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High frequency modelling of porcine brain tissue

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Abstract

The objective of this study is to contribute to the improvement of FE head models used to predict the mechanical response of brain during head impact. The topic of that research is the mechanical characterization of high frequency behaviour of porcine brain tissue from own experimental results obtained in small deformation, oscillatory shear experiments. These results are the first experimental data corresponding to a large frequency range associated with non-penetrating ballistic and accidental impacts or inertial loadings. Cylindrical samples of white matter of adult pigs (diameter: 10 mm, thickness: 150 - 250 μm) are harvested, conserved in physiological solution at 6°C and tested within the day post-mortem. The complex shear modulus of the samples are measured in a custom-designed oscillatory shear testing device at shear strain amplitudes of 0.002 % from 0.251 to 10 000 Hz, at 37°C and 100 % humidity. In this range, the elastic (G') and viscous (G'') component of the complex shear modulus increased with the frequency from 0.455 kPa to 133.9 kPa and 0.133 kPa to 63.7 kPa respectively. Results show two successive intersections between the two moduli which indicate that the viscous behaviour is predominant between 250 and 3700 Hz. Moreover, a constitutive description capable of capturing the material behaviour observed in the material experiments is developed. The model chosen is a linear multi-mode Maxwell model which allows to fit both storage and loss modulus at low and high frequency. It is important to note that up to now only the elastic part is taken into account in viscoelastic modelling of brain tissue in FE head models which has the effect of overestimating the elastic moduli and underestimating the viscosities of rheological model. Our work is expected to enhance the biofidelity of computational models and provide a better understanding for the mechanisms of traumatic brain injury.

Introduction

Traumatic brain injury (TBI) remains an increasingly common cause of death and disability around the world. In western countries, they are estimated to account for 15% of the burden of death and disability and are projected to account for 20% in 2020 when they will represent the third leading cause of death and disability. Nowadays, we note TBI are the leading cause of death in young adult [1,2]. According to an European Brain Injury Consortium (EBIC) survey, 52% of head injuries were motor vehicle related [3] and the other main causes are falls and assaults or firearm use [1,4]. More than 30 years of research into the mechanical properties of the brain tissue have been motivated by traumatic injury prevention [5-13]. In most of these studies it was assumed that the brain tissue is incompressible [14,15] and is therefore most likely to fail in shear. It's the reason why the results were usually presented in the form of frequency-dependant complex shear moduli. In this study we report the main results from the literature pertaining to the mechanical properties of the brain tissue in shear. For ethical and technical reasons, all these studies were performed on *in vitro* brain tissue. Fallenstein et al. (1969) [5] measured the storage (G') and the loss (G'') modulus of human brain at 10 Hz and found that G' and G'' lie between 0.6 and 1.10 kPa and 0.35 and 0.60 kPa respectively. Shuck et al. (1972) [7] reported the complex shear moduli of human brain between 5 and 350 Hz ranging from 7.6 to 39.4 kPa for G' and from 2.8 to 81.4 kPa for G''. They proposed a linear four-parameter-fluid model to fit the results at the higher frequencies but this model was not satisfactory below 100 Hz. Donnelly et al. (1997) [8] determined a non-linear, viscoelastic, standard solid model to represent the stress versus finite strain curves obtained from the human brain tissue testing at constant shear strain rate. They concluded that the stress versus strain curves had an increasing slope as both strain and strain rate increased. Peters et al. (1997) [9] applied the time/temperature superposition principle to brain tissue. They calculated a dynamic shear modulus ranging from 0.3 kPa to 10 kPa between 0.1 and 10^6 Hz for the porcine brain tissue. Brands et al. (2002) [10] applied this principle to determine a linear multi-mode Maxwell model from small strain oscillatory experiments on the porcine brain tissue. The extrapolated storage (G') and loss (G'') moduli lie between 0.5 and 1.8 kPa and 0.2 and 1.5 kPa respectively for a frequency ranging from 0.16 to 1000 Hz. By noting shear softening from shear stress relaxation experiments at high strain, he proposed a second Mooney-Rivlin model to fit the non-linear strain behaviour of the porcine brain tissue [11]. Finally, Arbogast et al. [12] measured the complex shear modulus of the porcine brain tissue and found G' ranging from 1.25 to 1.65 kPa and G'' ranging from 0.4 to 2.15 kPa as frequency increased from 20 to 200 Hz.

During an accident, the head is subjected to an external mechanical load which is transferred to the brain tissue. Brain damages are caused if this load exceeds the brain's tolerance threshold. Insight into brain behaviour is needed to improve not only prevention measures but also diagnosis and treatment of brain injury. Since a few years, Finite Element Models of the human head have been

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powerful tools used to understand and to predict the head's response under impact conditions [16,17,18,19]. Each component of this model has to be described accurately in term of geometry and material behaviour. However, one of the shortcomings of the actual models is the lack of data on constitutive law of brain tissue in short times. Indeed, typical frequencies during direct head impacts or non-penetrating ballistic impacts are on the order of 1000 Hz or more, i.e. corresponds with very short acceleration's peak. Until now, no result is available in this relevant dynamic range in the literature and the aim of this study is to complete the material characterisation of the brain tissue as well as its modelling. In the present paper, we report new data at small strain from oscillatory experiments performed on porcine brain tissue and we propose an analytical modelling capable of fitting our results in a very large frequency range.

Material and methods

Porcine brain tissue was harvested from two six-months-old pigs obtained from a local slaughterhouse. Immediately, the complete brains were preserved in a Ringer-Lactate solution to prevent dehydration. Sagittal core-samples were cut using a cylindrical sharp tube. All slices were taken in corona radiata and contained only white matter to avoid inhomogeneity's effects. In the same time, to eliminate scattering of measurement data by potential anisotropy, all core-samples were cut in the same direction with their cylindrical axis perpendicular to sagittal plane. From these slices, 10-mm-diameter cylindrical samples were cut using a microtome with vibrating razor blade. Each slice is glued on a plate which is fixed in a vat filled with physiological saline solution and surrounded with melting ice. The disc-shaped specimens heights varied between 150 and 265 μm. Each sample was submerged in Ringer-Lactate solution and preserved at 6°C before the test to slow down the degeneracy of the tissue. Testing was completed within the day.

The experimental setup consisted in a custom-designed oscillatory shear testing device associated with signal generator followed of an amplifier to generate the input signal and with a charge amplifier to observe the output signal. Samples (diameter: 10 mm, thickness: 150 to 265 μm) were placed between 10-mm-diameter flat parallel plates. The prescribed translation was applied on the one plate by transmitting piezoelectrical oscillator, while the resultant shear force was measured on the other plate by receiving piezoelectrical oscillator. The treatment of both signals allows to obtain the complex shear modulus and the phase according to Cagnon (1980) [20]. Acquisition program permits to correct the radiate signal due to parasitic electrostatic interaction of piezoelectrical oscillators. The imposed displacement was 50 Å and lead a strain of 0.002% approximately. The frequency-range was from 0.251 Hz to 10000 Hz.

All the tests were made at body temperature, 37°C, and dehydration of the brain tissue samples was prevented by 100% humidity chamber during testing. Five samples were tested under an initial compression rate of 10% while four other samples were experienced under an initial compression rate of 0.6%. Table 1 provides an overview of experimental conditions.

Table 1: Overview of experimental test matrix. N°: number of brain, h: samples thickness, n: number of samples, p: initial compression rate, T: testing temperature

N°	h [µm]	n	p [%]	T [°C]
1	265	3	9	37
	150	2		
2	243	4	0.6	

Experimental results and modelling

First, the experience showed that both samples thickness and initial compression rate had no significant influence on the mechanical properties of the brain tissue as shown in Figure1a and b. Second, regardless initial compression rate and samples thickness, the storage (G') and loss (G") modulus increased significantly as a function of frequency. Figure 2 represents the mean values of real and imaginary parts of the complex shear modulus of porcine brain tissue for all tests with their standard deviation. After analysis of the curves, the elastic (G') and viscous (G'') component of the complex shear modulus increased from 0.455 ± 0.171 kPa to 133.9 ± 49.2 kPa and 0.133 ± 0.055 kPa to 63.7 ± 59.8 kPa respectively between 0.251 and 10000 Hz. Finally, two successive intersections between the two moduli were observed and indicated that the viscous behaviour was predominant between 250 and 3700 Hz.

In terms of constitutive model, the brain tissue can be described, at small strains, by means of a linear viscoelastic three-mode-Maxwell model (Figure 3) which is completely defined by four elastic moduli (G_i) and three viscosity moduli (η_i) (Figure 4). These parameters (Table 2) were calculated from equations (1) and (2) using a Levenbergh-Marquardt algorithm [21].

$$G' = G_0 + \sum_{i=1}^{3} G_i \frac{\left(\eta_i / G_i\right)^2 \omega^2}{1 + \left(\eta_i / G_i\right)^2 \omega^2} \tag{1}$$

$$G'' = G_0 + \sum_{i=1}^{3} G_i \frac{\eta_i / G_i \, \omega}{1 + \left(\eta_i / G_i\right)^2 \omega^2} \tag{2}$$

In the literature, the material description of the brain is often implemented via the relaxation modulus in the FE models of the human head. Usually, this modulus is obtained from the experimental storage modulus (G') by the empirical interconversion equation of Christensen (1982) [22] to convert test data in the frequency domain into the time domain. Therefore, Figure 5 shows that the relaxation modulus deduced from our data is well-fitted with material parameters calculated from experimental real and imaginary parts of the complex shear modulus.

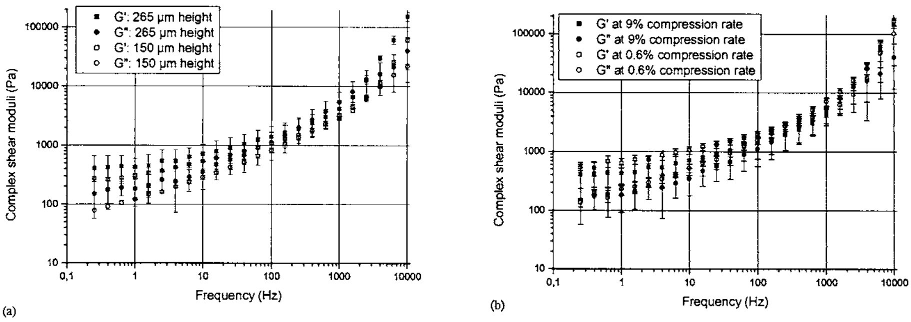

Figure 1: (a) Complex shear moduli versus frequency of the porcine brain tissue for 150 and 265 μm samples thickness and on initial compression rate of 9%.
(b) Complex shear moduli versus frequency of the porcine brain tissue for 9% and 0.6% initial compression rate.

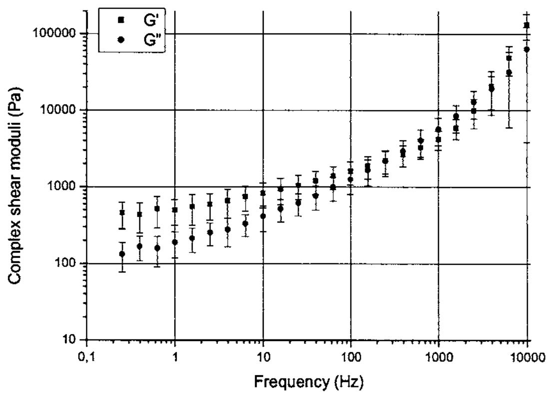

Figure 2: The mean frequency response of storage (G') and loss (G'') modulus of the white matter at 37°C. The disc-shaped samples heights ranged from 150 to 265 μm. The shear strain was 0.002% and the frequency ranged from 0.251 to 10000 Hz.

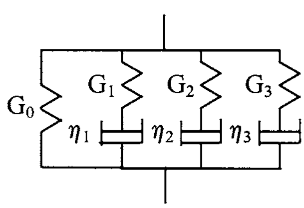

Figure 3: Linear viscoelastic three-mode-Maxwell model. G_i and η_i are respectively the purely elastic and purely viscous moduli of the model.

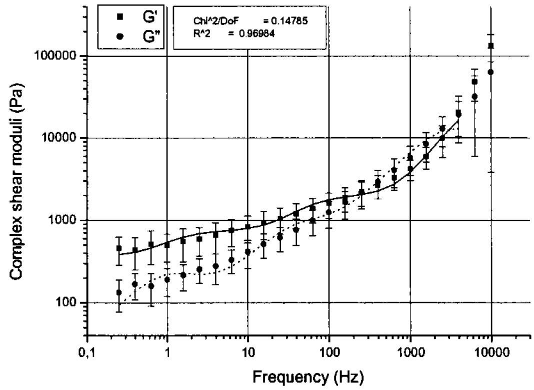

Figure 4: The mean frequency response of the complex shear moduli overplotted with the proposed constitutive model fit. Results fit accurately for a frequency range from 0.251 to 4000 Hz.

Table 2: Material parameters obtained from fitting the three-mode-Maxwell model on porcine brain tissue experimental shear data.

Mode i	**G_i (Pa)**	**η_i (Pa.s)**
0	359.9 ± 79.5	0
1	372.2 ± 75.9	56.5 ± 19.8
2	1217.4 ± 277.1	4.3 ± 1.2
3	25933 ± 8064	1.14 ± 0.16

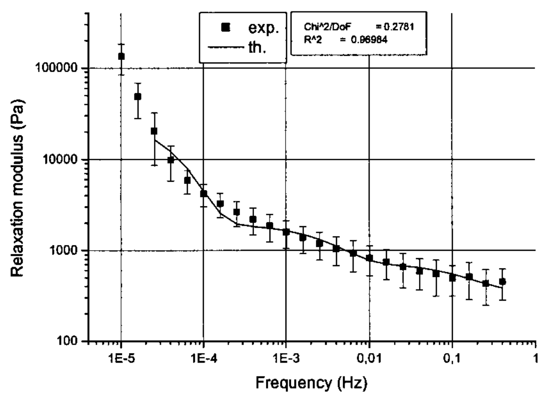

Figure 5: Relaxation modulus of the porcine brain tissue determined from experimental storage modulus (G') by the interconversion equation of Christensen [22] overplotted with the proposed constitutive model fit.

Discussion and conclusions

Dynamical behaviour of the brain is a great relevance to assess the risks of traumatic brain injury under impact loading. However, no result is available in the literature on the mechanical properties of the brain in shear corresponding to both relevant frequency ranges of accidental and ballistic direct impacts. An overview of literature data superimposed with our results is presented in Figure 6. We can observe that there is a great discrepancy in results which is likely due to different experimental protocols, different donors, different amplitude of applied strain, different post-mortem times and different species. However, by taking account of different thickness, our results are in agreement with Arbogast's results [12] who also studied the porcine brain tissue. Moreover, regardless of the differences in the relative magnitudes of the experimentally determined moduli, we can note that the general frequency-dependant behaviour of the porcine brain matched literature data excepted Brands results. Indeed, our findings bear remarkable resemblance to Shuck [7] and Arbogast [12] results which indicate an intersection of the two curves between 125 and 250 Hz. Another original result is the observation of a second intersection of G' and G" curves at 3700 Hz never reported in the literature. Our results are based on the linear viscoelastic theory which is justified by the amplitude of applied strain (0.002%). Indeed, this strain level is within linear range of the brain tissue determined by Brands [10] on the porcine brain tissue (< 1% of strain) or Shuck [7] on the human brain tissue (< 1.3% of strain). In view of the samples size, the inhomogeneity's effects are expected to be neglected in our study because all samples only consisted in white matter. For this reason, the reported material properties are to be considered as properties of the white matter only. So, future tests on grey matter might allow us to distinguish the mechanical properties of both matters in the future development of the numerical head model for a best biofidelity of the brain's response under impact loading.

In other respects, most of Finite Element Models have been used a standard 3-parameter Maxwell model fitted on Shuck's data [7] in shear on the human brain tissue. However, the modelling is still directly realised from the relaxation modulus deduced to the empirical interconversion equation of Christensen [22]. In other words, only elastic component of the complex shear modulus is taken into account in the numerical brain's model. As on example, Figure 7 shows Shuck's results [7] superimposed with a standard 3-parameter Maxwell model fit proposed by Zhang [23]. The shortcoming of this assumption leads to a bad modelling of the viscous behaviour of the brain tissue as shown in Figure 8. On Figure 8, we use the material parameters determined by Zhang [23] from direct fit of the relaxation modulus to calculate both storage and loss moduli. As explained, we note that the storage modulus (G') is correctly fitted but the loss modulus (G'') is less well-fitted.

Our study has three major limitations. First, brain tissue properties were determined from *in vitro* tests and the effects of *in vitro* versus *in vivo* mechanical behaviour of the brain have not been clearly elucidated and may be influenced substantially by the presence of the extensive pressurized cerebral vasculature [13] and the degeneracy's effects. Second, no scaling methods have been developed to facilitate extrapolation of biomechanical data from animal experiments to human being. Third, the brain tissue has to be also investigated in large strains to be used in a numerical head model under real impact conditions. Indeed, for higher strains as 1% the brain tissue behaves non-linear.

In conclusion, in this study we proposed a linear viscoelastic 3-mode-Maxwell model to fit new experimental data on white matter of the porcine brain tissue obtained at small shear strain and for both low and high frequencies. In this way, we expect to enhance the biofidelity of computational models and provide a better understanding for the mechanisms of traumatic brain injury.

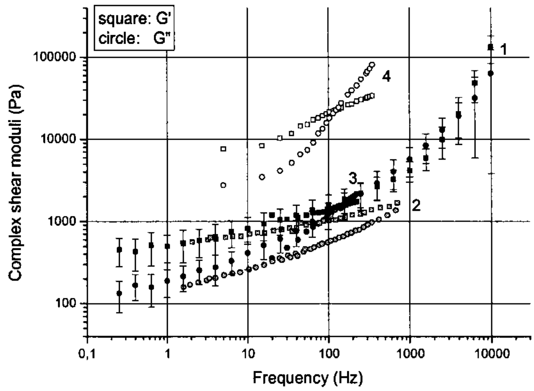

Figure 6: Complex shear moduli of measured results (1. porcine brain (ϵ = 0.002%)) and data from the literature: 2. porcine brain (ϵ = 1%) [10], 3. porcine brain (ϵ = 2.5%) [12], 4. human brain (ϵ = 1.3%) [7].

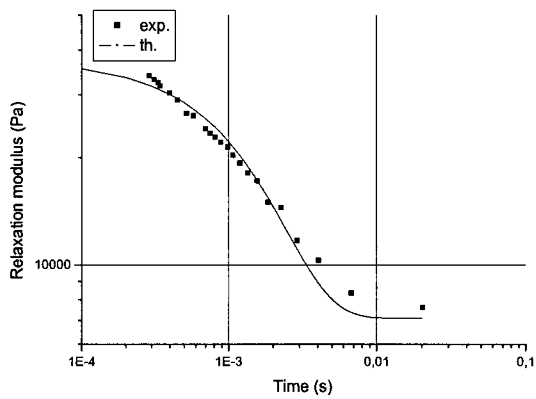

Figure 7: Relaxation modulus of the human brain tissue determined from Shuck experimental storage modulus (G') by Christensen [22] interconversion equation overplotted with Zhang's model (2001) [23].

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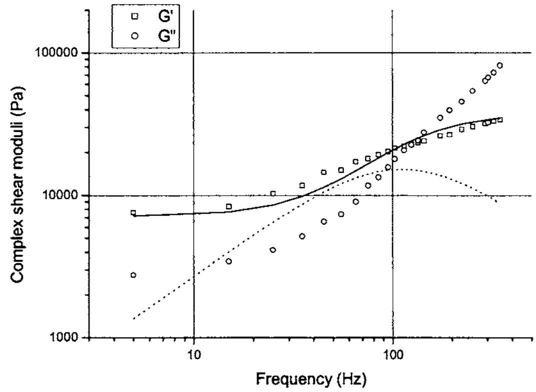

Figure 8: The mean frequency response of the complex shear moduli overplotted with 3-mode-Maxwell fit by using material parameters directly calculated from relaxation modulus.

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