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Modeling the lung: Integer-order viscoelastic models – Part 2

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Abstract

The mechanical behavior of lung tissue, especially under pathological conditions such as acute respiratory distress syndrome (ARDS), cannot be fully described by simple elastic or viscous models. Instead, the lung exhibits viscoelastic properties that depend on both the rate and duration of deformation. Integer-order viscoelastic models, including the Maxwell, Kelvin-Voigt, Zener, Anti-Zener, and Burgers models, have historically provided a conceptual framework for understanding lung mechanics by representing tissue as combinations of springs and dashpots governed by first- or second-order differential equations. These models are valuable for educational purposes and initial clinical interpretation, allowing quantification of phenomena such as stress relaxation and creep. However, their main limitation lies in their inability to capture the continuous distribution of relaxation times and the power-law response observed in biological tissues, particularly in heterogeneous and injured lungs as seen in ARDS. More complex models, such as the generalized Maxwell model, offer improved accuracy but at the cost of increased mathematical complexity and parameterization, restricting their routine clinical use. Recent evidence suggests that fractional-order models may provide a more physiologically accurate and parsimonious description of lung viscoelasticity, capturing frequency dependence and long-term responses with fewer parameters. The development of advanced models is essential for optimizing protective ventilation strategies and understanding the mechanisms underlying ventilator-induced lung injury.

Keywords: lung viscoelasticity, integer-order models, Maxwell model, Kelvin-Voigt model, Zener model, Anti-Zener model, Burgers model, ventilator-induced lung injury.

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Introduction

The study of the respiratory system, particularly in severe pathological states such as acute respiratory distress syndrome (ARDS), demands an understanding that transcends simple mechanical laws. The lung cannot be categorized as a purely elastic material that instantly recovers its shape (like an ideal solid), nor as a purely viscous fluid that deforms continuously under stress. Physical evidence demonstrates that lung tissue exhibits viscoelastic behavior, displaying intermediate properties that intrinsically depend on the rate of deformation and the duration of force application. [1]

Rheology, defined as the science that studies the deformation and flow of materials, provides the mathematical framework for analyzing pulmonary mechanics. [2]

Integer-order constitutive viscoelasticity models represent the respiratory system by combining ideal mechanical elements described by first or second-order differential equations with constant coefficients. These models, valid under the assumption of a linear relationship between stress and strain (generally limited to small deformations), form the basis of the “equation of motion” used at the patient's bedside. [3]

In practice, integer-order models assume that the viscoelastic response is governed by one- or a few-time constants (τ) and predict an exponential stress relaxation or creep behavior. Lung tissue (with its fractal structure and complex distribution of collagen, elastin, and fluids) exhibits a power-law response which is not exponential. These classical models can only approximate this response by connecting an infinite number of elements, which are impractical and have little physiological significance. [4]

Methods

A concise yet comprehensive literature review was conducted using online databases, employing search terms such as "rheology," "lung viscoelasticity," and "integer-order models." The authors critically evaluated and selected the publications deemed most relevant to the objectives of this study.

Objectives

- To review and synthesize the main integer-order viscoelastic models applied to lung tissue, highlighting their theoretical foundations and clinical relevance.
- To analyze the strengths and limitations of classical models such as Maxwell, Kelvin-Voigt, Zener, Anti-Zener, and Burgers in representing the mechanical behavior of the lung.
- To discuss the physiological and pathological implications of viscoelastic modeling in the context of lung diseases, particularly ARDS.
- To evaluate the applicability of integer-order models in describing stress relaxation, creep, and other dynamic phenomena observed in lung tissue.
- To identify the gaps in current modeling approaches and suggest directions for future research, including the potential advantages of fractional-order models.

Review

The viscoelastic behavior of the lung is a complex, multifactorial phenomenon governed by both the structural architecture and the biochemical composition of its tissues. [5] Under physiological conditions, the lung demonstrates an immediate response to changes in transpulmonary pressure (PTP); however, it also exhibits dynamic processes such as stress relaxation and creep. These phenomena are indicative of ongoing structural reorganization within the extracellular matrix, which is primarily composed of collagen, elastin, and proteoglycan fibers. This intricate structural and compositional complexity imparts mechanical properties to lung tissue that cannot be sufficiently characterized by simple elastic models, thereby necessitating the use of more advanced viscoelastic modeling approaches. [6]

In the setting of ARDS, where pronounced regional heterogeneity results in the coexistence of collapsed, normally aerated, and overdistended lung zones, a precise understanding of lung viscoelasticity is essential for optimizing protective ventilation strategies. The phenomena of atelectrauma characterized by cyclic alveolar opening and closing and stress concentration at the interfaces between regions with differing aeration are closely associated with the viscoelastic properties of lung tissue. [7]

Viscoelastic models provide a quantitative framework for characterizing the dynamic mechanical properties of lung tissue, enabling the formulation of mathematical relationships that link applied stress to the resulting deformation. [8]

Integer-order models are the simplest formulations of linear viscoelasticity, where the constitutive relationship is described using first or second-order time derivatives. These models are educational and provide a conceptual base, but they have serious limitations when describing the complexity of biological tissues. These are based on simple mechanical analogies of springs and dashpots and have traditionally been used to describe the elastic and viscous properties of the lung. These models, although simplified, have been instrumental in

establishing an initial understanding of lung mechanics, representing flow resistance and tissue compliance. [9]

The limitation of these models lies in their inability to fully capture the complexity of tissue time dependence especially with regard to phenomena such as stress relaxation and creep. [10]

1. Classical first-order constitutive models (integer order)

1A. Maxwell model (fluid model)

This model consists of a spring and a dashpot also known as damper (a mechanical device that resists motion via viscous damping) connected in series (Figure 1) and describes the behavior of materials that exhibit stress relaxation, a fundamental characteristic of lung tissue. [11] A series connection implies that both elements experience the same stress $\sigma(t)$, but their strain $\varepsilon(t)$ are separate and additive. [12]

It models the behavior of viscoelastic liquids and captures the stress memory of the material [13] and predicts an exponential decay of stress when the tissue is held at a constant strain, which has been observed in experimental studies of lung parenchyma. [11] Its main limitation is that when constant stress is applied (creep phenomenon), it predicts that strain will increase linearly over time, which is unrealistic for lung tissue. Therefore, while conceptually useful, its direct applicability to complete parenchymal modeling is limited. [14] In lung mechanics, Maxwell's model fails to capture the complex tissue response during prolonged respiratory cycles and underestimates the long-term elastic component. [8]

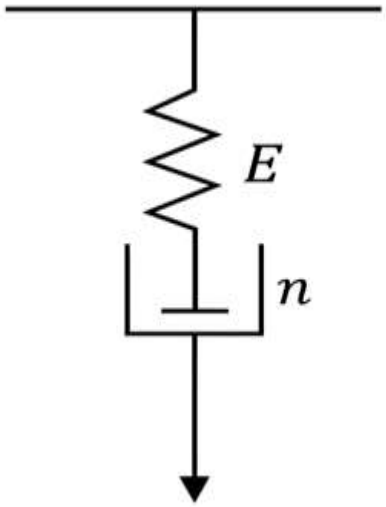

Figure 1: Maxwell model. A spring and a dashpot in series.

1B. Kelvin-Voigt model (solid model)

Or Voigt. It combines a spring and a dashpot in parallel (Figure 2) and is particularly suitable for modeling materials that exhibit creep, where the deformation increases progressively under constant stress. [15] The parallel configuration means that the total stress is distributed between the two elements, and the deformation is the same in both. This arrangement produces a retardation effect, [16] effectively capturing the delayed elastic response characteristic of viscoelastic materials. [17]

The key behavior of the Kelvin-Voigt model is that it exhibits additional resistance to rapid deformation but behaves purely elastic on slow timescales. [14]

One of its principal limitations is that it cannot describe stress relaxation: when applying a sudden deformation, it predicts a constant stress rather than the experimentally observed decay. [18] In lung tissue, its limitations are particularly relevant during recruitment maneuvers and rapid pressure changes in mechanical ventilation, where stress relaxation plays a crucial role. [7]

It is fundamental to understanding how the lung resists rapid deformation and how, under sustained loads, its apparent compliance can change due to stress redistribution. This model's ability to capture the temporal response and resistance to deformation makes it a valuable tool for interpreting clinical and experimental data related to lung mechanics. [19]

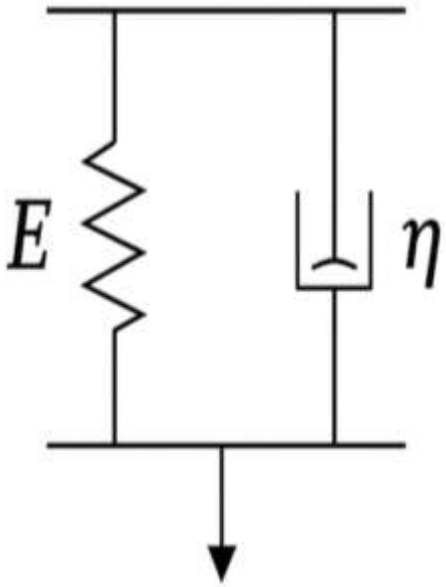

Figure 2: Kevin-Voigt. A spring and a dashpot in parallel.

2. More complex models

Integer-order models comprising three or more elements were developed to enhance rheological representations, enabling a more comprehensive characterization of stress relaxation and creep phenomena that simpler two-element models were unable to accurately simulate. [14]

2A. Zener model (viscoelastic solid)

Also known as the “relaxation oscillator” [20] or “standard linear solid" (SLS). [21] It is a second-order model. [14] It consists of two springs and a dashpot. It is the simplest model that describes both creep and stress relaxation behaviors of a viscoelastic material properly. The constitutive relations governing this model are illustrated in Figures 3a and 3b. [22] This configuration allows the parallel spring element to provide an immediate response, while the series unit contributes to the time-dependent behavior. [23]

This more complex configuration allows the Zener model to overcome the limitations of its predecessors. Unlike the Maxwell model, the Zener model is able to describe the recovery of deformation after loading (creep recovery). And unlike the Kelvin-Voigt model, it can describe stress relaxation. [20] Zener's model was revolutionary because it is the first simple model that predicts both phenomena simultaneously. [21] Furthermore, this model provides information on the material's behavior at high frequencies, which is highly relevant in mechanical ventilation, where respiratory rate can vary significantly. [20]

In the pulmonary context, each component of the Zener model represents specific anatomical structures:

- Parallel spring: elastin fibers of the alveolar parenchyma, providing immediate elastic recoil. [24]
- Series spring: collagen fibers, which are primarily activated at high lung volumes. [25]
- Series dashpot: tissue reorganization, interstitial fluid movement, and cellular mechanotransduction. [26]

One of the key properties of the Zener model is its ability to predict hysteresis. Its ability to capture this energy dissipation provides a metric of the mechanical load imposed on lung tissue, which is a known risk factor for the development of VILI. [20]

The Zener model is particularly useful for describing:
- The behavior of normal and mildly altered lung parenchyma. [27]
- The response to alveolar recruitment maneuvers. [28]
- The relaxation of pressures during prolonged inspiratory pauses. [29]

Limitations:
- Underestimates the extreme alveolar heterogeneity present in severe ARDS. [29]
- Does not fully capture cyclic collapse/opening phenomena (atelectrauma). [30]
- The model predicts that stress relaxation asymptotically approaches zero; however, experimental studies have demonstrated that, in lung tissue, stress relaxation is finite and tends toward a non-zero equilibrium value. [20]

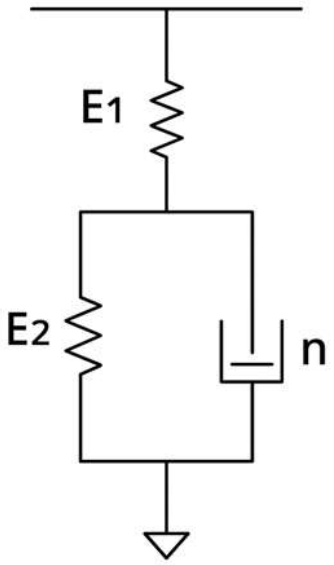

Figure 3a: Zener model. Kelvin representation.

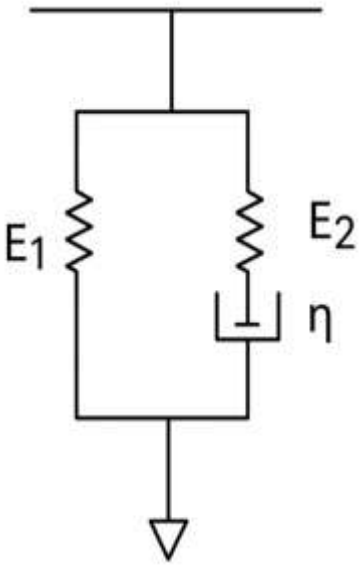

Figure 3b: Zener model. Maxwell representation.

2B. Anti Zener model (viscoelastic fluid)

Similar to the Zener model, this configuration is a three-element system consisting of two dashpots and a spring [31] (Figure 4). It is also referred to as "Jeffrey's fluid" or the "standard linear fluid model" or SLS. Although its theoretical structure is contemporary to Zener (both as extensions of the elements of Maxwell and Kelvin-Voigt), it was formalized later in the rheology literature. Its explicit recognition as a relevant alternative configuration for biological systems has emerged only recently, with active promotion for pulmonary applications occurring in recent years by research groups specializing in pulmonary mechanotransduction. [32]

This arrangement gives the system a fundamentally fluid behavior with temporary elastic characteristics. [33]

A healthy lung does not exhibit liquid-like behavior and does not undergo indefinite deformation. Nevertheless, this model acquires significant clinical relevance in pathological conditions where the structural integrity of the lung is compromised. [7] This model has limited application to intact lung parenchyma, but it is useful for:

- Mucous secretions in the airways (cystic fibrosis, bronchial asthma).
- Interstitial edema in the acute phases of ARDS.
- Long-term behavior of evolving fibrotic tissue. [33]

It is an even more precise tool than the Zener for describing lung mechanotransduction and could optimize treatments for diseases such as ARDS. [20]

Limitations:

- Not applicable to healthy lung parenchyma under physiological conditions.
- Does not adequately represent the characteristic elastic recoil of lung tissue.
- Clinical use restricted to specific pathologies with altered secretion rheology. [33]

The most complex models used in respiratory research, such as the generalized Kelvin-Voigt model, combine multiple Zener and anti-Zener elements to more accurately capture the actual viscoelastic behavior of the lung. These models incorporate multiple relaxation times that reflect the structural heterogeneity of the lung parenchyma at different anatomical scales. [34]

Despite their usefulness, integer-order models have inherent limitations in fully describing lung viscoelasticity, especially regarding the representation of frequency dependence and long-term response. These models often require multiple elements in series or parallel to approximate the observed behavior, which increases model complexity and hinders the interpretation of underlying physiological parameters. [35] In contrast, fractional order models offer a more parsimonious and accurate description of viscoelastic behavior, capturing frequency dependence and long-term responses with a reduced number of parameters. [36]

Although these models are more complex than two-element systems, they remain within the framework of integer-order descriptions (discrete-order differential equations) and are designed to incorporate delayed elasticity and viscous flow, thereby improving the fit to pulmonary dynamic curves.

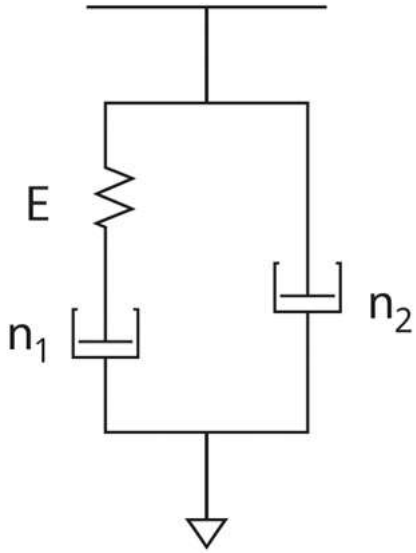

Figure 4: Anti Zener model.

2C. Burgers model (generalized standard linear solid)

This model consists of either two Maxwell components in parallel or a Kelvin–Voigt component, a spring and a dashpot in series [37] (Figure 5a and 5b). It incorporates second-order derivatives of both stress and strain. [38]
This four-element model is crucial because it can incorporate permanent viscous flow (a continuous linear increase in strain under constant load) into the SLS model. This is relevant for biological materials that, under prolonged stress, can exhibit plastic deformation or net flow. [14]

This model adequately describes both relaxation and creep, incorporates multiple characteristic times: relaxation time and delay time. It captures both viscoelastic solid behavior (Kelvin-Voigt component) and

viscoelastic liquid behavior (Maxwell component) and predicts a finite equilibrium modulus at low frequencies. [39]

As a limitation it still predicts exponential relaxation rather than the power-law behavior observed experimentally. [8]

The Burgers model, while structurally more complete, is unnecessarily complex for most clinical applications in mechanical ventilation. Its mathematical complexity requires more parameters and can lead to overfitting of experimental data. However, the Burgers model provides the most comprehensive representation when highly detailed analyses of pulmonary viscoelasticity are required in rigorous research studies. [32]

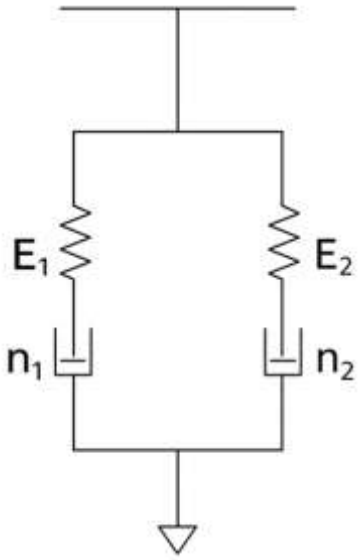

Figure 5a. Burgers model. Maxwell representation.

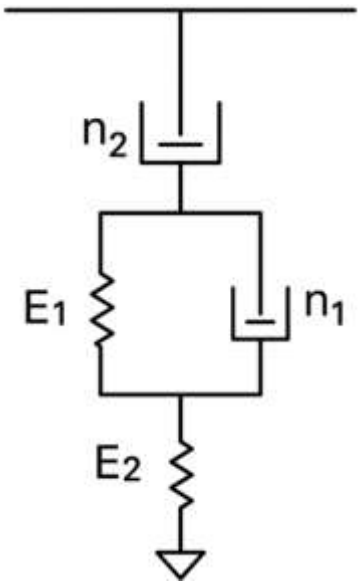

Figure 5b: Burgers model. Kelvin representation.

2D. Generalized Maxwell model

Also known as the Wiechert model, it is the most general form of the linear model for viscoelasticity. It takes into account that the relaxation does not occur at a single time, but at a distribution of time. The Wiechert model shows this by having as many spring–dashpot Maxwell elements as necessary to accurately represent the distribution [40] (Figure 6).

This model overcomes the main limitation of simple integer-order models: the inability to capture the continuous distribution of relaxation times that exist in real biological tissues. Instead of one or two elements, it uses multiple Maxwell elements in parallel, each with its own characteristic relaxation time. [41]

It is particularly useful for characterizing the heterogeneous viscoelasticity of lung parenchyma in ARDS. Each Maxwell unit can theoretically represent different populations of alveoli or acinar units with distinct time constants (e.g., dependent vs. non-dependent regions, or healthy vs. edematous or injured tissue). It allows for highly accurate modeling of stress relaxation over several seconds or even minutes. [42]

Its mathematical complexity increases linearly with the number of elements, making it difficult to estimate its multiple parameters. This needs to sum discrete models to approximate viscoelasticity underscores the fundamental limitation of all integer-order models in representing the “continuous distribution of relaxation times” (DRT) that characterizes the complex multiscale structure of the injured lung. [27]

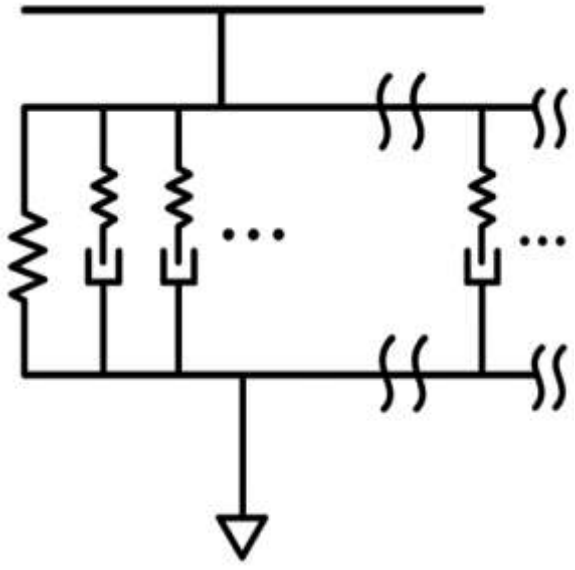

Figure 6: Generalized Maxwell model.

Table 1: Integer-order viscoelastic models: Comparative summary

Model name	Mechanical analogy	Elements	Key behaviors	Limitations	Clinical/research use
Maxwell	Spring & dashpot (series)	E, η	Stress relaxation	Poor creep fit; oscillatory	Rapid stress decay modeling
Kelvin-Voigt	Spring & dashpot (parallel)	E, η	Creep	No stress relaxation	Slow deformation scenarios
Zener (SLS)	Maxwell + spring (parallel)	E1, E2, η	Creep & relaxation	Limited frequency response	Physiological lung modeling
Anti-Zener	Kelvin-Voigt + spring (series)	E1, E2, η	Enhanced creep	Weak relaxation; complex	Pathological compliance study
Burgers	Maxwell + Kelvin-Voigt (series)	E1, E2, η1, η2	Creep & relaxation	Many parameters; complex	Detailed viscoelastic analysis
Generalized Maxwell	Multiple Maxwell (parallel)	Multiple E, η	Broad relaxation times	Calibration; overfitting	Advanced lung mechanics

Limitations of integer order models

Despite the greater complexity of models with three or more elements (Zener, Anti-Zener, Burgers) and models with multiple discrete components (Generalized Maxwell), all whole-order models share a fundamental limitation in pulmonary physiology: they assume that the tissue is homogeneous and that the mechanical response can be described by one or a few discrete relaxation times. [8,43] Rheological evidence from biological soft tissues, including lung parenchyma, shows that relaxation dynamics follow a power-law (rapid initial decay followed by very slow asymptotic relaxation) rather than a simple exponential function. This divergence between exponential prediction and power-law behavior is what has led to integer-order models showing a poor fit to experimental lung stress relaxation curves. [8]

The inherent limitations of integer-order models, which only capture a discrete number of relaxation times, make them unsuitable for accurately modeling the heterogeneous lung with ARDS. Injured biological tissue exhibits a continuous and broad DTR due to its multiscale and heterogeneous structure. Fractional calculus offers a powerful mathematical tool to overcome this limitation. [44]

Conclusions

Integer-order viscoelastic models (such as Maxwell, Kelvin-Voigt, Zener, Anti-Zener, and Burgers) have played a fundamental role in establishing the basic principles of lung mechanics. These models, based on simple mechanical analogies, have enabled the formulation of mathematical relationships between applied stress and resulting deformation in lung tissue. They have been valuable for educational purposes and for the initial interpretation of clinical and experimental data.

While integer-order models can describe phenomena such as stress relaxation and creep, they present substantial limitations when attempting to represent the true complexity of lung tissue, especially under pathological conditions such as ARDS. Their main weakness lies in their inability to capture the continuous distribution of relaxation times and the power-law response observed experimentally in biological tissues.

Although more complex models (such as Burgers or the generalized Maxwell model) can better fit the heterogeneous nature of the lung, their mathematical complexity and the large number of required parameters limit their routine use in clinical practice. As a result, their application is mainly restricted to advanced research and detailed characterization of pulmonary viscoelasticity.

Lung viscoelasticity is key to understanding phenomena such as pressure relaxation, stress redistribution, and the development of ventilator-induced lung injury (VILI). In the context of ARDS, regional heterogeneity and the coexistence of collapsed, overdistended, and normally aerated zones require models that reflect this complexity to optimize protective ventilation strategies.

Current evidence suggests that integer-order models, while useful, are insufficient to fully describe lung mechanics, particularly in injured tissues. The use of fractional-order models represents a promising alternative, as they can capture frequency dependence and long-term responses with fewer parameters and greater physiological accuracy.

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