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BIOLOGICAL SOFT TISSUES: MECHANICAL CHARACTERIZATION, DATA ANALYSIS, AND MODELS' EVALUATION

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Abstract: *Mechanical test procedures and a systematic data analysis of soft tissues are discussed with the view of providing experimental bases for the evaluation and validation of constitutive models for this class of biological materials. A new methodology and measures are presented for the quantitative and qualitative characterization of the mechanical response of soft tissues under monotonic (J-shape response) and quasi-static cyclic loading (stress softening effect) in different deformation modes. The general structure of constitutive theory and special models are shortly discussed within the same conceptual framework.*

Keywords: Soft tissues, Multiple-axial tests, Elasticity, Stress softening, Viscoelasticity.

1. Introduction

Soft tissues such as arteries muscle, skin, lung, mesentery, etc. exhibit qualitatively similar mechanical properties (Fung, 1993). They are inelastic (no single-valued relationship between stresses and strains exists), their stress-strain history relationships are nonlinear, they show hysteresis when subjected to cyclic loading-unloading, they exhibit stress relaxation and creep when held at constant strain and stress, respectively. Soft tissues are anisotropic and inhomogeneous, their properties vary with the sites, aging, etc. When all these factors are coupled, the problem of how to experimentally characterize and theoretically describe the mechanical properties of soft tissues becomes quite acute. Two main issues, which must be addressed in this respect, are: 1) advanced and efficient experimental methods to guarantee a high quality of comprehensive data for soft tissues; 2) reliable constitutive models with physically identified material parameters that represent mechanisms occurring in these biological materials.

There is a wide range of testing techniques available to characterize the mechanical behavior of soft tissues. These differing experimental methods and testing protocols have resulted in a large variance in the reported data making comparison of the mechanical behavior of soft tissues difficult and sometimes even impossible. In order to address these issues, this paper discusses in a unified way testing procedures under monotonic and quasi-static cyclic loading together with suitable methods of data analysis that provide a firm experimental basis for the evaluation of theoretical models for the biological soft tissues.

2. Test Procedures and Data Analysis

Mechanical properties of soft tissues can be experimentally studied by different test procedures, e.g. a) monotonic loading up to failure, b) cyclic pre-stressing to an assigned strain, c) cyclic pre-stressing to a fixed stress, and d) pre-stressing to successively higher strains or stresses. In addition, the viscoelastic behavior of these biological materials can be experimentally studied in the standard creep and relaxation tests as well as by the dynamical mechanical analysis. Moreover, all these tests may be performed in various deformation modes such as uniaxial tension (compression), equi-biaxial tension, pure or simple shear, planar tension, and multi-axial straining. A typical behavior of soft tissues observed under monotonic and cyclic loading is schematically shown in Fig. 1.

Under monotonic loading, most soft tissues exhibit characteristic J-shape stress-strain curves with three main phases. The best way to qualitatively describe this phenomenon is to measure the slope of the stress-strain curves and to plot this quantity as a function of strain or stress. This analysis of the monotonic

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tension data lies at the basis of the famous Fung model for the elastic behavior of soft tissues (Fung, 1993).

Under cyclic loading, all biological soft tissues exhibit the so-called stress softening phenomenon, first observed in elastomers (natural and synthetic rubber) where it is referred to as the Mullins effect. The main problem in qualitative characterization of this phenomenon is the variety of ways of expressing the degree of stress softening.

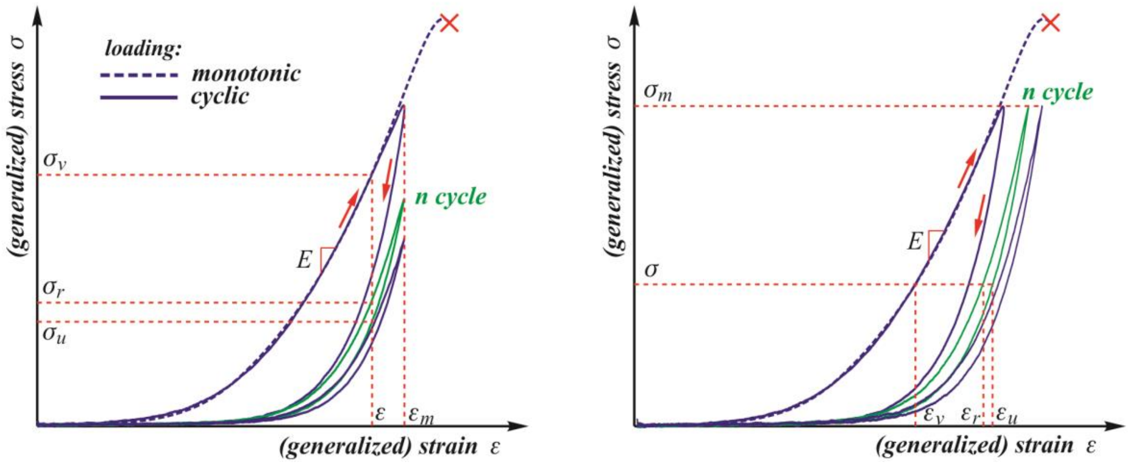

Fig. 1: Schematic response of soft tissues under monotonic and quasi-static cyclic loading to pre-scribed strain (left) and to pre-scribed stress (right).

In this study, the stress-strain response of soft tissues under monotonic and cyclic loading is characterized by the tangential modulus E defined as the slope of the stress-strain curve during loading, unloading, and reloading with E denoted by $E_v(\varepsilon)$, $E_u(\varepsilon;\varepsilon_m)$ and $E_r(\varepsilon;\varepsilon_m)$, respectively. The reduction of modulus caused by successive stretching serves as a measure of the amount of stress softening. In addition, this quantity during each deformation cycle for the specified value of pre-strain ε_m and pre-stress σ_m is described by the stress and strain retention $s(\varepsilon;\varepsilon_m)$ and $e(\sigma;\sigma_m)$, respectively, defined as (see Fig. 1)

$$s(\varepsilon;\varepsilon_m) = \frac{\sigma_s(\varepsilon;\varepsilon_m)}{\sigma_v(\varepsilon)}, \qquad e(\sigma;\sigma_m) = \frac{\varepsilon_s(\sigma;\sigma_m)}{\varepsilon_v(\sigma)}. \tag{1}$$

Here σ_s is a common notation for σ_u and σ_r (ε_s for ε_u and ε_r, respectively). Plots of $s(\varepsilon;\varepsilon_m)$ and $e(\sigma;\sigma_m)$ as functions of the normalized strain $\varepsilon/\varepsilon_m$ and stress σ/σ_m for different values of ε_m and σ_m, respectively, provide qualitative and quantitative measures of the stress softening in the tested soft tissues. These plots should be compared with corresponding theoretical results predicted by various models proposed in the literature.

Most experimental studies of the stress softening in soft tissues are confined to uniaxial tension tests. However, this phenomenon is also evidenced in cyclic compression, equi-biaxial tension, and shear deformation modes. The methodology of characterizing the stress softening described above applies to all these deformation modes with the uniaxial stress and strain replaced by their generalized counterparts. For example, the axial strain may be replaced by the measure of the deformation extent discussed below.

3. Modeling and Models' Evaluation

Macroscopic behavior of soft tissues may effectively be modeled within the thermodynamic framework of continua with internal variables or micro-forces (Kazakevičiūtė-Makovska and Steeb, 2011). For first order (local) models with time effects neglected or at constant strain rates, the latter theory reduces to the former one and the general constitutive law for the stress takes the form

$$\boldsymbol{T} = \tilde{\boldsymbol{T}}(\boldsymbol{F},\boldsymbol{\alpha}) + \boldsymbol{T}_R\,, \quad \tilde{\boldsymbol{T}}(\boldsymbol{F},\boldsymbol{\alpha}) = J^{-1}(\partial\Phi(\boldsymbol{F},\boldsymbol{\alpha})/\partial\boldsymbol{F})(\boldsymbol{F}^{-1})^T\,, \quad J = \det\boldsymbol{F}\,. \tag{2}$$

Here $\Phi = \Phi(\boldsymbol{F},\boldsymbol{\alpha})$ is the energy potential (free energy in isothermal processes or internal energy in adiabatic processes), which is a function of the deformation gradient $\boldsymbol{F}$ and a set of internal variables $\boldsymbol{\alpha} = (\alpha_1,\ldots\alpha_n)$. Moreover, $\boldsymbol{T}$ denotes the Cauchy (true) stress tensor and $\boldsymbol{T}_R$ is a constitutively indeterminate reactive stress due to possible material constraints (e.g. incompressibility of bulk material or fibre inextensibility). For unconstrained materials, $\boldsymbol{T}_R = \boldsymbol{0}$. The internal variables $\boldsymbol{\alpha} = (\alpha_1, \ldots \alpha_n)$ represent the state of deterioration (stress softening, permanent strain, etc.) of a material and their evolution during deformation process must be specified by additional constitutive laws. In general, the functional form of the constitutive relations (2) is delimited only by the frame-indifference principle and possible material symmetries. They can be rewritten in terms of the first (engineering) and second Piola-Kirchhoff stress tensors $\boldsymbol{P}$ and $\boldsymbol{S}$ using classical relations.

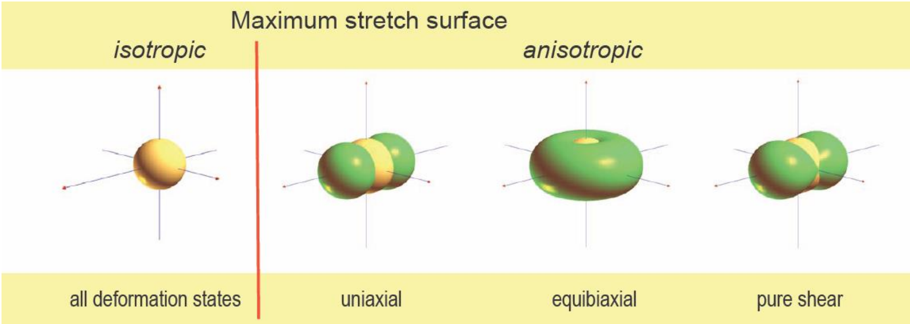

Fig. 2: Quantification of deformation extent under general loading conditions.

In formulating the evolution law for the softening and permanent set variables $\boldsymbol{\alpha} = (\alpha_1, \ldots \alpha_n)$, it is generally assumed that the response of soft tissues to cycling loading depends only on the maximum previous strain experienced during the deformation history (Horný et al., 2010; Peña et al., 2011). Accordingly, a suitable measure must be introduced to quantify the maximum strain experienced by the material during the entire deformation process for the three-dimensional state of strain. In general, such a measure is defined as $v = \hat{v}(\boldsymbol{F})$ subject to certain physically justified assumptions (Kazakevičiūtė-Makovska, 2007a). For both isotropic and anisotropic response of materials, the deformation extent may be defined as the maximum of stretches computed over all directions and the past history (this definition is graphically represented in Fig. 2). Most of models proposed in the literature for the stress softening of soft tissues use a single softening variable in which case the evolution law may be assumed in the following general form: $\alpha = \hat{\alpha}(v; v_m)$, $0 \le v \le v_m$. Here v is a measure of deformation extent at the current time instant t and v_m denotes the maximum value of v experienced by material during deformation process up to time t. The function $\hat{\alpha}(v; v_m)$ may be called the softening function because it determines the measure of softening in the tissue during the whole deformation process. It has been shown by Kazakevičiūtė-Makovska (2007, 2007a) that two broad classes of the evolution laws for the softening variable may be distinguished for elastomeric materials. It turn out that the same forms of the evolution law are used for soft tissues (e.g. Peña et al., 2011; Gultova et al., 2011; Maher et al., 2012):

$$\alpha = \begin{cases} \hat{\alpha}(v) \equiv \tilde{\alpha}(v; v) & \text{if} \quad v = v_m \quad \textit{(primary loading path)}, \\ \alpha_m \equiv \hat{\alpha}(v_m) & \text{if} \quad v < v_m \quad \textit{(unloading / reloading paths)}, \end{cases} \tag{3}$$

or (e.g. Weisbecker et al., 2012)

$$\alpha = \begin{cases} 0 & \text{if} \quad v = v_m \quad \textit{(primary loading path)}, \\ \tilde{\alpha}(v; v) & \text{if} \quad v < v_m \quad \textit{(unloading / reloading paths)}. \end{cases} \tag{4}$$

With evolution law assumed in either form (3) or (4), it remains to specify the dependence of the response function $\tilde{\boldsymbol{T}}(\boldsymbol{F}, \alpha)$, equivalently the energy function $\Phi = \Phi(\boldsymbol{F}, \alpha)$, on α but leaving the dependence on $\boldsymbol{F}$ arbitrary. The general assumption is that for $\alpha = 0$ the relations (2) reduce to the constitutive equation of the nonlinear elasticity $\boldsymbol{T}_0 = \tilde{\boldsymbol{T}}_0(\boldsymbol{F}) + \boldsymbol{T}_R$ with the elastic response function $\tilde{\boldsymbol{T}}_0(\boldsymbol{F}) \equiv \tilde{\boldsymbol{T}}(\boldsymbol{F}, \boldsymbol{0})$ derived from the strain energy density $W(\boldsymbol{F})$. In the context of elastomers, that there are four basic classes of models that differ in the manner the response function $\tilde{\boldsymbol{T}}(\boldsymbol{F}, \alpha)$ depends on the internal (softening) variable α (Kazakevičiūtė-Makovska, 2007, 2007a). The same classification applies to models proposed in the literature for the soft tissues.

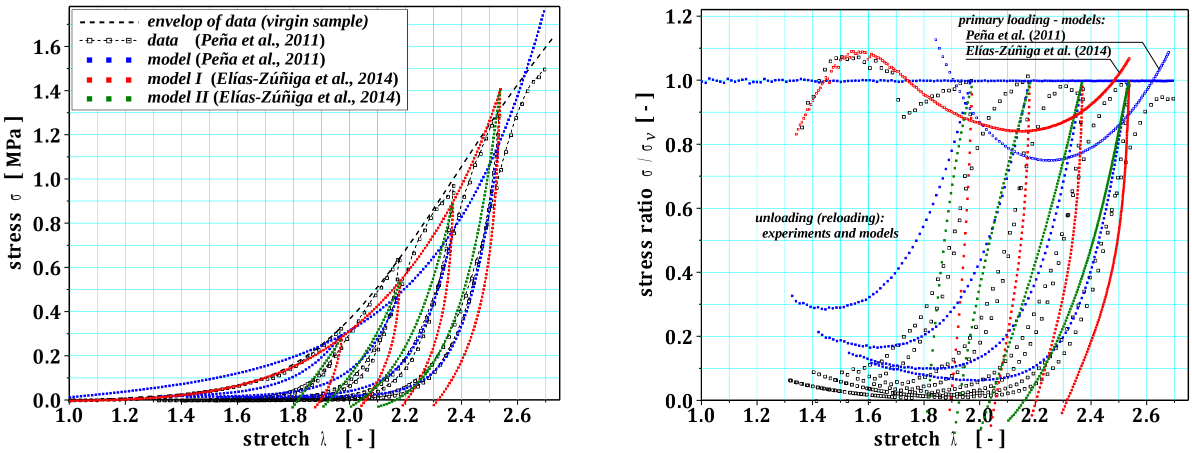

Fig. 3: Comparison of data with different models prediction: Conventional comparison of stress-strain curves (left); plots of stress ratio $(1)_1$ defined in this work (right).

4. Conclusions

Characterising and modelling the mechanical behaviour of soft tissues are an essential step in development of predictive computational models to assist research for a wide range of applications in medicine, biology, tissue engineering, pharmaceutics, consumer goods or cosmetics. Therefore, it is critical that constitutive models capture the main characteristic properties of this class of biological materials so that the proposed models are adapted for their intended applications. Results of this work provide reliable methods for the quantitative and qualitative evaluation of the theoretical models aiming to describe the response of soft tissues under monotonic and cyclic loading in different deformation modes. The proposed methodology is far more reliable than the usual comparison of theoretical and measured stress-strain curves. This is illustrated in Fig. 3 for the measured data and theoretical model prediction presented in Peña et al. (2011) and two models proposed by Elías-Zúñiga et al. (2014).

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