

Evaluation of Two Methods to Induce Mechanical Injury to Neuronal Cell Cultures

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INTRODUCTION

Disabilities due to traumatic brain injury are common, and a significant majority occurs as a consequence of automotive accidents (Morrison, 2006). Because this topic is of great interest, there are several methods by which neuronal injury of the brain can be tested. Two such methods are the pressure-driven system used by Ellis et al. (1995) and the biaxial stretch system used by Morrison (2006).

Ellis et al. utilized a pressurized system, where an elastomer-bottomed culture well was deformed outward by a transient pressure pulse. The deformation of the membrane was used to apply stretch injury to cultures of astrocytes, which are glial cells found in the brain or neonatal rat pups.

An alternative system used by Morrison et al. relied on a biaxial mechanism. By deforming the circular membrane along its plane, a uniform biaxial stretch was applied to slices of the hippocampus region of the brain of young rat pups. The slices incorporate all of the cells of the brain, including astrocytes, neurons, and the associated vascular cells.

The objective of this paper is to evaluate, via finite element analysis, the relative merits of each type of injury control system. The local strains induced in the membrane, and

presumably the cell culture, will be examined.

METHODS

A finite element model was developed to model the two systems. A circular mesh was used to represent the elastomer membrane in both of the models, with the loading conditions differing between the two.

In order to model the system used by Ellis, a pressure was applied to each element. This load pulse was of the form of a sinusoid. The membrane, which lay in the X-Y plane, would then deform in the Z direction. The outer edge of the membrane was restrained from all displacements but allowed to rotate.

The system used by Morrison was modeled by applying prescribed displacements to the nodes making up the outer edge of the membrane. A gravitational force was the only applied loading.

RESULTS AND DISCUSSION

The model of the pressure driven system was completed and validated against the data published by Ellis (1995). These results are shown in Figure 1. As shown, there was a good agreement between the finite element model and the experimental results (R^2 value of 0.996).

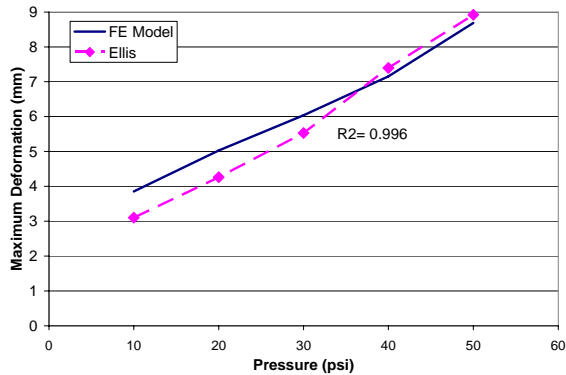


Figure 1: Pressure-driven membrane deflection as a function of the pressure pulse magnitude.

The strain profiles for each of the models were of particular interest, as tissue strain is believed to be a predictor of injury. Figure 2 shows a plot of the strain profiles as a function of the radial position on the membrane.

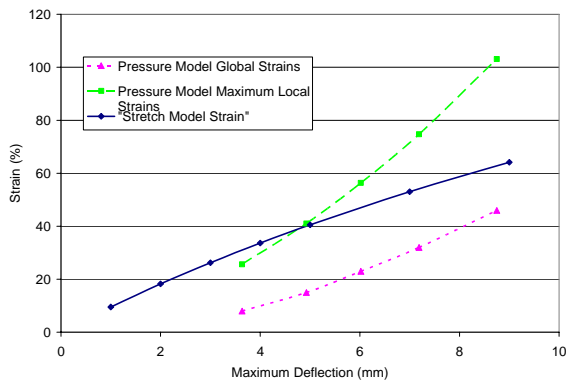


Figure 2: Strain profiles for each for the two model types.

The strain profile of the pressure driven system was the most complex. Both the average and maximum strains were non-linear. The strain also varied by the distance from the center.

The biaxial stretch model showed a near uniform distribution of strain across the entire membrane. Small differences in the element strains (< 1%) were attributed to the meshing pattern and considered insignificant.

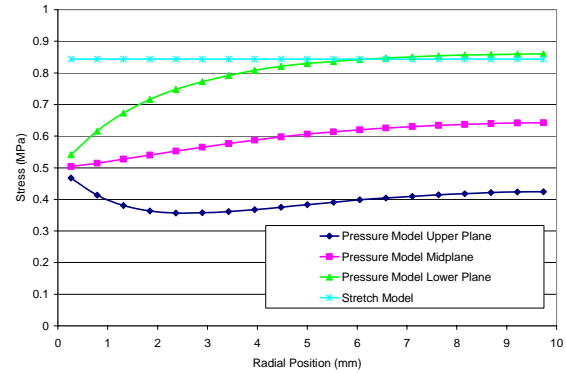


Figure 3: Stress profiles for the two models.

The stress profiles of the pressure driven model were found to vary at the different thicknesses. The membrane upper surface, which is in flexion, was under a smaller stress than the lower surface. The stretch model had equal stresses at all levels of thickness due to its lack of deformation in the Z-direction.

CONCLUSIONS

Two viable methods for inducing injury to cellular cultures were evaluated. The two devices possess differing stress and strain profiles. The strain profiles were uniform in the stretch model and were both variable and non-linear in the pressure driven model.

The virtues of the stretch model include its uniform strain profile and its flat, planar surface that makes video analysis possible. The pressure model is useful for its ease of use. There is no need to transplant cell cultures and the culture medium can be maintained if desired.

REFERENCES

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- Morrison et al. (2006) *Journal of Neuroscience Methods*, **150**, 2, 192-201
- LS-DYNA User's Manual*, Livermore Software Technology Corporation