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Arterial viscoelasticity: a fractional derivative model

Damian O. Craiem, Ricardo L. Armentano, *Member, IEEE*

Abstract—**Arteries are viscoelastic materials. Viscoelastic laws are fully characterized by measuring a complex modulus. Arterial mechanics can be described using stress-strain dynamic measurements applied to the particular cylindrical geometry. Most materials show an energy loss per cycle that increases steadily with frequency. By contrast, the frequency modulus response in arteries presents a frequency independence describing a plateau above a corner frequency near 4Hz. Traditional methods to fit this response include several spring and dashpot elements to model integer order differential equations in time domain. Recently, fractional derivative models proved to be efficient to describe rheological tissues, reducing the number of parameters and showing a natural power-law response. In this work a fractional derivative model with 4-parameter was selected to describe the arterial wall mechanics in-vivo. Strain and stress were measured simultaneously in an anaesthetized sheep. A fractional model was applied. The order resulted α=0.12, confirming the manifest elastic response of the aorta. The fractional derivative model proved to naturally mimic the elastic modulus spectrum with only 4 parameters and a reasonable small computational effort.**

Keywords: **fractional models, arteries, viscoelasticity, complex modulus**

I. Introduction

Arterial wall materials, as many soft biological tissues, reveal elastic and viscous properties. Many articles described these viscoelastic properties to get insight of wall structure under normal and pathological situations but few measurements were made in-vivo [1]-[3]. Based on stress-strain measurements, many methods were developed to study the arterial wall. In time domain, stress-strain relations are associated with linear differential equations. In addition, the determination of the frequency dependent Young modulus appeared as an alternative method. This complex modulus E* has real and imaginary parts. The former is associated with the elastic response (i.e. storage modulus) and shows a constant behavior in arteries, within the physiologic range (0.1-20Hz). The latter (i.e. loss modulus) denotes a viscous behavior. Pure viscous materials exhibit a proportional energy loss with frequency. Conversely, the loss modulus in conduit arteries increases with frequency but has a marked plateau at high frequencies. There are some known deficiencies fitting this frequency response to a broad range of frequencies [4]. The constitutive equation of rheological models is based on stress-strain analysis and traditionally represented with derivatives of integer order. These classical derivatives can be extended including fractional derivatives. This generalization to any real-order derivative was applied to many fields and eventually in rheological cases including molecular theories [5]-[10]. Some important advantages must be emphasized i) They proved to describe accurately complex model with less number of parameters (model order) ii) They improved the curve fitting, principally with power-law frequency responses iii) They allowed a physical justification in rheological and tissue cases. As far as we know this methodology was not applied before to characterize the mechanics of complete conduit arteries.

The E^* can be estimated in-vivo. A stress strain analysis can be accomplished measuring pressure and diameter simultaneously in the aorta. In an invasive in-vivo experiment, geometrical factors can be combined to calculate the complex modulus and the so called constitutive equation, which contains information on the underlying mechanisms and structure contributing to the viscoelastic behavior [11]-[12].

The aim of the present work was to propose a fractional derivative model to describe the aorta viscoelastic response in-vivo.

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D. O. Craiem and R.L Armentano are in the Favaloro University, Av.Belgrano 1723 (1093), Buenos Aires, Argentina. Phone: +54 11 4378 1132 (dcraiem@favaloro.edu.ar) and in the CPSI, FRBA, UTN, Argentina.

II. Methods

A. Modelling

At a mean distension pressure, stress-strain analysis can be measured in the aorta of a living animal. Assuming a linear behaviour around the working point, a complex viscoelastic modulus E^* can be derived to describe the viscoelastic properties of the vessel tissue and its frequency (ω) dependence

$$E^*(\omega) = \frac{\sigma(\omega)}{\varepsilon(\omega)} = E_S(\omega) + iE_L(\omega)$$

where σ and ε are the stress and strain harmonics respectively and $i = \sqrt{-1}$ the imaginary unit. The real part of E^* was designated as the storage modulus E_S and the imaginary part will be called loss modulus E_L.

Common viscoelastic materials present storage and loss modules that increase steadily with frequency. This response resulted very different in arteries and motivated the present model. Bergel, in widely quoted publications [13], observed in-vitro the frequency dependence of E^* in different arteries. The real part of E^* showed a steep increase from zero frequency and an almost stable behaviour beyond 2Hz. The imaginary part showed a continuous increase following an apparent power law with a plateau at 4Hz.

The simplest viscoelastic model that can store and dissipate energy is the Voigt body, consisting in a perfectly elastic element i.e. spring, arranged in parallel with a purely viscous element, a dashpot.

$$\sigma(t) = E_0\varepsilon(t) + E_1\frac{d\varepsilon(t)}{dt}$$

where E_0 denotes the elastic constant of the spring and E_1 the viscous coefficient of the dashpot.

The minimum combination to contemplate both, stress relaxation and creep, can be derived including a derivative term in the left side of the Voigt equation,

$$\sigma(t) + B_1\frac{d\varepsilon(t)}{dt} = E_0\varepsilon(t) + E_1\frac{d\varepsilon(t)}{dt} \quad (1)$$

This 3-parameter model is able to mimic stress relaxation and creep with exponential time functions. Using a Fourier transform, the modeled complex modulus E^* can be obtained as

$$E^*(\omega) = \frac{\sigma(\omega)}{\varepsilon(\omega)} = \frac{E_0 + iE_1\omega}{1 + iB_1\omega} \quad (2)$$

To fit the measured data, a generalized model can be adopted, including additional coefficients in both, numerator and denominator [4],

$$E^*(\omega) = \frac{E_0 + \sum_{n=1}^{N} E_n (i\omega)^n}{1 + \sum_{m=1}^{M} B_m (i\omega)^m}$$

Here, the constants E_n and B_n result real assuming that the stress relaxation in soft tissues would show no oscillations. Furthermore, adopting the orders (N=M) bounded creep and stress relaxations responses are guaranteed [4].

A fractional derivative model will be proposed to accomplish this fitting with i) less number of parameters to fit, ii) a power-law response, iii) appropriate fit with mild computational effort.

The most classical definition of a fractional derivate is attributed to Rienman and Liouville, for the fractional order (α) derivative of a function f(t) can be expressed as

$$D^\alpha f(t) = \frac{1}{\Gamma(1-\alpha)}\frac{d}{dt}\int_0^t \frac{f(\tau)}{(t-\tau)^\alpha d\tau} \quad (3)$$

where Γ is the Euler gamma function. Finite element and numerical implementation of this integral can be found elsewhere [14]-[15]. By replacing this fractional derivative in equation (1), the constitutive equation becomes the following fractional differential equation,

$$\sigma(t) + B_1\frac{d\varepsilon^\alpha(t)}{dt^\alpha} = E_0\varepsilon(t) + E_1\frac{d\varepsilon^\beta(t)}{dt^\beta} \quad (4)$$

This simple 5 element model has proved to be reliable and robust describing real materials [5], [8], [9], [16]. As analyzed by Bagley and Torvik [7], the constraint $\alpha=\beta$ predicts positive energy dissipation for all frequencies. Applying the Fourier Transform and following a direct integer analogy to the fractional derivatives, the complex modulus yields a 4-parameter model of the form

$$E^*(\omega) = \frac{E_0 + E_1(i\omega)^\alpha}{1 + B_1(i\omega)^\alpha} \quad (5)$$

For very low frequencies, E^* approaches to E_0 (static elastic modulus). In the transition region, the amplitude of E^* increases with frequency, following a power-law response and reaching a plateau at high frequencies with an asymptote in E_1/B_1. The storage and loss module can be obtained from (5) as the real and imaginary part respectively. The 4-parameters can be determined by a least-squares fit, over the physiological frequency band, to either the real or imaginary part.

B. Measurements

Previous data from an instrumented sheep were used to test the model. The surgical procedure can be found elsewhere [17]. Pressure (microtransducer, model P7, 1200 Hz flat frequency response, Konigsberg Instruments, Inc., Pasadena, CA) and external diameter (ultrasonic crystals 5 MHz, 3 mm diameter) were measured in the aorta simultaneously. Both signals were digitized at a frequency rate of 250Hz (12 bits) for off-line processing.

The periods of both pressure and diameter signals were automatically detected and converted to stress strain as described in previous works of our group [11], [17]. Fifty representative cycles were selected. Fourier transform was applied to an averaged period to obtain the complex modulus in basal state. As the hear rate was near 2Hz, 15 harmonics were calculated avoiding higher frequency dispersion. The 4-parameter fractional model described in (5) was fitted. The minimization of the squared magnitude of the residuals of E^* was performed using Microsoft Excel solver over the real and imaginary parts simultaneously. Mean squared error was averaged for each harmonic.

III. RESULTS

Fig. 1 shows the stress and strain signals. The strain was normalized to the unstressed radius. In Table 1 all the sheep hemodynamic values are presented, including the pressure/diameter to stress/strain conversion.

TABLE 1.
HEMODYNAMIC VALUES (Mean±MAX and MIN)

	CTL		PHE	
Pressure [mmHg]	**63.48**	72.2 55.2	**63.35**	71.4 55.1
Diameter [mm]	**15.88**	16.6 15.2	**14.38**	14.61 14.16
Stress [kPa]	**84.34**	117.3 54.5	**37.16**	51.8 26.0
Strain [ ]	**1.17**	1.19 1.14	**1.05**	1.07 1.04

Using the model of equation (5) and after the 4-parameter adaptation, the parameters resulted E_0=72.0kPa, α=0.124, B_1=3.68s^{α} and E_1=2833kPa s^{α}.

The measured and estimated complex modules are represented normalized to the mean elastic value (E_0), in the frequency domain. Accordingly, the storage and dissipating modulus are showed in Fig. 2. The absolute value of the elastic modulus averaged for high frequencies along the plateau resulted $\approx 7.10^5$ Pa whereas the phase response attained $\approx$0.3 radians. A clear potential relationship can be confirmed together with the model fit. An abrupt elastic increase can be seen from low to high frequencies, reaching a plateau at 4Hz, for both states. Mean squared error was calculated for each harmonic and resulted <5%.

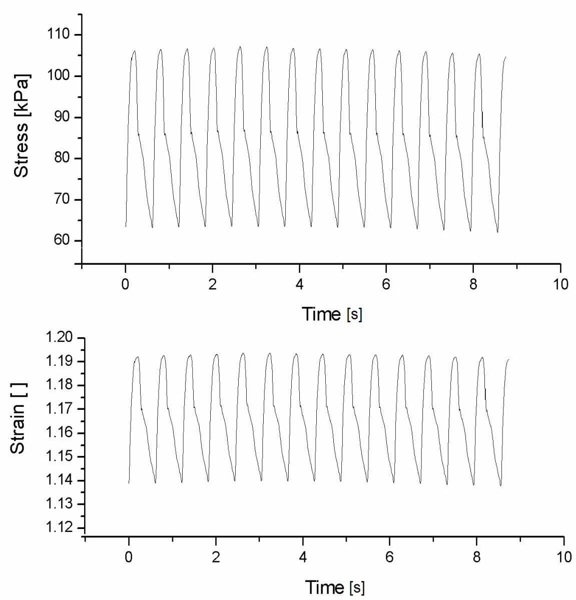

Fig. 1. Stress and strain signals derived from pressure and diameter measurements in the aorta of an anesthetized sheep.

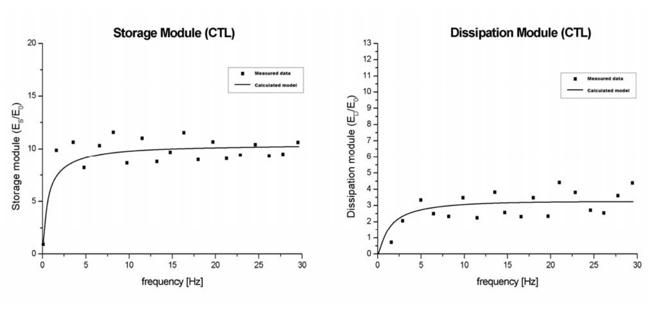

Fig. 2. The real (left) and imaginary (right) parts of the calculated complex modulus E* with the adapted fractional model (thick line). CTL=control state.

IV. Discussion

To analyze the arterial wall mechanics in vivo, a complex modulus (E^*) approach was adopted. Linear viscoelasticity assumes that stress is a function of strain history. This translates naturally into the existence of a relaxation function given by a convolution integral

$$\sigma(t) = \int_{-\infty}^{0} \varepsilon(\tau) E^*(t-\tau)\, d\tau$$

Using the Fourier transform, this hypothesis is equivalent to the existence of a complex modulus E^* such that $\tau(\omega)=\varepsilon(\omega)\, E^*(\omega)$.

From a practical point of view, viscoelasticity problems can be solved fitting a model to the frequency dependent $E^*(\omega)$. The real part of E^* is associated with the elastic behavior of the material, usually called storage modulus. Arterial mechanics depends intimately not only on this real part but to the imaginary part (loss modulus) related to viscous responses.

In conduit arteries, not only the storage but the loss modules showed to increase with frequency, attaining a plateau for high rates of stress/strain. As remarked by Bergel [13] many attempts were made to fit these responses to simple models, combining linear voigt/Maxwell elements. The quality of the fit depended strongly on the model order. The inclusion of new non-linear elements or more complicated terms to the equations tended to systematically blur the physical meaning of the added parameters.

Our results confirm that using a fractional derivative model, with only 4 parameters, the complex modulus shows an appropriate fit. Whereas an integer order derivate is a local operator, fractional derivatives depend on the material past, evidencing a memory mechanism that can be adjusted using the fractional order α [18]. Fractional derivatives are such an intimate descriptor of rheological materials behaviour that only four parameters resulted enough to accurately represent a particular material. Our E* confirms other findings: the storage modulus approaches to its static value E_0 at low frequencies and increases towards an asymptote at high frequencies. Accordingly, the loss modulus attains zero values for low frequencies and increases steadily towards a plateau. Storage module resulted higher with respect to the loss module and confirming the predominant elastic nature of the aorta. The natural potential behaviour of the fractional derivative models matches naturally to those responses. The mean squared errors, accumulated by the real and the imaginary parts for each harmonic from 0 to 30Hz, confirmed a proper fit. For each harmonic there was an average error that doesn't exceed 5%. Moreover, our elastic curves, calculated in-vivo based on pressure-diameter measurements, also showed a reasonable agreement with results reported not only in-vivo but in-vitro [19].

In contrast to in-vitro studies, our in-vivo experiments yielded information from the mechanical properties of the living animal where the complete artery remained intact with all the natural variability. The complex modulus in the living animal was determined at a mean distending pressure for multiples of the heart rate. Variations around this working point were considered. Although non-linear behaviour of the arterial wall is well reported, small strains are present under our stable physiologic conditions, allowing a linear approximation. The arterial wall constituents are essentially elastin, collagen and smooth muscle. We assumed that at low pressure values, as those found in the anesthetized sheep, the mechanical response is mainly governed by the elastic component. Consequently, a linear model can be adopted permitting the complex modulus analysis to be a reasonable approach. The absolute value for the complex modulus in vivo resulted near 7.10^5 Pa. These values don't differ from the reported elsewhere [18]. The phase response attaining 0.3 rad for higher frequencies resulted similar to some measurements [3] although a little higher from others [19]. This difference is probably due to the scatter in phase measurements, reported to be about 0.1 rad.

The viscous properties of the wall are responsible for the frequency dependence of E^*. Many evidences of this viscous presence can be enumerated including the hysteresis of the pressure-diameter loop, creep and stress relaxation responses and ultimately the power-law response of E^*. Arterial smooth muscle is thought to be a natural contributor to this viscous evidence and should play a key element in arterial mechanics modeling [11].

Finally, physical models can be found to represent viscoelastic materials, combining Maxwell-Voigt elements as suggested by Magin in his vast review [18]. Special attention should be paid to give each element a physical correlation that describes the arterial mechanical response.

V. Conclusion and Perspectives

The complex elastic modulus was calculated for a sheep in-vivo measuring aortic pressure and diameter simultaneously. The spectrum of this viscoelastic modulus was calculated, showing frequency independence above 4Hz, in accordance with the literature. The fractional derivative model allowed this power-law to be naturally fitted. The main interest of fractional derivative models is to allow fairly good approximations of realistic material behavior with a low number of parameters.

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