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Mechanically Similar Gel Simulants for Brain Tissues

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ABSTRACT
Various gels have been used to evaluate the dynamic response of soft tissues. In dynamic experiments studying the brain response to impact loading, gel materials are used as surrogates in the exploration and calibration stages of the experimental research. Gels are simpler in handling and can be made in large quantities. In such experiments, it is clear that the dynamic mechanical behavior of the gels must be similar to that of the brain tissues they are representing. The objective of this study is to experimentally determine the mechanical properties of artificial gels over a wide range of strain rates, in addition to rheological analysis. The behaviors are then compared to that of the brain tissues under identical loading conditions to find candidate gel materials that respond to dynamic loading in a similar manner as the brain tissues. The gels investigated include Perma gel, collagen gel, and Agarose gel. Each type of the gels has multiple concentration levels. The results show that the mechanical properties of agarose gel with concentration of 0.4-0.6% are close to that of brain tissues.

INTRODUCTION
Different types of gels have been generally used for the cell culture of soft tissues [1]. Gel has unique feature which has drawn attention to the researchers. These gels are chemically and electrically neutral and have good elasticity. They are available easily and easy to fabricate. The mechanical behaviors of gels are important since these gels will be used to model the human head to study the injury mechanism. Agarose is a natural polysaccharide. It has the greatest gelling capacity. The contents of agarose vary depending on the source from which the agar was extracted. This fact is important as it will affect the physicochemical, mechanical, and rheological properties of agar [2]. Traditionally, ballistics gelatins have been used as human tissue simulants in a wide variety of impact and injury studies and provided a natural initial material [3]. The limitations of traditional gelatins include room temperature decomposition, translucence, and single use behavior. Perma-Gel^{TM} ballistics gelatin is characterized as a styrene-ethylene-butylene copolymer. The benefits of the Perma-Gel^{TM} gelatin over traditional gelatins include the superior transparency and lack of decomposition at room temperature. This allows for multiple uses of the gelatin by melting and recasting of the model. In this present study, the dynamic mechanical properties of gel materials at different strain rate have been characterized. Our concentration is on the agar gel.

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Dynamic mechanical analysis (DMA) on gel materials can be used to validate dynamic measurement as well as to provide better understanding for the mechanical response of the brain tissues to the dynamic loading in artificial brain tissue studies. DMA is a non-destructive technique to characterize the viscoelastic properties of materials. This instrument deforms a sample in a constant or step fashion or under fixed rate or in a sinusoidal oscillation (stress or strain); and measures the sample response as function of time or temperature. The mechanical response monitored in DMA instrument can be termed as elastic modulus, viscous modulus and the phase angle or phase shift between the deformation and response. The DMA compressive test provides information for low to moderate modulus materials such as foams, gel and elastomer. A DMA compression experiment has advantage to directly measure the frequency-dependency of the materials, and has a better comparability with dynamic material testing experiment. Chen et al [4] performed dynamic mechanical analysis on agarose gel to validate the magnetic resonance elastography measurement. They investigated systematically the effect of sample thickness, shear strain, testing frequency and compressive clamping strain in DMA shear modulus measurements. Their multi-frequency sweep data showed that the shear modulus increased slowly with the frequency.

MANUFACTURING METHOD

Several procedures for the preparation of gel material are available in literature (2). Here, we have fabricated the agarose gel. Gels with agarose (Agarose, BPI 365-100, Fisher Scientific, USA) concentration (weight/volume, w/v) of 0.6%, 0.5%, 0.4%, and 0.3% were prepared by dissolving powdered agarose in distilled water. The solution was sealed and heated for 15 mins at 90-95 ^{0}C and magnetically stirred; and finally cooled down to 35 ^{o}C (gelation temperature) which is then poured into a vertical mold for curing. The mold is kept at room temperature overnight to cure the gel. The sheet was kept in Ziploc bag to maintain humidity. The mold is designed to prepare 3 mm thick sheet. Here, we have discussed the fabrication of agarose gel only.

EXPERIMENTAL METHOD

Dynamic Mechanical Analysis

For the DMA experiment, cylindrical specimen of 16 mm diameter and 3 mm thickness were cut from the 3mm thick sheet with a punch. The samples are taken from the top and bottom part of the sheets to check the density difference of the material. Dynamic mechanical analysis was performed in frequency sweep compression mode at 30 ^{o}C temperature with DMA (Q800-0127, TA instrument) over a frequency range 0.1-100 Hz at constant amplitude of 15 μm with 1% strain. Samples were subjected to 0.01N preloading before testing. Storage modulus and loss modulus were recorded.

Mechanical Analysis (quasi static, low and intermediate strain rates)

Quasi-static, low and intermediate experiments were performed using a hydraulically driven machine (MTS810). The MTS machine was set to the mode of displacement control at five speeds, which correspond to the strain rate 0.01/s, 0.1/s, 1/s, 10/s and 100 /s. 25 lb load cell (1500 Standard low capacity, Interface, Arizona) was used for quasi-static and 50lb low impedance piezoelectric load cell (9712A50, Kistler Inc. Corp, NY, USA) was used for intermediate strain rates. Samples with OD 10 mm and ID 5 mm and thickness of 1.7 mm were taken from the sheet.

RESULTS AND DISCUSSION

Figure 1-3 show the experimental results obtained from uniaxial compression tests conducted at quasi-static and intermediate strain rates. At each strain-rate, five repeated experiments were performed under identical testing conditions. These results reveal that the each gel material exhibits non-linear stress-strain behavior. The gel's responses stiffen up with increasing loading rates, suggesting the rate dependency of the gels.

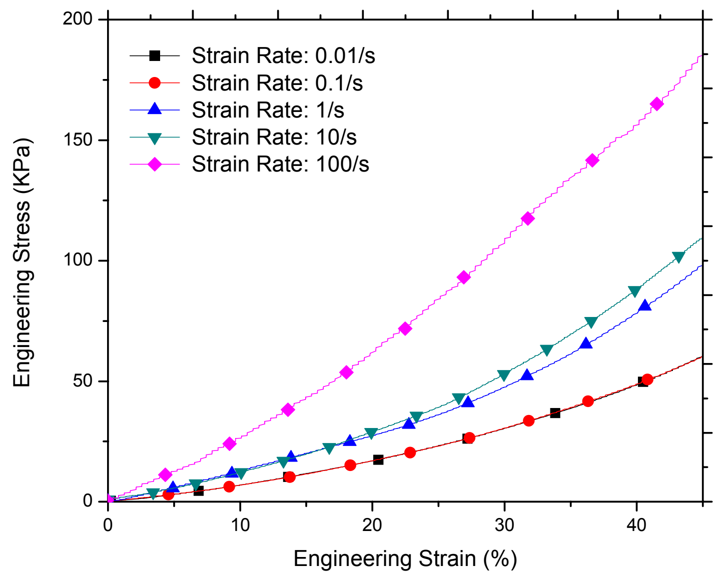


Figure 1: Compressive stress-strain response of Perma gel

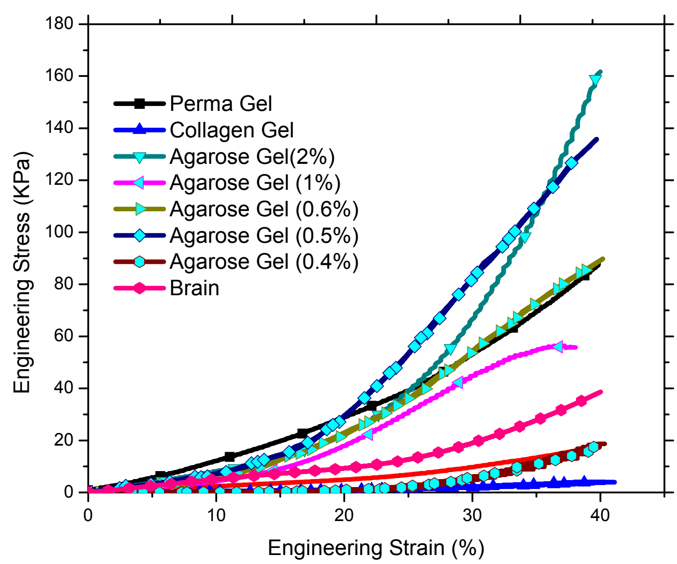


Figure 2: Average stress-strain curve of different gel materials at strain rate of 10/s

Figure 2 represents the average stress- strain curve of different gel materials at strain rate of 10/s. The brain response of bovine white matter was compared with the different candidate gels and it was found that agarose 0.4% has close mechanical properties compared to the brain tissue response. The DMA data shows that the elastic modulus and viscous modulus of the gel increase significantly with the frequency and gel concentration (Fig 2). These are consistent with the previous study [1, 2, 4, 5, 6 and 7]. Agarose 0.5% shows a decrease in modulus resulted from irreversible effects such as slippage or micro-cracking that occurred at high frequency

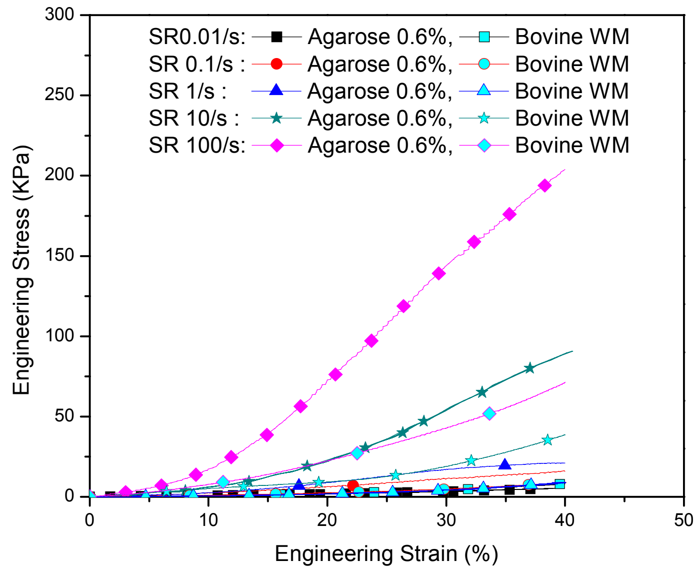
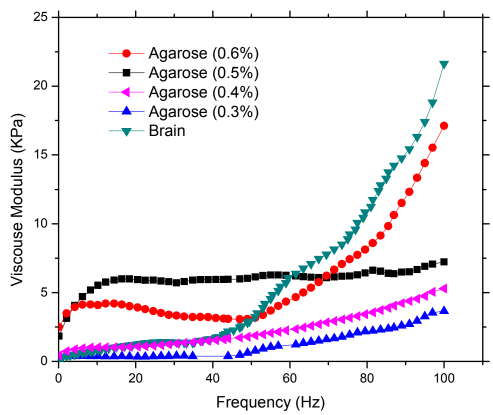


Figure 3: Comparison of stress-strain behavior of Agarose gel with concentration of 0.6% and brain white matter



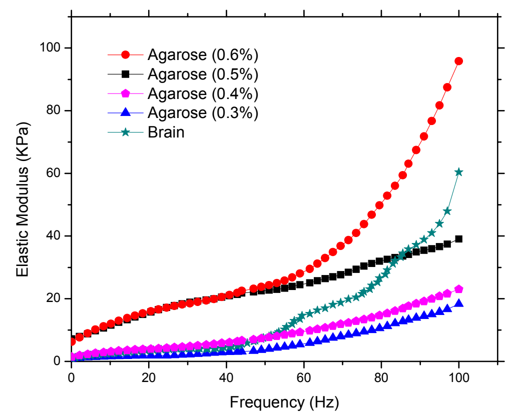


Figure 4: Average viscous and elastic modulus of agarose gel with different concentration as a function of frequency

CONCLUSIONS

This study involved manufacturing candidate gel material to simulate the brain tissue behavior. The mechanical behaviors of gels must closely match the tissues they are simulating to produce realistic results. In this study we experimentally determined the dynamic mechanical properties of gels with different integrants and concentrations to evaluate the stress-strain behavior of gel materials for wide range of strain and strain rates. The mechanical and rheological behaviors are then compared to that of the brain tissues under identical loading conditions to find candidate gel materials that respond to the loading in a similar manner as the brain tissues. This study evaluated the candidate gel materials for simulated brain tissues and agarose gel with concentration of 0.4~0.6% could be a good candidate for brain tissues. The mechanical properties of gel materials are critical for designing and performing the measurements on gels for various biomedical investigation purposes and also developing a model head for numerical simulations.

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