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SOME TOPICS FROM CONTINUUM MECHANICS RELATED TO BRAIN NEURO-MECHANICS

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Abstract. A number of topics from continuum mechanics are presented that are useful in developing mathematical models of brain neuromechanics. Part I reviews basic concepts used to describe deformation or distortion of brain tissue, strains, stresses, their connection and material stiffness. Part II presents concepts from viscoelasticity used to describe the time dependent response of brain tissue such as stress relaxation, creep, response to sinusoidal loading, energy dissipation, characteristic response times and their alteration due to non-mechanical influences. Part III describes recent modeling approaches that can be used to describe microstructural changes in materials due to large deformation, disease or other non-mechanical sources.

Key words. continuum mechanics, microstructural changes, large deformations.

1. Introduction

Continuum mechanics encompasses many topics that can contribute to the investigation of brain injuries resulting from concussions in sports and improvised explosive devices in military theaters, as well as brain diseases such as hydrocephalus. This article presents an overview of three such topics that should be useful in research in brain neuro-mechanics. The subject matter was selected based on two criteria. First, it was apparent from the current literature that research in brain neuro-mechanics could benefit from deeper insights into the implications of many fundamental concepts of continuum mechanics. The article aims to improve that insight. Second, there are a number of recent research directions within continuum mechanics that are potentially useful in the study of brain neuromechanics. The article provides an overview of two of these.

Section 2 contains a review of the notions of stress, strain and constitutive equations. It points out several issues that are generally not considered in the formulation of mechanical models, but could influence the mechanical response. Section 3 presents the essentials of viscoelasticity, namely stress relaxation, creep, linearity and the response to sinusoidal oscillations. Two important consequences of time dependent response are pointed out. Section 4 introduces a mechanical model that can account for chemical changes in materials such as brain tissue that are composed of networks of macromolecules. Among these may be chemical changes associated with disease, age or medication as well as large deformation due to swelling. Concluding comments are made in Section 5.

2. Basic Notions from Continuum Mechanics

Thorough presentations of the material of this section can be found in the classic reference by Fung [1] and the recent book by Cowin and Doty [2].

2.1. Reference Configuration, Material Elements, Strains. In developing a mathematical model for its mechanical response, the brain is idealized as a solid body composed of a continuous distribution of material particles. At a given instant,

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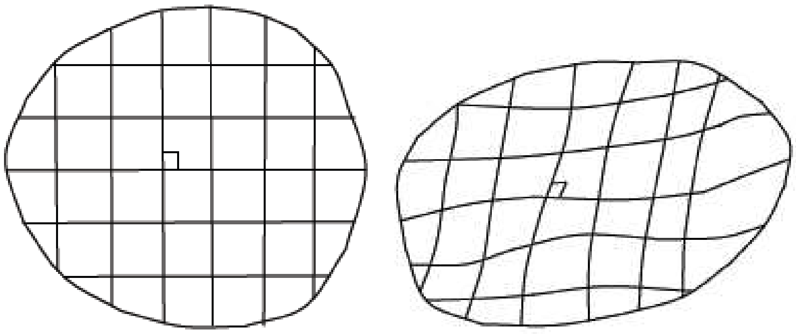


FIGURE 1. (a) Body, orthogonal grid and differential block in reference configuration; (b) deformed body, grid and differential block in a later configuration.

a material particle is associated with a spatial point. The distribution of material particles is visualized by the set of such points, i.e. the spatial configuration they occupy. The configurations of the brain can vary with time. For this reason, one is chosen as a reference and is used as a base state for defining material properties and determining changes.

Figure 1a shows a reference configuration with a grid of orthogonal straight lines. The points of the grid coincide with material particles. As time varies, the material particles can occupy different spatial points and the grid undergoes a distortion. Straight lines change length and become curved and the right angles increase or decrease. A deformed grid in shown in Figure 1b. In continuum mechanics, the material particles are regarded as differential cubes whose edges are line segments of the grid. As a result of the local distortion of the grid, each differential cube becomes a differential parallelepiped whose edges have new lengths and whose surfaces are no longer orthogonal. This introduces the two basic modes of deformation:

Normal Strains due to Changes in Length

Figure 2a shows a differential cube of material in the reference configuration whose three edges have the same length $dA_x = dA_y = dA_z = dA$. Figure 2b shows the differential cube in a later configuration when its edges have changed length and it has become a differential rectangular parallelepiped with edges da_x, da_y and da_z. The normal strain is defined as the change in length per unit length and is usually denoted by the symbol ϵ. The block has three normal strains, one associated with each edge,

$$\epsilon_x = \frac{da_x - dA_x}{dA_x}, \ \epsilon_y = \frac{da_y - dA_y}{dA_y}, \ \epsilon_z = \frac{da_z - dA_z}{dA_z} \tag{1}$$

Shear Strains due to Changes in Angle

Figure 2c shows the differential cube in a later configuration when the top surface has displaced distance da with respect to the bottom surface thereby

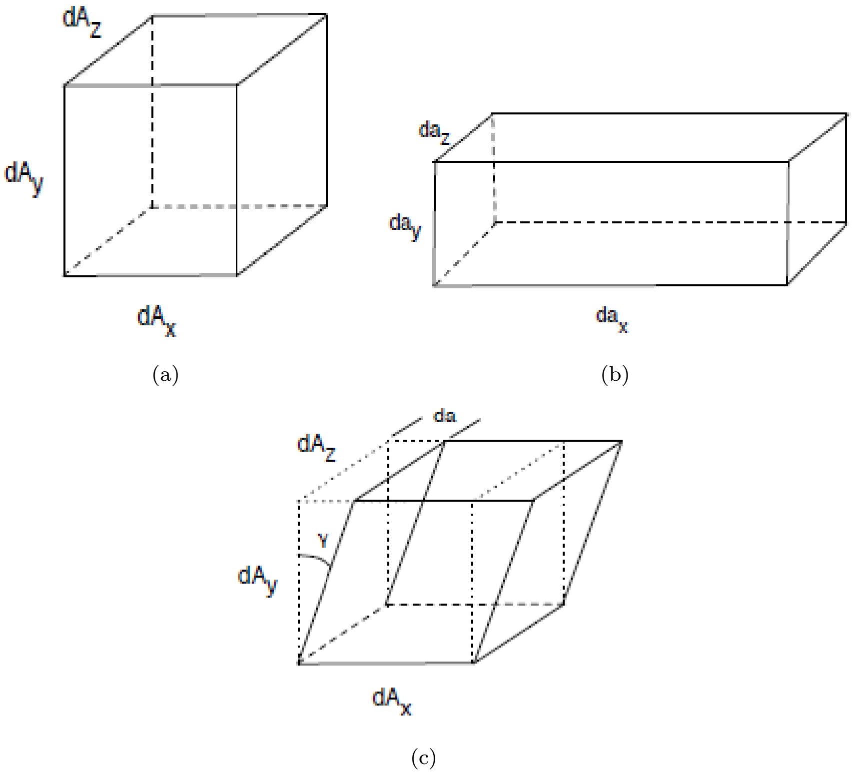


FIGURE 2. (a) Differential block in reference state with dimensions; (b) Differential block after extension along its edges: (c) Differential block after a shear deformation.

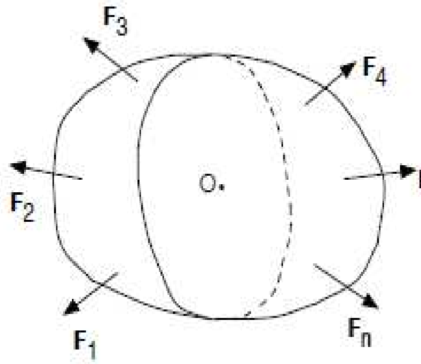
causing an angle change between two edges. The change in angle, the shear strain, is denoted by the symbol γ and is defined by

$$\tan\gamma_{xy} = \frac{da}{dA_y}. \tag{2}$$

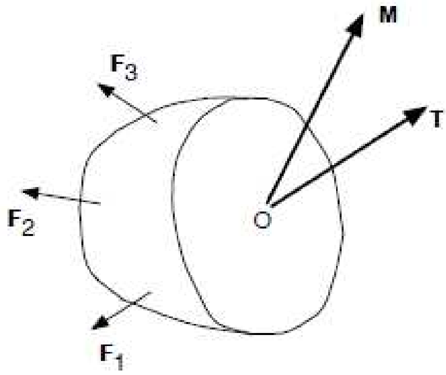
When the strain is very small in magnitude, it is common to use the approximation $\tan\gamma_{xy} \approx \gamma_{xy}$.

Comments: A differential cube generally undergoes simultaneous normal and shear strains in all three directions. At a fixed time, the strains vary throughout the body. At a fixed cube the strains vary with time. The strains describe the distortion of the microstructure of the material in the cube.

2.2. Cohesive Forces, Normal and Shear Stress. When a body deforms from the reference to a later configuration, parts of the body move relative to other parts. In order to maintain its continuity and not be torn apart, the body produces internal cohesive forces and moments. In continuum mechanics, these are visualized



(a)



(b)

FIGURE 3. (a) Body in deformed configuration showing applied forces and its intersection with a plane through point O: (b) A portion of the body showing its external surface and an internal planar surface with resultant internal moment and force.

as acting across internal surfaces. Figure 3a shows a body that is subjected to a system of external forces with an internal surface passing through some internal point O. Figure 3b shows the portion of the body to one side of the internal surface. The action of the portion of the body on the other side of the internal surface is represented by the resultant force vector $\mathbf{F}$ and moment vector $\mathbf{M}$. These represent the internal cohesive force and moment that is transmitted from the material on one side of the surface to the material on the other. The internal cohesive force and moment are distributed over the internal surface. That is, part of the total force and moment act on each area increment of the internal surface. The ratio $\Delta\mathbf{F}/\Delta A$ represents the average cohesive force per unit area on the area increment of amount ΔA. This can also be thought of as cohesive force intensity. A finer measure of the cohesive force intensity is obtained by decreasing the size of the area increment, and with it the corresponding force increment. A precise description of the force intensity is obtained by letting the size of the area become arbitrarily small, and leads to the vector $\mathbf{T} = \lim_{\Delta A\to 0}\Delta\mathbf{F}/\Delta A$. The quantity $\mathbf{T}$ represents the cohesive force per unit area, cohesive force intensity or stress vector acting on a differential area increment. The stress vector $\mathbf{T}$ is usually decomposed into the normal stress component T_n and the tangential or shear stress component T_t , as shown in Figure 4. This discussion implies that the stress vector $\mathbf{T}$ depends on the orientation of the internal surface. That is, there are an infinite number of internal surfaces through a point of the body, each having a different stress vector. It is of interest to know the stress vector on each of these surfaces so that the surfaces with the most severe normal or shear stress can be identified. This information can be determined by introducing the stress vectors acting on three mutually perpendicular differential surfaces though a point as shown in Figure 5. The nine components of the three stress vectors are shown on the figure. In the

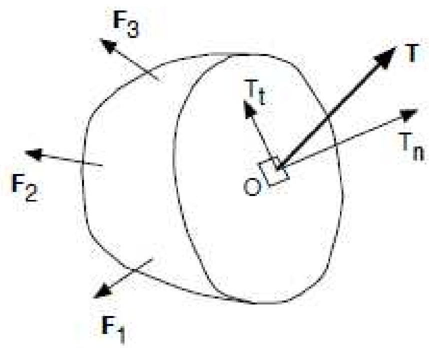


FIGURE 4. Decomposition of the force on an internal planar surface through point O into normal force and shear force components.

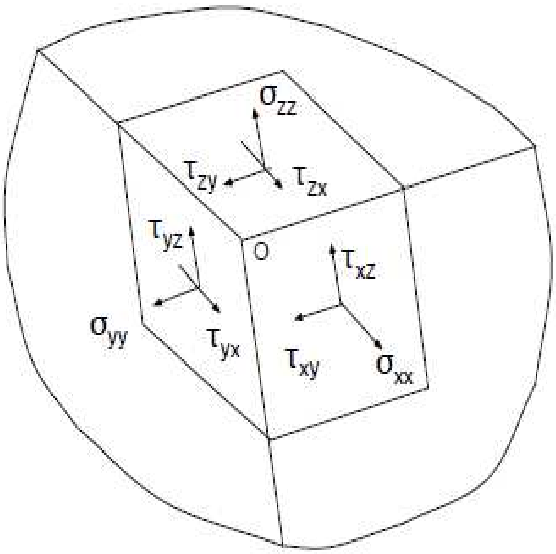


FIGURE 5. Components of the stress vectors acting on three mutually perpendicular surfaces intersecting at point O.

notation σ_{ij}, the first subscript denotes the direction of the normal to the surface and the second subscript denotes the direction of the component. Thus, σ_{xx} is a normal stress on a surface perpendicular to the x-axis, while σ_{xy} is a shear stress on the same surface acting in the y-direction. Let $(T_x,\, T_y,\, T_z)$ be the components with respect to the x-, y-, z- axes of the stress vector on the surface area increment having a unit outer normal vector **n** with components $(n_x,\, n_y,\, n_z)$. It can be shown that $(T_x,\, T_y,\, T_z)$ are related to $(n_x,\, n_y, n_z)$ and the stress components by means of the matrix relation:

$$\begin{bmatrix} T_x \\ T_y \\ T_z \end{bmatrix} = \begin{bmatrix} \sigma_{xx} & \sigma_{xy} & \sigma_{xz} \\ \sigma_{yx} & \sigma_{yy} & \sigma_{yz} \\ \sigma_{zx} & \sigma_{zy} & \sigma_{zz} \end{bmatrix} \begin{bmatrix} n_x \\ n_y \\ n_z \end{bmatrix} \tag{3}$$

From knowledge of $(T_x,\, T_y,\, T_z)$, the normal and shear stresses on the surface are readily determined.

Comment: Application of the equation of linear momentum to the body leads to a system of partial differential equations for determining the spatial variation of the stresses within the body. Application of the equation of angular momentum to the body leads to the relations $\sigma_{xy} = \sigma_{yx},\ \sigma_{xz} = \sigma_{zx},\ \sigma_{yz} = \sigma_{zy}$ at each point in the body.

2.3. Stress - Strain Relations. The cohesive force intensity, or stress, on the surface of a differential block of material arises in response to the distortion of the material, as measured by the strain. The stress-strain relation accounts for this distortion of the material's microstructure by considering a number of different factors. Among these are the magnitude of the strains, time dependence of the response and directional properties of the response. For the purpose of illustrating these concepts in this article, a number of simplifying assumptions are made:

(1) The magnitudes of the strains are small, of the order of magnitude of 0.001 - 0.1. This should characterize the strains produced in the brain in most circumstances.
(2) It is assumed that the mechanical response of the brain is independent of time, *i.e.* it is linearly elastic. Modifications when the material exhibits time dependent or viscoelastic response are discussed in Part II of this paper.

The directional properties of a material, such as brain, are determined by the material microstructure. For example, there may be a dominant orientation of its macromolecules in a particular direction. A set of unit vectors defines these directions with respect to the material, and these are called the preferred directions. When a material is described as orthotropic, transversely isotropic or isotropic, these vectors are mutually perpendicular.

An isotropic material has the same properties with respect to all sets of unit vectors, whatever their orientation. A transversely isotropic material has the same properties with respect to all unit vectors that lie in a plane perpendicular to a specific unit vector. An orthotropic material has different properties with respect to each of the different unit vectors. Figure 6a shows a block of material that is assumed to be orthotropic, transversely isotropic or isotropic. Its surfaces are perpendicular to the preferred material directions, which coincide with the x-, y-, z- axes of a Cartesian coordinate system. With respect to these directions, normal stresses are related only normal strains and shear stresses are related only to shear strains. In applications in continuum mechanics, in general, and in brain neuromechanics, in particular, this block is assumed to be free of stress. That is, there are no residual stresses.

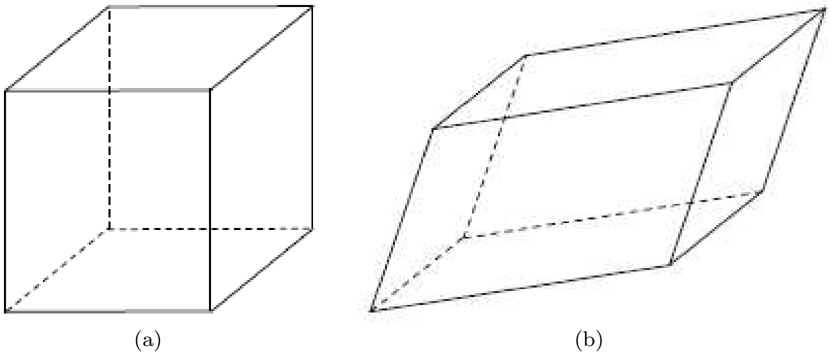


FIGURE 6. (a) Enlarged view of differential block in reference configuration; (b) Deformed into a parallelopiped in a later configuration.

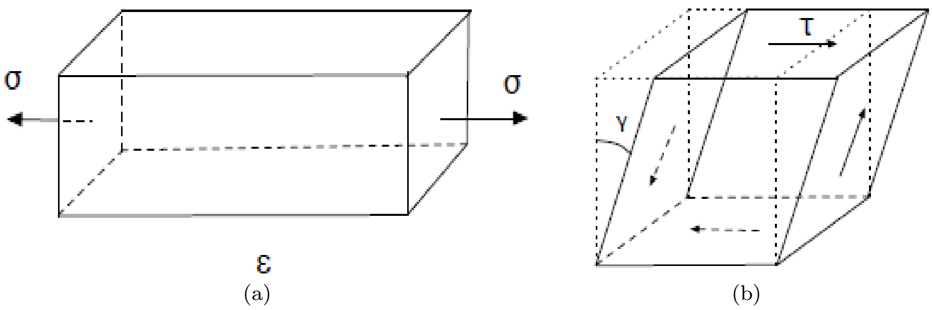


FIGURE 7. Differential block (a) after uniaxial extension, showing normal stress and elongational strain; (b) after shear showing shear stress and shear strain.

When this is the case, an applied normal stress σ_{xx} produces only normal strains, as seen in Figure 7a. The strain in the same direction as the normal stress is called a longitudinal strain and is denoted by ϵ_x. For linearly elastic response, these are related by

$$\sigma_{xx} = E\epsilon_x. \tag{4}$$

The coefficient E is a material property called Young's modulus or the elastic modulus. As there are a number of moduli that can be introduced to represent different phenomena, E will be termed the tensile modulus. A relation similar to (4) can also be written for normal stresses and strains with respect to the y- or z- directions. When the material is orthotropic, there is a different value of E associated with each direction. When the material is transversely isotropic, there is a value of E associated with the x- direction and another value associated with the y- and z- directions. When the material is isotropic, the value of E is independent of direction.

As shown in Figure 7b, an applied shear stress σ_{xy} produces only a shear strain γ_{xy} in the same direction as the stress. For linearly elastic response, these are related by:

$$\sigma_{xy} = \mu\gamma_{xy}. \tag{5}$$

The coefficient μ is called the shear modulus. As in the case of the tensile modulus, the value of the shear modulus for orthotropic, transversely isotropic or isotropic materials can depend on the direction in which the material is sheared.

It is necessary to add a number of comments to this overview of stress-strain relations. (i) It was mentioned earlier that the body is regarded as an assemblage of differential blocks. The material properties can vary from one block to another, in which case the material is described as being inhomogeneous. If this is the case, the tensile moduli E and shear moduli μ become dependent on location. (ii) The moduli E and μ characterize the stiffness of the material. The larger the value of the modulus, the larger is the stress required to produce a given strain, *i.e.* the material with the larger value of the modulus is *stiffer*. (iii) Equation (4) can be written in the form $\epsilon_x = \sigma_{xx}/E$. The coefficient of the stress $1/E$ is called the compliance. Thus, a material with a larger value of E, a stiffer material, is less compliant. (iv) The preferred material directions may not coincide with the directions that are utilized when analyzing the mechanical response of a body. It is possible, in such a case to transform the stress-strain relations so that they hold in these non-preferred directions. If the material is isotropic, the form of the stress-strain relations will be the same. However, if the material is transversely isotropic or orthotropic, the transformed equations introduce new phenomena. Normal stresses may produce shear strains, shear stresses may produce normal strains or shear strains in different directions. (v) The influence of residual stresses is a subject of current research. If there are residual stresses, the stress-strain relations (4) and (5) will change. For example, (4) may become of the form

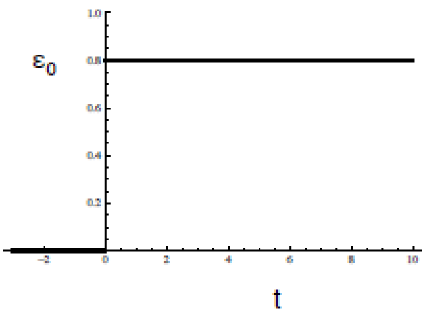
$$\sigma_{xx} = E(\sigma_{res})\epsilon_x + \sigma_{res}, \tag{6}$$

in which σ_{res} denotes a residual stress. Thus, the term $E(\sigma_{res})\epsilon_x$ represents a modification of the residual stress due to distortion from the reference configuration. In addition, $E(\sigma_{res})$ suggests that the moduli may depend on the residual stress.

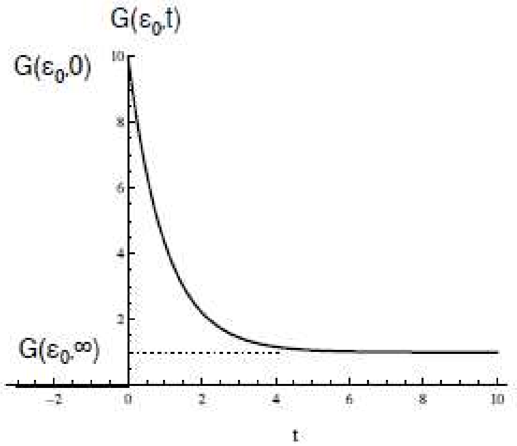
3. Elements of Viscoelasticity

A thorough treatment of linear viscoelasticity can be found in [3]. Although there is not yet a corresponding reference for nonlinear viscoelasticity, much useful information is presented in the recent review article [4].

The viscoelastic response of materials is characterized by its dependence on time. This arises from their microstructure, which consists of long-chained or macromolecules. When a viscoelastic material is deformed, its macromolecules undergo reconfigurations. The reconfiguration does not occur simultaneously over the entire macromolecule, but over shorter segments during short time intervals and over



(a)



(b)

FIGURE 8. (a) Step strain history: (b) Corresponding stress relaxation function.

longer segments during larger time intervals. Thus, the description of the mechanical response requires consideration of time as well as strain and stress. This is illustrated by discussing two distinct fundamental experiments: stress relaxation and creep.

3.1. Stress Relaxation. Let the block of material in Figure 6a be undeformed and unstressed for all times $t < 0$. Let Figure 7a now represent the block at a time $t > 0$, when there are both a (possibly time-dependent) longitudinal strain and a corresponding normal stress. The block is subjected to a longitudinal strain of amount ϵ_0 that is applied instantaneously at $t = 0$ and then held constant. This strain *vs.* time sequence, shown in Figure 8a, is called a step strain history. The corresponding normal stress varies with time as shown in Figure 8b and is represented by a function of strain and time, $\sigma = G(\epsilon_0, t)$.

In response to the jump in strain at $t = 0$, the stress jumps to the value $G(\epsilon_0, 0)$. It then gradually decreases with time to a steady state value $G(\epsilon_0, \infty)$. The jump in stress is called instantaneous springiness or elasticity, the decrease with time is called stress relaxation and the asymptotic value $G(\epsilon_0, \infty)$ is called long time equilibrium elasticity. The function $G(\epsilon_0, t)$ is called the stress relaxation function. Of interest in describing a viscoelastic material is the size of the jump in stress $G(\epsilon_0, 0)$, a measure of the amount of stress relaxation such as $G(\epsilon_0, \infty)/G(\epsilon_0, 0)$ and a measure of the time during which stress relaxation occurs. There are various definitions for such a time. For the purpose of this article, a characteristic relaxation time $\tau_R(\epsilon_0)$ is defined as the centroid of the graph of $\Delta G(\epsilon_0, t) = G(\epsilon_0, t) - G(\epsilon_0, \infty)$ *vs.* t. This defines a time at which there has been a substantial amount of stress relaxation. The mathematical form of the dependence of $G(\epsilon_0, t)$ on ϵ_0 and t varies with the material. Hence, the function $G(\epsilon_0, t)$ itself is a material property. This points out a vital distinction between the concept of a material property in linear elasticity and that in viscoelasticity. In linear elasticity, the material properties are constants. In viscoelasticity, the material properties are functions.

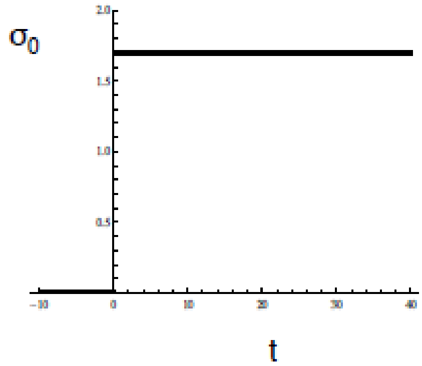
3.2. Creep. Consider again the block of material shown in Figures 6a and 7a. Let the block now be subjected to a normal stress of amount σ_0 that is applied instantaneously at $t = 0$ and then held constant. This stress *vs.* time sequence, shown in Figure 9a, is called a step stress history. The corresponding normal strain varies with time as shown in Figure 9b and is represented by a function of stress and time, $\epsilon = J(\sigma_0, t)$.

In response to the jump in stress at $t = 0$, the strain jumps to the value $J(\sigma_0, 0)$. It then gradually increases with time to a steady state value $J(\sigma_0, \infty)$. The jump in strain is again called instantaneous springiness or elasticity, the increase with time is called creep and the asymptotic value $J(\sigma_0, \infty)$ is again called long time equilibrium elasticity. The function $J(\sigma_0, t)$ is called the creep function. Of interest in describing a viscoelastic material is the size of the jump in strain $J(\sigma_0, 0)$, a measure of the amount of creep such as $J(\sigma_0, \infty)/J(\sigma_0, 0)$ and a measure of the time during which creep occurs. For the purpose of this article, a characteristic creep time $\tau_C(\sigma_0)$ is defined as the centroid of the graph of $\Delta J(\sigma_0, t) = J(\sigma_0, \infty) - J(\sigma_0, t)$ *vs.* t. This defines a time at which there has been a substantial amount of creep.

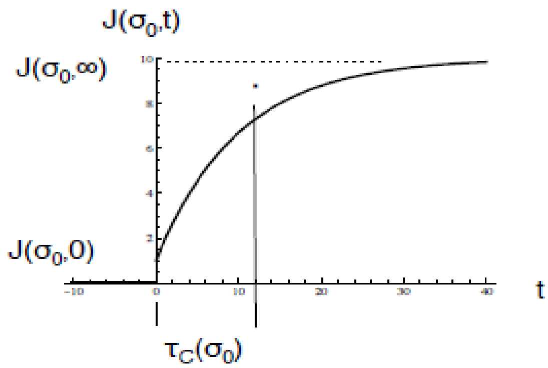
As in the case of stress relaxation, the function $J(\sigma_0, t)$ is a material property. In general, there is no simple relation between the stress relaxation function $G(\epsilon_0, t)$ and the creep function $J(\sigma_0, t)$.

3.3. Linear Response. Linearity is a property that simplifies the interpretation of experimental data and leads to a model that is convenient for analyzing mechanical response. In order for a material to be described as linear, its mechanical response must exhibit scaling and superposition. Scaling can be determined by considering how $G(\epsilon_0, t)$ depends on ϵ_0 or how $J(\sigma_0, t)$ depends on σ_0. One method for doing this is through an experimental program in which specimens are subjected to longitudinal step strain histories at different strains ϵ_1, ϵ_2, ..., ϵ_N. Plots of $G(\epsilon_i, \tilde{t})$ versus ϵ_i for different times $\tilde{t}$ are called stress relaxation isochrones. These isochrones may be straight lines or curves. Isochrones that are straight lines indicate scaling while curved isochrones indicate nonlinear response. In the former case,

$$\sigma = \epsilon_0 G(t), \tag{7}$$



(a)



(b)

FIGURE 9. (a) Step strain history; (b) Corresponding creep function.

$G(t)$ is called the stress relaxation modulus. A similar discussion, carried out for the creep response, introduces creep isochrones. If these are straight lines,

$$\epsilon = \sigma_0 J(t), \tag{8}$$

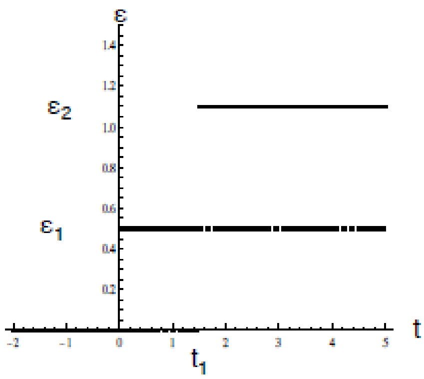
and $J(t)$ is called the creep compliance.

Superposition can be determined by experiments involving two-step strain histories, shown in Figure 10a. When the total stress is the superposition of the stresses for the individual step strain histories, *i.e.*

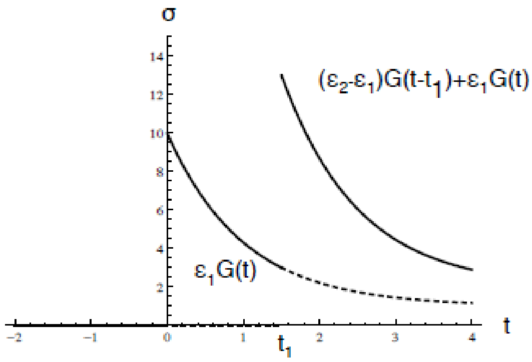
$$\sigma = \epsilon_1 G(t) + (\epsilon_2 - \epsilon_1) G(t - t_1), \tag{9}$$

the material exhibits the property of superposition.When the mechanical response satisfies (7) and (9), it is said to be linear.

3.4. Sinusoidal Oscillations. Another indication of linearity is given by the response to small amplitude oscillations. Let the longitudinal strain of the block of



(a)



(b)

FIGURE 10. (a) Two-step strain history; (b) Response to the two-step strain history assuming linearity of response.

material in Figure 7a vary sinusoidally with frequency ω, *e.g.*

$$\epsilon(t) = \epsilon_0 \sin(\omega t) \tag{10}$$

where $|\epsilon_0| << 1$. When there is linearity of response, the stress has a steady state response that is described by

$$\sigma(t) = \epsilon_0 \left[G'(\omega)\sin(\omega t) + G''(\omega)\cos(\omega t) \right], \tag{11}$$

or, equivalently,

$$\sigma(t) = \epsilon_0 G^\star(\omega)\sin(\omega t + \delta(\omega)), \tag{12}$$

where

$$G^\star(\omega) = \left[G'(\omega)^2 + G''(\omega)^2 \right]^{1/2}, \ \tan\delta(\omega) = G''(\omega)/G'(\omega). \tag{13}$$

The stress varies sinusoidally at the same frequency ω as the strain, but is out of phase with the strain by $\delta(\omega)$. Both the ratio of the stress and strain amplitudes

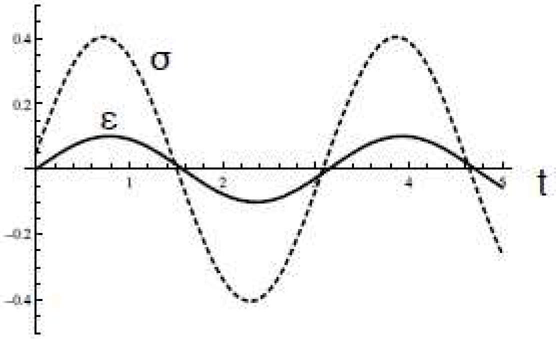


FIGURE 11. Applied sinusoidal strain history and corresponding stress response, assuming linearity of response.

$G^{\star}(\omega)$ and the phase difference vary with frequency ω. These features of the strain and stress variation are shown in Figure 11.

$G'(\omega)$ is called the storage modulus and $G''(\omega)$ is called the loss modulus. They are an alternate set of material properties that vary with frequency. $G'(\omega)$ and $G''(\omega)$ can be calculated from the stress relaxation modulus $G(t)$ and vice versa, but such relations are not presented here.

Similarly, let the normal stress on the block of material in Figure 7a vary sinusoidally,

$$\sigma(t) = \sigma_0 \sin(\omega t). \tag{14}$$

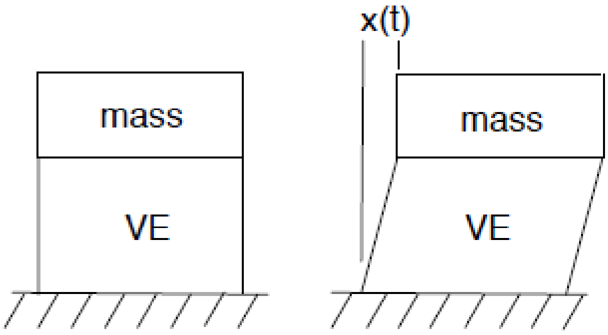
When there is linearity of response, the steady state strain is

$$\epsilon(t) = \sigma_0 \left[J'(\omega)\sin(\omega t) + J''(\omega)\cos(\omega t) \right]. \tag{15}$$

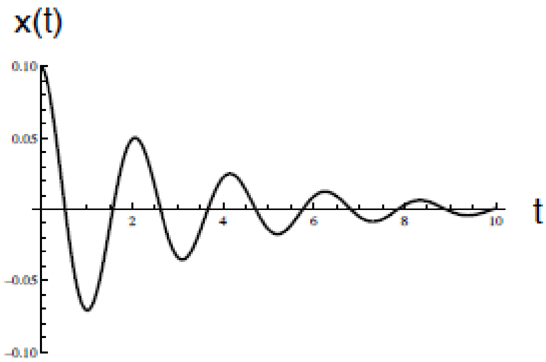
$J'(\omega)$ is called the storage compliance and $J''(\omega)$ is called the loss compliance. They are another set of material properties that vary with frequency. $J'(\omega)$ and $J''(\omega)$ can be calculated from the creep compliance $J(t)$ and vice versa. They can also be expressed in terms of $G'(\omega)$ and $G''(\omega)$.

Comments: It is expected that the response is linear when the strain magnitude $|\epsilon_0|$ is sufficiently small. The onset of nonlinear response can be detected by carrying out experiments with progressively larger strain amplitudes and determining when the stress is no longer sinusoidal. This discussion has been carried out using longitudinal strains and normal stresses. Analogous statements can be made for shear strains and shear stresses, in which case the modulus in extension $G(t)$ is to be interpreted as a modulus in shear.

3.5. Dissipation of Energy. Figure 12a shows a block of viscoelastic material that is fixed to a rigid support over its bottom surface and a mass over its top surface. The mass is given an initial horizontal displacement $x(0)$ that produces a shear strain $y = x(0)/h$ in the viscoelastic block. The mass is released and the block of material tries to recover its original shape, *i.e.* the shear strain starts to decrease.



(a)



(b)

FIGURE 12. (a) Viscoelastic block and an attached mass in the reference state; (b) Lateral disturbance of the mass at a later time.

Figure 12b shows a possible displacement time variation. The displacement will decrease to zero by means of decaying oscillations or by a monotonic decrease. Either way, the kinetic energy of the motion is dissipated because of the viscoelastic nature of the material. In short, viscoelastic materials dissipate energy. The process of dissipation is a consequence of the process of stress relaxation, $\Delta G(\epsilon_0, t) = G(\epsilon_0, t) - G(\epsilon_0, \infty) > 0$. When there is linear viscoelastic response, it can be shown that $\Delta G(t) = G(t) - G(\infty) > 0$ implies $G^{''}(\omega) > 0$ and $\delta(\omega) > 0$. Thus, stress relaxation in step strain tests or a difference in phase between stress and strain in sinusoidal tests indicate that the material dissipates energy. Therefore, when the brain is subjected to a sudden motion, brought on by a blow to the head, it becomes distorted. If the brain were composed of an elastic material, it would continue to vibrate, *i.e.* ring like a bell. Because of its viscoelasticity, the brain gradually recovers its original shape and returns to its rest state.

3.6. Arbitrary Variation of Strain with Time. The preceding comments considered only strains that undergo step changes or sinusoidal variation with time. In order determine the stress variation with time for other strain histories, it is necessary to develop a stress-strain-time or constitutive relation. When there is linear viscoelastic response, there are two methods for developing a constitutive relation. One method utilizes mechanical analogs composed of linear elastic springs and linear viscous dampers. It leads to a relation that expresses stress and its time derivatives to strain and its time derivatives. There are also complicated initial conditions associated with these equations. The second method makes use of the properties of scaling and superposition and results in the integral relation

$$\sigma(t) = G(0)\epsilon(t) + \int_0^t \epsilon(s)\frac{dG(t-s)}{d(t-s)}ds, \tag{16}$$

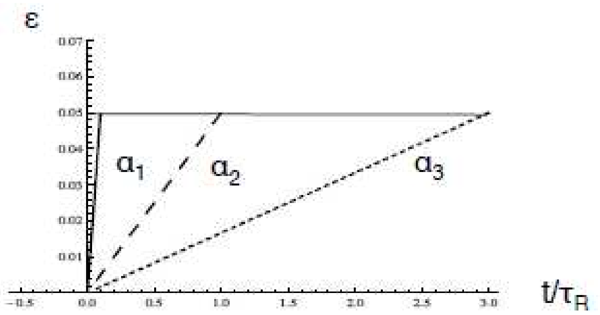
in which $G(t)$ is the stress relaxation modulus for the material. When there is non-linear viscoelastic response, there is no current generally accepted relation between stress, strain and time.

3.7. Process Time Relative to Stress Relaxation Time. Viscoelastic response of a material depends on the time during which a strain is applied relative to a time that characterizes the duration of the stress relaxation process, *i.e.* a characteristic stress relaxation time. This can be illustrated by means of a simple example for linear viscoelastic response. Let the stress relaxation modulus for a material have the form

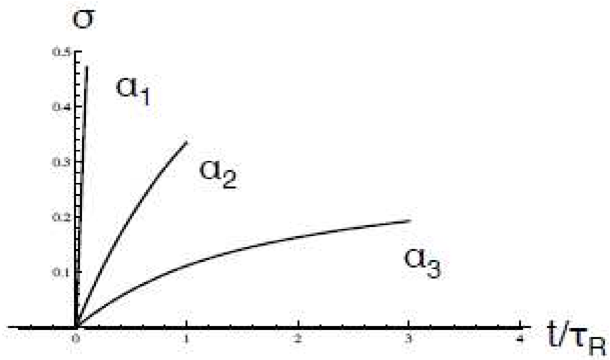
$$G(t) = G_\infty + (G_0 - G_\infty)\,\mathrm{e}^{-t/\tau_R}. \tag{17}$$

$G_0 = G(0)$ is the initial value of the stress relaxation function, $G_\infty = G(\infty)$ is the long time asymptotic value and τ_R is the characteristic stress relaxation time, corresponding to the centroid of the plot of $\Delta G(t) = G(t) - G_\infty = (G_0 - G_\infty)\,\mathrm{e}^{-t/\tau_R}$ *vs.* t, shown in Figure 8b. Let the material be subjected to a constant strain rate deformation history of the form $\epsilon(t) = \alpha t$, in which α denotes the strain rate. Suppose the strain is increased to a specific value, denoted by ϵ_0 at time τ_P, so that $\alpha = \epsilon_0/\tau_P$. Figure 13a shows the strain ϵ_0 being reached at three different rates corresponding to three different time intervals of straining relative to the stress relaxation time: time interval $\tau_{P1} = 0.1\tau_R$ at strain rate α_1, time interval $\tau_{P2} = \tau_R$ at strain rate α_2, time interval $\tau_{P3} = 3\tau_R$ at strain rate α_3. Figure 13b shows plots of σ/G_0 vs. t/τ_R for the three cases. Note that the stress at strain ϵ_0 is largest at the largest strain rate α_1 or when the time interval is the shortest relative to stress relaxation time τ_R. The stress at strain ϵ_0 decreases as the strain rate decreases and the time interval increases relative to stress relaxation time τ_R.

This simple example points out two main consequences of viscoelasticity. The first is that different stresses correspond to the same strain. The stress at a time depends not only on the strain at that time but also on the preceding strain history. The second is that the stress depends on a loading time τ_P relative to the stress relaxation time τ_R. It has been suggested that the stress relaxation time τ_R may be changed by age, disease or medication. This simple example shows that a mathematical model such as viscoelasticity can be used to explore the implications of these factors on the mechanical response of brain.



(a)



(b)

FIGURE 13. (a) Constant strain rate histories arriving at the same strain at different rates; (b) Corresponding stress histories showing the strain rate dependence.

4. Models of Microstructural Change

The material presented in this section is relatively recent and has only appeared in journal articles. Further details can be found in [5] and [6] and the references contained therein. The mechanical response of soft biological tissue is often assumed to be elastic or viscoelastic. The list of such tissues includes heart, arteries, uterus, tendons and ligaments and brain. A common feature of non-biological elastomeric materials and soft biological tissue is that they are composed of macromolecules that form networks and have lateral connections such as crosslinks. These lateral connections give the material its solid-like properties, *i.e.* recovery of shape upon release of stress. The elastic response of soft biological tissue is described using mathematical models for non-biological elastomeric materials. The material parameters in such models are generally determined by experiment. However, in the case of elastomers, research in polymer science has provided a connection between macromolecular structure and the material parameters. For example, the tensile modulus E is given by

$$E = NkT, \tag{18}$$

where N is the crosslink density, k is Boltzmann's constant and T is the absolute temperature.

The connection between the tensile modulus E of an elastomer and its macromolecular network, as represented by the expression for E in (18), has been used by Tobolsky [7] to explain changes in the mechanical response of elastomers resulting from changes in its macromolecular structure. Tobolsky [7] described experiments on rubber strips that were given different fixed uniaxial extensions, held at different constant elevated temperatures for various time periods, cooled down and then evaluated for the stress-strain response. The rubber was observed to have a reduced tensile modulus and permanent set on release of load. These were attributed to changes in the macromolecular structure arising from the scission of macromolecular network junctions and the formation of new networks by crosslinking. The decrease of modulus E was attributed to the decrease by scission of the crosslink density N.

In these experiments, scission and crosslinking were a result of oxidation at elevated temperatures. Subsequent research has introduced other causes that may produce similar microstructural changes. Scission and crosslinking due to large deformations was studied in [5], while the coupled influence of high temperature and large deformation were treated in [6]. Sodhi and Rao [8] discussed scission and crosslinking in stents resulting from ultraviolet radiation while Soares, Moore and Rajagopal [9] analyzed biodegradation of stents due to their interaction with a diffusing fluid. Regardless of the cause, scission and crosslinking were shown to have a significant impact on mechanical response. These studies for non-biological elastomeric materials suggest that it may be useful to consider the possibility of microstructural changes in soft biological tissue as a result of large deformation, interaction with a diffusing fluid or some other biochemical factor. For this reason, this section contains an overview of a recently developed constitutive theory for non-biological elastomeric materials that could be used in a study of the mechanical consequences of microstructural changes in brain tissue. The basic premise is that there is continuously occurring scission of crosslinks of the original macromolecular network while it deforms. The crosslinks re-connect to form new networks in new reference configurations. Each network can carry stress and the total stress in the material is the sum of the stresses in all of the networks. A small strain version of the general constitutive theory, applicable to uniaxial response, has the form

$$\sigma(t) = b^{(1)}(t)E_0\epsilon(t) + \int_{t_s}^{t} a(\hat{t})b^{(2)}(t,\hat{t})\bar{E}(\hat{t})[\epsilon(t) - \epsilon(\hat{t})]d\hat{t}. \tag{19}$$

$\epsilon(t)$ is the strain in the original network at time t and E_0 is the tensile modulus of this network. Thus, $E_0\epsilon(t)$ is the stress in the original network before scission occurs. t_s is the time at the start of the process of scission and crosslinking. $b^{(1)}(t)$ is the crosslink density of the original network that remains at time t and, thus, $b^{(t)}E_0\epsilon(t)$ is the current stress carried by that network. $a(\hat{t})$ represents the rate of formation by crosslinking of a new network at time $\hat{t}$. Its reference configuration coincides with that of the original material at time $\hat{t}$. The network that was formed at time $\hat{t}$ has undergone the strain $\epsilon(t) - \epsilon(\hat{t})$ at time t and is presumed to act as a linear elastic material with elastic modulus $\bar{E}(\hat{t})$, which may differ from E_0. This new network may also undergo scission, and $b^{(2)}(t,\hat{t})$ is the volume fraction of network formed at time $\hat{t}$ that remains at time t. The integral represents the sum of the stresses in all networks that form from the start of scission at time t_s to the current time. $b^{(1)}(t)$, $a(\hat{t})$ and $b^{(2)}(t,\,\hat{t})$ are non-mechanical quantities that are determined by experiment or from biochemical kinetics.

Before the onset of the process of scission and crosslinking, $b^{(1)}(0) = 1$ and $a(\hat{t}) = 0$. Equation (19) then gives $\sigma(t) = E_0\epsilon(t)$, which states that the stress arises only from the original network. During the process of scission and crosslinking, (19) can be written in the form

$$\sigma(t) = E(t)\left[\epsilon(t) - \epsilon^{\star}(t)\right], \tag{20}$$

in which

$$E(t) = b^{(1)}(t)E_0 + \int_{t_s}^{t} a(\hat{t})b^{(2)}(t,\hat{t})\bar{E}(\hat{t})d\hat{t}, \tag{21}$$

and

$$\epsilon^{\star}(t) = \frac{\int_{t_s}^{t} a(\hat{t})b^{(2)}(t,\hat{t})\bar{E}(\hat{t})\epsilon(\hat{t})d\hat{t}}{b^{(1)}(t)E_0 + \displaystyle\int_{t_s}^{t} a(\hat{t})b^{(2)}(t,\hat{t})\bar{E}(\hat{t})d\hat{t}} \tag{22}$$

$E(t)$ represents an evolving tensile modulus and $\epsilon^{\star}(t)$ represents an evolving strain that the material would return to if the stress were to be removed. If the process of scission and crosslinking were to be stopped at time t, (20) would give the new stress-strain relation. If the material were to completely remodel, then there is a time t_f when $b^{(1)}(t_f) = 0$. Assuming there is no scission of new networks after time t_f, the stress-strain response for the remodeled material would be

$$\sigma = E(t_f)\left[\epsilon - \epsilon^{\star}(t_f)\right], \tag{23}$$

$$E(t_f) = \int_{t_s}^{t_f} a(\hat{t})b^{(2)}(t,\hat{t})\bar{E}(\hat{t})d\hat{t} \tag{24}$$

and

$$\epsilon^{\star}(t_f) = \frac{\int_{t_s}^{t_f} a(\hat{t})b^{(2)}(t,\hat{t})\bar{E}(\hat{t})\epsilon(\hat{t})d\hat{t}}{\int_{t_s}^{t_f} a(\hat{t})b^{(2)}(t,\hat{t})\bar{E}(\hat{t})d\hat{t}} \tag{25}$$

This mathematical model may be useful in studying the mechanical consequences of changes in brain tissue caused by such diverse events as: (1) large deformation due to swelling, (2) large deformation during sloshing of the brain following a sudden motion of the head, (2) wave propagation from a blow to the head or (3) naturally occurring changes due to disease or aging.

5. Concluding Comments

This article has presented an overview of three topics from continuum mechanics that should be useful in research in brain neuro-mechanics. The first topic reviewed the notions of stress, strain and constitutive equations. It emphasized the significance of the reference configuration, its role in the development of mathematical models and the influence of residual stresses in the reference configuration on the mechanical response of brain tissue. The second topic reviewed the essentials of viscoelasticity, namely stress relaxation, creep, linearity and the response to sinusoidal oscillations. Two important consequences of these phenomena were addressed. The first was their connection to the dissipation of kinetic energy of brain tissue, *i.e.*

the settling down of disturbances with time. The second was the influence of disease, age or other non-mechanical factors on stress relaxation and how this could affect the response of brain tissue to disturbances. The third topic introduced a mechanical model that accounts for microstructural changes in materials composed of networks of macromolecules, and which should include soft biological tissue such as brain tissue. The chemical changes of scission and crosslinking at macromolecular network junctions can lead to modified material properties and permanent shape change and, thereby, altered mechanical response. It was pointed out that there are various causes for this process that could be relevant to the study of brain neuro-mechanics. Among these may be chemical changes associated with disease, age or medication as well as large deformation due to swelling. These last two topics, viscoelasticity and microstructural modification, provide a framework in which mechanical concepts such as stress and strain can be combined with non-mechanical concepts such as biochemical kinetics. This coupling should be useful in research in brain neuro-mechanics.

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