

Mechanical properties of brain tissue in tension

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Abstract

This paper contains experimental results of in vitro, uniaxial tension of swine brain tissue in finite deformation as well as proposes a new hyper-viscoelastic constitutive model for the brain tissue. The experimental results obtained for two loading velocities, corresponding to strain rates of 0.64 and $0.64 \times 10^{-2} \text{ s}^{-1}$, are presented. We believe that these are the first ever experiments of this kind. The applied strain rates were similar to those applied in our previous study, focused on explaining brain tissue properties in compression. The stress–strain curves are convex downward for all extension rates. The tissue response stiffened as the loading speed increased, indicating a strong stress–strain rate dependence. Swine brain tissue was found to be considerably softer in extension than in compression. Previously proposed in the literature brain tissue constitutive models, developed based on experimental data collected in compression are shown to be inadequate to explain tissue behaviour in tension. A new, non-linear, viscoelastic model based on the generalisation of the Ogden strain energy hyperelastic constitutive equation is proposed. The new model accounts well for brain tissue deformation behaviour in both tension and compression (natural strain $\in \langle -0.3, 0.2 \rangle$) for strain rates ranging over five orders of magnitude. © 2002 Elsevier Science Ltd. All rights reserved.

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1. Introduction

Mechanical properties of living tissues form a central subject in Biomechanics. In particular, the properties of the muscular-skeletal system, skin, lungs, blood and blood vessels have attracted much attention, for examples, see Borowski et al. (1992), Fung (1981), Gallagher et al. (1982), Mow et al. (1993), Schmid-Schonbein et al. (1986) and references cited therein. The properties of “very” soft tissues, which do not bear mechanical loads (such as brain, liver, kidney, etc.), have not been so thoroughly investigated.

However, recent developments in robotics technology, especially the emergence of automatic surgical tools and robots (e.g. Brett et al., 1995) as well as advances in virtual reality techniques (Burdea, 1996), call for closer examination of the mechanical properties of these tissues. The ultimate goal of our research into the biomechanics of these tissues is development of corresponding, realistic mathematical models.

Mathematical models of brain tissue mechanical properties may find applications, for example, in a surgical robot control system, where the prediction of deformation is needed (Miller and Chinzei, 1995, 2000), surgical operation planning and surgeon training systems based on the virtual reality techniques (Burdea, 1996 and references cited therein), where *force feedback* is needed, and *registration* (Lavallée, 1995), where knowledge of local deformation is required.

There is wealth of information available in the literature about the mechanical properties of brain tissue in vitro (Ommaya, 1968; Estes and McElhaney, 1970; Galford and McElhaney, 1970; Pamidi and Advani, 1978; Bilston et al., 1997; Donnelly and Medige, 1997; Miller and Chinzei, 1997). The experimental results available in literature are limited to compression, indentation and impact tests. To the best of the authors’ knowledge, there are no results in the literature concerning soft tissue (such as brain, liver and kidney) properties in tension. Why is that? We believe that, besides technical problems with conducting extension tests on brain and other soft tissues, the main reason is that the analytical relation between the tensile

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stress machine head displacement and strain had not been known for cylindrical samples with low aspect ratio. This obstacle was removed by Miller (2001).

In this paper we present the first results of swine brain tissue extension in finite deformation. We attempt to prove that brain tissue behaviour in tension is considerably different from its behaviour in compression and, therefore, tissue constitutive models based on compression experiments are not suitable for description of tissue behaviour in extension. Hence, previously proposed constitutive models of brain tissue cannot be confidently used in general finite element calculations, which may involve various loading states. Using results of a rigorous mathematical description of the deformation in the uniaxial extension experiment and the earlier derived relation between the strain in the sample and machine head displacement (Miller, 2001) we analyse results of uniaxial extension in the analogous way to that used for unconfined compression. Finally, we propose the new constitutive model of brain tissue, valid for both compression and extension.

2. Tension experiment of swine brain tissue

2.1. Specimen preparation

Specimen preparation follows closely the procedure described in Miller and Chinzei (1997). Eight brains from six-month old swines were collected from a slaughter house. Pigs were terminated according to standard slaughtering procedure and the samples were taken as a by-product. Specimens were not frozen at any time during the procedure. Brain weights ranged between 93.5 and 102.0 g, close to the weight of a healthy adult swine (Kumagaya and Namioka, 1987). After being removed from the dura, each brain was stored in physiological solution at 5°C. Usually, transportation of brains and sample preparation took one night before experiments.

Cylindrical samples of diameter ~30 mm and height ~10 mm were cut. A steel pipe (30 mm diameter) with sharp edges was used to cut the samples. The faces of the cylindrical brain specimens were smoothed manually using a surgical scalpel. Four samples were taken from the frontal and posterior portions of the Sylvian fissure of each hemisphere for each swine brain. The ventricle surface and the arachnoid membrane formed the top and bottom faces of the sample cylinder. Thus the arachnoid membrane and the structure of the sulci remained as parts of each specimen.

Brain tissue is very soft and adheres upon contacting almost any material. Consequently, it was very difficult to obtain an exact cylindrical shape. Usually, the diameters of opposite faces of the sample differed by ~2–3 mm. Therefore, we could not assume the cross-

section area to be constant across all samples. The average cross-section of each specimen was measured.

2.2. Experimental setup

Uniaxial tension of swine brain tissue was performed in a testing stand shown in Fig. 1. This particular geometry was dictated by the difficulties in attaching faces of cylindrical specimens to platens of the stress-strain machine.

The main testing apparatus was a Tensilon (Universal Testing Instrument, TMI, model RTM-1T made by Toyo Baldwin, Co., Ltd., Japan) with a load cell that allowed measurement of vertical force in the range 0.05–9.0 N for loading velocities between 0.005 and 500 mm/min. The vertical displacement (along *z*-axis in Fig. 1b) was measured by a micrometer with electric analog output. The experiment was documented by automatically taking CCD camera images, Fig. 1a. The images were used to ensure that during the loading phase samples had uniformly contracted in the middle section of the specimen as well as that upper or lower faces of the specimen had remained adhered to the moving platen and support.

2.3. Experimental protocol

Cylindrical samples of tissue were axially extended between two impermeable platens. As a result of brain tissue delicacy and adhesiveness, no pre-conditioning was performed. Only one loading cycle was executed on each sample.

One of the practical difficulties in conducting tension experiments was placing samples in the testing machine in reliable and repeatable way. After preparing a specimen we attached it to a glass plate using Zero-Time Jelly (cyanoacrylate, surgical glue made by Cemedine, Japan). Next the glass plate was rigidly fixed to the support of the testing apparatus by four screws. The glue was then applied to the upper platen of the testing apparatus and the platen was moved very slowly so that it touched the upper surface of the specimen. To assure proper attachment of two surfaces the upper platen was moved additional 1 mm (so that it stayed 9 mm above the glass plate) and maintained in this position for 20 s. Next the platen was slowly reversed back to the initial touching position, i.e. 10 mm above glass plate. In this position the specimen was left for about 1 min before the actual test began. As a result bottom and top surfaces of the sample were rigidly attached to the support and moving platen of the testing apparatus. This prevented any movement of sample faces relative to the platens of testing apparatus and enabled the use of the no-slip boundary condition during the analysis of results.

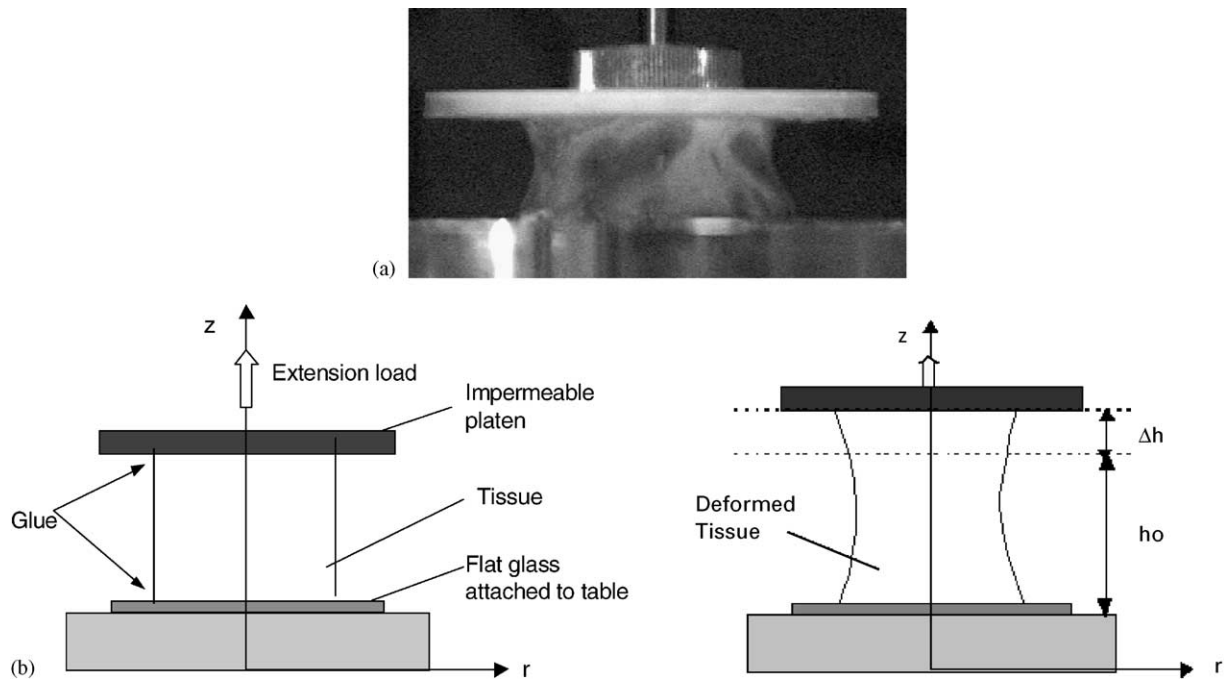


Fig. 1. (a) Swine brain tissue sample subjected to extension and (b) sketch of the experimental set-up. Δh and vertical force are measured.

The tests were performed at room temperature ($\sim 22^\circ\text{C}$). At the end of the procedure no signs of dehydration were observed. The start of the loading phase was indicated by the first non-zero reading of the micrometer. The tests were continued until the failure of the specimen. In the paper the results obtained for the loading phase are discussed. The measurements for the following two loading velocities were conducted:

- *fast*: 500 mm min^{-1} —the fastest loading speed possible with our equipment—corresponding to the (nominal) strain rate of about 0.64 s^{-1} ,
- *medium*: 5 mm min^{-1} , corresponding to the (nominal) strain rate of about $0.64 \times 10^{-2} \text{ s}^{-1}$.

The desired velocity was achieved very quickly. Therefore, in the analysis of the results we assumed that the prescribed loading velocity was achieved instantly.

The applied loading speeds are the same as in Miller and Chinzei (1997). Eleven fast and 10 medium speed tests were performed. Each sample was tested once only. Extension tests corresponding to the slow compression in Miller and Chinzei (1997)—strain rate $0.64 \times 10^{-5} \text{ s}^{-1}$ —proved impossible to conduct using our technique. Such experiments would require the upper platen of the machine to move for at least 11 h. At such long times the surgical glue used did not provide appropriate adhesion of the tissue to the top platen of the machine.

2.4. Measurement results

To assess the repeatability of measurements, the vertical force divided by initial cross-section area (which is the average Lagrange stresses in the plane of symmetry) versus time for each loading velocity are presented in Fig. 2a and b and standard deviation bars are included in Fig. 2c and d. The coefficient of variation (standard deviation divided by the mean) for medium speed tests was approximately constant and equal to 0.2. The coefficient of variation for fast test was larger—0.5. Value 0.2 is similar to that reported in Miller and Chinzei (1997) and significantly lower than 0.5—the value estimated from Figs. 3–6 in Estes and MacElhane (1970). Value 0.5 is larger than that reported for compression experiments in Miller and Chinzei (1997) but comparable to the results of (Estes and MacElhane, 1970). This suggesting that the repeatability of experiments is satisfactory.

The experimental errors are affected by a number of factors, whose relative influence is difficult to judge. The most important are variations between tissue samples taken from eight swines, inherent for biological materials, and errors in estimation of sample cross-section area, due to deviations from cylindrical shape (up to 4%). The possible effect of the orientation of the material with respect to the test axis was overwhelmed by between-sample variations and was not detected. Also, the “necking” of specimens appeared very close to the plane of symmetry of the samples, Fig. 1. The errors of force and displacement measurements are

insignificant (not more than 0.1% of maximum force and displacement).

The stress–displacement curves are convex downward for all extension rates. The tissue response stiffened with

the increasing loading speed, indicating strong stress–strain rate dependence. It needs to be pointed out here that there is no other data for slow strain rates typical for surgical procedures available for comparisons.

3. Analysis of experimental results

3.1. Brain as a hyper-viscoelastic, single-phase continuum

The measurement results indicate that brain tissue properties in extension are very different to those in compression and therefore the previously used assumption of equality of the energy of the reciprocal deformation to that of the original deformation (Mooney, 1940; Miller and Chinzei, 1997; Miller, 1999) has to be abandoned.

Recently, brain tissue constitutive models based on the strain energy function in polynomial form with time dependent coefficients have been proposed (Mendis et al., 1995; Miller and Chinzei, 1997; Miller, 1999). These models cannot, unfortunately, account for a different behaviour in extension than in compression, exhibited by brain tissue. Therefore, they have to be modified if the objective is to implement the constitutive model in the finite element code capable of computing brain deformation under general loading conditions.

The limited flexibility of energy functions in polynomial form results from the use of integer powers of the first and second strain invariants and, consequently, only even powers of stretches, i.e.:

$$I_1 = \lambda_1^2 + \lambda_2^2 + \lambda_3^2 \Rightarrow I_1^2 = \lambda_1^4 + 2\lambda_1^2\lambda_2^2 + \lambda_2^4 + 2\lambda_1^2\lambda_3^2 + 2\lambda_3^2\lambda_2^2 + \lambda_3^4. \quad (1)$$

The obvious alternative is to use fractional powers of stretches in the definition of the energy function. This idea, for hyperelastic materials, was developed by Ogden (1972). The following form of energy function for hyperelastic solids was proposed:

$$W = \frac{2\mu}{\alpha^2}(\lambda_1^\alpha + \lambda_2^\alpha + \lambda_3^\alpha - 3), \quad (2)$$

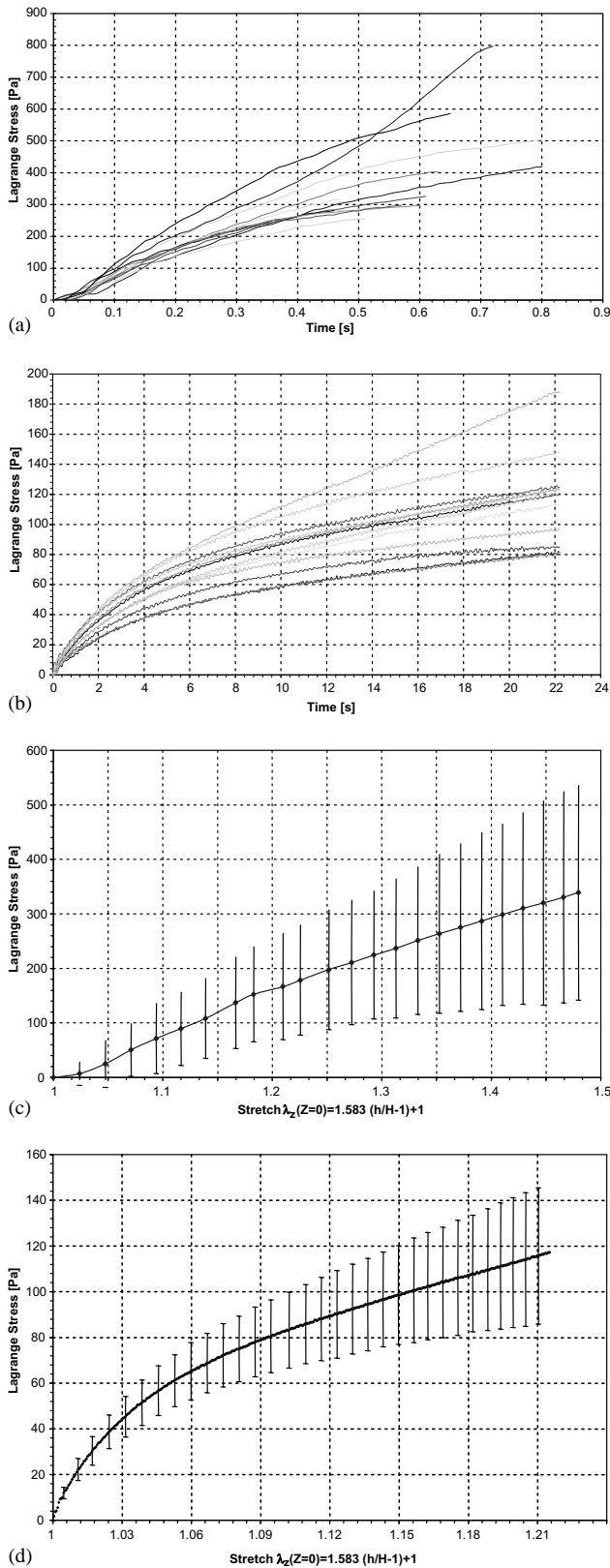


Fig. 2. Repeatability of the extension experiment: (a) Lagrange stress (force divided by original cross-section area) versus time for loading velocity $v = 5.0 \times 10^2$ mm/min; corresponding to the strain rate strain-rate approx. 0.64 s^{-1} . (b) Lagrange stress versus time for loading velocity $v = 5.0$ mm/min; corresponding to the strain rate strain-rate approx. $0.64 \times 10^{-2} \text{ s}^{-1}$. (c) Lagrange stress (averaged over all samples) versus stretch in the plane of symmetry $\lambda_z(Z=0) = 1.583(h/H-1) + 1$ (see Eq. (5)) for loading velocity $v = 5.0 \times 10^2$ mm/min; corresponding to the strain rate strain-rate approx. 0.64 s^{-1} . Error bars indicate standard deviation. (d) Lagrange stress averaged over all samples versus stretch in the plane of symmetry $\lambda_z(Z=0) = 1.583(h/H-1) + 1$ (see Eq. (5)) for loading velocity $v = 5.0$ mm/min; corresponding to the strain rate strain-rate approx. $0.64 \times 10^{-2} \text{ s}^{-1}$. Error bars indicate standard deviation.

where μ is a shear modulus in undeformed state and α is a material coefficient, which can assume any real value without restrictions.

The brain exhibits stress–strain rate dependency (Fig. 2). Therefore, in order to be used in brain tissue biomechanics, Eq. (2) has to be generalised. We propose the following form of the energy function for very soft biological tissues:

$$W = \frac{2}{\alpha^2} \int_0^t \left[\mu(t - \tau) \frac{d}{d\tau} (\lambda_1^\alpha + \lambda_2^\alpha + \lambda_3^\alpha - 3) \right] d\tau. \quad (3)$$

The strain energy function is represented in the form of a convolution integral, where

$$\mu = \mu_0 \left[1 - \sum_{k=1}^n g_k (1 - e^{-t/\tau_k}) \right] \quad (4)$$

describes the relaxation of the shear modulus of the tissue. μ_0 is the instantaneous shear modulus in undeformed state. τ_k are characteristic times.

3.2. Material constants for brain tissue

In the analysis of the extension experiment the theoretical results of Miller (2001) were used. The major result of Miller (2001) is the proof that, for practical purposes, the vertical stretch in the plane of symmetry can be treated as proportional to the displacement of the machine head, at least for h/H (Fig. 3) between 1 and 1.3

$$\lambda_z(Z = 0) - 1 = K \left(\frac{h}{H} - 1 \right), \quad K = 1.583 \quad (5)$$

so that, the results of uniaxial extension of brain tissue can be analysed using the same methods as for unconfined compression (Miller and Chinzei, 1997; Miller, 1999) provided the correction by factor $K = 1.583$ for stretch and stretch rate is included:

Unconfined compression

$$\lambda_z(Z = 0) = \frac{h}{H}. \quad (6)$$

Uniaxial extension (Figs. 1 and 3)

$$\lambda_z(Z = 0) - 1 = K \left(\frac{h}{H} - 1 \right), \quad K = 1.583. \quad (7)$$

As shown in Miller (2001), in a uniaxial extension experiment, in the plane of symmetry $Z = z = 0$ (Fig. 3) the orthogonal state of deformation can be assumed. This state of deformation can be described, as in the case of the unconfined compression experiment (Miller and Chinzei, 1997), by a diagonal deformation gradient

$$F(Z = 0) = \begin{bmatrix} \lambda_z^{-1/2} & 0 & 0 \\ 0 & \lambda_z^{-1/2} & 0 \\ 0 & 0 & \lambda_z \end{bmatrix}. \quad (8)$$

In such case, one can compute the only non-zero Lagrange stress component from the simple formula

$$T_{zz} = \frac{\partial W}{\partial \lambda_z}. \quad (9)$$

After substituting Eq. (3) for the energy function one obtains

$$\begin{aligned} T_{zz} = & \frac{1}{\alpha} \left\{ \mu_0 \left[2 \left(1 + \frac{K\dot{h}}{H} \right)^{-1-\alpha/2} \left(-1 + \left(1 + \frac{K\dot{h}}{H} \right)^{3\alpha/2} \right) \right. \right. \\ & + \sum_{i=1}^n \left\{ e^{-(H+K\dot{h})/K\dot{h}\tau_i} n g_i \left(2(-1 + \alpha)\gamma \left[-1 + \alpha, -\frac{H}{K\dot{h}\tau_i} \right] \right. \right. \\ & + (2 + \alpha)\gamma \left[-1 - \frac{\alpha}{2}, -\frac{H}{K\dot{h}\tau_i} \right] \left(-\frac{H}{K\dot{h}\tau_i} \right)^{3\alpha/2} \left(-\frac{H}{K\dot{h}\tau_i} \right)^{1-\alpha} \\ & + \frac{1}{K^2 \dot{h}^2 \tau_i^2} \left\{ e^{-(H+K\dot{h})/K\dot{h}\tau_i} H^2 \left(1 + \frac{K\dot{h}}{H} \right)^{\alpha/2} g_i \left(-\frac{H + K\dot{h}}{K\dot{h}\tau_i} \right)^{-1-\alpha} \right. \\ & \left. \left. \left. \frac{\left\{ K(2 + \alpha)\gamma \left[-1 - \frac{\alpha}{2}, -\frac{H + K\dot{h}}{K\dot{h}\tau_i} \right] \dot{h} \left(-\frac{H + K\dot{h}}{K\dot{h}\tau_i} \right)^{1+3\alpha/2} \right\} \tau_i}{H} \right. \right. \\ & + 2 \left\{ (1 - \alpha)\gamma \left[-1 + \alpha, -\frac{H + K\dot{h}}{K\dot{h}\tau_i} \right] \left(1 + \frac{K\dot{h}}{H} \right)^{1+3\alpha/2} \right. \\ & \left. \left. \left. \left. \left. \left. \frac{e^{(H+K\dot{h})/K\dot{h}\tau_i} K \dot{h} \left(-1 + \left(1 + \frac{K\dot{h}}{H} \right)^{3\alpha/2} \right) \left(-\frac{H + K\dot{h}}{K\dot{h}\tau_i} \right)^\alpha \right\} \tau_i}{H} \right\} \right\} \right\}, \end{aligned}$$

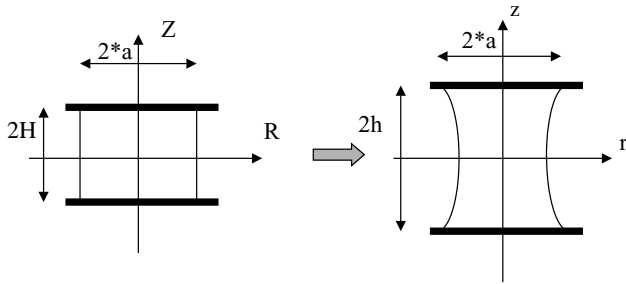


Fig. 3. Description of deformation in extension experiment.

Table 1
List of material constants for constitutive model of brain tissue, Eqs. (3) and (4), $n = 2$

Instantaneous response	$k = 1$	$k = 2$
$\mu_0 = 842$ (Pa); $\alpha = -4.7$	Characteristic time $t_1 = 0.5$ (s); $g_1 = 0.450$	Characteristic time $t_2 = 50$ (s); $g_2 = 0.365$

where n is number of terms in series expansion (4), τ_i are the characteristic times, g_i the relaxation coefficients, \dot{h} is a velocity of the machine head, and t the time. The solution for stress contains the incomplete γ function.

To identify material constants of the brain tissue the assumption of strain-time separability of the energy function describing the tissue properties was adopted (Larson, 1988). The same assumption was (implicitly) used e.g. in Mendis et al. (1995), Miller (1999). Therefore, the values of the relaxation coefficients g_i and characteristic times τ_i could be taken from Miller (1999). α and shear modulus μ_0 were left as the only parameters to be identified. This was accomplished by fitting the model to extension and compression (without correction by K) experimental results using a NonlinearFit command available in Mathematica (Wolfram Research, 1996). Values $\alpha = -4.7$ and $\mu_0 = 842$ Pa—about Pa—about 20% lower value than that reported in Miller (1999)—were obtained. The complete list of material constants for brain tissue is given in Table 1.

As can be seen in Fig. 4 the proposed model accounts well for brain tissue behaviour in compression and extension for strains up to 30% and strain rates ranging over a few orders of magnitude.

4. Discussion and conclusions

In this study the results of in vitro extension of swine brain tissue and the analysis of mathematical models of tissue deformation behaviour are discussed. Non-linear stress–strain relations were observed. A strong dependence between stresses and strain rate was recorded. The

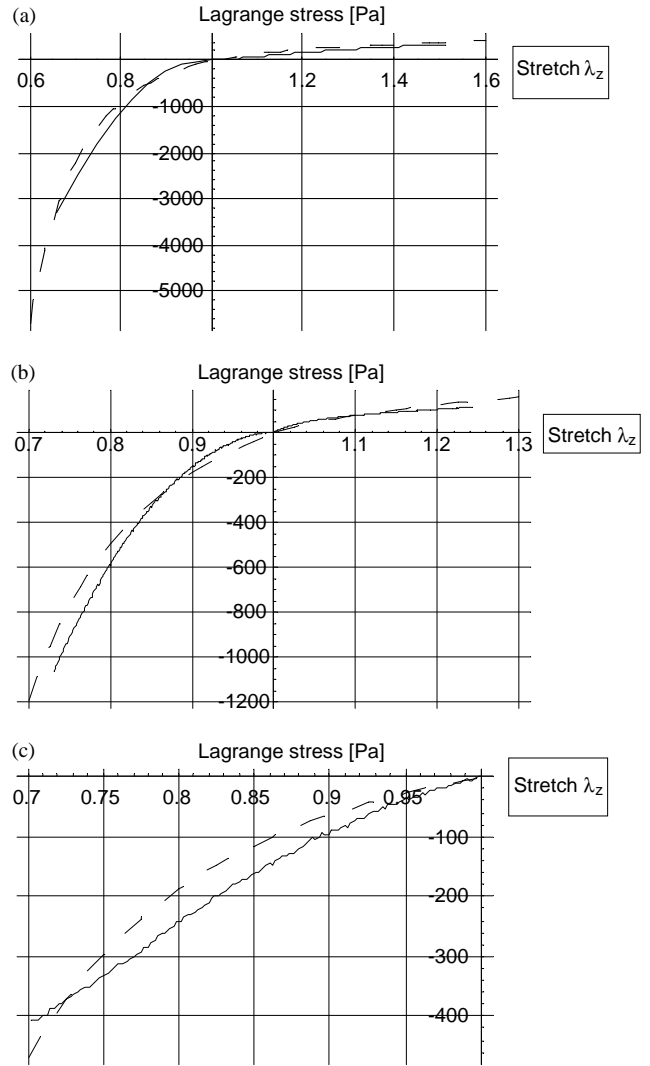


Fig. 4. Experimental (solid line) versus theoretical (dashed line, Eq. (10)) results for compression (Miller and Chinzei, 1997) and extension of brain tissue for various loading velocities. (a) Loading velocity $v = 5.0 \times 10^2$ mm/min; corresponding to the strain rate strain-rate approx. 0.64 s^{-1} . (b) Loading velocity $v = 5.0$ mm/min; corresponding to the strain rate strain-rate approx. $0.64 \times 10^{-2} \text{ s}^{-1}$. (c) Loading velocity $v = 5.0 \times 10^{-3}$ mm/min; corresponding to the strain rate strain-rate approx. $0.64 \times 10^{-5} \text{ s}^{-1}$ (compression only).

experiments conducted in this work were designed to give more insight into the tissue behaviour at lower strains and strain rates, which are typical for surgical procedures. We believe that presented here results of brain tension in finite deformation are the first to be made public.

Unfortunately, the behaviour of brain tissue in extension is completely different to that in compression. Previously proposed models, based on the concept of the polynomial strain energy function in the form of convolution integral with coefficients expressed in the form of exponential series, could not account for such material behaviour. In particular, the assumption of the

equality of the energy of deformation and the energy of reciprocal deformation had to be abandoned. In this paper we proposed a new hyper-viscoelastic constitutive model including fractional powers of principal stretches. The model was shown to account well for tissue mechanical properties in compression as well as in extension for strains up to 30% and strain rates ranging over five orders of magnitude. An additional advantage of the proposed model is that it contains fewer constants to be estimated from the data than previously used second order polynomial hyper-viscoelastic constitutive equations.

The model proposed can be immediately applied to larger scale finite element computations, e.g. by directly using ABAQUS (ABAQUS, 1992), which contains built-in commands to model Ogden-type instantaneous hyper-elasticity of the tissue and time dependent material behaviour.

The specimens used in the experiments consisted of the arachnoid membrane, white matter and grey matter. Subsequently, the criticism may arise that the experimental results are only valid for such a composite. However, we think that our results are still useful in approximate modelling the behaviour of the brain tissue, which includes spatial averaging of material properties. Furthermore, the average properties of the specimen consisting of white and grey matter, and arachnoid membrane are meaningful in the clinical situations. In the case of brain surgery, the sulcus is pushed aside to access lesions. To avoid damage to the brain, neurosurgeons try not to destroy the arachnoid membrane.

How to use the in vitro experimental results in the more realistic in vivo environment remains an open question. More experimental work is required to verify the validity of the assumptions used for model derivation as well as the numerical values of brain tissue material constants. Further research is needed to determine brain tissue constitutive models, which would incorporate the influence of the blood and cerebrospinal fluid pressure and flow. However, recent computer simulation results (Miller et al., 2000) suggest that brain properties obtained in vitro are close to those needed to model a realistic brain deformation under surgical load in vivo.

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