Spinal Cord Modelling for Understanding and Preventing Injury

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Dear Professor Dell

I am pleased to submit this thesis, entitled, “Spinal Cord Modeling for Understanding and Preventing Injury”, as part of the requirement for the postgraduate degree of Master of Professional Engineering.

Yours Sincerely,

Jason Chan Chim Yuk
Abstract:

Spinal cord injuries often result from compressive loads. The spinal cord may be compressed by various scenarios including: fractured vertebrae, cancerous tumours and hematoma. Methods of computational biomechanics can be utilised to complement experimental studies. These simulations can increase our understanding of the mechanisms involved in spinal cord injuries and in the creation of injury criteria. Whilst many experimental studies have been conducted on the mechanical properties of the spinal cord in tension, very few have looked at the properties of the spinal cord in compression that are crucial for understanding the mechanisms of injury due to compressive loading. The aim of this study is to investigate the validity of a hyper-viscoelastic constitutive model of spinal cord white matter in uniaxial unconfined compression and to investigate whether this model can accurately predict the mechanical response of the spinal cord under transverse compression. A three-dimensional, non-linear explicit dynamics finite element model was created utilising the finite element analysis software ABAQUS. A model replicating a cylindrical sample of spinal cord tissue was created, consisting of 1920 elements with 2385 nodes. The elements used were eight-noded three dimensional hexahedral elements with reduced integration (element type C3D8R in ABAQUS). An unconfined uniaxial compression test for four different strain rates (0.005, 0.05, 0.5 and 5/sec) was simulated to determine the strain-stress curve. The general behaviour of the stress-strain curves obtained from the ABAQUS simulation was similar to the curves obtained experimentally. However the stress-strain curve obtained using the computational simulation differed by 15% compared with those recorded during the experiment. The validity of the constitutive model was also investigated in transverse compression. It was found that the hyper-viscoelastic constitutive model could be utilised in both axial and transverse compression.
Acknowledgements:

This work would not have been possible without the guidance and assistance of several individuals, who contributed in various ways over the course of the past year.

Firstly I would like to thank my supervisor, Professor Adam Wittek, for his help and guidance throughout this year. Thank you for your comments and advice while preparing not only this thesis, but also the other components of my final year project.

I would also like to thank my parents, and my cousin, Jeremy, for their support and guidance throughout the five years that I have been at university and particularly through this process of researching and writing this thesis. Your support of all my endeavours, whether academic, sporting, or musical is something that I will always be grateful for.

And finally, thanks be to my Lord and Saviour, Jesus Christ, for nothing is possible without him.
Abbreviations:

aCSF: ARTIFICIAL CEREBROSPINAL FLUID
CSF: CEREBROSPINAL FLUID
FE: FINITE ELEMENT
MRI: MAGNETIC RESONANCE IMAGING
NHP: NON-HUMAN PRIMATE
SCI: SPINAL CORD INJURY
SCIs: SPINAL CORD INJURIES
1. Introduction:

Worldwide, between 250,000 and 500,000 people suffer from Spinal Cord Injuries every year. In 2009 a study for the Victorian Neurotrauma Initiative estimated the cost of Spinal Cord Injuries (SCIs) in Australia alone is $2 billion per year (Access Economics 2009). A greater understanding of these injuries can help in the design of preventative measures, leading to a reduction of the domestic cost of spinal cord injuries.

SCIs can occur in various circumstances. The most common causes of SCIs worldwide are motor vehicle accidents (39.08%), falls (29.54%), gunshot wounds (13.01%) and sporting related accidents (8.39%), (NSCISC 2015). SCIs often result from axial and transverse compressive loads. Axial compression occurs from impacts to the crown of the head, typically occurring in vehicle rollover crashes and in football tackles (Bilston 1995). The spinal cord can be transversely compressed through many different scenarios including: fractured vertebrae, cancerous tumours and hematoma.

Experimental studies have already been conducted in an attempt to understand the mechanical response of the spinal cord. However, there are strict ethical constraints and technical limitations in such studies. Due to these limitations and constraints, there is greater emphasis on the creation of computer models that can simulate the mechanical response of the spinal cord. As methods and algorithms of computational biomechanics have improved, along with the increased computing capabilities of the 21st century, more reliable and efficient computer models can be created.
2. Problem Identification

The aim of this study is to improve our understanding of injury mechanisms of the spinal cord through computer simulations using the methods of computational biomechanics. The focus will primarily be on investigating a hyper-viscoelastic constitutive model that can be used to accurately model both the axial and transverse compression behaviour of the spinal cord tissue.

A number of studies have been conducted to determine the mechanical properties of the spinal cord tissue in tension. These studies have determined that spinal cord tissue is a non-linear viscoelastic material. However, the mechanical properties of the spinal cord tissue in axial and transverse compression are largely unknown. This is due to technical difficulties in characterising the mechanical properties of the spinal cord in transverse compression (Clarke 2011). Experimental studies conducted on brain and spinal cord tissue have shown that such materials are isotropic and tensile-compressive asymmetric (Miller & Chinzei 2002; Sparrey 2008).

The creation of realistic computer simulations is dependent on the use of accurate mechanical properties. As a high number of SCIs occur due to compressive loading, the mechanical properties of the spinal cord in compression must be understood to create realistic computer simulations. Due to the limitations of experimental studies, computer simulations are increasingly being used to complement experimental studies.

One such limitation is the ethical issues surrounding the use of post mortem human subjects. Even if post mortem human subjects can be obtained, there are great difficulties in obtaining large sample sizes to perform experiments. There are also technical limitations with experimental studies and, as a result, a greater insight into injury mechanisms can be obtained through computational simulations. Computer models can predict deformations, stresses and strains that cannot be determined in experimental studies (e.g. deformation of a spinal cord sample can only be measured on the sample surface) and can also predict the response of the spinal cord under different conditions/loadings. Computer models can also act as a precursor to future experiments, to increase the initial understanding of spinal cord injuries, and to also predict expected results of a future experiment, therefore reducing the necessity for preliminary testing to obtain results.
Due to the lack of knowledge surrounding the compressive behaviour of the spinal cord, computational simulations typically utilise the mechanical behaviour of the spinal cord in tension. As spinal cord tissue is considered tensile-compressive asymmetric, the validity of using the tensile properties of the spinal cord tissue in biomechanics models simulating compressive loading can be questioned.

Increasing our understanding of injury mechanisms can aid in the research and development of preventative countermeasures. Understanding the behaviour of the spinal cord tissue in compression is imperative in accurately modelling deformations occurring under compressive loading. Understanding the locations of maximum displacements can help in developing potential countermeasures to reduce the risk of injuries (e.g. protective equipment in sports).
3. Literature Review:

3.1. The Anatomy of the Cervical Spine and Spinal Cord:

An anatomical understanding of both the spine and spinal cord is important to this project, as it enables an anatomically correct computational biomechanics model to be created. The spinal cord is protected by 33 vertebrae, which combine to form the spine. The spinal cord can be considered a cylindrical bundle of nerve cell bodies that occupy the vertebral canal. The primary function of these nerve cell bodies is to process and transmit sensory information to the brain and motor information from the brain (Anatomica: The Complete Home Medical Reference 2010). The spinal cord is surrounded by the spinal meninges, which consist of the dura mater, the arachnoid mater and the pia mater (Moore & Dalley 1999). When the spinal cord is cut or damaged, it impairs the ability of the nerve cell bundles to transmit information to the brain and receive information from the brain. Depending on the severity of damage to the spinal cord, it can lead to minor impairment such as temporary numbness in extremities to major impairment such as paraplegia and tetraplegia.

3.2. Geometry of the Spinal Cord:

To create an anatomically correct model of the spinal cord, the geometry of the spinal cord must also be known. Determination of the physical properties of the spinal cord can be conducted through magnetic resonance imaging (MRI) or measuring cadaver samples. Measurements obtained from MRI studies differ greatly from those using cadaver samples. For example, at the C4 level, one study using cadaver samples obtained an average cross sectional area of 74mm$^2$, however using MRI an average cross sectional area of 121.8mm$^2$ was recorded (Ko et al. 2004; Sherman, Nassaux & Citrin 1990). The large differences in cross sectional area may be partially attributed to the irregular shape of the spinal cord. Methods utilised to calculate the cross sectional area varies in the literature. The study conducted by Sherman, Nassaux & Citrin (1990) calculated the area as the product of the transverse and anterior-posterior diameters of the spinal cord, which would result in an overestimation of the area (Sherman, Nassaux & Citrin 1990). In other studies, the method utilised to calculate the area has not been stated, making it difficult to determine the accuracy of the results (Ko et al. 2004; Prasad et al. 2003).

Another factor influencing the differences in cross sectional area may be due to sampling methods. Due to the difficulty in obtaining spinal cord samples, sample sizes for the studies
using the cadavers were much smaller than the studies using MRI. Studies measuring cadaver tissue samples give little indication as to the method/s used to preserve the spinal cord samples. Incorrect preservation of samples may cause dehydration, leading to shrinkage of the spinal cord cross section, therefore altering results. Both human and instrumentation errors could be present in both of the methods utilized. Human error could exist as a result of the difficulty in measuring the MRI images (MRI images shown in the literature are low resolution, making it difficult to determine the extent of the spinal cord) and difficulty in measurement of the cadaver sample, due to the size of the spinal cord. The low resolution of the MRI images is also a source of instrumentation error. Errors could also be introduced when measurements of the spinal cord were recorded, if measurement tools are not calibrated correctly.

3.3. Mechanical Properties of the Spinal Cord and Spinal Cord Tissue:

To accurately predict the response of the spinal cord using computational simulations, the mechanical properties of the spinal cord tissue must be known. Many experimental studies have been conducted to determine both the mechanical and physical properties of the spinal cord tissue under tension.

There are two methods to determine the mechanical properties of the spinal cord. The first utilises solely experimental studies, and the second a combination of computer simulations and experimental studies.

The first method of determining the mechanical properties of the spinal cord/spinal cord tissue is through experimental studies, primarily through tensile testing due to the simplicity of obtaining results using this process. These experiments are conducted by fixing a spinal cord sample and applying a force to one end to cause deformation of the sample. The Young’s modulus of the spinal cord can then be found using the average cross sectional area, the tensile force exerted on the sample and the change in length of the sample.

Whilst the testing method is simple, the results between different experiments differ greatly with Young’s moduli ranging from 0.012MPa to 1.37MPa (see Table 1.).
The differing values of experimentally obtained mechanical properties can be partially attributed to the non-linearity of spinal cord tissue. Studies conducted by Lynne E. Bilston using both rat and human samples, have shown that spinal cord tissue exhibits a ‘J-Shaped’ stress-strain response (Bilston & Thibault 1995). From Table 1, it can be seen that samples were tested under various loading conditions (different strain rates), with studies using a higher strain rate producing a much higher value for the moduli of the spinal cord/spinal cord tissue.

The specimen preservation method used can also influence results. Incorrect preservation techniques can lead to dehydration of the sample. Dehydration of the sample can alter the material properties of the spinal cord tissue (Bilston & Thibault 1995; Fiford & Bilston 2004). Post-mortem delay can also affect the accuracy of results, with studies conducted on brain tissue showing that the stiffness remains unchanged up to a delay of 6 hours, however the stiffness of brain tissue increased by approximately 14% each subsequent hour (Sparrey 2008). Some studies only rejected samples if more than 48 hours had elapsed since death, which could increase the stiffness of the spinal cord tissue by up to 500% (Mazuchowski & Thibault 2003). Many studies are also vague about both the methods used to preserve samples and post-mortem delay, introducing concern about the results obtained.

Preconditioning of the sample can also affect the results obtained. Preconditioning is predominantly used as a method to allow samples to undergo multiple tests, however it is also believed to create a consistent pre-testing state and reduces variability between samples (Clarke 2011). Some studies state that preconditioning should be performed at the same strain rate as any testing to be conducted (Cheng, Clarke & Bilston 2009). If testing is conducted using a high strain rate, preconditioning at this strain rate may damage the sample, affecting the results. The use of preconditioning has also been criticised due to spinal cord tissue being considered as a hyperelastic/viscoelastic material (models which predict history-dependent behaviour), and therefore, preconditioning can alter the mechanical behaviour of the sample.
To compare the mechanical properties between studies, it must be ensured that the samples tested are anatomically similar. Some studies have been conducted utilising the spinal cord with the spinal meninges intact whereas others have obtained the mechanical properties of the spinal cord tissue white and grey matter alone by removing the spinal meninges. Experimental studies have determined the dura mater has a Young’s modulus of the order 1MPa (Maikos, Elias & Shreiber 2008). Testing of a sample with the spinal meninges had the same order of Young’s modulus (~1MPa) as the dura mater (Bilston & Thibault 1995). The Young’s modulus for rat brain tissue is of the order 0.1-1kPa (brain tissue and spinal cord tissue are assumed to have similar mechanical properties), approximately three orders below the Young’s modulus of the spinal cord with spinal meninges (Gefen et al. 2003).

Whilst experimental studies of the mechanical properties of spinal cord tissue are extensive, it is evident that it is often difficult to compare results from different studies, due to the inconsistency of both the methods used and the differences between the samples/specimens. Many factors can lead to differences in the calculation of mechanical properties, for example: preservation technique, testing methods, strain rate and preconditioning. This is due to the lack of commonly accepted standards/practices for tissue testing.

The second method involves replicating an experimental study using a computer simulation. This method could be used to complement indentation compression experimental studies, because of the difficulty in determining mechanical properties with studies of this type. The mechanical properties of human tissue have been determined using this method (Moerman et al. 2009). Understanding the mechanical properties under indentation compression is important, as indentation of the spinal cord by vertebrae fragments accounts for a high percentage of spinal cord injuries (Young 2009). When the experimental study is conducted, the indentation force on the specimen and the displacement due to this force is recorded. Using a computer simulation utilising the principles of computational biomechanics, the experiment is replicated with an estimate for the material parameters. The parameters are then altered until the displacement results achieved in the experimental study are achieved in the computational model.

Whilst studies have been conducted on the behaviour of the spinal cord under tension, few have been conducted under compression to determine the mechanical properties. This means that the compressive behaviour of the spinal cord is not well known. The lack of experimental studies can be partially attributed to experimental difficulties. One study on the compressive behaviour of the spinal cord was conducted by Sparrey, which compressed porcine spinal cord white matter under four different strain rates. It was determined that under compressive
loading, the spinal white matter exhibits a ‘J-Shaped’ stress-strain response, similar to under tensile loading. It was found that a first order Ogden hyperelastic model along with a three-term Prony viscoelastic model was the best fit.

3.4. Causes of SCIs

A definite mechanism that causes SCIs is yet to be discovered. Experimental studies have been conducted in attempt to understand the conditions required to cause SCIs. Some have focused on the relationship between spinal cord displacement and level of impairment in rats, others on the interaction between velocity and spinal cord compression in determining the severity of SCI in ferrets, whereas other studies have focused on the damage to axons and neurons after an SCI (Behrmann et al. 1992; Fehlings & Tator 1995; Kearney et al. 1988). Different methods are used to attempt to quantify the level of SCI sustained. The most commonly used method is the Tarlov scale, which is used to grade recovery of locomotor function (Behrmann et al. 1992). Due to the ambiguity of this scale, it is difficult to compare the severity of injury caused by each method. An understanding of the conditions required to cause SCIs could result in the implementation of solutions preventing those conditions from occurring, and thus attempt to reduce the number and severity of spinal cord injuries.

3.5. Biomechanical Analysis of SCIs using Computational Simulations:

Many studies have been conducted on computational biomechanical analysis of the spinal cord. The replication of SCIs is often conducted using finite element (FE) models. Some examples of injuries replicated using computational simulations are: SCIs in rats caused by weight drop and SCIs caused by burst fracture of the human spinal cord (Greaves, Gadala & Oxland 2008; Maikos et al. 2008). However, the accuracy of some studies can be questioned, as the FE models created are often not validated.

The American Society of Mechanical Engineers defines validation as ‘the process of determining the degree to which a model is an accurate representation of the real world from the perspective of the intended uses of the model’ (Guide for Verification and Validation in Computational Solid Mechanics 2006). There are two types of model validation, indirect and direct. Indirect validation is the comparison between experimental results (from sources such as literature and clinical studies) and model predictions, when the exact experimental conditions are not known and thus cannot be input into the model (Henninger et al. 2010). Studies conducted on computational simulations have utilized indirect validation, as literature
on experimental studies lack key data (e.g. dimensions of the spinal cord). Caution is needed when applying the results of experimental studies in validation of computational biomechanics models of the spinal cord.
4. Model Formulation:

4.1 Description of Experimental Studies:

The primary aim of this study is to determine whether the hyper-viscoelastic constitutive model suggested by an experimental study conducted by Sparrey and Keaveny (2011) is suitable for use in a FE model in both axial and transverse compression.

The experimental study conducted by Sparrey and Keaveny was chosen as it is one of the few studies to quantify the unconfined compression response of the spinal cord white matter (Sparrey & Keaveny 2011).

Sparrey and Keaveny (2011) conducted an unconfined uniaxial compression test on the porcine spinal cord white matter. In this study, porcine spinal cord white matter was obtained by harvesting spinal cords from freshly sacrificed Yorkshire pigs. The spinal cords were then segmented into 1.5mm transverse slices and 3mm diameter samples were cut from these slices using a biopsy punch. The force on the sample was determined by using an Electroforce 3200 equipped with a 10N load cell. The samples were compressed with aluminium plates and kept hydrated with drops of artificial cerebral spinal fluid (aCSF). The samples were then tested at four strain rates (5.0, 0.5, 0.05 and 0.005/sec) to a maximum strain of 0.4 (Sparrey & Keaveny 2011). A hyper-viscoelastic constitutive model was developed from the resulting stress-strain curves. The suitability of this hyper-viscoelastic constitutive model was investigated by simulating this experiment using a computational biomechanics model implemented using ABAQUS finite element code (non-linear explicit dynamics finite element solver).

Due to the isotropic nature of spinal cord tissue, the suitability of this hyper-viscoelastic constitutive model in transverse compression was also investigated by simulating the experimental study conducted by Fradet et al. (2016). This experimental study was selected as it is one of the few studies to report stress-strain curves under transverse compression. This allowed for comparison of stress-strain curves between the experimental study and the hyper-viscoelastic constitutive model. The limited number of studies of this nature reporting stress-strain curves is largely due to experimental difficulties (Clarke 2011). In this study porcine spinal cords were harvested from freshly sacrificed Land Race pigs. The dura mater was removed and the spinal cord samples were then cut into 25mm longitudinal samples. The samples were then transversely compressed using a 5mm diameter impactor, under three different strain rates (50, 5.0 and 0.5/sec) to a maximum strain of 0.9. Force and displacement
data was obtained using a 225N force transducer and displacement transducer (Fradet et al. 2016).

4.2 Description of Finite Element Model:

To analyse the results obtained from the experimental studies and to determine the appropriateness of the constitutive model proposed in this study in axial and transverse compression, three dimensional, non-linear dynamic finite element models were created. The commercially available finite element software package ABAQUS was used.

Description of Spinal Cord White Matter:

As shown in the literature review, neurological tissue has been represented by a variety of models such as; linear elastic and hyper-viscoelastic. Whilst a variety of models can be utilised, literature suggests that a combination of hyperelastic and viscoelastic models best represents the spinal cord tissue. The material behaviour of the spinal cord tissue was incorporated in the computational simulation using a first term Ogden hyperelastic model and a three-term Prony series viscoelastic expression.

The Ogden model is a hyperelastic model that is used to describe the non-linear stress-strain behaviour of materials such as rubbers and biological tissue. Hyperelastic models define the strain energy stored in the material per unit of reference volume as a function of the strain at that point in the material (ABAQUS/CAE 6.13 User's Manual 2013). The Ogden model represents strain energy density as:

\[
U = \sum_{i=1}^{N} \frac{2\mu_i}{\alpha_i^2} (\tilde{\lambda}_1^{\alpha_i} + \tilde{\lambda}_2^{\alpha_i} + \tilde{\lambda}_3^{\alpha_i} - 3) \quad (1.1)
\]

A first order Ogden model (N = 1), reduces the strain energy density equation to:

\[
U = \frac{2\mu_0}{\alpha_i^2} (\tilde{\lambda}_1^{\alpha_1} + \tilde{\lambda}_2^{\alpha_1} + \tilde{\lambda}_3^{\alpha_1} - 3) \quad (1.2)
\]

Where \(\tilde{\lambda}\) is the deviatoric principal stretch, \(\mu_0\) is the initial shear modulus and \(\alpha\) is an Ogden material parameter.
The Prony series for a viscoelastic material is given by the following formula:

\[ g_R(t) = \sum_{i=1}^{N} \tilde{g}_i \frac{\tau}{\tau_0} \left( 1 - e^{-\frac{t}{\tau_0}} \right) \]  \hspace{1cm} (1.3)

Where \( g_R(t) \) and \( \tilde{g}_i \) are shear relaxation modulus ratios, and \( \tau_0 \) is the relaxation time.

Table 2 shows the coefficients for the hyperelastic and viscoelastic models obtained by Sparrey and Keaveny (2011). The density of the white matter was taken as 1045kg/m\(^3\).

<table>
<thead>
<tr>
<th>( \mu_1 ) (kPa)</th>
<th>( \alpha )</th>
<th>( g_1 )</th>
<th>( \tau_1 )</th>
<th>( g_2 )</th>
<th>( \tau_2 )</th>
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</table>

**Table 2**: Hyper-viscoelastic material parameters

**Incompressibility:**

Soft tissues are typically assumed to be incompressible, however ABAQUS does not allow the assumption of a fully incompressible material. This is because ABAQUS has no mechanism to impose an incompressible constraint at each material calculation point (*ABAQUS/CAE 6.13 User's Manual* 2013). To introduce this incompressibility it was initially assumed that the Poisson’s ratio was 0.495. The compressibility of a hyperelastic material can be input in ABAQUS through the parameter D, which is given as:

\[ D = \frac{2}{K_0} = \frac{3(1 - v)}{\mu_0(1 + v)} \]  \hspace{1cm} (1.4)

**Element Type:**

Selecting the correct element in computational simulations is important, as they can affect both the type and accuracy of the results. It can also control the computational cost. Each element is described by five aspects; family, degrees of freedom, number of nodes, formulation and integration. Eight-noded three dimensional hexahedral continuum elements with first order reduced integration and hourglass control were created on the spinal cord tissue.
The pia and dura mater were modelled as shell-membrane elements rather than shell elements, as shell membrane elements do not have any bending stiffness (*ABAQUS/CAE 6.13 User’s Manual* 2013). Four-noded quadrilateral shell membrane elements were utilized with first order reduced integration and hourglass control.

**Finite Element Mesh:**

Mesh element quality is important as poorly shaped elements can result in solution errors. Mesh of the spinal cord tissue samples were generated using the in-built meshing tool in ABAQUS. Whilst third-party meshing programs could have been used (e.g. HyperMesh), an effective mesh was created in ABAQUS by partitioning the spinal cord samples into quarters. For medium/coarse meshes, the in-built meshing tool in ABAQUS was sufficient, however for finer meshes, third-party software would be required, as poor quality elements are created.

![Figure 1: Mesh created using ABAQUS by partitioning cylinder](image)

**4.3 Uniaxial Unconfined Compression:**

To replicate the study conducted by Sparrey and Keaveny (2011), a cylinder was created in ABAQUS. The cylinder had a diameter of 3.0mm and a height of 1.5mm, congruent with the samples tested experimentally.

**Loading and Boundary Conditions:**

To model the physical experiments accurately, the correct loading and boundary conditions are required. Typically in axial compressive and tensile tests, a constant velocity is applied to the sample. Thus, the loading was described by prescribing a velocity on the top surface of the tissue sample. The velocity was calculated from the maximum strain and the strain rate at
which the sample was compressed. The maximum strain applied to the sample in the experimental study was 0.4, thus with an initial sample height of 1.5mm, a displacement of 0.6mm is required to produce this strain. To replicate the strain rates of 5/sec, 0.5/sec, 0.005/sec and 0.0005/sec, the time over which this maximum displacement was required was calculated. The velocity applied to the sample could then be calculated.

In a uniaxial unconfined compression test, the aim is to limit friction between the testing plates and the specimen ensuring that the sample can deform freely along the x-y plane. Artificial cerebrospinal cord fluid was utilized to minimize friction (Sparrey & Keaveny 2011). In order to replicate these boundary conditions in ABAQUS, the sample was not constrained in the x-y plane. The bottom surface of the spinal cord sample was not allowed to move up or down, thus the nodes on this surface were fixed in the z-direction.

![Figure 2: Boundary conditions on the bottom of sample](image)

4.4 Transverse Compression:

The experimental study conducted by Fradet et. al (2016) investigated the behaviour of strain rate dependent behaviour of the porcine spinal cord under transverse compression. The experimental study removed the dura mater from the spinal cord, so only the spinal cord and pia mater were modelled, as CSF leaks when the dura mater is removed.

The spinal cord was idealised as an elliptic cylinder, with an anterior-posterior diameter of 6.4mm, a transverse diameter of 9.4mm and a total length of 25mm, congruent with the experimental study.
The experimental study by Fradet et al. (2016) was simulated in ABAQUS by creating a cylindrical impactor of diameter 5mm and a rectangular plate of height, 4mm, width, 10mm and length, 30mm. It was assumed that both the impactor and the plate were made of steel (E = 200GPa, ν = 0.3, ρ = 8050kg/m³), as it was not specified in the literature. The pia mater was assumed to be a linear elastic material, with a Young’s modulus of 2.3MPa, a Poisson’s ratio of 0.45, a density of 1075kg/m³ and a thickness of 12µm (Ozawa et al. 2004).

*Loading and Boundary Conditions:*

In the experimental study conducted by Fradet et al. (2016), there were no constraints imposed upon the spinal cord sample. The plate was fixed in all directions and the impactor was given a velocity that was dependent on the strain rate.

The interaction between the pia mater and the spinal cord was modelled as general contact, with a shell-solid coupling to represent that the pia mater is fixed to the spinal cord white matter. The interaction between the pia mater and the testing apparatus (impactor and plate) were modelled as frictionless, as the experimental study utilised saline solution to minimise friction between the testing apparatus and spinal cord sample.
The strain rates imposed onto the sample were 0.5 and 5/sec. In the experiment conducted by Fradet et al. (2016) a strain rate of 50/sec was also imposed upon the sample, however the accuracy of the hyper-viscoelastic constitutive model under strain rates above 5/sec is not known, thus the strain rate of 50/sec was not imposed. The maximum strain caused by the impactor in the experiment was 0.9 and the sample had an anterior-posterior diameter of 6.4mm, thus the total displacement of the impactor required was 5.76mm. To replicate the strain rates of 0.5 and 5/sec, the time over which the maximum strain was required was calculated. The velocity of the impactor could then be calculated.

4.5 Uniaxial Tension:

Spinal cord injuries rarely occur solely due to compression. The validity of this hyper-viscoelastic model in tension needs to be verified. This was achieved through replicating two uniaxial tensile experiments; one with the pia mater attached to the spinal cord and one with the pia mater removed.

*Loading and Boundary Conditions:*

For tensile testing of the spinal cord, the aim is to prevent slippage between the specimen and the clamps. This is typically achieved by using an adhesive to fix the spinal cord ends to clamps. To replicate these boundary conditions in ABAQUS, the bottom of the spinal cord and pia mater were fixed in all directions and the top surface of the sample was fixed in the x-y direction.

![Figure 5: Boundary conditions on bottom of spinal cord for tensile testing](image)

The dimensions of the sample were kept the same as the dimensions of the spinal cord in the transverse compression experiment. The velocity imposed on the top of the spinal cord
sample was calculated in a similar manner to both the axial and transverse compression, with strain rates of 0.5 & 5/sec and a maximum strain of 0.1.

Table 3: Summary of loading conditions

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<th>Compression</th>
<th>Strain Rate (1/s)</th>
<th>Peak Strain</th>
<th>Sample Length (m)</th>
<th>Max Displacement (m)</th>
<th>Time (s)</th>
<th>Velocity (m/s)</th>
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<th>Strain Rate (1/s)</th>
<th>Peak Strain</th>
<th>Sample Depth (m)</th>
<th>Max Displacement (m)</th>
<th>Time (s)</th>
<th>Velocity (m/s)</th>
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4.6 Investigation of Injury Criteria:

Finally, to investigate the creation of injury criteria, the transverse compression model was utilised to represent the compression of the human spinal cord. The spinal cord was scaled to the geometry of the human spinal cord at the C4 level, with an anterior-posterior diameter of 8.7mm and a transverse diameter of 14mm (Sherman, Nassaux & Citrin 1990). The dura mater and the CSF were not modelled for simplicity.

Figure 6: Dimensions of human spinal cord at C4 level
Loading and Boundary Conditions:

An experimental study conducted by Salegio et al. (2016) investigated a unilateral spinal cord contusion model in non-human primates (NHPs). This study was conducted on Macaca mulatta in-vivo by attempting to cause SCIs in primates by indenting the spinal cord under different loading conditions.

Two separate experiments were conducted, looking at SCIs caused by applying the indentor with a velocity of 0.27m/s over a period of 0.02 seconds and SCIs caused by applying the indentor with a velocity of 0.58m/s over the same time period (Salegio et al. 2016). Only the velocity of 0.27m/s was simulated utilising the FE model, as the NHP subject that was subjected to the velocity of 0.58m/s had a spinal deformity, which resulted in an angled impact. The boundary conditions for this FE model remained the same as the transverse compression model, with only the plate being fixed.
5. Results & Discussion:

5.1 Mesh Convergence Study:

To determine an appropriate mesh size, the results obtained with three different mesh sizes were analysed. A coarse, intermediate and fine mesh was created to evaluate mesh convergence. Whilst a finer mesh gives more accurate results, a more coarse mesh can lead to lower computational times. For the uniaxial compression model, the difference in stress obtained with the fine and intermediate mesh was less than 1% and the difference in stress between the dense and fine mesh was less than 2%. This gives evidence that the mesh has converged and that the results are satisfactory. Whilst there were small differences in the results obtained, there was a great reduction in computational times as a result of using an intermediate mesh as opposed to a fine mesh. The computational time for the intermediate mesh was 12% of the required computational time for the fine mesh. Thus, an intermediate mesh was utilised due to the reduced computational times whilst giving results very similar to those obtained with the fine mesh. Similar studies were conducted with the tensile model and the transverse compression models to determine convergence mesh sizes.

![Mesh Convergence Study](image)

**Figure 7:** a) Coarse mesh b) Intermediate mesh c) Fine mesh.

<table>
<thead>
<tr>
<th>Model</th>
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<th>Nodes</th>
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<tr>
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<td>2385</td>
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<tr>
<td>Transverse Compression (Porcine Geometry)</td>
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</tr>
<tr>
<td>Tension</td>
<td>5084</td>
<td>5922</td>
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</table>

**Table 4:** Number of nodes and elements utilised for each model
5.2 Uniaxial Unconfined Compression:

Figure 8 shows the comparison of the experimental stress-strain curve with the results obtained with computer simulations using a hyper-viscoelastic constitutive model of spinal cord white matter for the strain rates 0.5 and 5/sec. The stress was calculated by the sum of the reaction forces at the fixed end of the sample and dividing this by the cross sectional area and the strain calculated by the change in sample length divided by the initial sample length.

![Stress-Strain Comparison](image)

**Figure 8:** Comparison of stress-strain curves

It can be seen that the general behaviour of the stress-strain curve obtained via the FE model was similar to the behaviour obtained by the experimental study. The stresses calculated by the FE model for strain rates of 0.5 and 5/sec were approximately 15% higher than that measured in vitro. However, for the lower strain rates, the model was inaccurate, with stresses differing by over 75% and thus it would not be advised to use this constitutive model in ABAQUS for low strain rates.

The inaccuracy at low strain rates could be due to the miscalculation of the Prony series coefficients, as the viscoelastic Prony series dictates the response of the sample under different strain rates. Typically a Prony series is fitted to strain-relaxation curves, however it can be fitted to stress-strain curves. The three-term Prony series was fitted to the data, using iterative methods, however the fit was only optimised for two strain rates.

The results obtained experimentally also had an uncertainty of approximately 20%. This is primarily due to the difficulties in cutting the samples, as the samples of porcine spinal cord white matter had a diameter of only 3mm. There is also difficulty in the measurement of such small samples, due to both human and instrumental errors. The computational model also assumed frictionless contact between the sample and plates, however it is unlikely that the application of aCSF to the sample and the plates would make the interface between the
sample and plate completely frictionless. Depending on the coefficient of friction, friction can alter the reaction force of a sample by over 15% (Miller 2005).

5.3 Transverse Compression:

Figure 9 shows the comparison of the experimental stress-strain curve with the results obtained with computer simulations using a hyper-viscoelastic constitutive model of spinal cord white matter. Engineering stress and strain could not be calculated in this experiment, as the load was not applied to the entire sample of spinal cord. The stress was calculated by dividing the reaction force at the bottom of the indenter by the cross-sectional area of the indenter. The strain was calculated by the change in anterior-posterior diameter of the sample and dividing by the original diameter.

![Figure 9: Comparison of stress-strain curves](image)

The general behaviour of the stress-strain curve obtained via computer simulation is similar to the behaviour obtained by the experimental study. However, the stresses obtained utilising the hyper-viscoelastic constitutive model differed by 20% when compared to those obtained experimentally. Taking into account the variability of spinal cord tissue, the difference in stress in my opinion, is acceptable. As discussed in the literature review, the mechanical properties of the spinal cord tissue can be affected by the age and species of the samples tested, preservation methods utilised and the time elapsed between the death of the animal and testing. A comparison of the tissue samples utilised by Sparrey and Keaveny (2011) and Fradet et al. (2016), shows differences in species, age and weight of the porcine samples, along with differences in preservation method and the time between death of the sample and testing. A combination of these factors could lead to the differences seen in the values of the...
stress-strain curve. Another factor that could cause the difference in stress is an experimental limitation of the study conducted by Sparrey & Keaveny (2011). The cutting of such small samples may result in obtaining localised mechanical properties of the spinal cord, which may not represent the mechanical properties of the entire spinal cord.

5.4 Uniaxial Tension:

Figure 10 shows the stress-strain curves obtained from the tensile test simulation with and without pia mater.

![Stress-strain curves from tensile simulation](image)

**Figure 10:** Stress-strain curves from tensile simulation (no pia mater – LHS, with pia mater – RHS)

From the stress-strain curves obtained from the computational model, the average Young’s modulus of the sample without pia mater was approximately 4.5kPa and with pia mater approximately 18kPa. The values of Young’s modulus only varied slightly as a result of the differing strain rates. A study conducted on the mechanical properties of the pia mater found that the Young’s modulus for the spinal cord with pia mater was 16kPa and without pia was 5kPa (Ozawa et al. 2004). The slight underestimation of the Young’s modulus of the spinal cord without pia could be as a result of the fact that the white and grey matter were assumed to have the same mechanical properties.

As shown in the literature review, the Young’s modulus calculated from different experimental studies varies from 0.017MPa to 1.37MPa. In the FE model, the Young’s modulus obtained through a tensile simulation of the spinal cord with pia mater is highly dependent on the choice of material properties of the pia. If the pia mater were assigned a much higher Young’s modulus, the Young’s modulus of the combined pia and white matter would be higher.
5.5 Investigation of Injury Criteria:

The simulation of the NHP experiment overestimated the maximum displacement caused by the indentor. With the indentor impacting the spinal cord at 0.27 m/s, the maximum displacement predicted by the computational model was 5.1 mm. However, the experimental study recorded a displacement of only 2 mm. The overprediction of displacement was primarily due to the CSF not being modelled, due to difficulties in modelling the fluid properties of the CSF.

![Figure 11: Cross section – compression of human spinal cord](image)

The experimental study conducted by Choo et al. (2009) on contusion injuries in the rat, found that the damage caused by a contusion was concentrated centrally (Choo et al. 2009). This is consistent with the findings found in the model, with the maximum displacements occurring in the central region of the spinal cord.

Bain and Meaney (2000) investigated a tissue-level threshold for axonal damage in white matter. It was determined that the strain required for SCIs was approximately 20% (Bain & Meaney 2000). The NHP experimental study, caused a displacement of 2 mm, which would result in a strain of over 20%, thus according to Bain and Meaney (2000) this contusion experiment would cause a spinal cord injury. However in the experimental study conducted on NHPs, it was found that the Macaca mulatta did not suffer a spinal cord injury due to this compression.

As can be seen in the Figure 11, strains are localised around the location of the indentor. If the CSF were also modelled, there would be a much larger proportion of spinal cord tissue not affected by the indentor. There is believed to be a relationship between the number of...
surviving axons at the injury site and severity of spinal cord injury (Fehlings & Tator 1995). If no injury occurs due to an indentation of 2mm, this suggests that the number of surviving axons is sufficient.

The spinal cord injury caused by an increased displacement was not replicated, due to external factors which may have assisted in the creation of a spinal cord injury. Thus a comparison between a contusion causing injury and one not causing injury could not be conducted. A comparison between the two different scenarios could aid in the creation of injury criteria.

The FE model also allows us to see the displacement occurring at different sections of the spinal cord. It can be seen that the damage caused by the impactor primarily impacted the dorsal funiculus area at locations surrounding the impactor (upper central area of the spinal cord).

![Figure 12: Cross section at different locations (distance from LHS of model)](image)

![Figure 13: Cross section at different locations (distance from LHS of model)](image)
6. Limitations:

This study attempts to show that the previously proposed hyper-viscoelastic constitutive model of spinal cord white matter can be applied in finite element simulations of spinal cord deformation for moderate and low strain rates in axial and compressive loading. One of the key strengths in this study is the fact that both of the papers utilised tested porcine spinal cord reducing the potential variability in the mechanical properties due to specimen variation (Fradet et al. 2016; Sparrey & Keaveny 2011). However, there are limitations in both the experimental studies that this study was based on, and also the FE model created. Whilst there are limitations in the experimental studies, the key limitations can be found in the respective papers (Fradet et al. 2016; Sparrey & Keaveny 2011). The focus of this section will be on limitations within the FE model.

Poisson’s Ratio:

The primary limitation in this study was that the Poisson’s ratio of the spinal cord white matter was assumed to be 0.42. This is much lower than what is typically utilised in FE models, as it is assumed that biological soft tissue, including the spinal cord tissue, is incompressible (Miller 2005; Pamidi & Advani 1978). To introduce this incompressibility, it was initially assumed that the Poisson’s ratio of the spinal cord white matter was 0.495. However, it was clear that assuming that the white matter was incompressible would lead to major errors in the magnitude of stress. The FE model was tuned by varying the Poisson’s ratio until similar results to the experimental data were obtained. It was found that a Poisson’s ratio of 0.42 gives close values of stress with similar stress-strain behaviour. An experimental study conducted by Ichihara calculated that the Poisson’s ratio of bovine white matter was approximately 0.42, which correlates with the Poisson’s ratio utilised within the FE model, however further investigation is required (Ichihara et al. 2001). Figure 14 shows the differences in values of stress obtained for different Poisson’s ratio for an applied strain rate of 0.5/sec.
An alternative method that could be utilised in order to replicate the stress-strain curve, without having to assume a low value of Poisson’s ratio, is to alter the parameters of the hyper-viscoelastic model. However if only the shear modulus is altered in the hyperelastic constitutive model, it would need to be reduced to approximately 50Pa.

Another limitation is that the spinal cord created in the FE models was much simpler than in reality. The CSF was not modelled in the experiment conducted on the human spinal cord, due to difficulties in modelling fluid properties in ABAQUS. The geometry of the spinal cord was also simplified. The transverse and tensile models both assumed that the spinal cord cross section could be idealised as an ellipse, however in reality, the shape of the spinal cord is more complex. Literature only specified the anterior-posterior and transverse diameter of samples, making it difficult to create an accurate cross-section of the spinal cord. It was also assumed that the cross-sectional dimensions did not change over the length of the sample, however the spinal cord varies in dimensions. For more accurate simulations, the spinal cord geometry implemented in ABAQUS should be more consistent with the actual geometry. Some FE models have utilised MRI scans to create more geometrically accurate models.

Another simplification that was made was that the material properties of the white and grey matter were assumed to be identical for the transverse compression simulation, however this is not the case. It is not well known if the grey matter is stiffer than the white matter, with studies providing conflicting results in relation to the stiffness of the grey matter compared to white matter (Budday et al. 2015; Dommelen et al. 2009; Ichihara et al. 2001). Given the experimental difficulties of obtaining samples of grey matter, a lack of experimental studies

**Figure 14:** Comparison of stress-strain curves for different Poisson’s ratio
have been conducted on the mechanical properties of the spinal cord grey matter. As a result, white and grey matter was assumed to be identical in this project. Another limitation is the lack of research that has been conducted on the compressive behaviour of the spinal cord. Other papers could not be used to compare the results that were obtained from the Sparrey experiment.

The study conducted by Sparrey & Keaveny was also conducted in-vitro. The suitability of the mechanical properties obtained with in-vitro experiments must be checked to determine whether they can be applied in-vitro.
7. Conclusion and Future Work:

Knowledge of the compressive behaviour of the spinal cord is required to simulate spinal cord injuries occurring due to compressive loading. The aim of this study was to determine the suitability of a hyper-viscoelastic constitutive model in both axial and transverse compression. The FE solver, ABAQUS, was utilised to create three dimensional, non-linear dynamic finite element models to simulate three separate experiments. The constitutive model was deemed to be acceptable in both axial and transverse compression and in tension. This confirms that the assumption of isotropy can be utilised in FE models.

This project also aimed to increase the understanding of injury mechanisms of the spinal cord. The FE model showed that the contusion created by the impactor at a velocity of 0.27m/s may not have caused an SCI due to the large region of spinal cord tissue that was unaffected by the impactor. However, as a comparison between an impact causing an SCI and one not causing a SCI could not be simulated, it is difficult to comprehensively explore potential reasons why SCIs occur.

The advancement of finite element analysis and technological progress means that computational methods are more likely to be present in the future as a way of simulating injuries. Much more future work is required to be able to accurately simulate these injuries.

Further investigation needs to be conducted on the compressive behaviour of the spinal cord tissue. The small size of the samples of porcine spinal cord white matter means that there is a possibility that the mechanical properties of the spinal cord obtained by Sparrey and Keaveny are only localised properties and cannot represent the entire spinal cord tissue. Experimental studies also need to be conducted on the mechanical properties of the human spinal cord in compression, to improve the accuracy of FE models simulating human SCIs. The axial and transverse compressive behaviour of the spinal cord should also be compared in a single study, to reduce the variability of both the samples utilised and also testing methods used to characterize the behaviour.

In creating any FE model, the material properties of each part must be known. The main limitation in FE models of the spinal cord is that there are no commonly accepted material properties for each component of the spinal cord. The general behaviour of the spinal cord in tension is well known, but as seen in the literature review, the exact values for stiffness and the non-linear model utilised vary. This introduces difficulty when creating any
computational model, as it is difficult to determine the accuracy of parameters. Currently, the material properties utilised in FE studies are obtained from many different sources within the one model, often without any validation of such properties.

Future work should involve the creation of accepted practices and standards for the testing of soft biological tissue, similar to testing of any other material, for example the tensile testing of metal requires adherence to the Australian Standard AS1391 (Standards Australia 2007). Papers have been published suggesting methods that should be utilised for the testing of biological tissue, however these are merely suggestions (Miller 2005). Commonly accepted practices and standards would lead to less variation in the results obtained, as standard practices for tissue preservation, preconditioning etc. would be utilised. The creation of a database of accepted material parameters, whilst very difficult to create, would also aid greatly in the creation of finite element models.

A reduction in the number of SCIs would aid not only in the reduction of the cost associated with such injuries, but also in a reduction of the number of lives which are impacted by these often life altering injuries. The use of computer simulations utilising the methods of computational biomechanics can be utilised to further our understanding of SCIs and to aid in the design of preventative countermeasures. However there is much work to be done to enable the use of computational models to accurately complement experimental studies.
8. References


Gefen, A, Green, N, Zhu, Q, Raghupathi, R & Margulies, SS 2003, 'Age-Dependent Changes in Material Properties of the Brain and Braincase of the Rat', *Journal of Neurotrauma*, vol. 20, no. 11, p. 16.


