Note di Matematica **27,** n. 2, 2007, 229–247.

A model for the kinetics of thermal damage of biological membranes

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Received: 21/08/2006; accepted: 20/09/2006.

Abstract. The increased use of heating in many medical specialties is driven by the availability of new devices, not an understanding of the underlying physics. Whereas most prior studies have quantified material response characteristics before and after thermal damage, the goal of this work is to describe changing response characteristics during a particular class of thermal damage tests—biaxial isometric tests on collagenous biomembranes. Evolution equations are derived/postulated that provide a good fit to data but more generally provide direction for future work.

Keywords: biological membrane, modeling, thermal damage

MSC 2000 classification: primary 92C10, secondary 74L15

1 Introduction

Various procedures commonly used to treat disease or injury within a clinical setting employ lasers, microwaves, radio waves and related technologies to produce changes in the thermal state of the tissue that is being treated. An increase in the temperature tends to kill cells and shrink the collagen, in contrast to metals which tend to expand, bringing to the fore the distinction in the response due to changes in temperature. Such clinical procedures can also induce changes in the mechanical, electrical, optical, acoustical, chemical and magnetic properties of the tissue undergoing treatment. In this study we are

primarily interested in the coupling between the thermal and the mechanical response characteristics of soft tissues. The shrinking of the collagen (the most abundant structural protein in the body) due to heating suggests procedures for tightening sprained joints or reshaping geometries and the killing of cells suggests its use in the treatment of tumors. In fact, one can find the application of heat in many specialties, including dermatology, cardiology, oncology, gynecology, opthalmology, orthopedics, and urology.

Denaturing collagen by heat treatment leads to significant changes in its response characteristics. It has been found in both uniaxial and biaxial experiments that the extensibility of the specimen often increases with heat treatment (see [1]– [5]). Harris et al. [2] also found that heat treatment tended to reduce the extent of anisotropy of the specimen. Wells et al. [4] investigated the effect of heating under the constraint of biaxial isometry in isothermal processes. They determined the forces generated under isometric conditions.

Collagenous tissues exhibit viscoelastic response characteristics. Rigby et al. [6] carried out stress relaxation experiments on rat tail tendon and Cohen et al. [7] carried out creep tests on human digital tendon. Chen and Humphrey [1] studied the effect of thermal damage on the hysteresis during cyclic loading of bovine chordae tendineae.

It is worth noting that the stress relaxation that can manifest itself due to damage is markedly different from the stress relaxation in a viscoelastic solid (see Rajagopal and Wineman [8]). Even a material, that is initially elastic that is suffering damage and is such that the response of the material is elastic if there is no further damage, can exhibit stress relaxation while being damaged (see Soares et al. [9], Rajagopal et al. [10]).

In this paper we are interested in describing responses of biological membranes during the thermal damage process. We shall model the membrane, which is a multiconstituent body, as a homogenized single continuum. As the body suffers thermal damage and its response changes by virtue of this, we will introduce parameters that reflect and quantify this damage. The process of thermal damage, which is largely due to the breakage of hydrogen bonds, causes the body to shrink. We can interpret this situation as the natural configuration of the body changing due to heat treatment. This suggests a multiplicative decomposition for the deformation gradient with a deformation gradient associated with the elastic response $\mathbf{F}^E$ from the evolving natural configurations (see Rajagopal [11] for a discussion of the notion of natural configuration, its material symmetry, and the connection of its evolution with the rate of entropy production) and the linear transformation $\mathbf{G}$ that reflects the shrinking, namely $\mathbf{G}$ is the mapping from material points in the configuration of the body in its initial natural configuration to the corresponding material points in the natural configuration

at time t. While such an approach might superficially resemble the multiplicative decomposition that one comes across in plasticity, its physical origins and the role that it plays in the response of the material is markedly different. The tensor $\mathbf{G}$ is a consequence of the damage that is taking place due to the heat treatment. In order to capture the physics, we need to introduce a parameter that reflects the stiffening or hardening of the material due to the damage as well as that the hardening is different along different directions. We also need to take into account that material (molecules) is being altered due to the debonding. Once, we introduce physical parameters to reflect these facts, we will have a model in place.

In this paper we study the biaxial stretching of a membrane of biological material as the body undergoes heat treatment and the attendant damage.

2 Preliminaries

Assume that the membrane has two principal directions, X_1 and X_2, and that the fibers and the water in the membrane undergo the same planar motion described by

$$x_i = \chi_i\left(X_j, t\right), \quad i, j = 1, 2\,. \tag{1}$$

The matrix associated with the deformation gradient tensor $\mathbf{F}$ is given by

$$\mathbf{F} = \left[\frac{\partial x_i}{\partial X_j}\right]. \tag{2}$$

The balance of mass is given by

$$\rho \det \mathbf{F} = \rho_0\,, \quad \text{or } \frac{\partial \rho}{\partial t} + \left(\rho v_j\right)_{,j} = 0\,, \tag{3}$$

where ρ_0 and ρ are, respectively, the mass densities of the membrane (per unit area) in its initial and its present configuration, and $\mathbf{v}$ is the velocity of the membrane. The diffusion of water in or out of the membrane during the deformation process is ignored in the following analysis.

The balance of linear momentum takes the form

$$\rho\frac{dv_i}{dt} = \sigma_{ji,j}\,, \quad \frac{dv_i}{dt} = \frac{\partial v_i}{\partial t} + v_j v_{i,j}\,, \quad i = 1, 2\,, \tag{4}$$

where $\boldsymbol{\sigma}$ $\left(= \boldsymbol{\sigma}^T\right)$ is the Cauchy stress; the effect of gravity is neglected.

Under the premise that the membrane has a uniform temperature field T (independent of the spatial positions (x_1, x_2)) and is undergoing an isothermal process during damage, the balance of energy reduces to

$$\rho\frac{de}{dt} = \operatorname{tr}\left[\left(\boldsymbol{\sigma} + hP^w\mathbf{1}\right)\mathbf{L}\right] + q\,. \tag{5}$$

Here, e is the internal energy of the membrane, P^w the pressure of the water surrounding the membrane, h the thickness of the membrane in the present state, $L_{ij} = v_{i,j}$, and q the heat source by virtue of the hot water bath. The presence of P^w results from changes in the membrane thickness while the membrane is being stretched or damaged. The heat flux due to conduction (in both the direction normal to the membrane and the directions x_1 and x_2) is ignored and is a consequence of the assumption of a uniform temperature field. This idealization is mainly justified by the thinness of the membrane and the setup of the experimental test in which the membrane is submerged in a water bath of constant temperature T_f. Calculations of the heat transfer upon immersion suggest that the centerline temperature of the membrane reaches T_f within $1.5s$ [3], which is much shorter than the time scales of interest ($10^3 s$).

The entropy production equation during the process of damage may be written as

$$\rho \frac{d\eta}{dt} - \frac{q}{T} = \xi \geq 0\,, \tag{6}$$

or

$$-\rho \left(\dot{A} + \eta \dot{T} \right) + \operatorname{tr} \left[\left(\boldsymbol{\sigma} + h P^w \mathbf{1} \right) \mathbf{L} \right] = T\xi \geq 0\,, \tag{7}$$

where η is the entropy, q/T the entropy flux due to convective heating, $A = e - T\eta$ the Helmholtz potential, ξ the rate of dissipation, and the dot denotes material time derivative. Equation (5) has been used to derive (7).

During the process of thermal damage, chemical bonds in the membrane such as hydrogen bonds are damaged progressively, which causes permanent shrinkage or extension of the membrane under certain stretching conditions. To simulate this phenomenon of shrinkage or extension (i.e., the inelastic deformation or evolution of the natural configuration) due to heating, we decompose the deformation gradient $\mathbf{F}$ as

$$\mathbf{F} = \mathbf{F}^E \mathbf{G} \tag{8}$$

where $\mathbf{G}$ characterizes the part of the deformation associated with the damage of the material whose evolution is to be described by a differential equation, and $\mathbf{F}^E$ the elastic part relative to the evolving reference configuration. Assume that the Helmholtz potential is determined through

$$A = A \left(\mathbf{F}^E, \mathbf{G}, \boldsymbol{\gamma}, \boldsymbol{\alpha}, T \right), \tag{9}$$

where the quantity $\boldsymbol{\gamma}$ is a tensor that is a measure of the "hardening" of the biological membrane due to the damage. This effect of hardening is reflected by the stiffer mechanical response of a thermally damaged membrane than that of the corresponding native membrane, and the tensor character of $\boldsymbol{\gamma}$ attempts to

reflect the different degrees of hardening along different directions. The role of tensor $\boldsymbol{\alpha}$ will be demonstrated later, but without the inclusion of $\boldsymbol{\alpha}$ the solutions of $\mathbf{G}$ and $\boldsymbol{\gamma}$ would not be physically adequate under certain circumstance. For the moment, we will treat both $\boldsymbol{\gamma}$ and $\boldsymbol{\alpha}$ as dimensionless internal variables but provide a physical meaning for the same, later. Here we seek an approximate way to simulate the damage process with the use of internal variables such as $\mathbf{G}$, $\boldsymbol{\gamma}$ and $\boldsymbol{\alpha}$ to capture the macroscopic behavior of the membrane. We do not consider explicitly the bio-chemical reactions at the molecular level due to our limited understanding of these reactions.

Now, (7) can be expressed as

$$\rho \operatorname{tr}\left[\left(\frac{\partial A}{\partial \mathbf{F}^{E^T}}\mathbf{F}^E - \mathbf{G}\frac{\partial A}{\partial \mathbf{G}^T}\right)\dot{\mathbf{G}}\mathbf{G}^{-1} - \frac{\partial A}{\partial \boldsymbol{\gamma}^T}\dot{\boldsymbol{\gamma}} - \frac{\partial A}{\partial \boldsymbol{\alpha}^T}\dot{\boldsymbol{\alpha}}\right] + \operatorname{tr}\left[\left(\boldsymbol{\sigma} - \rho\mathbf{F}^E\frac{\partial A}{\partial \mathbf{F}^{E^T}}\right)\mathbf{L}\right] - \rho\left(\eta + \frac{\partial A}{\partial T}\right)\dot{T} = T\xi \geq 0\,. \quad (10)$$

Based on the above inequality and the assumption that the mechanical response of the membrane relative to the current reference configuration is elastic, we choose

$$\boldsymbol{\sigma} = \rho\mathbf{F}^E\frac{\partial A}{\partial \mathbf{F}^{E^T}} = \frac{1}{\det\mathbf{F}}\mathbf{F}^E\frac{\partial W}{\partial \mathbf{F}^{E^T}}, \quad W = \rho_0 A\,. \quad (11)$$

or, in terms of the nominal stress tensor $\mathbf{S}$,

$$\mathbf{S} = (\det\mathbf{F})\,\mathbf{F}^{-1}\boldsymbol{\sigma} = \mathbf{G}^{-1}\frac{\partial W}{\partial \mathbf{F}^{E^T}}\,. \quad (12)$$

Thus, (10) reduces to

$$\frac{\rho}{\rho_0}\operatorname{tr}\left[\left(\frac{\partial W}{\partial \mathbf{F}^{E^T}}\mathbf{F}^E - \mathbf{G}\frac{\partial W}{\partial \mathbf{G}^T}\right)\dot{\mathbf{G}}\mathbf{G}^{-1} - \frac{\partial W}{\partial \boldsymbol{\gamma}^T}\dot{\boldsymbol{\gamma}} - \frac{\partial W}{\partial \boldsymbol{\alpha}^T}\dot{\boldsymbol{\alpha}}\right] - \rho\left(\eta + \frac{1}{\rho_0}\frac{\partial W}{\partial T}\right)\dot{T} = T\xi \geq 0\,. \quad (13)$$

To exploit the entropy inequality further, we restrict our consideration to the damage processes of the membrane under biaxial stretch along the two principal directions, i.e.,

$$\mathbf{F} = \begin{bmatrix} \frac{\partial x_1}{\partial X_1} & 0 \\ 0 & \frac{\partial x_2}{\partial X_2} \end{bmatrix}, \quad \mathbf{G} = \begin{bmatrix} G_1 & 0 \\ 0 & G_2 \end{bmatrix}, \quad \boldsymbol{\gamma} = \begin{bmatrix} \gamma_1 & 0 \\ 0 & \gamma_2 \end{bmatrix},$$
$$\boldsymbol{\alpha} = \begin{bmatrix} \alpha_1 & 0 \\ 0 & \alpha_2 \end{bmatrix}, \quad \mathbf{F}^E = \begin{bmatrix} F_1^E & 0 \\ 0 & F_2^E \end{bmatrix} = \begin{bmatrix} \frac{F_1}{G_1} & 0 \\ 0 & \frac{F_2}{G_2} \end{bmatrix}. \quad (14)$$

With these simplifications, (13) reduces to

$$D_1\dot{G}_1 + \left(-\frac{\partial W}{\partial \gamma_1}\right)\dot{\gamma}_1 + D_2\dot{G}_2 + \left(-\frac{\partial W}{\partial \gamma_2}\right)\dot{\gamma}_2 + \left(-\frac{\partial W}{\partial \alpha_1}\right)\dot{\alpha}_1 + \left(-\frac{\partial W}{\partial \alpha_2}\right)\dot{\alpha}_2 - \rho_0\left(\eta + \frac{1}{\rho_0}\frac{\partial W}{\partial T}\right)\dot{T} = \frac{\rho_0 T\xi}{\rho} \geq 0\,, \quad (15)$$

where

$$D_1 := \frac{F_1^E}{G_1}\frac{\partial W}{\partial F_1^E} - \frac{\partial W}{\partial G_1}, \quad D_2 := \frac{F_2^E}{G_2}\frac{\partial W}{\partial F_2^E} - \frac{\partial W}{\partial G_2}\,. \quad (16)$$

Based on this inequality, we construct the following constitutive assumptions for the evolution of $\mathbf{G}$, $\boldsymbol{\gamma}$ and $\boldsymbol{\alpha}$:

$$\dot{G}_1 = (\beta_{11} + \beta_{\gamma_1})\left(\frac{\partial W}{\partial \gamma_1}\right)^2 D_1 + \beta_{12}\frac{\partial W}{\partial \gamma_1}\frac{\partial W}{\partial \gamma_2}D_2 + \beta_{1T}\dot{T}\,, \quad (17)$$

$$\dot{G}_2 = (\beta_{22} + \beta_{\gamma_2})\left(\frac{\partial W}{\partial \gamma_2}\right)^2 D_2 + \beta_{21}\frac{\partial W}{\partial \gamma_2}\frac{\partial W}{\partial \gamma_1}D_1 + \beta_{2T}\dot{T}\,, \quad (18)$$

$$\dot{\gamma}_1 = \beta_{\gamma_1}\frac{\partial W}{\partial \gamma_1}(D_1)^2 - \beta_{\gamma_1\alpha_1}\frac{\partial W}{\partial \alpha_1} + \beta_{\gamma_1 T}\dot{T}\,, \quad (19)$$

$$\dot{\gamma}_2 = \beta_{\gamma_2}\frac{\partial W}{\partial \gamma_2}(D_2)^2 - \beta_{\gamma_2\alpha_2}\frac{\partial W}{\partial \alpha_2} + \beta_{\gamma_2 T}\dot{T}\,, \quad (20)$$

$$\dot{\alpha}_1 = \beta_{\alpha_1\gamma_1}\frac{\partial W}{\partial \gamma_1} + \beta_{\alpha_1 T}\dot{T}\,, \quad (21)$$

$$\dot{\alpha}_2 = \beta_{\alpha_2\gamma_2}\frac{\partial W}{\partial \gamma_2} + \beta_{\alpha_2 T}\dot{T}\,. \quad (22)$$

Here, we do not propose an equation for the evolution of temperature since the balance of energy (5) will provide the required equation. Additional cross terms may be added to (17) through (22). In a fully thermodynamic framework, the manner in which the natural configuration, and hence $\mathbf{G}$, evolves will be determined by the second law and possibly additional assumptions such as the maximization of the rate of entropy production. Unfortunately, as we have no understanding of how entropy is produced due to damage, we will have to assume evolution equations that are able to capture the experimental results.

We shall now discuss some issues concerning the forms of the coefficients β's in the above equations.

(i) Substituting the above relations into (15) gives

$$0 \leq \frac{\rho_0 T\xi}{\rho} = \beta_{11}\left(\frac{\partial W}{\partial \gamma_1}D_1\right)^2 + \beta_{22}\left(\frac{\partial W}{\partial \gamma_2}D_2\right)^2 + (\beta_{12}+\beta_{21})\frac{\partial W}{\partial \gamma_1}\frac{\partial W}{\partial \gamma_2}D_1D_2 + (\beta_{\gamma_1\alpha_1}-\beta_{\alpha_1\gamma_1})\frac{\partial W}{\partial \gamma_1}\frac{\partial W}{\partial \alpha_1} + (\beta_{\gamma_2\alpha_2}-\beta_{\alpha_2\gamma_2})\frac{\partial W}{\partial \gamma_2}\frac{\partial W}{\partial \alpha_2} - \rho_0\left(\eta + \frac{1}{\rho_0}\frac{\partial W}{\partial T} + \frac{\beta_{\gamma_1 T}}{\rho_0}\frac{\partial W}{\partial \gamma_1} + \frac{\beta_{\gamma_2 T}}{\rho_0}\frac{\partial W}{\partial \gamma_2} + \frac{\beta_{\alpha_1 T}}{\rho_0}\frac{\partial W}{\partial \alpha_1} + \frac{\beta_{\alpha_2 T}}{\rho_0}\frac{\partial W}{\partial \alpha_2} - \frac{\beta_{1T}}{\rho_0}D_1 - \frac{\beta_{2T}}{\rho_0}D_2\right)\dot{T}\,. \quad (23)$$

To satisfy this inequality, it is sufficient to choose

$$\beta_{11} \geq 0, \quad \beta_{22} \geq 0, \quad \beta_{11}\beta_{22} \geq \left(\frac{\beta_{12}+\beta_{21}}{2}\right)^2, \quad (24)$$

$$(\beta_{\gamma_1\alpha_1}-\beta_{\alpha_1\gamma_1})\frac{\partial W}{\partial \gamma_1}\frac{\partial W}{\partial \alpha_1} \geq 0, \quad (\beta_{\gamma_2\alpha_2}-\beta_{\alpha_2\gamma_2})\frac{\partial W}{\partial \gamma_2}\frac{\partial W}{\partial \alpha_2} \geq 0\,, \quad (25)$$

and

$$\eta = -\frac{1}{\rho_0}\frac{\partial W}{\partial T} - \frac{\beta_{\gamma_1 T}}{\rho_0}\frac{\partial W}{\partial \gamma_1} - \frac{\beta_{\gamma_2 T}}{\rho_0}\frac{\partial W}{\partial \gamma_2} - \frac{\beta_{\alpha_1 T}}{\rho_0}\frac{\partial W}{\partial \alpha_1} - \frac{\beta_{\alpha_2 T}}{\rho_0}\frac{\partial W}{\partial \alpha_2} + \frac{\beta_{1T}}{\rho_0}D_1 + \frac{\beta_{2T}}{\rho_0}D_2\,. \quad (26)$$

(ii) If we think of $\boldsymbol{\gamma}$ as characterizing the number of chemical bonds along different directions being altered or created during the damage process and if we assume that this number is increasing as the damage progresses, we could require that

$$\dot{\gamma}_1 \geq 0\,, \quad \dot{\gamma}_2 \geq 0\,. \quad (27)$$

Accordingly, we view $\boldsymbol{\alpha}$ as indicating the number of molecules which are involved in altering or creating the bonds associated with $\boldsymbol{\gamma}$, and as the damage progresses, the number of molecules being altered or created increases. That is,

$$\dot{\alpha}_1 \geq 0\,, \quad \dot{\alpha}_2 \geq 0\,. \quad (28)$$

Further, we assume that

$$\frac{\partial W}{\partial \gamma_1} > 0\,, \quad \frac{\partial W}{\partial \gamma_2} > 0\,, \quad (29)$$

to reflect the hardening that is observed in the response of the membrane.

To meet the inequalities (25), (27) and (28), we require that

$$\begin{gathered}\beta_{\alpha_1\gamma_1} \geq \beta_{\gamma_1\alpha_1} \geq 0, \quad \frac{\partial W}{\partial \alpha_1} < 0\,, \quad \beta_{\alpha_2\gamma_2} \geq \beta_{\gamma_2\alpha_2} \geq 0\,, \quad \frac{\partial W}{\partial \alpha_2} < 0\,, \\ \beta_{\gamma_1} \geq 0\,, \quad \beta_{\gamma_2} \geq 0\,, \\ \beta_{1T} \geq 0\,, \quad \beta_{2T} \geq 0\,, \quad \beta_{\gamma_1 T} \geq 0\,, \quad \beta_{\gamma_2 T} \geq 0\,, \quad \beta_{\alpha_1 T} \geq 0\,, \quad \beta_{\alpha_2 T} \geq 0\,.\end{gathered} \tag{30}$$

(iii) The experimental test data demonstrate that, under a given constant stretch $\mathbf{F}$ (isometric loading) and a heating history from the initial room temperature T_0 instantly rising to the final temperature $T_f = 75^0 C$, there is a time period t_c during which the membrane is at the equilibrium temperature T_f and the stress $\boldsymbol{\sigma}$ is essentially constant; after this period, the stress starts to increase. We may infer that, during this time, thermal damage to the membrane is negligible, though the elastic property of the membrane is affected by the temperature rise to T_f (hardening as indicated by the data). It then follows that we can set

$$\dot{T} = 0\,. \tag{31}$$

in the above equations, and thus, the coefficients of β_{1T}, β_{2T}, $\beta_{\gamma_1 T}$, $\beta_{\gamma_2 T}$, $\beta_{\alpha_1 T}$ and $\beta_{\alpha_2 T}$ do not play active roles in the present simulation. More importantly, the observed change of the stress motivates the introduction of an activation criterion that characterizes whether the thermal damage to the membrane is activated. We expect this criterion to be a function of the heating and loading history and will be described by

$$\int_0^t f\left(\mathbf{F}, T\right) dt - 1 \begin{cases} < 0 & \text{(when no damage occurs)} \\ = 0 & \text{(commencement of damage).} \end{cases} \tag{32}$$

(iv) To calibrate the coefficients in equations (17) through (22) and the forms of W and f, we need to solve the equations to obtain the relations between stress and time (and/or stretch and time) and then compare these relations with the corresponding experimental data. We adopt the initial conditions

$$G_1 = G_2 = 1\,, \quad \gamma_1 = \gamma_2 = 0\,, \quad \alpha_1 = \alpha_2 = 0\,, \quad \text{at } t = 0\,. \tag{33}$$

Further, on using (31), (17) through (22) reduce to

$$\dot{G}_1 = \left(\beta_{11} + \beta_{\gamma_1}\right) \left(\frac{\partial W}{\partial \gamma_1}\right)^2 D_1 + \beta_{12} \frac{\partial W}{\partial \gamma_1} \frac{\partial W}{\partial \gamma_2} D_2\,, \tag{34}$$

$$\dot{G}_2 = \left(\beta_{22} + \beta_{\gamma_2}\right) \left(\frac{\partial W}{\partial \gamma_2}\right)^2 D_2 + \beta_{21} \frac{\partial W}{\partial \gamma_2} \frac{\partial W}{\partial \gamma_1} D_1\,, \tag{35}$$

$$\dot{\gamma}_1 = \beta_{\gamma_1} \frac{\partial W}{\partial \gamma_1} (D_1)^2 - \beta_{\gamma_1 \alpha_1} \frac{\partial W}{\partial \alpha_1}, \tag{36}$$

$$\dot{\gamma}_2 = \beta_{\gamma_2} \frac{\partial W}{\partial \gamma_2} (D_2)^2 - \beta_{\gamma_2 \alpha_2} \frac{\partial W}{\partial \alpha_2}, \tag{37}$$

$$\dot{\alpha}_1 = \beta_{\alpha_1 \gamma_1} \frac{\partial W}{\partial \gamma_1}, \tag{38}$$

$$\dot{\alpha}_2 = \beta_{\alpha_2 \gamma_2} \frac{\partial W}{\partial \gamma_2}. \tag{39}$$

The solutions to above equations (34) through (39) will be our basis for correlating with the experimental data.

(v) In the case of free shrinkage, that is, thermal damage in the absence of applied tractions, $S_1 = S_2 = 0$, $D_1 = -\frac{\partial W}{\partial G_1}$ and $D_2 = -\frac{\partial W}{\partial G_2}$. Equations (34) and (35) reduce to

$$\dot{G}_1 = -(\beta_{11} + \beta_{\gamma_1}) \left(\frac{\partial W}{\partial \gamma_1} \right)^2 \frac{\partial W}{\partial G_1} - \beta_{12} \frac{\partial W}{\partial \gamma_1} \frac{\partial W}{\partial \gamma_2} \frac{\partial W}{\partial G_2},$$

$$\dot{G}_2 = -(\beta_{22} + \beta_{\gamma_2}) \left(\frac{\partial W}{\partial \gamma_2} \right)^2 \frac{\partial W}{\partial G_2} - \beta_{21} \frac{\partial W}{\partial \gamma_2} \frac{\partial W}{\partial \gamma_1} \frac{\partial W}{\partial G_1}.$$

To reproduce the observed lower bounds for G_1 and G_2 and the upper bound of hardening, we will ensure that the model satisfies the limits

$$\frac{\partial W}{\partial \gamma_1} \to 0, \quad \frac{\partial W}{\partial \gamma_2} \to 0, \tag{40}$$

as $t \to \infty$. Moreover, to guarantee the shrinkage of the membranes, it is preferable to have

$$\frac{\partial W}{\partial G_1} > 0, \quad \frac{\partial W}{\partial G_2} > 0, \tag{41}$$

in a certain range of $\mathbf{F}^E$, $\mathbf{G}$, $\boldsymbol{\gamma}$ and $\boldsymbol{\alpha}$. This constraint may also help to simulate the phenomenon of extension, which may occur under applied tractions.

(vi) To explain the necessity of including the quantity $\boldsymbol{\alpha}$ in the present formulation, we consider the case of $D_1|_{t=0} = D_2|_{t=0} = 0$. Under this condition, (34) through (39) reduce to, at $t = 0$,

$$\dot{G}_1 = \dot{G}_2 = 0, \tag{42}$$

$$\dot{\gamma}_1 = -\beta_{\gamma_1 \alpha_1} \frac{\partial W}{\partial \alpha_1}, \quad \dot{\gamma}_2 = -\beta_{\gamma_2 \alpha_2} \frac{\partial W}{\partial \alpha_2}, \tag{43}$$

$$\dot{\alpha}_1 = \beta_{\alpha_1 \gamma_1} \frac{\partial W}{\partial \gamma_1}, \tag{44}$$

$$\dot{\alpha}_2 = \beta_{\alpha_2 \gamma_2} \frac{\partial W}{\partial \gamma_2}. \tag{45}$$

If $\boldsymbol{\alpha}$ were not included, $G_1 = G_2 = 1$ and $\gamma_1 = \gamma_2 = 0$ is a solution, that is, G's and γ's would not change under the isometric or isotonic conditions that give rise to $D_1|_{t=0} = D_2|_{t=0} = 0$, and this is not consistent with the expectation that, under the loading conditions considered here, a membrane will experience substantial damage.

(vii) We consider the following structure for the stored energy W,

$$W = W^E\left(C_1^E, C_2^E, \gamma_1, \gamma_2, G_1, G_2\right) + W^D\left(\gamma_1, \gamma_2, G_1, G_2, \alpha_1, \alpha_2\right), \quad \mathbf{C}^E := \mathbf{F}^{E^T}\mathbf{F}^E. \tag{46}$$

W^E is the part of W corresponding to the elastic response and it will take the form of an exponential function, following Fung's model. That is,

$$W^E = a_0\Big\{\exp\Big[a_1\left(C_1^E - 1\right)^2 + a_2\left(C_2^E - 1\right)^2 + 2a_{12}\left(C_1^E - 1\right)\left(C_2^E - 1\right)\Big] - 1\Big\}, \tag{47}$$

where

$$a_i = a_i\left(\gamma_1, \gamma_2, G_1, G_2\right) > 0\,, \quad \frac{\partial a_i}{\partial \gamma_1} > 0\,, \quad \frac{\partial a_i}{\partial \gamma_2} > 0\,, \quad i = 0, 1, 2, 12\,; \quad a_{12} \le \sqrt{a_1 a_2}\,. \tag{48}$$

The main advantage of (47) is its simplicity and the reasonable agreement that it provides between theory and experimental data for a thermally damaged membrane under biaxial stretch tests, but it does not work well in that it poorly fits data for some native membranes under biaxial stretching. The dependence of the elastic coefficients on γ_1 and γ_2 reflects the effect of hardening. The suggested form for W^E should be restricted by the condition $S_1 \ge 0$ and $S_2 \ge 0$ to ensure the convexity for W^E, which appears reasonable for soft bio-membranes.

(viii) To determine the specific forms for a's in W^E, the form of W^D, and the coefficients β's in equations (34) through (39), we use averaged test data from experiments on several membranes that were taken from the same region (left posterior ventricle) of the epicardium of bovine hearts. The samples were thermally damaged at 75^oC under various isometric stretches. We use the following specific relations to correlate the isometric test data of the Cauchy stresses versus time (Figure 1 through Figure 3):

$$a_0 = 0.498, \quad a_1 = 0.756\exp\left(\frac{1.9\gamma_1}{1+\gamma_1}\right), \quad a_2 = 1.59\exp\left(\frac{3.74\gamma_2}{1+2\gamma_2}\right), \quad a_{12} = 1.07\exp\left[0.5\left(\frac{1.9\gamma_1}{1+\gamma_1} + \frac{3.74\gamma_2}{1+2\gamma_2}\right)\right], \tag{49}$$

$$W^D = \int_1^{G_1} 2\exp\left[20\left(-2\left(G_1\right)^{-6} + \left(G_1\right)^{-12} + 1\right)\right] dG_1 + \int_1^{G_2} 3\exp\left[20\left(-2\left(G_2\right)^{-6} + \left(G_2\right)^{-12} + 1\right)\right] dG_2 + \int_0^{\gamma_1} \exp\left(-0.1\gamma_1\right) d\gamma_1 + \int_0^{\gamma_2} \exp\left(-0.1\gamma_2\right) d\gamma_2 - \int_0^{\alpha_1} 2\,\exp\left(-0.1\alpha_1\right) d\alpha_1 - \int_0^{\alpha_2} 2\exp\left(-0.1\alpha_2\right) d\alpha_2\,, \quad (50)$$

$$\beta_{11} = M\frac{\left[1 + \left(\frac{\partial W}{\partial \gamma_1}\right)^4 \left(D_1\right)^2\right]^{-.5}}{\cosh\left[10\left(\left(G_1\right)^{10} - 1\right)\right]} \exp\left\{3.8\left(C_1 - 1.35\right)^2 \left(C_1\right)^3 - \left[.5 + .17\left(C_1 - 1.35\right)\right]\left[1 + .5\left(C_1^E - 1.64\right)^2 \gamma_1\right] \frac{\sigma_1}{\left(C_1^E\right)^2}\right\}, \quad (51)$$

$$\beta_{22} = M\frac{\left[1 + \left(\frac{\partial W}{\partial \gamma_2}\right)^4 \left(D_2\right)^2\right]^{-.5}}{\cosh\left[10\left(\left(G_2\right)^{10} - 1\right)\right]} \exp\left\{26\left(C_2 - 1.35\right)^2 \left(C_2\right)^{-.6} - \left[.7 + .51\left(C_2 - 1.35\right)\right]\left[1 + .1\left(C_2^E - 1.64\right)^2 \gamma_2\right] \frac{\sigma_2}{\left(C_2^E\right)^3}\right\}, \quad (52)$$

$$\beta_{12} = \beta_{21} = \beta_{\gamma_1} = \beta_{\gamma_2} = 0\,, \quad (53)$$

$$\beta_{\gamma_1\alpha_1} = M\exp\left\{-.0186\left[1 + .77\left(1 + \left(C_1^E - 1.64\right)^2 \gamma_1\right) \times \frac{\left(C_1\right)^8 \gamma_1}{1 + \left(C_1\right)^2 \gamma_1}\right]\left(C_1\right)^2 \sigma_1\right\}, \quad (54)$$

$$\beta_{\gamma_2\alpha_2} = M\exp\left\{-.0186\left[1 + .51\left(1 + \left(C_2^E - 1.64\right)^2 \gamma_2\right) \times \frac{\left(C_2\right)^8 \gamma_2}{1 + \left(C_2\right)^2 \gamma_2}\right]\left(C_2\right)^2 \sigma_2\right\}, \quad (55)$$

$$\beta_{\alpha_1\gamma_1} = 2\,\beta_{\gamma_1\alpha_1}\,, \quad \beta_{\alpha_2\gamma_2} = 2\,\beta_{\gamma_2\alpha_2}\,. \quad (56)$$

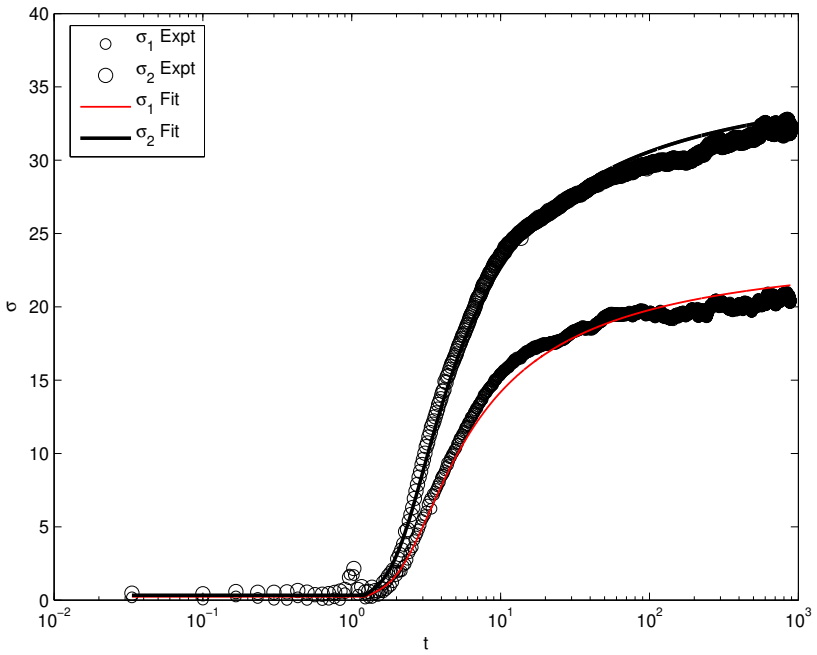

Figure 1. Stress versus time under fixed stretch ratio of $F_1 = F_2 = 1.03$.

Here, $\mathbf{C} = \mathbf{F}^T\mathbf{F}$. The coefficient M reflects the effect of the activation criterion (32). For the process under consideration here, both $\mathbf{F}$ and T are constant, therefore (32) reduces to

$$f(\mathbf{F}, T_f)\, t - 1 \begin{cases} < 0 & \text{(when no damage occurs)} \\ = 0 & \text{(commencement of damage).} \end{cases} \tag{57}$$

We set

$$M = \frac{\max\left(f(\mathbf{F}, T_f)\, t - 1, 0\right)}{1 + \max\left(f(\mathbf{F}, T_f)\, t - 1, 0\right)}\,. \tag{58}$$

Equations (34) through (39), along with the initial condition (33), were solved numerically using the 'ode15s' solver in MATLAB (tolerance at 10^{-12}), under a fixed stretch ratio. We choose three equibiaxial isometric conditions, $F_1 = F_2 = 1.03$, $F_1 = F_2 = 1.16$ and $F_1 = F_2 = 1.28$, that correspond to the experimental tests. The values of $f(\mathbf{F}, T_f)$ can be estimated from the test data: $f(F_1 = 1.03, F_2 = 1.03, T_f) = 1/1.2$ (1/s); $f(F_1 = 1.16, F_2 = 1.16, T_f) =$

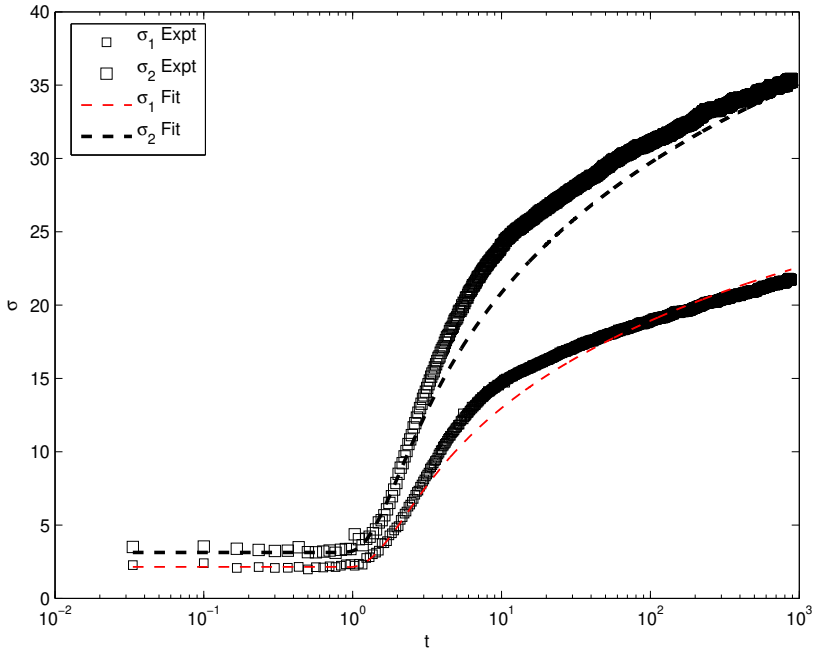

Figure 2. Stress versus time under fixed stretch ratio of $F_1 = F_2 = 1.16$.

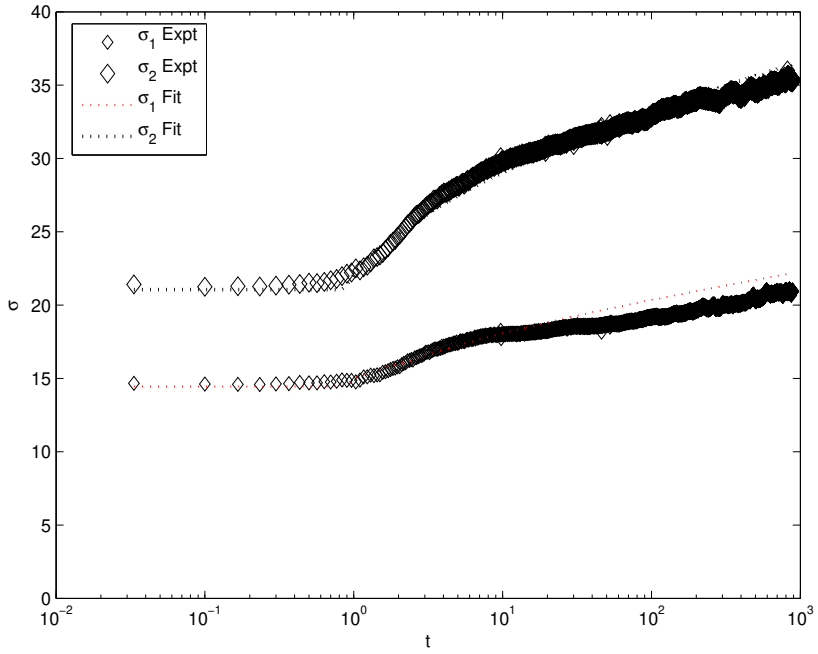

Figure 3. Stress versus time under fixed stretch ratio of $F_1 = F_2 = 1.28$.

$1/0.8$ (1/s); $f\,(F_1 = 1.28, F_2 = 1.28, T_f) = 1/0.8$ (1/s). It is clear that the model fits the experimental results for stresses versus time, at the three fixed stretch ratios, reasonably well. Further, the computed final inelastic deformations are $(0.945, 0.924)$, $(1.041, 1.03)$ and $(1.064, 1.045)$, under $F_1 = F_2 = 1.03$, $F_1 = F_2 = 1.16$ and $F_1 = F_2 = 1.28$, respectively, which are in the range the experimentally obtained values of $(0.97, 0.90)$, $(1.05, 1.05)$ and $(1.05, 1.03)$. The hardening trend with respect to the isometric constraints is also consistent with the experimental observation (see Figure 4). Finally, Figures 5 and 6 depict how the hardening parameter $\boldsymbol{\gamma}$ and the extent of damage $\boldsymbol{\alpha}$ change with time and these results seem to be in keeping with physical expectation.

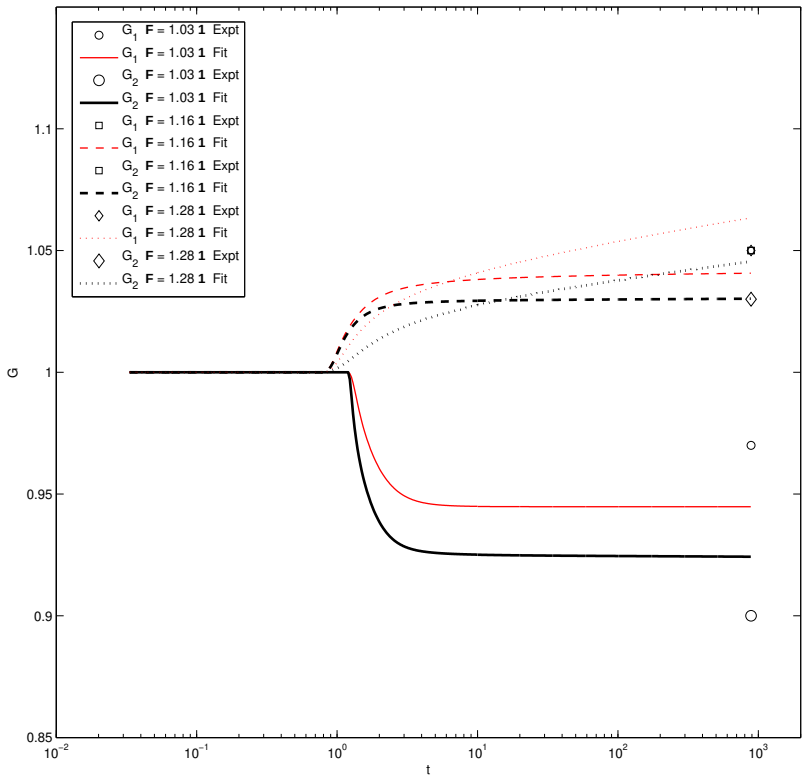

Figure 4. Inelastic deformation versus time under fixed stretch ratios. The formulas of $\mathbf{F} = 1.03\mathbf{1}$ stands for $F_1 = F_2 = 1.03$. Similar representations hold for the other cases.

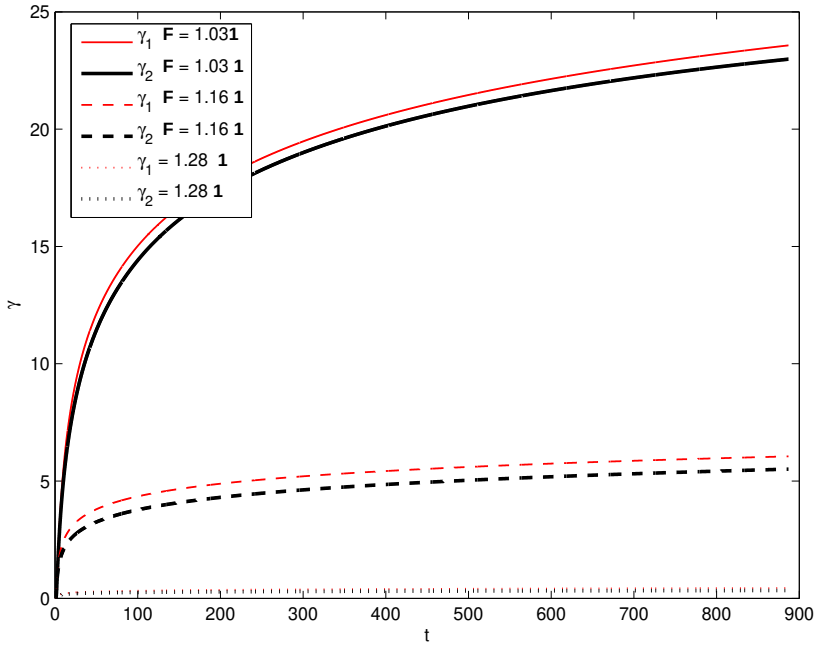

Figure 5. Hardenning versus time under fixed stretch ratios.

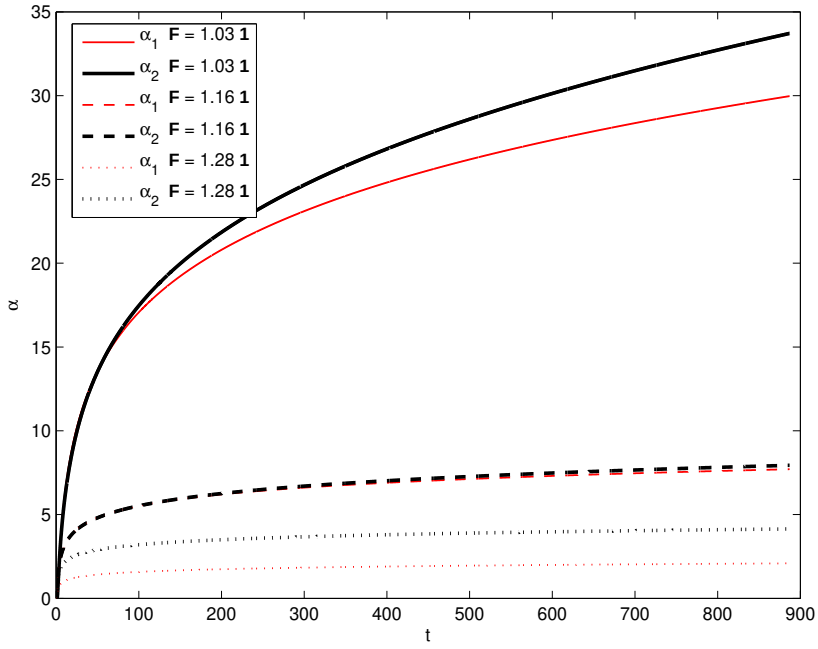

Figure 6. $\boldsymbol{\alpha}$ versus time under fixed stretch ratios.

Acknowledgements. The authors thank the National Science Foundation (BES-9634109) and the National Institute of Health (HL-68118) for support of this work.

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