Technical Note

A fiber-reinforced composite model of the viscoelastic behavior of the brainstem in shear

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Abstract

Brainstem trauma occurs frequently in severe head injury, often resulting in fatal lesions due to importance of brainstem in crucial neural functions. Structurally, the brainstem is composed of bundles of axonal fibers distinctly oriented in a longitudinal direction surrounded by an extracellular matrix. We hypothesize that the oriented structure and architecture of the brainstem dictates this mechanical response and results in its selective vulnerability in rotational loading. In order to understand the relationship between the biologic architecture and the mechanical response and provide further insight into the high vulnerability of this region, a structural and mathematical model was created. A fiber-reinforced composite model composed of viscoelastic fibers surrounded by a viscoelastic matrix was used to relate the biological architecture of the brainstem to its anisotropic mechanical response. Relevant model parameters measured include the brainstem’s composite complex moduli and relative fraction of matrix and fiber. The model predicted that the fiber component is three times stiffer and more viscous than the matrix. The fiber modulus predictions were compared with experimental tissue measurements. The optic nerve, a bundle of tightly packed longitudinally arranged myelinated fibers with little matrix, served as a surrogate for the brainstem fiber component. Model predictions agreed with experimental measures, offering a validation of the model. This approach provided an understanding of the relationship between the specific biologic architecture of the brainstem and the anisotropic mechanical response and allowed insight into reasons for the selective vulnerability of this region in rotational head injury. © 1999 Elsevier Science Ltd. All rights reserved.

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1. Introduction

Brainstem trauma occurs in more than 50% of cases of severe head injury and more frequently (70%) in those with survival times less than 48 hours (Jellinger, 1983). These lesions are often fatal because these sites serve as neural relay stations and as center for vital functions (Rosenblum et al., 1981; Gentry et al., 1989). Previous material tests have confirmed that the brainstem exhibits a transversely isotropic response at high strain rates that may lead to sensitivity to rotational load direction and magnitude (Arbogast and Margulies, 1998).

Structurally, the brainstem is composed of bundles of axonal fibers distinctly oriented in a longitudinal direction. Surrounding these axons is a matrix of extracellular components and oligodendrocytes, cells of the CNS responsible for the production and maintenance of myelin. We hypothesize that the oriented structure and architecture of the brainstem dictates this mechanical response and results in its selective vulnerability in rotational loading. In order to understand the relationship between the biologic architecture and the mechanical response and provide further insight into the high vulnerability of this region, a structural and mathematical model was created.

A micromechanical composite model predicts composite behavior from the individual properties of the constituents, the geometrical structure, and fractional content and represents the most useful method to gain this insight. Several micromechanical models have been developed for the analysis of composite materials including the rule of mixtures, the dilute approximation, the
self-consistent scheme, the Mori–Tanaka-type models, and the method of cells. Comprehensive reviews of these models can be found in Christensen (Christensen, 1994) and Stellbrink (Stellbrink, 1996). Micromechanical models have been used to predict the response of biological materials (e.g. tendon in Ault and Hoffman, 1992b). Finite-element micromechanical models have also been applied to biological materials such as the intervertebral disk (Spilker et al., 1986) and Haversian cortical bone tissue (Hogan, 1992). Most of these models determined the material response of the composite as a whole; none proposed property descriptions of the individual components of these structures. The composite cylinder assemblage model developed by Hashin and colleagues (Hashin, 1970b) was composed of isotropic or transversely isotropic elastic fibers surrounded by an isotropic viscoelastic matrix. With this model, Hashin et al. developed expressions for complex moduli of both the fibers and the matrix. This model has been used previously to predict elastic constants of biological tissues such as rat tail tendon and cat knee joint capsule (Ault and Hoffman, 1992a,b).

In this paper, we extend Hashin’s fiber-reinforced composite model using the correspondence principle to include both viscoelastic fibers and matrix to provide novel information about the anisotropic response of the brainstem which will be useful in understanding the high vulnerability of this region during rotational head injury.

2. Materials and methods

The composite cylinder assemblage model developed by Hashin et al. (Hashin and Rosen, 1964; Hashin, 1966, 1970a,b) consists of \( n \) right circular cylinders composed of an inner cylindrical fiber, with a radius \( a_n \), surrounded by a concentric cylindrical shell (matrix). The radius of the combined cylinder and shell is \( b_n \). Both matrix and fibers are assumed to be isotropic. All cylinders are continuous and of equal height, \( h \), and possess the same radii ratio, \( a_n/b_n \). The overall structure is constructed by randomly filling the entire area with non-overlapping composite cylinders of varying radii until the volume not occupied by composite cylinders is infinitely small (Fig. 1).

For an assemblage composed of elastic fibers and an elastic matrix, Hashin and colleagues developed expressions for the two elastic shear moduli (transverse and axial) characteristic of a transversely isotropic structure, \( G_{\text{Trans}} \) and \( G_{\text{Axial}} \), using the principles of minimum potential energy and minimum complementary energy (Hashin and Rosen, 1964). From these equations, expressions for the elastic shear moduli of the matrix and fibers were developed. These moduli are dependent on the volume fractions, \( x_m \) and \( x_f \), and the Poisson’s ratios, \( \nu_m \) and \( \nu_f \), of the matrix and fibers.

The correspondence principle (Christensen, 1994) was used to extend this model to include linear viscoelastic fibers surrounded by a linear viscoelastic matrix. In practice, this theory involves the replacement of the component elastic moduli (\( G_m \) and \( G_f \)) by component complex moduli (\( G_m^{\ast}(io\omega) \) and \( G_f^{\ast}(io\omega) \)) in the expressions for the elastic moduli of the composite assemblage where \( \omega = 2\pi f \). The Poisson’s ratios have been assumed to have no imaginary component. The result of this substitution is an expression for the complex moduli of
the viscoelastic composite, where all moduli are of the form: \( G^*(i\omega) = G' + iG'' \).

\[
G_{\text{Axial}}^*(i\omega) = G_{\text{m}}^*(i\omega) x_m + G_{\text{f}}^*(i\omega)(1 + x_f)
\]

\[
G_{\text{trans}}^*(i\omega) = G_{\text{m}}^*(i\omega)(1 + 2\gamma(i\omega)x_f^3(\rho(i\omega) + \beta_m x_f) - 3x_f x_m^2\beta_m^2 - 1 + 2\gamma(i\omega)x_f^3(\rho(i\omega) - x_f) - 3x_f x_m^2\beta_m^2),
\]

where \( f \) is frequency in Hz and the moduli are in Pa.

Eqs. (3) were set equal to the relations in (1) and solved simultaneously for matrix and fiber complex moduli, \( G_{\text{m}}^*(i\omega) \) and \( G_{\text{f}}^*(i\omega) \), respectively, using MAPLE™ mathematical software, and exact expressions for the storage \( (G_m' \text{ and } G_f') \) and loss moduli \( (G_m'' \text{ and } G_f'') \) for the matrix and fibers were obtained. These moduli are functions of the linear relations for moduli of the composite structure as a whole (Eqs. (3)), the Poisson’s ratios \( (\nu_m \text{ and } \nu_f) \), and the volume fractions \( (x_m \text{ and } x_f) \).

To determine the volume fraction of porcine brainstem, a staining technique in which bundles of white matter are stained dark, while areas of gray matter remain light (Schmued, 1990). A fresh adult porcine brain was fixed, freeze-sectioned in the horizontal plane. The slides were then soaked for approximately 2–3 h in a histological stain that consists of a solution of 0.2% gold chloride solution dissolved in 0.02 M neutral phosphate buffer and 0.9% sodium chloride.

Two randomly chosen regions from each of the three sections \( (n = 6 \text{ regions}) \), magnified at 50 \( \times \), were captured using an AIS imaging system (Imaging Research Inc., St. Catherines, Ont.). A thresholding technique (NIH Image software) was used to determine the fraction of myelinated fibers in the entire cross-section. Average fiber and matrix volume fraction were obtained \( (x_f \text{ and } x_m) \) and these values were used in the fiber-reinforced composite model for brainstem.

3. Results

The gold chloride stain for myelin produced cross-sections of dark stained white matter bundles surrounded by areas of unstained gray matter (Fig. 2). The ratio of white matter area to entire cross-sectional area was calculated as 0.53 \( \pm \) 0.07 (mean \( \pm \) S.D.) and was defined as the fiber volume fraction, \( x_f \). The matrix fraction, \( x_m \), was defined as the remaining fraction (0.47).

Calculated fiber and matrix complex moduli predicted that the fibers are three times stiffer and more viscous than the matrix, as indicated by the more pronounced frequency dependence of the fiber loss modulus (Fig. 3). Results are expressed as modulus versus frequency with the error bars representing \( \pm \) 1 S.D. in fiber volume fraction.

The guinea pig optic nerve moduli showed excellent agreement with the theoretical predictions of fiber
Fig. 2. A representative histology slide using a gold-chloride stain sensitive to myelin shows the typical cross-section of the adult porcine brainstem. Myelinated axonal bundles (fibers) are stained dark, while the surrounding gray matter (matrix) remains unstained. The fiber volume fraction ratio was calculated as $0.53 \pm 0.07$ (mean $\pm$ S.D.). The matrix fraction was defined as the remaining fraction ($0.47$).

Fig. 3. Predicted frequency response of the storage modulus, $G'$, and loss modulus, $G''$, for the fibers ($G_f, G'_f$) and matrix ($G_m, G'_m$) of the fiber reinforced composite model. The model predicted that the fibers are three times stiffer and more viscous than the matrix. Results are expressed as modulus versus frequency with the error bars representing $\pm$ 1 S.D. in fiber volume fraction.

Fig. 4. The theoretical fiber (a) storage modulus and (b) loss modulus from the fiber reinforced composite model (mean volume fraction $\pm$ S.D.) show excellent agreement with the experimentally determined moduli from the optic nerve oscillatory tests (mean $\pm$ S.D.) confirming the predictive capability of the model.

complex moduli from the model (Fig. 4). In particular, the deviation (one-half the difference between the modulus values at each frequency expressed as a percentage of the mean) associated with the storage modulus and

the loss modulus over the frequency range was $< 5\%$ and $< 7\%$, respectively.

4. Discussion

In this paper, we extended Hashin’s fiber-reinforced composite model using the correspondence principle to include viscoelastic components to provide novel information about the anisotropic structural response of the brainstem. To develop the model, we made simplifying assumptions regarding the structure and material properties of the brainstem. Structurally, the mechanical response of fiber-reinforced materials is dictated by three parameters: (a) the volume fraction of fiber and matrix, (b) the direction of fiber reinforcement, and (c) the cross-sectional geometry of the fiber.

A parametric analysis was performed to assess the sensitivity of the predicted complex moduli to volume fraction. With a four-fold increase in fiber volume fraction from $x_f = 0.20$ to $x_f = 0.80$, the matrix complex modulus, $G''_m$, decreased by $119\%$, and the fiber complex modulus, $G''_f$, decreased by $221\%$. In our volume fraction calculations, serial sections were sliced perpendicular to the main axis of the axonal tracts to obtain a true cross-section, and each section was analyzed three times and
averaged. The small coefficient of variation (S.D./mean = 13%) across sections in the measurements supports the reproducibility of this method of analysis, but does not include biological variability across subjects.

In the model, all fibers were assumed to be aligned parallel in the vertical direction, continuous throughout the height of the sample, and circular in cross section. These geometrical assumptions represent an idealization of the brainstem structure that is based on anatomic evidence (Nolte, 1993).

The mechanical response of the model is not only influenced by structural assumptions, but also affected by the choice of material parameters. Both components of the composite structure have been assumed to be incompressible with Poisson’s ratios, $v = 0.5$, due to the high fraction of water (Dickerson and Dobbing, 1966) and large bulk modulus (McElhaney et al., 1976) of these tissues.

This model assumes that the composite structure as a whole and its two components are linear viscoelastic materials. Although it was shown that CNS tissue responds non-linearly to mechanical deformation over a broad range of strains (Donnelly and Medige, 1997), at the small strains used in our study ($\leq 5\%$), the assumption of linearity is reasonable. As strain magnitude increases, non-linear representation becomes important.

Both matrix and fibers have been treated as homogenous, isotropic materials. The assumption of isotropy is a logical one for the matrix due to the random arrangement of oligodendrocytes and extracellular matrix. However, the axonal fibers, characterized by a longitudinal arrangement of neurofilaments and microtubules that support the cell membrane, are probably transversely isotropic. To incorporate transversely isotropic fibers, one step would be to replace the moduli of the fibers in the equations for $G_{Axial}$ and $G_{Trans}$ of the composite structure (Eq. (1)) with the fiber axial and transverse complex moduli, but no material data currently exists about these subcomponents.

The interface between the fiber and matrix is another material parameter that influences the mechanical response of the composite structure. We have assumed the deformation at the outer radius of a fiber is equal to the deformation at the inner radius of its surrounding matrix. Anatomically the oligodendrocytes of the matrix physically attach in a random manner to surrounding fibers justifying a no-slip interface as a reasonable mathematical description of this biological interaction.

We simplified the optic nerve as containing no surrounding matrix ($x_d = 1.00$), and therefore assumed that the complex moduli obtained from these experiments were equal to the complex moduli of a single fiber. This simplification contains two limiting assumptions. First, due to the natural undulation of axons within the optic nerve, these experiments most likely underestimate the complex moduli of a single axonal fiber. Upon loading, an initial force is required to straighten the axon, loading the connections between the fiber and surrounding matrix rather than the fiber itself. As a result, the individual fibers experience less stretch than the applied macroscopic deformation, thereby underestimating the individual fiber modulus. By assuming the optic nerve is composed of taut axons, we assume that all of the force is applied to stretch the axon and that the individual fibers experience the same strain as applied macroscopically to the optic nerve. Second, the complex moduli of a single axonal fiber is further underestimated due to the presence of an actual matrix in the optic nerve ($x_d \sim 0.90$). As the fractions of fibers decrease in a cross-section, the moduli of single fiber must increase to sustain the same load. However, we suspect that this small decrease in fiber volume fraction ($100 - 90\%$) will result in only minor increases in the moduli.

The model predictions of fiber properties demonstrated close agreement with independently determined experimental results, thus validating the viscoelastic fiber reinforced model of the brainstem. Specifically, the fiber-reinforced composite model predicted the complex modulus of the fibers was approximately three times higher than that of matrix indicating that the fiber is a much stiffer material. In addition, the frequency dependence of the fiber loss modulus was more pronounced than the matrix suggesting that the fibers are relatively more viscous. Consequently, we conclude that the axonal fibers, rather than the surrounding matrix, impart the stiffness to the structure.

In summary, a viscoelastic fiber-reinforced composite model based on variational calculus techniques was implemented and validated with experimental data to describe the mechanical response of the brainstem. This model predicted individual complex moduli of the fibers and matrix using data from the complex moduli of the brainstem, and the volume fraction of fibers in a typical brainstem cross-section. The fiber complex modulus predictions agreed with data from oscillatory shear tests on guinea pig optic nerve. This approach provided an understanding of the relationship between the specific biologic architecture of the brainstem and the anisotropic mechanical response and allowed insight into reasons for the selective vulnerability of this region in rotational head injury.

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References


