEEP). *Bottom*: corresponding time courses of the fraction of open lung units.

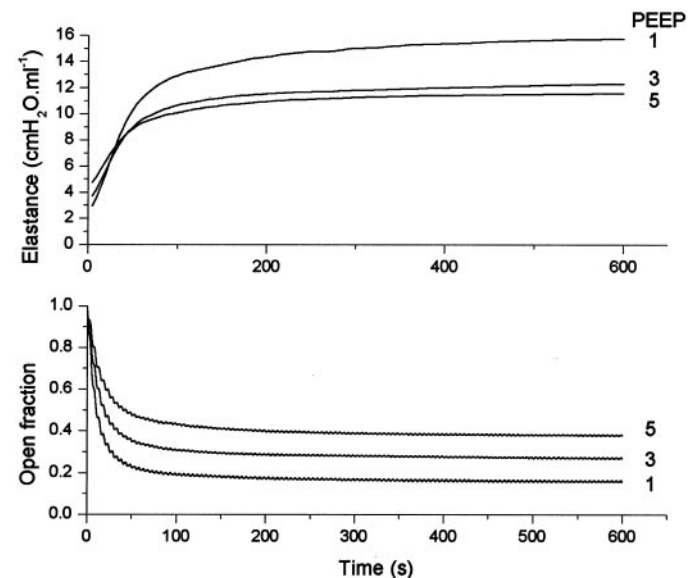


Fig. 8. Derecruitment in an injured lung simulation. Model parameters were the same as for the injured lung simulation in Fig. 6D. *Top*: time course of elastance starting from a fully open lung ventilated for 10 min at 5, 3, and 1 cmH₂O PEEP. *Bottom*: corresponding time courses of the fraction of open lung units.

on pulmonary mechanics, namely the opening and closing of airways with the attendant gain or loss of lung volume. To allow this mechanism to have a time-dependent influence on lung mechanics, it was necessary to have opening and closing occur with a certain latency once the P_{crit} had been reached. This was achieved by the novel procedure of having airway closure and opening determined by the position of a virtual state that moved continuously along a finite trajectory, the extremes of which signaled either opening or closure (Figs. 1 and 2). Although Alencar et al. (1) invoked the notion of finite opening times of airways to account for the distribution of crackle-like sounds observed as a degassed lung is slowly inflated, previous models of lung mechanics have only considered airway opening and closure to give rise to purely static nonlinear effects. These effects have been invoked to account for the finite width (hysteresis) of the P-V loop of the lung when cycled over a wide volume range (5, 14–16). However, there is a body of experimental evidence (e.g., Refs. 8, 11, 17, 29) that suggests that opening and closure is a very time-dependent phenomenon. We thus decided to explore how R/D dynamics might be incorporated into a model of the lung.

The responsible mechanisms for the long-term transients in lung E seen during mechanical ventilation remain controversial. For example, this phenomenon may be due to either tissue viscoelastic effects or to gas redistribution (“pendelluft”) because both these mechanisms give rise to transient mechanical behavior that is qualitatively similar to that due to the time dependence of airway opening and closure. However, when the transients take place over a time scale of minutes or more, as is the case for the very slow P-V cycling of the lung or for the increases in E during mechanical ventilation after a sigh, it is unlikely that either tissue viscoelasticity or gas redistribution could be responsible because they both resolve far too quickly on the order of seconds or less.

Another possible mechanism responsible for slow mechanical transients in the lung is the dynamics of surfactant function at the air-liquid interface. If the distribution of surfactant molecules gradually changes as ventilation proceeds, the resulting changes in surface tension at the air-liquid interface will alter lung elastic recoil. Williams et al. (45) ascribed slow changes in lung E entirely to this mechanism. However, Horie and Hildebrandt (18) proposed that a combination of surfactant dynamics together with airway closure at low lung volumes could be responsible, whereas Dechman et al. (8) invoked only the derecruitment mechanism to account for the accelerated E transients they found in dog lungs at low PEEP. Although it may be impossible to distinguish between these two possibilities experimentally, recent interest in optimal ventilation of critically ill patients has focused attention on R/D as an important process in the lung. Thus, even if the dynamics of R/D are not particularly important in normal lungs, it seems likely that they could be significant in lung injury, as R/D is widely proposed to account for the greatly increased hysteresis of the

quasistatic P-V curve in lung injury (5–7, 14, 15, 19, 24, 31, 34). On the other hand, Wilson et al. (46) have just proposed a model for edematous lungs that ascribes the knee in the P-V curve to the nonlinear coupled behavior of the parenchyma and alveolar fluid, which does not invoke R/D at all. In reality, P-V hysteresis in the lung may well involve contributions from all these mechanisms.

There have been a number of previous attempts to account for R/D in the lung by using mathematical models. All these models have assumed that opening and closing are triggered immediately on pressure reaching a certain critical threshold. For example, Suki et al. (39) used such a model to show how randomizing each breath during ventilation can improve oxygenation compared with ventilating with fixed breaths. Hickling (15) used a somewhat similar model to explore the possible relationship between amount of open lung and PEEP. P-V hysteresis in models such as these is achieved by having the opening P_{crit} be higher than the corresponding closing pressures. However, these kinds of models are not able to account for the R/D transients in compliance that occur, for example, when a lung is ventilated from an initial either fully opened or fully closed state.

By contrast, the present model is able to reproduce this transient behavior, provided appropriate distributions are chosen for the quantities P_{crit} , s_o , and s_c . The choice of these distributions is thus of critical importance, but unfortunately we have relatively little data available to guide us. Choices for these parameters were thus made on the basis of what seemed reasonable and what gave the appropriate model behavior. A Gaussian distribution for P_{crit} seemed a logical first guess, particularly as there have been reports that opening and closing P_{crit} may indeed follow this kind of distribution (7, 31). The mean and standard deviation of this Gaussian distribution were chosen to obtain model behavior similar to that seen experimentally. Moreover, their values are not unreasonable. For the normal lung, we chose a value for μ_P of 5 cmH₂O. This is not too far above the normal end-expiratory transpulmonary pressure of the lung, whereas the value for σ_P of 3 cmH₂O encapsulates the notion that most R/D takes place over the lower half of the vital capacity range. For the diseased lung, we doubled μ_P to 10 cmH₂O and doubled σ_P to 6 cmH₂O to produce a model with a greatly increased propensity for closure over most of the vital capacity range, as has been recently suggested to occur (5, 15). These parameters caused P-V hysteresis (Fig. 4) to be increased substantially, as occurs in lung injury (19, 24, 34, 42).

It was less obvious how to choose appropriate distributions for s_o and s_c . We thought it reasonable that most lung units would open or close rather slowly, enabling the organ to function in a consistently open state during regular ventilation, with only a small number of units being actively recruited and derecruited. This behavior is conveniently embodied in hyperbolic distributions for s_o and s_c . We also felt that hyperbolic distributions might be a suitable choice

because of the well-known ubiquity of power-law phenomena in nature (2) and in the lung in particular (1, 4, 41, 44). The scale factors (S_o and S_c) applied to these hyperbolic distributions were chosen by trial and error to give reasonable behavior for the model. However, we also used uniform distributions for s_o and s_c and found that realistic P-V curves and E-time profiles could be achieved if these distributions were scaled to span the appropriate intervals (Fig. 5B). Indeed, it is also possible to obtain dynamic R/D in the model when all lung units have the same values of s_o and s_c , provided P_{crit} follows a distribution with a finite width. Nevertheless, it is more likely that the lung would exhibit a variety of values of s_o and s_c , as perfect uniformity has not been observed in any other quantities measured within the lung. In any case, the model is rather robust with regard to the particular choice of distributions for s_o and s_c . Furthermore, these results do not indicate exactly what the distribution should be but, rather, demonstrate that a distribution on the basis of some degree of physical reasoning leads to realistic predictions.

We have also assumed that a simple linear relationship exists between ($P - P_{crit}$) and both s_o and s_c (Fig. 2). This was motivated by the notion that airways close by the formation of liquid bridges (9, 17) and the *in vitro* work of Gaver et al. (11), which showed a linear relationship between the pressure applied to a collapsed tube and the speed with which the tube was opened by a moving finger of air. However, airway closure can also occur by mechanical collapse of the airway walls (30). We do not know whether our formula for the rate of opening and closing (Fig. 2, Eq. 2) also applies to wall collapse or, alternatively, whether the formula should be more complicated than the linear relationship depicted in Fig. 2. Also, airway closure is not the only R/D mechanism that is likely to be time dependent and important in the lung. There are three mechanisms by which R/D might be postulated to occur: 1) R/D of airways, 2) R/D of alveoli (atelectasis), and 3) microstructural R/D within the alveoli themselves. In the last case, tension is maintained in the alveolar wall by having extra wall material sequestered into the alveolar corners, from which it may be recruited as needed to expand alveolar volume (43). It is possible that some or all of these mechanisms may contribute to the dynamics of R/D within the lung, the net effect merely being represented in an empirical fashion in our model.

We have thus developed a model of the lung capable of producing realistic time-dependent mechanical behavior on the basis of R/D. This is not to say, however, that the mechanisms by which we achieved this are entirely accurate representations of what actually happens in nature nor that R/D are the only processes responsible for long-term transients in lung mechanics. Although we have discounted the possibility of tissue rheology being responsible for mechanical transients occurring over a time scale of minutes or more, this may be open to debate. Stress adaptation of lung tissue has been shown to obey a power-law function of

time (4) for which there is no characteristic time scale. Thus it is possible that ongoing stress adaption could contribute, albeit in a probably very small way, to transient events over the scale of minutes or more.

We have also assumed that R/D is governed by a single P_{crit} and that there are not separate opening and closing pressures. This implies that P-V hysteresis is fundamentally dynamic and that, given a long enough cycling period, the width of the P-V loop would collapse toward a single curve. Changes in the loop area of our model are seen in Fig. 5 as the cycling period varies from 50 to 200 s. To have this loop close to a single curve, it would be necessary to cycle the model at a rate far too slow to test experimentally *in vivo*, as gas exchange would be compromised. In any case, we would not expect to find this result even if the experiment could be done because true static hysteresis appears to be exhibited by the lungs when they are cycled over the vital capacity range (16, 18). Therefore, our model would be more realistic if it combined the time-dependent R/D mechanism we have developed together with opening P_{crit} that are higher than closing P_{crit} . This would also make the model produce second P-V curves with loop areas that are more independent of cycling rate than those shown in Fig. 5. Such frequency independence has been reported in isolated lungs (16) and may be due to the existence of a true static hysteresis, although a rate dependence of hysteresis has also been reported (13). One particular prediction of our model is open to experimental verification, namely the increased gas trapping that occurs when the cycling rate of a degassed lung is decreased (Fig. 5). Frazer and Weber (10) found precisely this phenomenon when degassed isolated rat lungs were cycled at different rates. They also showed successively more gas trapping with each cycle, which supports the notion that the dynamics of R/D do indeed play a role in lung dynamics.

Our model is also somewhat simplistic in structure. For example, it assumes that the various lung regions taking place in R/D are mechanically independent and arranged in parallel. Although this facilitated the model's implementation, it would have been more accurate to arrange the lung units in a combined parallel and serial fashion as dictated by the tree structure of the airways. Suki et al. (40, 41) have shown that this causes R/D events to occur in avalanches, which raises the interesting question of how such avalanches would be affected by a latency in the opening and closing of airways along each avalanche pathway. Another simplistic aspect of our model is that it does not include any large-scale spatial structure in the distributions of s_o , s_c , and P_{crit} , such as would likely be determined by gravity. This may be particularly important in lung injury (14, 15).

Thus there are many simplifications and assumptions that we made in devising our model of dynamic R/D in the lung, and many of these are easily assailable in view of the rather scant experimental evidence currently available. Nevertheless, it seems reasonable to

suppose that some dynamic R/D mechanism, such as the one we propose, does exist in the lung and contributes to long-term mechanical transients. It may be that surface tension effects constitute the predominant mechanism behind P-V hysteresis in the normal lung, as has been suggested previously (38). However, it is also well known that, in some kinds of lung injury, there is a greatly increased propensity for airspace closure (19, 31, 33). Furthermore, airway closure is thought to feature prominently in the pathophysiology of asthma (20, 23). It is thus very likely that R/D is a significant phenomenon in the injured lung. It also seems reasonable to suppose that closure of open units in an injured lung might take place significantly more rapidly than in a normal lung, as our model predicts. We simulated a substantially increased level of closure by increasing the mean value of P_{crit} , whereas we achieved more rapid closure by increasing the values of s_c . This allowed us, for example, to simulate how effective a sigh might be at opening the lung and how long the effect might last. Currently there is a great deal of debate as to the best way to ventilate an injured lung. The temporal dynamics of R/D are clearly critical considerations in this debate, and a model such as the one presented here may be useful in addressing this issue in a more mechanistic way. In particular, the conventional viewpoint is that the lower inflection point of the inspiratory quasistatic P-V curve reflects the majority of the recruitment events that take place in the lung during inflation (14, 15, 34). Our model is based on the same notion. However, as our model posits that R/D is a dynamic phenomenon, the position of the lower inflection point is predicted to depend on the rate of inflation, as can be seen in Fig. 5. In particular, this means that the position of the lower inflection point, as determined by a quasi-static inflation maneuver, may be rather different to its position during the dynamic process of conventional mechanical ventilation. This calls into question the relevance of the lower inflection point, as it is usually measured, for optimal ventilation of the lung.

In conclusion, we have developed a model of the lung that incorporates a novel mechanism by which R/D may give rise to transient behavior in lung mechanics. We have shown that, with an appropriate choice of parameters, the model can realistically mimic the first and second P-V loops of a degassed lung and the transient decreases in lung compliance that follow a deep lung inflation. We have also shown how the model parameters may be adjusted to represent an injured lung, resulting in increased P-V hysteresis and a greater degree of derecruitment after a sigh. We suggest that this model may be useful for exploring how the timing of ventilation strategies can influence the extent to which an injured lung is kept open.

This work was supported by National Heart, Lung, and Blood Institute Grants RO1 HL-62746, RO1 HL-76004, and RO1 HL-67273, and National Center for Research Resources Center of Biomedical Research Excellence P20RR15557.

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