



Brain Mechanics at Loading Rates Relevant to Blast

By

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Declaration

The work presented within this thesis is my own unless otherwise specified.

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Abstract

The use of explosive weapons is becoming increasingly prevalent in the modern world, from the recent military conflicts in Iraq, Afghanistan, Syria, Yemen, Israel, Palestine and many more, to the increasing regularity of terror and guerrilla attacks on both civilian and military personnel, the damage and injuries wrought by these inherently indiscriminate weapons cannot be ignored.

Despite the use of explosives for industrial and military applications for hundreds of years, many aspects of blast injury remain poorly understood. In recent years, with the advances made in computational science and the increasing processing power available to researchers, the use of computational models as an effective tool to study blast injury has risen dramatically. These models are capable of accurately simulating blast events and reporting a vast swathe of information not available from traditional experiments. These models rely on accurate information and characterization of the geometries and material properties of the structures involved, in this case the human brain.

The behaviour of the brain at high strain rates is still poorly understood, and this understanding is critical if we are to develop accurate models for blast events, which are by their very nature, high strain rate phenomena. Due to its soft nature, as well as the hazards associated with tissue handling and the lack of suitable apparatus available commercially, brain tissue is traditionally extremely difficult to characterize accurately, particularly at high strain rates relevant to both blast and impacts.

In this work, a novel custom apparatus for mechanically testing soft tissue such as brain tissue was developed, prototyped and built. The apparatus offered a number of advantages over comparable apparatus available commercially or in literature, being sensitive enough to test extremely small samples of soft tissue, while being able to test at strain rates far in excess of other apparatus. The apparatus was validated against surrogate materials, including soft gels (Ecoflex) and strongly viscoelastic materials (Armourgel) and was shown to be able to accurately capture viscoelastic behaviour at high strain rates, a key property of brain tissue under impact and blast loading.

The apparatus was subsequently used to characterize porcine white matter brain tissue from the corona radiata, using tensile mechanical experiments up to failure at strain rates between 15 s^{-1} and 250 s^{-1} . This represents an almost threefold increase over the maximum strain rate in current literature and the widest range of strain rates investigated using a single apparatus under the same conditions.

Following this, the experimental data was used to characterize a hyper-viscoelastic model for brain tissue. The hyper-viscoelastic model used in this work was the sum of a 2 term Ogden model to represent the long-term non-linear response and a convolution integral with a 6 term Prony series to represent viscoelasticity. To this end, a novel analytical approach was developed which is significantly less resource intensive than the traditional inverse finite element modelling methods. This was achieved by fitting a 6th order polynomial curve to the recorded displacement, allowing stretch to be modelled analytically. The hyper-viscoelastic model was solved analytically providing a closed form relationship between the 1st Piola-Kirchoff stress, stretch and rate of stretch.

Using these methods, a set of viscoelastic properties, namely the constants of the Prony series representing the relaxation modulus, were extracted for the corona radiata of a porcine brain. These properties, when combined with hyperelastic properties from literature, were shown to apply across the full range of strain rates investigated (15 s^{-1} to 250 s^{-1}), with statistically similar values being determined for the full range of strain rates. While more work needs to be done to validate and expand upon these findings, they strongly support the use of the hyper-viscoelastic model that we have characterized in this work to represent the mechanical behaviour of brain tissue across a wide range of scenarios, up to and including blast injury.

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List of abbreviations

TBI	-	Traumatic Brain Injury
bTBI	-	Blast Induced Traumatic Brain Injury
cTBI	-	Closed Traumatic Brain Injury
mTBI	-	Mild Traumatic Brain Injury
CDC	-	Centres for Disease Control and Prevention (a US institution)
OEF	-	Operation Enduring Freedom
OIF	-	Operation Iraqi Freedom
PPE	-	Personal Protective Equipment
CFD	-	Computational Fluid Dynamics
FE	-	Finite Element
CNS	-	Central Nervous System
PNS	-	Peripheral Nervous System
GCS	-	Glasgow Coma Score
CTE	-	Chronic Traumatic Encephalopathy
DAI	-	Diffuse Axonal Injury
CSF	-	Cerebrospinal Fluid
CAD	-	Computer Aided Design

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1 Introduction

1.1 Relevance in the world today

Traumatic Brain Injury (TBI), both from blast and impact events is a leading cause of death and disability worldwide. According to a report by (Taylor *et al.*, 2017) and cited by the US Centres for Disease Control and Prevention (CDC) (TBI: Get the Facts), TBI contributes to approximately 30% of all injury related deaths, an average of 153 deaths per day in the United States alone. Additionally, TBI can have long lasting effects on injury survivors that can drastically affect quality of life, including impaired memory, cognitive function, movement and sensory perception (such as loss of sight, balance or hearing) as well as psychological and emotional effects such as trauma or depression, particularly in military personnel. The impact of these issues is not limited to the individual, but can have long lasting consequences for their families, friends and communities.

The effect on the military population is more pronounced still, with TBI often referred to as the ‘signature injury of modern war’ (Warden, 2006; Martin *et al.*, 2008). This is primarily due to the widespread use of improvised explosive devices (IEDs) in modern theatres of war such as Afghanistan and Iraq, where explosive events primarily from such devices are the cause of over 60% of combat casualties (Ling *et al.*, 2009). Furthermore, it has been extrapolated (Tanielain *et al.*, 2008) that a full 19% of soldiers deployed in Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF) will return suffering from some degree of TBI. While it should be noted that this figure is based on self-reporting rather than a standardized test and suffers from a limited sample size, it is still a telling statistic.

Blast Induced Traumatic Brain Injury (bTBI) is becoming increasingly prevalent in modern conflicts, with 29.4% of injured soldiers presenting with wounds to the head or neck according

to the Joint Theatre Trauma Registry (Owens *et al.*, 2008). This represents a marked increase from the 17.3% in Operation Desert Storm (Carey, 1996), and 12-14% in Vietnam (Okie, Das and Moorthi, 2005). This increase has been linked to greatly improved survival rates for injured troops, with a survival ratio of 7.4:1 (16,906, wounded with 2296 deaths) in OIF, compared with 2.6:1 in Vietnam, 2.8:1 in Korea and 2:1 in World War II (Armonda *et al.*, 2006). These increased survival rates can likely be attributed to improved personal protective equipment (PPE) (Okie, Das and Moorthi, 2005) as well as more comprehensive forward care and evacuation procedures (Armonda *et al.*, 2006), the result of which is that a soldier suffering from a blast injury that would have proven fatal in earlier conflicts can now survive and be treated for their injuries including bTBI.

These figures are especially concerning as soldiers whose injuries include bTBI have been shown to be 500% more likely to suffer a major health decline in the 6 months following their injury. After 6 months, a further 41.3% go on to report a more gradual decline over 5 years (Heltemes *et al.*, 2012). Again, it should be noted that this is based on self-reporting rather than a standardized test. However, the effect bTBI has on long term health, combined with its substantial and growing prevalence is concerning. Interestingly, this post injury health decline is at odds with civilian literature, which broadly shows a gradual recovery pattern for TBI that results from impact alone (McCrea *et al.*, 2009). This suggests that there may be additional unknown factors associated with bTBI that cause this marked health decline and merit further study.

The head is one of the most commonly affected areas during an explosion, with 59% of soldiers exposed to a blast event suffering from some degree of bTBI, even if they suffered no further injuries. Of these bTBI cases, 56% are classed as severe (Okie, Das and Moorthi, 2005). Both these figures are theorized to be underestimates, however, due to the difficulty in catching and diagnosing TBI, especially Closed TBI (cTBI) where no skull fracture is present and there may be no outward marks or injuries to suggest head injury.

Blast events are not limited to military personnel, indeed, 74% of those killed or injured by explosive weapons are civilians, with 31904 recorded casualties in 2017, of which 16289 were fatalities (Action on Armed Violence, 2017), although true figures will sadly almost certainly be higher.

From the increasing number of explosive based terrorist attacks in the west to the widespread use of explosives in civilian population centres in the middle east, notably Syria, Iraq and Afghanistan, civilian bTBI is a global issue. Much like in military personnel, the frequency of such injuries is increasing in the civilian population, with 38% more civilian deaths in 2017 due to explosive weapons than in 2016, and 165% more than in 2011 (Action on Armed Violence, 2017). The majority of those injured suffer a combination of blast, penetrating, impact and thermal injuries that fall outside the day to day experience of most civilian physicians (Lucci, 2006).

bTBI is an ever-increasing problem in today's world, one which can sadly affect people from all walks of life. Accurate understanding of the underlying mechanics of such injuries is paramount, since it will allow the informed development of treatments and therapies for those affected, as well as more advanced and effective preventative measures and evacuation procedures. Considering the prevalence of bTBI on the global scene today, and its increasing trend that shows no sign of abating, studies to help us understand blast injury are critical and are becoming more and more relevant. It is to be hoped such studies would lead to treatments and preventative measures that would save lives.

1.2 Objectives

The overarching goal of this work is to characterize brain mechanical behaviour at loading rates relevant to blast in a format suitable for advanced computational biomechanics models of TBI, in line with recent trends in the approach to this research area.

More specifically

1. To design and build a custom desktop apparatus for testing brain tissue at rates relevant to blast, up to 1000 s^{-1}
2. To validate this apparatus against known materials for high rate viscoelastic characterization
3. To determine the mechanical response of brain tissue across a range of strain rates experimentally
4. To test whether the 2 term Ogden model summed with a convolution integral commonly used in literature and commercial FE packages can adequately model brain tissue behaviour across a range of strain rates
5. To determine values for the viscoelastic constants using experimental data across a range of strain rates

1.3 Outline and structure

In this thesis the biomechanics of brain tissue at loading rates relevant to blast are investigated using a selection of tools specially designed and built for this research, including a novel new apparatus for the mechanical testing of soft tissue.

In the current chapter, chapter 1, an overview of the current relevance of blast in the world today is conducted, giving context to the work reported in this thesis and outlining the relevance, practicality and need for this research and other similar projects.

In chapter 2 an overview of current blast injury, physics and modelling research is presented, outlining the foundation of background literature that underpins this research. While assumption

of scientific knowledge is, to a certain degree, unavoidable in a technical thesis such as this, chapter 2 seeks to provide the reader with much of the knowledge and background specific to this field of study that the research presented in this thesis is built upon.

Chapter 0 reviews the current available literature describing the characterization of brain tissue and identifies avenues where a greater understanding is required. Following this, chapter 0 details the design, construction and validation of a new high rate tissue testing apparatus designed specifically to investigate these relatively unexplored areas.

Chapter 4 describes the experimental methods, tools and materials used alongside this new apparatus to investigate the behaviour of brain tissue at strain rates relevant to blast. The type, freshness and preservation methods of the experimental tissue are reviewed, along with tissue cutting methods and experimental procedure. Chapter 4 also details the parameters and filtering methods used with the experimental data before processing.

Chapter 5 reviews the experimental results, comparing the results from this study with those from comparable experiments in literature. Rate dependent (viscoelastic) behaviour is statistically confirmed by an analysis of the tissue response to loading across the full range of strain rates investigated in this work.

Chapter 6 details the mathematical foundation of the hyper-viscoelastic model used as a foundation to characterize brain tissue. Working from the original papers the two components of the model were originally published in, chapter 6 details, step by step, the process of combining the two components and converting them into the format used by this work. This format matches the format this model is implemented in in much of the literature as well as commercial FE software packages. Following this, chapter 6 details a novel new analytical approach for characterizing material using this model, significantly reducing the difficulty and computational power required for such a characterization, as well as removing the need for FE software.

Chapter 7 illustrates the use of this analytical process in order to extract values for the viscoelastic constants of brain tissue. G values are extracted from the experimental data for the whole range of strain rates and are shown to have no statistical differences, supporting the use of the aforementioned hyper-viscoelastic model to describe the mechanical behaviour of brain tissue across a range of strain rates.

Chapter 8 analyses and reviews the work, presenting the main findings and conclusions as well as discussing the potential avenues for expansion and future work.

2 Blast physics, injury and modelling

2.1 Blast injury

Blast injury is a matter of growing concern, and with the prevalence of terrorist attacks on civilians as well as the indiscriminate nature of landmines, roadside bombs, IEDs and similar devices it cannot be thought of as a solely military matter. Although it should be noted that civilian blast injury often does not follow the same pattern as military, with civilians not typically having access to body armour and helmets, as well as being a much more heterogenous population that includes a higher proportion of women as well as children and the elderly (Hicks *et al.*, 2010).

2.1.1 Types of blast injury

An explosion in the real world is typically a complex scenario that can produce a variety of injuries via several mechanisms. Although many different types of injury have been recorded following blast exposure, they can be broken down into 4 categories based on the injury mechanism (Ling *et al.*, 2009; Moore *et al.*, 2009; CDC, 2015; Singh, 2015).

2.1.1.1 Primary blast injury

A non-penetrating injury caused by the blast shockwave travelling through the subject, causing injury as a result of the loading applied by the wave. This ‘blast wave’ should be distinguished from the ‘blast wind’, which is a much slower flow of superheated air following an explosion, rather than a shockwave. The majority of primary blast injuries are internal rather than external, and consequently harder to diagnose.

Much of the literature on primary blast injury concentrates on the injuries caused by the waves interaction with blood vessels and air filled organs, such as Blast Lung (Bowen *et al.*, 1968) and Traumatic Cerebral Vasospasm (Armonda *et al.*, 2006). However, computational models have predicted sufficient conditions in the brain for injury to occur during a blast wave (Radovitzky *et al.*, 2012), supporting primary blast injury as a mechanism for TBI.

2.1.1.2 Secondary blast injury

Injuries resulting from objects such as shrapnel, fragments or debris originating from either the environment or the explosive device being propelled through the air at high velocity by the blast and impacting upon the subject, causing injury.

2.1.1.3 Tertiary blast injury

Injuries resulting from the subject being propelled through the air by the force of the blast, the so called ‘blast wind’, causing injury upon impact with the ground or surrounding environment. It is particularly common in urban environments or when the subject is riding in a vehicle during the blast event.

2.1.1.4 Quaternary blast injury

Injuries, commonly burns, resulting from thermal exposure during the blast or from thermal, radioactive or chemical components used in the explosive device.

Note: Quaternary Blast Injury is alternately defined as ‘All explosion-related injuries, illnesses, or diseases not due to primary, secondary, or tertiary mechanisms’ (CDC, 2015)

2.1.2 Overview of primary blast injury

Primary blast injury in particular is a matter of growing concern, particularly in the military. Military personnel have access to a range of preventative measures such as advanced PPE and

armoured vehicles which provide a great deal of protection against secondary blast injury in particular, which is what much of the existing literature focusses on and is the primary design concern when producing PPE (Underwood, 1981) and vehicle armour.

However, these protective measures have revealed primary blast injury as a widespread injury mechanism. In earlier conflicts a soldier exposed to a certain blast event might have been killed by secondary blast injury, which produces much more visual signs of trauma and is expected to prevent any additional primary blast injury from being diagnosed. However, in modern conflicts a soldier exposed to a similar blast event is much more likely to be protected from secondary blast injury to a greater degree by their more advanced PPE and potentially vehicles. This may let them survive the blast event and go onto display symptoms of primary injury. On the extreme end of the scale injuries and deaths have been observed where the victims show no signs of external trauma (Glasser, 2007), while it has not been conclusively proven, it can be inferred and it is widely believed that the mechanism for these injuries is primary blast injury.

While a great deal more work needs to be done on characterizing primary blast injury, a goal which it is sincerely hoped this work will contribute to in some small way, certain patterns and injury pathologies have emerged from the research that has gone into it in the recent years since it has emerged as a prevalent injury mechanism. Blast events cause a range of injuries across a broad spectrum of severity and both ends of the spectrum present unique challenges when studying their pathology. Severe blast injury is rarely incurred in isolation, particularly in civilian cases where there is limited access to protection from the blast event, leading to difficulties in pinpointing primary blast injury amongst all the noise. In contrast, mild TBI is often non-penetrative, or closed TBI (cTBI) where the skull is not breached, meaning injuries are not always apparent, lowering the likelihood of a successful diagnosis (Schlifka, 2007).

bTBI severity is classed using the Glasgow Coma Score (GCS), with mild-moderate TBI (mTBI) being classed as a GCS score of 9-15 and severe TBI requiring a GCS of 8 or lower (Ling and Ecklund, 2011). Most of our knowledge regarding severe blast injury (GCS < 8) comes from civilian studies (Hicks *et al.*, 2010)(Schwartz *et al.*, 2008) since they sadly make up the majority of blast victims as reported in the first section.

Edemas, contusions, haematomas and haemorrhages have all been recorded as injuries resulting from bTBI (Levi *et al.*, 1990; Schwartz *et al.*, 2008), as well as pituitary dysfunction (Baxter *et al.*,

2013), neurovascular injury (Armonda *et al.*, 2006; Shahlaie *et al.*, 2009), diffuse axonal injury (DAI) (Harris *et al.*, 2010; Hicks *et al.*, 2010) and Chronic Traumatic Encephalopathy (CTE) (Goldstein *et al.*, 2012).

Much of the literature on TBI focusses on impact scenarios, where (aside from physical damage from the object the head impacts) acceleration of the head is thought to be the primary cause of injury. However in a blast event acceleration-based symptoms would generally constitute tertiary blast injury, with primary blast injury being caused by the pressure wave released by the explosive. It has been shown with shock tube experiments (Cernak *et al.*, 2001) that intra-cranial pressures generated by fairly typical blast scenarios are sufficient to cause TBI without any subsequent impacts or overall head acceleration, validating the focus on primary blast injury as an avenue of research.

2.2 Anatomy

This section presents a brief overview of the anatomy of the head, at both the cellular (microscopic) level, covering the predominant cell type, the axon and its features, and at the macroscopic level detailing the major structures in the head and brain, focusing on brain anatomy.

2.2.1 The Central Nervous System (CNS)

The brain is the central hub of the Central Nervous System (CNS) which, together with the peripheral nervous system (PNS), is responsible for the human bodies control, coordination and response to stimuli. The CNS, which consists of the brain and spinal cord, is a continual source of fascination for anyone with an appreciation of the sciences, being responsible for such human fundamentals as our movements, thoughts and emotions, as well as performing a variety of baser functions such as regulating our body temperature, breathing and heart rate and is one of the most complicated and intricate systems in the human body.

2.2.2 The nerve cell

The majority of cells that make up the structure of the brain can be divided into 3 broad categories.

1. Neurons

These highly specialized cells carry out the primary functions of the CNS by transmitting electrochemical signals to cells throughout the body. Often thought of as the ‘wires’ of the CNS, they form an incredibly complex structure. It is estimated that there are approximately 100 billion neurons in the human brain (Herculano-Houzel, 2009). They come together to form bundles, called ‘nerves’ (Figure 1C) which run throughout the larger structures of the CNS (Figure 1D & Figure 1E)

2. Neuroglia

The Neuroglia are a variety of cells that are involved in supporting and maintaining the neuron network (Figure 1B), they provide structural support for the network as well as insulating the neurons from one another, preventing signal interference. Additionally, they supply nutrients and oxygen to the neurons, remove dead neurons, debris and pathogens and play a role in the bridging of synaptic connections.

3. Blood vessels

These provide bulk oxygen and nutrients to the neuroglia and neurons in the brain. The walls of these blood vessels include a highly selective semi-permeable membrane called the Blood Brain Barrier (BBB), which prevents the majority of harmful or undesired substances from leaving the blood and interacting with the CNS

The basic structure of a neuron can be seen below in Figure 1 A. It consists of a cell body, containing the nucleus, mitochondria, ribosomes and other major cellular components as well as dendrites and an axon, which are specialized structures for impulse transmission. The dendrites receive information from other neurons across specialized bridges called synapses, the action potential then passes through the cell body and down the axon to its destination, which could be another neuron or a specialized actuator cell that produces a response. Neurons typically have many dendrites and can therefore receive information from multiple sources creating a branched network, however neurons are normally specialized to one destination and so only have one axon.

The axon is typically wrapped in a fatty sheath called a Myelin sheath, separated by Nodes of Ranvier as can be seen below in Figure 1 A. This sheath serves to protect the axon as well as greatly increase the speed of impulse transmission, a necessity in larger organisms for effective response to stimuli. Axons can vary greatly in length, from a few millimetres to a meter long or more.

Despite this protection, the nature of neurons as long thin cells means they are inherently one of the most vulnerable structures to a blast wave, with DAI being a common symptom in patients exposed to blast, as stated in the 'Blast injury' section previously.

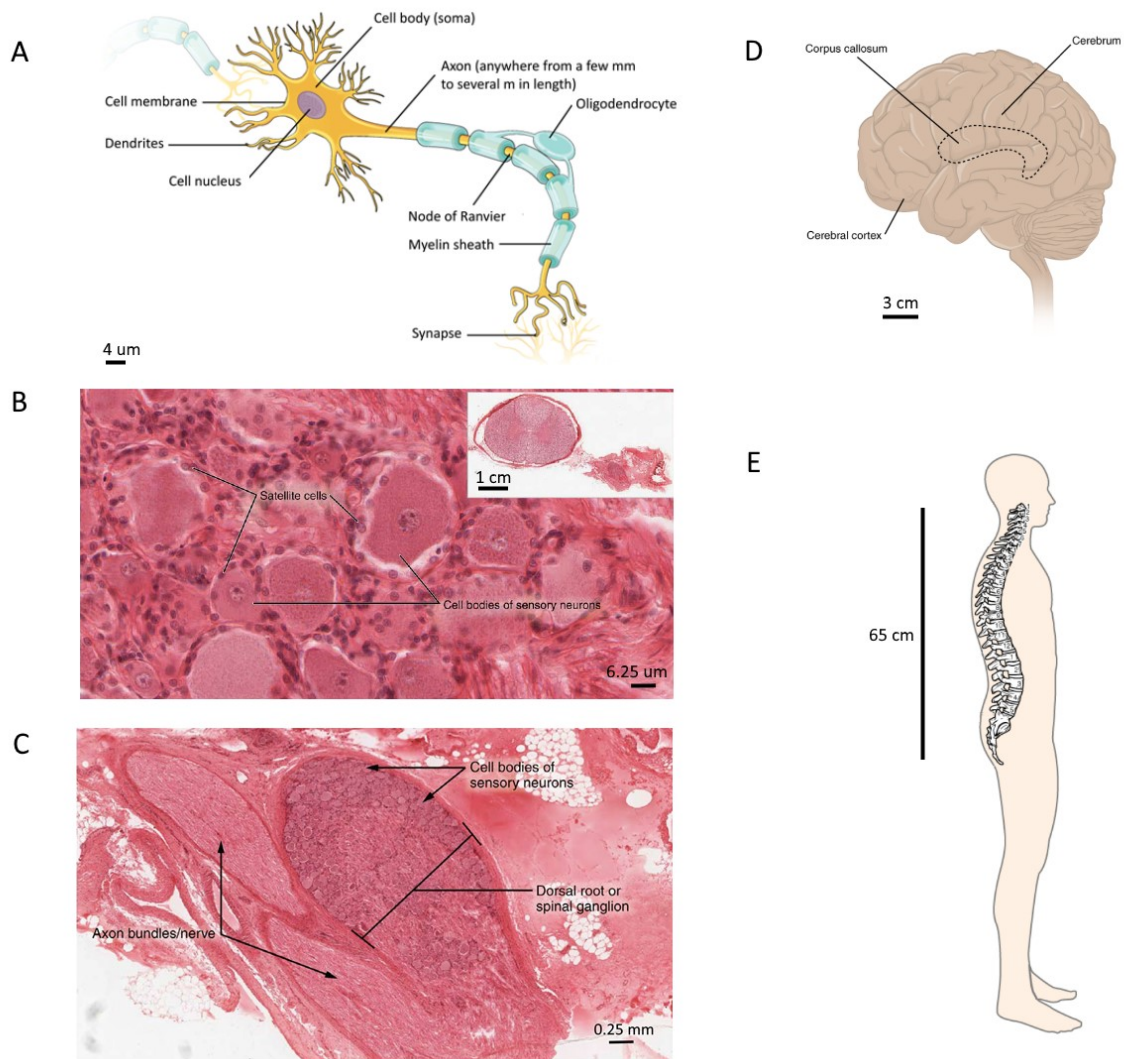


Figure 1: Diagram of the multi-scale nature of the central nervous system (CNS), consisting of (A) A diagram of a typical axon. (B) These nerve cells embedded in a tissue matrix, taken from a cross section of the spinal cord and root ganglion under 1600x magnification with a light microscope. (C) The axons shown collected into bundles to form nerves, taken from a cross section of the spinal cord and root ganglion under 40x magnification with a light microscope. (D) the whole brain and (E) the full spinal cord. (A-E) reproduced with modification from (OpenStax, Anatomy & Physiology)

2.2.3 The Frankfurt convention

When talking about the brain it is necessary to define a coordinate system for spatial reference, the most common being the Frankfurt reference plane coordinate system, displayed below in Figure 2. This coordinate system will be used throughout this text, particularly in the Methodology section and so should be noted.

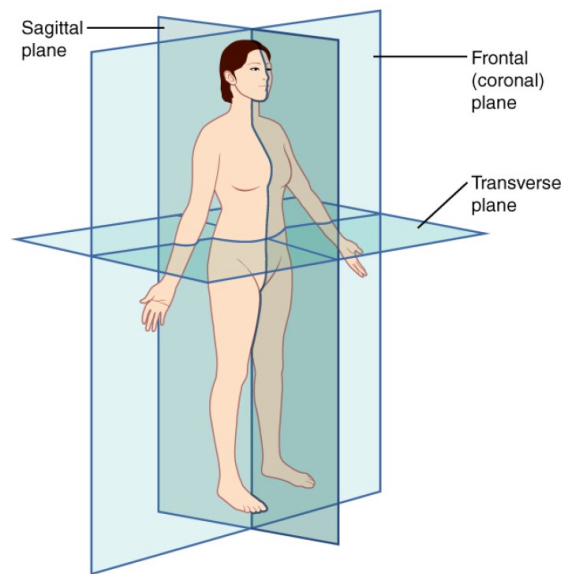


Figure 2: An illustration of the Frankfort reference plane coordinate system, reproduced from (OpenStax, Anatomy & Physiology)

2.2.4 The brain

While the brain consists of numerous structures, it can be broadly divided into 2 sections, the cerebrum and the cerebellum.

The cerebellum is the smaller of the two sections, sitting in the lower posterior (back) portion of the brain, it is responsible for the body's coordination and balance.

The cerebrum is the largest part of the brain and is the most recognisable, forming its iconic shape and bulk. It is covered by the cerebral cortex, which contains the characteristic wrinkles in the brain surface, the sulci (fissures) and gyri (ridges). The cerebrum is notably divided into 2 hemispheres, the right and left cerebral hemisphere, by a gap called the longitudinal fissure. This gap is bridged by the corpus callosum, a bridge of axon dense tissue which facilitates communication between the two hemispheres. A simplified diagram can be seen below in Figure

3

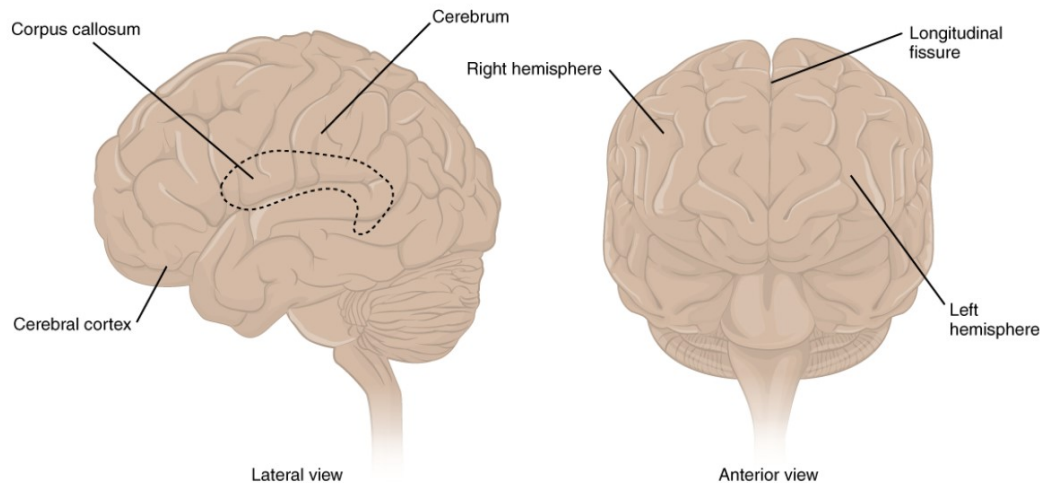


Figure 3: An illustration of the general structure of the brain detailing the major structures, reproduced from (OpenStax, Anatomy & Physiology)

The cerebrum (and the cerebellum) consist primarily of two tissue types, an outer layer of grey matter and an inner structure of white matter (Figure 4). The grey matter is a pinkish-grey tissue that contains the cell bodies of all the axons, as well as the dendrites, axon terminals and synapses. The white matter contains primarily axons that connect different parts of grey matter to each other, as well as connecting to the spinal cord and PNS. It is the myelin sheaths on the axons (see Figure 1) that give white matter its characteristic colour. The two matter types can be clearly seen on a coronal cross section of the cerebrum, where the white matter forms a tree like structure in each hemisphere called the corona radiata.

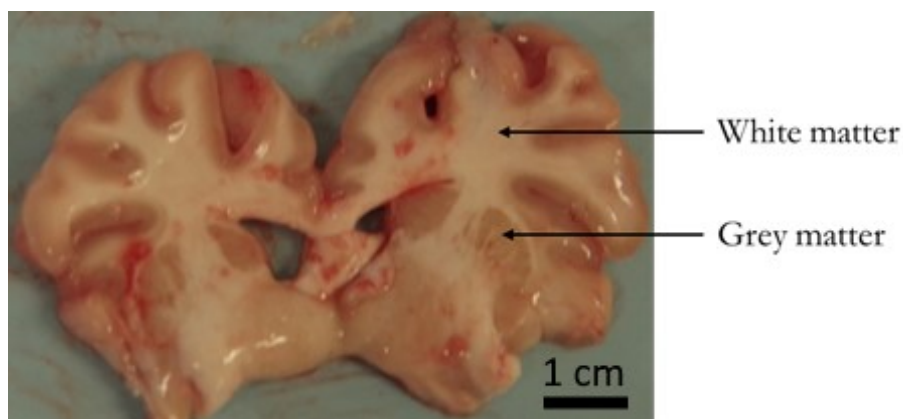


Figure 4: A coronal cross section of a porcine brain, taken from work done for this report, showing grey and white matter in the cerebrum

2.2.5 Surrounding structures

The brain is held in a cavity inside the skull, which is a bony structure that provides the majority of mechanical protection to the brain, in the manner shown by Figure 5B. It can be separated into the cranium, or 'brain case', which is the bone surrounding the cavity that holds the brain, and the face, which are the bones of the attached anterior structure that support the eyes, muscles and various other components of the face (Figure 5B). With the exception of the lower mandible, the skull is a single structure.

The bones of the cranium consist of 3 layers, a comparatively spongy diploë layer sandwiched between 2 layers of hard cortical bone which gives the cranium both strength and flexibility in the same manner as a composite. The thickness of the skull generally varies between 4-10mm (Ghajari *et al.*, 2011) depending on the location, however this is in turn affected by variables such as age, biological gender and genetic variables.

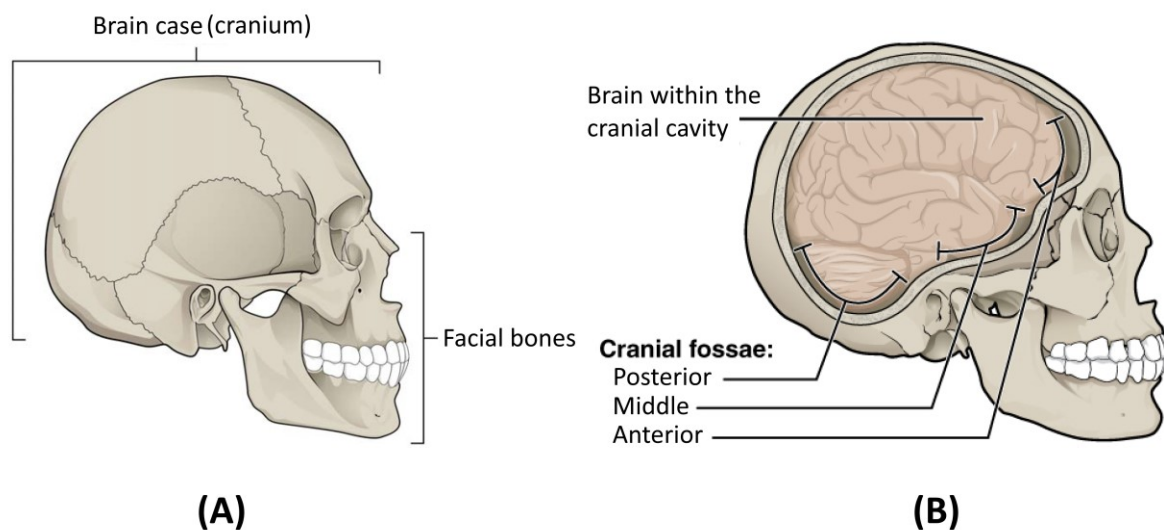


Figure 5: (A) An illustration of the cranium and facial structure, (B) An illustration of the brain inside the skull, both reproduced with modification from (OpenStax, Anatomy & Physiology)

The skull is in turn enveloped by the scalp, a roughly 5-7mm thick structure composed of skin and connective tissue that provides a mechanical buffer to the skull, further protecting the brain from shocks and impacts.

Inside the cranial cavity the brain is surrounded by a clear and colourless fluid called the Cerebrospinal Fluid (CSF) which serves as immunological protection as well as acting as a

mechanical buffer. The CSF is primarily water with a variety of biological molecules and components in suspension.

Surrounding the brain are the meninges, 3 layers of membrane that couple the brain to the skull and are the origin of the ‘tethered bag’ analogy. Starting from the inside, the meninges are known respectively as the dura mater, the arachnoid mater, and the pia mater. They serve a number of functions, but their primary mechanical function is to anchor the brain and provide additional mechanical protection and shock absorption.

2.3 Blast physics

2.3.1 The blast wave

When a high order explosive such as C-4, Trinitrotoluene, Dynamite or Semtex is detonated it rapidly releases energy into the surrounding environment in the form of heat, light, sound and pressure. Among other effects, this creates a pressure front which moves through the air at supersonic speeds, unlike a low order explosive such as gasoline or gunpowder which produce subsonic explosions (CDC, 2015).

This ‘shockwave’ is represented by a sudden, discontinuous pressure increase at the pressure front, in a similar manner to step loading, followed by an exponential decay that leads to a region of negative pressure after the pressure front where objects are sucked back towards the source of the explosion in a phenomenon known as ‘blast wind’ (Moore *et al.*, 2009; Dass Goel *et al.*, 2012). Although it should be noted that this is the mathematical model of the blast wave. In reality blasts rarely occur in open field conditions so the eventual pressure profile is likely to be significantly different due to reflections, diffraction and interference.

This pressure front can be modelled in the open field by the Friedlander equation:

$$P(t) = P_0 + P_{pos} \left(1 - \frac{t}{t_{pos}} \right) e^{-b \frac{t}{t_{pos}}}$$

Equation 1: The Friedlander Equation

where $P(t)$ represents pressure, P_0 is ambient pressure, P_{pos} is the pressure difference between peak and ambient pressure, t is time (the independent variable), t_{pos} is the duration of positive overpressure and b is the decay parameter of the curve. These are illustrated graphically on the plot of the Friedlander waveform (Figure 6) below.

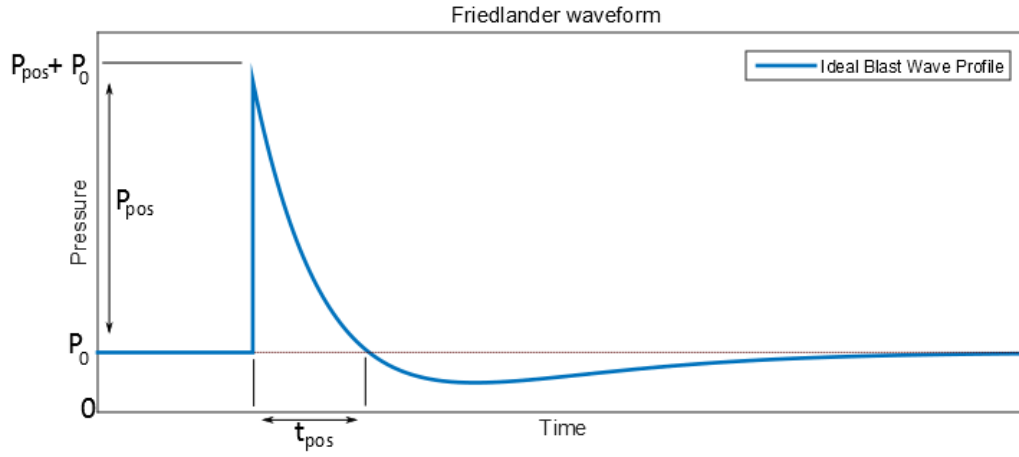


Figure 6: A plot of the Friedlander Waveform

Each of these parameters, P_{pos} , t_{pos} , P_{neg} and t_{neg} as well as the decay parameter b can be determined by their own equation.

2.3.1.1 The overpressure parameters

The overpressure parameters are often determined by the equations proposed by Kinney and Graham (Kinney and Graham, 1985), due to their close agreement with experimental data

$$P_{pos} = P_0 \frac{808 \left[1 + \left(\frac{Z}{4.5} \right)^2 \right]}{\sqrt{\left[1 + \left(\frac{Z}{0.048} \right)^2 \right]} \times \sqrt{\left[1 + \left(\frac{Z}{0.32} \right)^2 \right]} \times \sqrt{\left[1 + \left(\frac{Z}{1.35} \right)^2 \right]}} \quad (bar)$$

Equation 2: The equation for the pressure overpressure parameter in the Friedlander equation (Kinney and Graham, 1985)

$$t_{pos} = W^{\frac{1}{3}} \frac{980 \left[1 + \left(\frac{Z}{0.54} \right)^{10} \right]}{\sqrt{\left[1 + \left(\frac{Z}{0.02} \right)^3 \right]} \times \sqrt{\left[1 + \left(\frac{Z}{0.74} \right)^6 \right]} \times \sqrt{\left[1 + \left(\frac{Z}{6.9} \right)^2 \right]}} \quad (ms)$$

Equation 3: The equation for the time overpressure parameter in the Friedlander equation (Kinney and Graham, 1985)

Where W is the weight (in kg) of TNT used in the explosive charged, or appropriately scaled weight of the relevant explosive, R is the standoff distance (in meters) from the centre of the initial explosion and Z is the scaled distance.

$$Z = \frac{R}{W^{\frac{1}{3}}}$$

Equation 4: The equation for the scaled distance from the explosion (Kinney and Graham, 1985)

2.3.1.2 The underpressure parameters

For the underpressure parameters, several equations by Krauthammer and Altenberg (Krauthammer and Altenberg, 2000) are commonly used, as suggested by the comprehensive review of blast wave parameters by Dass Goel et al (Dass Goel *et al.*, 2012). The appropriate equation for the underpressure parameters varies depending on the scaled distance Z , as given by Equation 4 above.

If Z is less than 3.5, P_{neg} converges to a value of 10^4 (Pa), If the Z value is greater than 3.5 it uses the following equation (Equation 5).

$$(Z > 3.5) \rightarrow P_{neg} = \frac{0.35}{Z} \times 10^5 \text{ (Pa)}$$

Equation 5: The equation for the underpressure pressure parameter in the Friedlander equation when $Z > 3.5$

$$(Z < 3.5) \rightarrow P_{neg} = 10^4 \text{ (Pa)}$$

Equation 6: The equation for the underpressure pressure in the Friedlander equation when $Z < 3.5$

In a similar manner, the time underpressure parameter is represented by 1 of 3 equations depending upon the scaled distance Z in the problem

$$(Z < 0.3) \rightarrow t_{neg} = 0.0104 \times W^{\frac{1}{3}} \text{ (s)}$$

Equation 7: The equation for the underpressure time parameter when in the Friedlander equation $Z < 0.3$

$$(0.3 < Z < 1.9) \rightarrow t_{neg} = [0.0003125 \times \log_{10}[(Z)] + 0.01201] \times W^{\frac{1}{3}} \text{ (s)}$$

Equation 8: The equation for the underpressure time parameter in the Friedlander equation when $0.3 < Z < 1.9$

$$(Z > 1.9) \rightarrow t_{neg} = 0.0139 \times W^{\frac{1}{3}} \text{ (s)}$$

Equation 9: The equation for the underpressure time parameter in the Friedlander equation when $Z > 1.9$

2.3.1.3 The decay parameter

The decay parameter b is similarly defined by Krauthammer and Altenberg (Krauthammer and Altenberg, 2000), and their equation is the most commonly used in

literature as stated by Dass Goel (Dass Goel *et al.*, 2012). The equation (Equation 10) for b Krauthammer and Altenberg put forward is only defined for Z values between 0.1 and 30, however it should be noted that considering Z is a scaled distance, $Z < 30$ encompasses most reasonable applications.

$$(0.1 < Z < 30) \rightarrow b = 1.5 \times Z^{-0.38}$$

Equation 10: The equation for the decay parameter in the Friedlander equation

2.3.2 Limitations of the analytical model

The Friedlander waveform can accurately describe the propagation of a blast wave from a known explosive charge suspended in an open field and forms the basis for many of the methods used to model a blast wave, as well as being the equation used in many commercial Computational Fluid Dynamics (CFD) packages to model blast propagation. However it is one tool that must be used in tandem with other tools (such as CFD packages and other computational modelling methods) to accurately model blast waves.

A blast wave follows wave mechanics like any other wave. It diffracts when passing through a narrow opening and it will be partially reflected, absorbed and transmitted when it encounters a surface or otherwise boundary between two media depending upon their relative impedances. These mechanics are an important consideration when considering a real world blast wave, as the eventual wave profile will almost always be considerably more complicated than the ideal Friedlander waveform described above (Figure 6). In even the simplest cases, an explosion will normally be on or close to the ground as opposed to suspended in space, creating a hemispherical shock wave, visualized below in Figure 7.

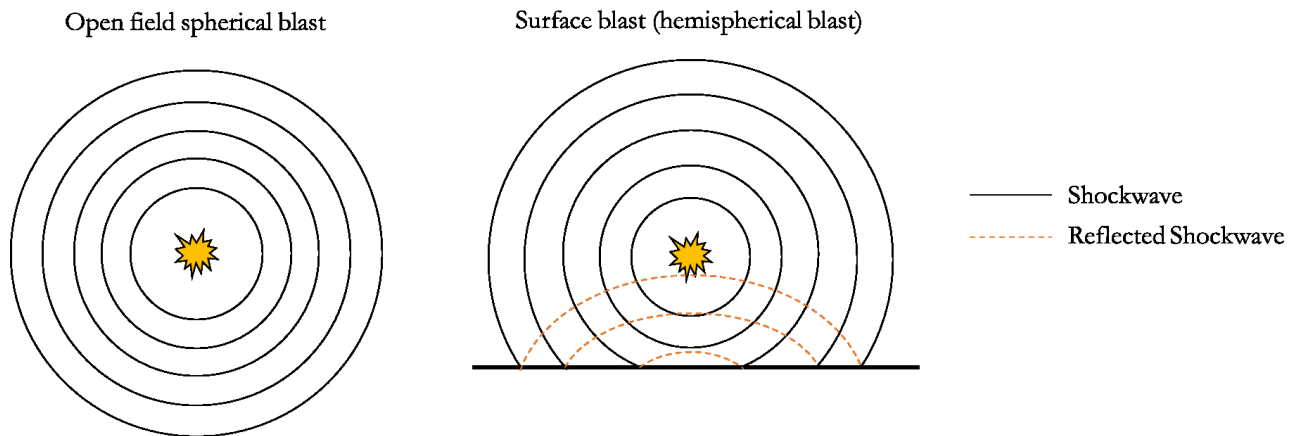


Figure 7: A comparison of open field and surface blast shockwaves

In the case of a hemispherical blast, the wave reflecting off the ground constructively interferes with the shock front, creating a single incident shockwave known as a Mach Stem, visualised below in Figure 8, which has a theoretical overpressure magnitude of double the original overpressure magnitude at that time, an effect modelled extensively (Cullis, 2001).

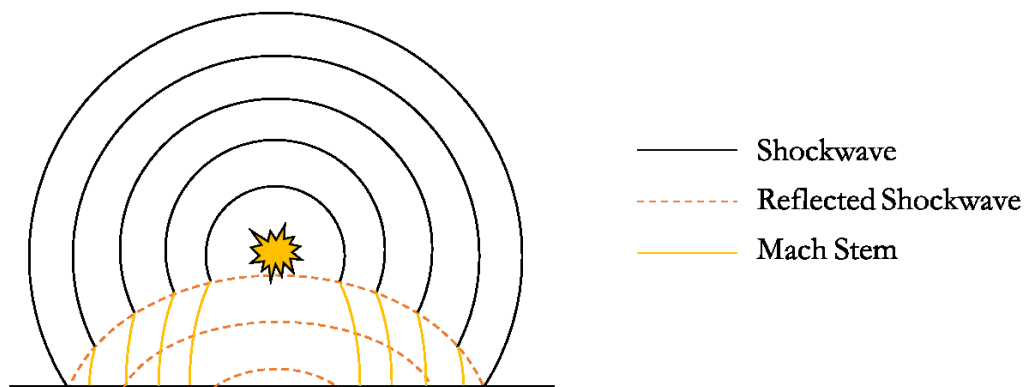


Figure 8: A visualisation of Mach Stem formation

While an open field spherical blast or even simple Mach Stems in a hemispherical surface blast can be modelled analytically, overpressure in real world blast scenarios is far too complex to realistically be determined using such methods, leading to the need for computational simulations to model such events. Cullis (Cullis, 2001) modelled a 1kg TNT charge exploding 50cm above the ground and showed that recorded pressure could be reinforced by wave reflections to reach an overpressure magnitude of up to 8 times the incident pressure. This shows that computational simulations are essential for modelling blast events, as an analytical solution such as the Friedlander equation that doesn't take reflection and interference into account has been shown to be off by a factor of 8 in some cases, and potentially more in complex blast scenarios such as inside a structure or vehicle.

A special mention should be made of the ‘underwash effect’, as it has a specific relevance to the behaviour of a blast wave in the context of military helmets. It was observed by Moss et al (Moss, King and Blackman, 2009) that, when a blast wave was modelled impacting upon a helmeted head model, a local high pressure region occurred in the gap between the helmet and the head on the side opposite to the blast. This effect was also observed by Ganpule et al (Ganpule *et al.*, 2012) and is visualised below in Figure 9 below. Ganpule did note however that the inclusion of a padding layer into the model attenuated this effect to some degree (the model by Moss et al included no padding).

The underwash effect was extensively investigated using CFD modelling by Sarvghad-Moghaddam et al (Sarvghad-Moghaddam *et al.*, 2017), including the effect of differing head orientations. It was noted that the pressure region developed by the underwash effect, like the Mach Stem, can exceed the pressure of the incident blast wave. This represents another example of a complex blast scenario leading to the analytical wave equation under-estimating the severity of a shockwave, this time in a direct military scenario due to it being an effect of military helmets, supporting the need for computational modelling to accurately model a blast event.

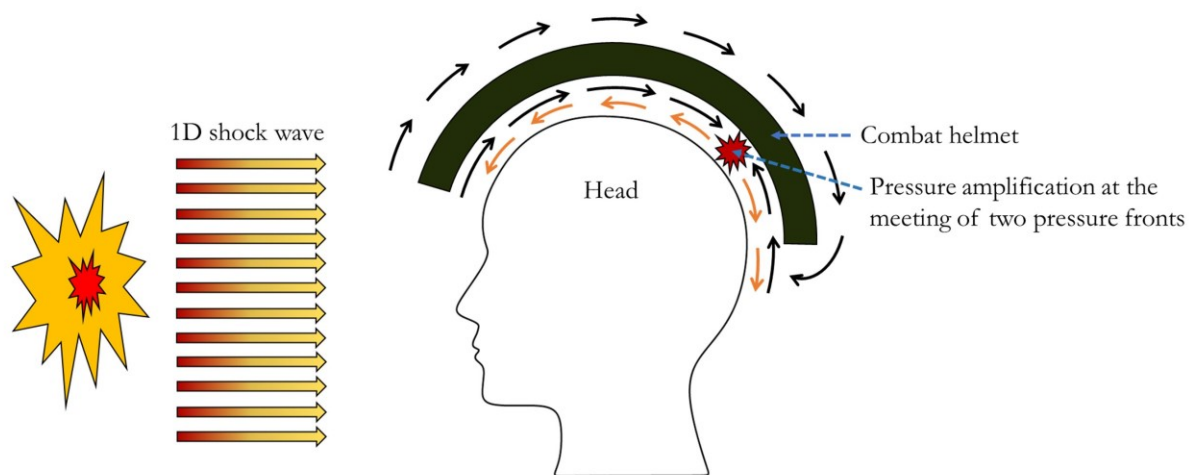


Figure 9: A visualisation of the underwash effect

2.4 Blast modelling

2.4.1 Existing models

As the previous section established, there is a need for computational models to accurately model blast injury in the brain. Blast wave propagation, including reflections and interference, is generally best modelled with Computational Fluid Dynamics (CFD) methods. However, propagation of the blast wave through a structure such as the human head lends itself much more to Finite Element (FE) modelling methods, which will be the focus of this work. Modelling the propagation of the blast wave through the brain is the critical tool which allows a researcher to predict such things as injury location and severity, as well as the effectiveness of new preventative measures such as helmets. It does this by allowing a researcher to model the magnitude and duration of various parameters expected to cause injury, such as pressure, strain, strain rate etc, at different locations within the brain.

Computational modelling of any sort is a fast-moving field due mainly to the quickly advancing nature of available computing resources. Computers today are vastly more powerful than those several years ago and are capable of ever more advanced simulations. In line with this, the degree of complexity in FE models in literature tends to advance quite quickly with time and it is expected to continue to do so into the future, allowing more and more accurate simulations. The only real exceptions to this are in studies where the FE modelling component is either not the primary focus of the work, or one of several focuses, in which case an older or simplified model may be used.

There are a number of models (Kleiven, 2007; Moore *et al.*, 2009; Moss, King and Blackman, 2009; Nyein *et al.*, 2011; Panzer *et al.*, 2012; Singh *et al.*, 2012; Ganpule *et al.*, 2013; Zhang, Makwana and Sharma, 2013; Taylor, Ludwigsen and Ford, 2014; Sahoo, Deck and Willinger, 2014; Singh, 2015; Ghajari, Hellyer and Sharp, 2017) used in literature for investigating the effects of a blast wave on the human brain and they vary significantly in detail and complexity depending upon their application. In the aforementioned paper by Moss *et al.* (Moss, King and Blackman, 2009) where the underwash effect was noticed, a greatly simplified geometry and level of detail was used, representing the brain as a simple half hemisphere shape (Figure 10).

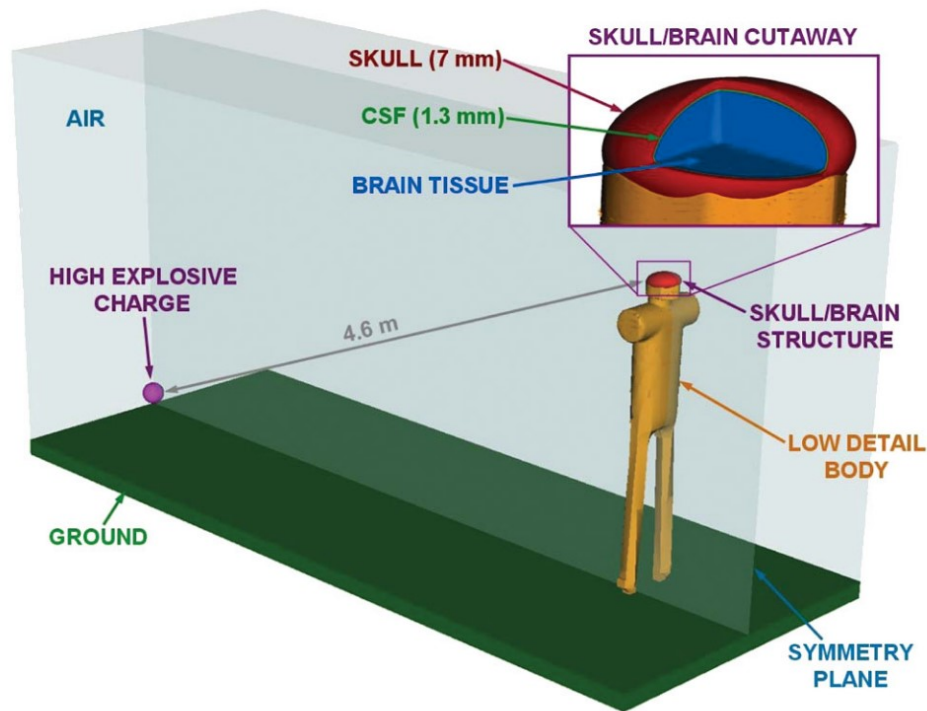


Figure 10: The simplified FE model used by Moss et al (Moss, King and Blackman, 2009)

At the other end of the spectrum there are some extremely detailed 3D FE models in literature, notably the WSUBIM model developed by Zhang et al (Zhang, Yang and King, 2001) at the Wayne State University of Detroit, the SIMon model developed by Takhounts (Takhounts *et al.*, 2008) et al at the National Highway Traffic Safety Administration, the SUFEHM developed by Kang et al (Kang *et al.*, 1997) at Strasbourg University under Willinger and the UC DTBM model developed by Horgan and Gilchrist (T J Horgan and Gilchrist, 2003) at the University of Dublin. There are also several detailed unnamed models such as the one developed by Chafi et al (Chafi, Karami and Ziejewski, 2010) at North Dakota State University, the one developed by Moore et al (Moore *et al.*, 2009) at MIT under Radovitzky, the one developed by Grujicic et al (Grujicic, Arakere and He, 2010) at Clemson University South Carolina and most recently the one developed by Ghajari et al (Ghajari, Hellyer and Sharp, 2017) at Imperial College London, the group from which this work originates, which can be seen below in Figure 11.

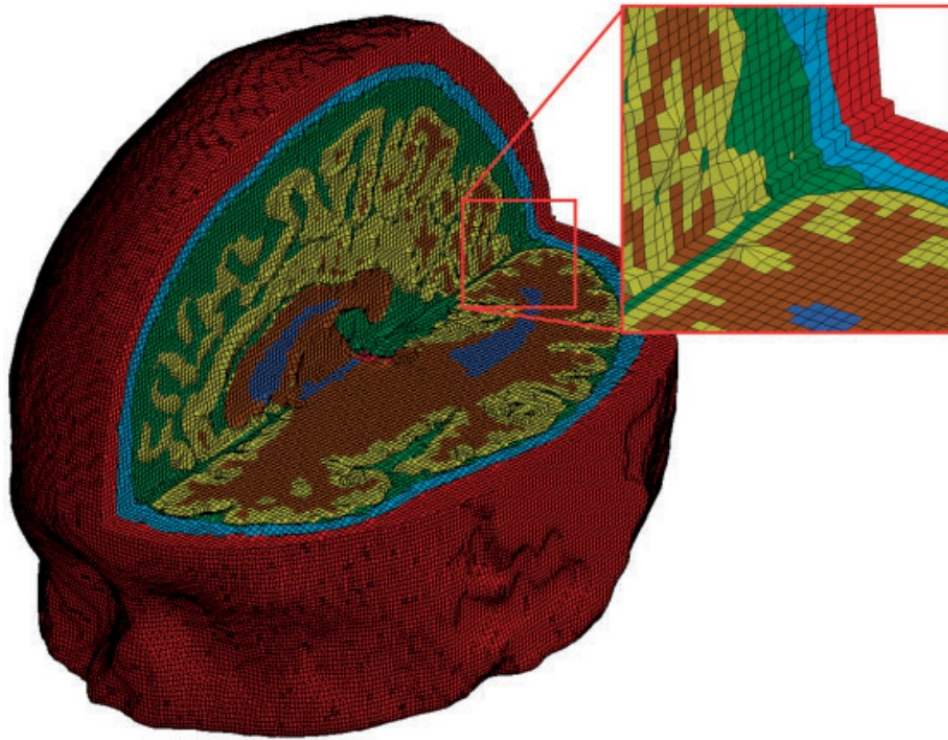


Figure 11: The FE model used by (Ghajari, Hellyer and Sharp, 2017), showing a fine mesh and a high level of detail with many different structures represented within the model

In FE head modelling ‘detail’ can mean one of two things. It can firstly mean the number of elements in the model, directly related to element size and otherwise known as the ‘resolution’ of the model. It can also be a measure of how closely the FE structure mimics the structure of the human head and what details, structures and regions are represented in the model.

Generally, in terms of ‘resolution’, the smaller the elements used in a model, the more accurate the results, since the model is a closer approximation of the (super-atomic) continuum nature of reality. However, it is a system of diminishing returns where past a certain point decreasing the element size in a model will produce a negligible increase in accuracy while greatly increasing the computational power required to run the simulation. One partial solution to this problem is to use a 2 dimensional model, otherwise known as a planar model, such as those used by Panzer et al (Panzer *et al.*, 2012) at Duke University, and Singh (Singh, 2015) at the University of Waterloo. This involves modelling the behaviour of a 2-dimensional slice of the brain and has the advantage of greatly reducing the number of elements in the model, allowing them to be made smaller than previously feasible while still being viable to run. The drawback is the separate loss

of accuracy with these models, as 3D effects and structures can only be modelled to a limited degree.

All of these models have been created with a specific function in mind and as such have different advantages and disadvantages relative to each other. One common differentiator between these models is the amount they compromise in the structural detail they represent. By way of an example, the model by Ganpule et al (Ganpule *et al.*, 2013) models the brain as a single homogeneous structure, the models by Taylor et al (Taylor, Ludwigsen and Ford, 2014) and Kang and Willinger (Kang *et al.*, 1997) include the Falx and Tentorium but no further membranes such as the meninges. The model by Ghajari et al (Ghajari, Hellyer and Sharp, 2017) is the only one currently to represent higher structures such as sulci, which is an important feature in predicting the presence of CTE. CTE can be characterised by hyper-phosphorylated tau deposits, shown as darker areas in Figure 12 below and these were observed by (McKee *et al.*, 2013) to concentrate in the depths of the sulci (Figure 12).

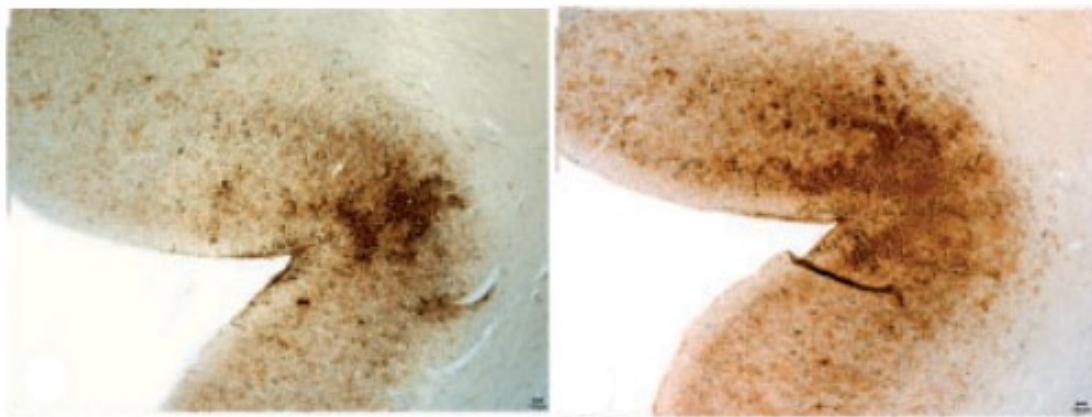


Figure 12: Stained microscopy images showing hyper phosphorylated tau protein concentrations (dark areas) in the depths of the sulci, reproduced from (McKee *et al.*, 2013)

The model by (Ghajari, Hellyer and Sharp, 2017) predicts both high stresses and high strain rates concentrated at these locations during impacts, as shown by the areas of darker red in Figure 13 below. This directly links a probable indicator (stress and strain rate concentrations) to the observed effect (tau concentrations and CTE), underlining the importance of incorporating such detailed geometry and structures into a model, as a less detailed model would be unable to detect these results.

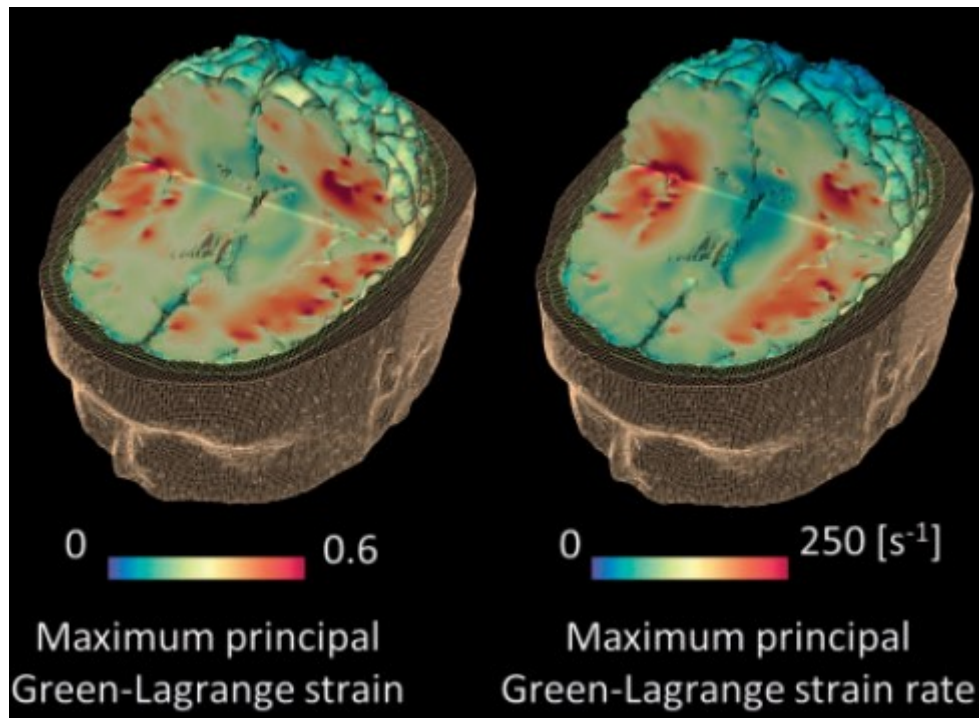


Figure 13: The model by Ghajari et al, showing stress and strain rate concentrations at the depths of the sulci, reproduced from (Ghajari, Hellyer and Sharp, 2017)

As can be seen, a wide variety of computational models are present in literature, an exhaustive review of which is beyond the scope of this work. However several stand out in literature, either because of their widespread use or their relevance to this work, and these models are summarised below (Table 1).

Table 1: An overview of the major FE models of the human head in literature

FE Model	Number of elements	Regions modelled	Brain material model	Detail
(Ghajari, Hellyer and Sharp, 2017)	1250000 (1000000 Hexahedral, 250000 quadrilateral)	11 different tissues including skin, skull, CSF, grey matter, white matter, meninges, subarachnoid space, ventricles	Hyperelastic 2 term Ogden model with 6 term viscoelastic convolution integral	Very high - Includes several different brain regions and differentiates between grey and white matter, includes fine structures and geometric details like the gyri and sulci
(Sahoo, Deck and Willinger, 2014) (SUFEHM)	13208 (5320 in the brain)	Brain tissue (homogenized), CSF, Falx, Tentorium scalp, skull (3 layers), face	3 term Maxwell viscoelastic model	Medium - uses a homogenized brain tissue material without differentiating the different structures. Comparatively high level of detail in the skull.
(Kleiven, 2007)	7128	Brain tissue (multiple structures but homogenous properties) CSF, sinuses, dura, falx, tentorium, pia Compact bone, porous bone, neck bone, scalp, bridging veins	Hyperelastic 2 term Ogden model with 6 term viscoelastic convolution integral	Medium - Many different structures accounted for within the brain, however large element size and no fine geometric details.
(Takhounts <i>et al.</i> , 2008) (SiMON)	45875	Cerebrum, cerebellum, brainstem, ventricles, combined CSF and pia arachnoid complex layer, falx, tentorium, parasagittal blood vessels	Kelvin-Maxwell Viscoelastic model	High - large number of structures accounted for within the brain, but no fine geometric details
(T. J. Horgan and Gilchrist, 2003) (UCDTBM)	9000-50000	Homogenised brain tissue, CSF, pia, dura, falx, tentorium, Skull (cortical bone + trabecular bone, facial bones)	3 term Maxwell viscoelastic model	Medium - detailed skull and several different structures accounted for, however no fine geometric details
(Moore <i>et al.</i> , 2009)	808766	Ventricles, glia, white matter, grey matter, eyes, venous sinus, CSF, air sinus, muscle, skin/fat, skull	Tait equation of state with parameters tuned to the bulk modulus of the various tissue types Neo-Hookean model for	Very High - high level of detail with fine geometric structures present. Differentiates between gray and white matter. Intended for use with blast modelling

			deviatoric response	
(Ganpule <i>et al.</i> , 2013)	255626	Homogenised brain tissue, skin, skull, subarachnoidal space, neck	Elastic volumetric response with viscoelastic shear response	High- high level of detail with a small degree of fine geometric structures. Used for blast loading.
(Yang <i>et al.</i> , 2001) (WSUHIM)	330000	Dura, falx, tentorium, pia, sagittal sinus, transverse sinus, CSF, white matter, grey matter, cerebellum, brainstem, lateral ventricles, third ventricles, bridging veins Scalp, skull (3 layers, cortical + trabecular bone)	3 term Maxwell viscoelastic model	High - high level of detail, differentiates between grey and white matter, large amount of structures modelled but no apparent fine geometric structures
(Chafi, Karami and Ziejewski, 2010)	27971	Homogenised brain tissue, dura, falx, tentorium, pia, CSF, scalp, skull	Mooney-Rivlin hyperelastic model with 2 term viscoelastic convolution integral	Medium – several different brain structures and membranes accounted for, however no fine geometric structures

2.4.2 Constitutive modelling

The level of detail in a computational model is certainly an important factor in the accuracy of the model. However, it should be remembered that the accuracy of results also hinges upon the constitutive model and material parameters used. The constitutive model is an important consideration for any FE modelling problem since it governs the relationship between stress, strain and, when viscoelasticity is incorporated into the model, strain rate in the elements, it essentially tells the model how to behave. For viscoelastic materials such as brain tissue, constitutive equations capable of capturing that behaviour is necessary.

Brain tissue is typically modelled with two components, an elastic/hyperelastic component and a viscoelastic one, which is the approach the many of the computational models take (Kleiven, 2007; Chafi, Karami and Ziejewski, 2010; Ghajari, Hellyer and Sharp, 2017).

2.4.2.1 Hyperelasticity

There are many methods for modelling the elastic/hyperelastic component of brain behaviour, but six stand out in literature, the Neo-Hookean model as used by (Nyein *et al.*, 2011), the Mooney-Rivlen model as used by Chafi et al (Chafi, Karami and Ziejewski, 2010), the Gent model (Gent, 1996) as used by (Rashid, Destrade and Gilchrist, 2014), the Fung model (Fung, 1967) as used by (Rashid, Destrade and Gilchrist, 2012b), the Demiray model (Demiray, 1972) and the Ogden model (Ogden, 1972, 1997) as used by (Kleiven, 2007; Ghajari, Hellyer and Sharp, 2017), as well as in this work.

The Neo-Hookean, Mooney-Rivlen, Gent, Demiray and Ogden models were compared by (Budday *et al.*, 2017) across both tension and compression. Of the models compared, the Neo-Hookean and Mooney-Rivlin were found not to represent the data in (Budday *et al.*, 2017) satisfactorily. Of the three remaining, only the Ogden model was found to satisfactorily represent the experimental data in both tension and compression, with the Gent and Demiray models requiring calibration to represent tensile behaviour, and then recalibration to accurately represent compressive behaviour.

Interestingly, the Ogden model used in Budday's work (Budday *et al.*, 2017) does not conform to the model originally published by Ogden (Ogden, 1997), although it is extremely similar. The differences are further elaborated upon in section 7.2, however the values used for the constants in the variant model are not valid for use in the original, and vice versa. The variant model is also not implemented in LS-DYNA by default, limiting its ease of use. The 2 term Ogden model used by Kleiven *et al* (Kleiven, 2007) and Ghajari *et al* (Ghajari, Hellyer and Sharp, 2017) is an established variant of the Ogden model that is more in line with the original publication and is implemented in that form in several common FE modelling packages.

2.4.2.2 Viscoelasticity

Many of the modern computational models include viscoelasticity in their constitutive model for brain behaviour, as the brain is generally recognised to display rate dependent behaviour. Linear viscoelastic models were used by (Zhang, Yang and King, 2001; Takhoumts *et al.*, 2008; Singh, 2015) either because they were deemed sufficient for purpose, or because of the increased availability of linear viscoelastic parameters in literature at the time of publication. However, brain tissue has been shown to exhibit non-linear viscoelasticity (Jin *et al.*, 2013) and, in the opinion of the author, needs to be modelled as such. Quasi-linear viscoelastic models have been used in literature (Kleiven, 2007; Chafi, Karami and Ziejewski, 2010; Ghajari, Hellyer and Sharp, 2017) and go a long way towards modelling this behaviour, however they have not been widely adopted yet.

Quasi-linear viscoelasticity is most commonly modelled by a convolution integral as detailed by Christensen (Christensen, 1980) and explained in section 6.2, which was the approach used by the aforementioned papers.

2.5 Literature discussion

Blast injury has been shown to be a significant issue in the world today, and one that is gaining more and more relevance as blast injuries, both in civilians and military personnel, are on the rise due to the ever-increasing use of explosives in military and terror operations. FE modelling is an invaluable tool in the investigation, analysis and research of these injuries.

Increasing levels of technology play a role in this, and arguments can be made that technology exacerbates the issue, with more advanced explosives creating larger more devastating explosions and encouraging greater and more widespread use of such weapons. Conversely it can also be said that the increased level of technology going into such weapons allow them to be used more precisely, eliminating or damaging their intended target while minimizing the collateral damage which is characteristic of such inherently indiscriminate weapons. A thorough analysis or a resolution to this discrepancy is beyond the scope of this work. However, it cannot be argued that improvements in technology greatly aid in the prevention and treatment of injuries resulting from blasts.

One of the primary areas of improvement that technology offers is in the use of advanced computational models. Computer power is one of the fastest moving areas of technology in recent years, and the complexity and accuracy of computational models has increased in line with this.

Computational models allow us to simulate blasts in a risk-free environment, removing the need for potentially traumatic animal tests, or human tests that are severely limited in scope due to the need to ensure the subjects safety. Additionally computational models offer a wealth of information that physical experiments lack. Stresses in all directions, strains, temperature, loading history and many more quantities are available for every single element in a FE model, whereas physical experiments are limited to a number of sensors that will typically measure a single quantity, often external to the brain.

The downside to these models is they have to be calibrated. Unlike a physical experiment which is generally a direct measurement of the scenario in question, a computational model measures a simulation of that scenario. Care must be taken to ensure the simulation is accurate in order to acquire valid data.

The geometry of current leading FE models is generally very detailed and is constantly improving. The main area where the models appear to be lacking is in accurate material properties for the brain, without which the model will not behave in a biofidelic manner. Brain tissue is especially poorly characterized at high strain rates such as those experienced in a traumatic impact or blast scenario. Despite brain tissue being known to be non-linearly viscoelastic (Jin *et al.*, 2013), a number of modern studies such as (Zhang, Makwana and Sharma, 2013) and (Singh, 2015) use linear properties due to the lack of non-linear (or quasi-linear) parameters available in literature.

Consequently, there is a need to characterize brain tissue across a range of strain rates and to fit that characterization to a quasi-linear, or otherwise non-linear viscoelastic constitutive model. This is especially important in blast and impact modelling since brain tissue has not been very extensively characterized at dynamic strain rates, and certainly not those comparable to blast scenarios as seen in section 3.1. This is largely due to the lack of suitable apparatus that are capable of performing such a characterization available, both commercially and in literature. It is this lack of high rate characterization that this work aims to address.

3 A new apparatus for high-rate tissue experiments

3.1 The need for the apparatus

There have been various attempts to characterize brain tissue experimentally in the past. Using a variety of materials testing lab equipment, stretch, compression and shear have all been applied to various samples from a variety of species (see Table 2). The results of these various studies differ greatly as illustrated below in Figure 14, with no clear indication of which may be the most valid. The probable cause for this is the variety of testing conditions and apparatus used, with no clear standard across literature.

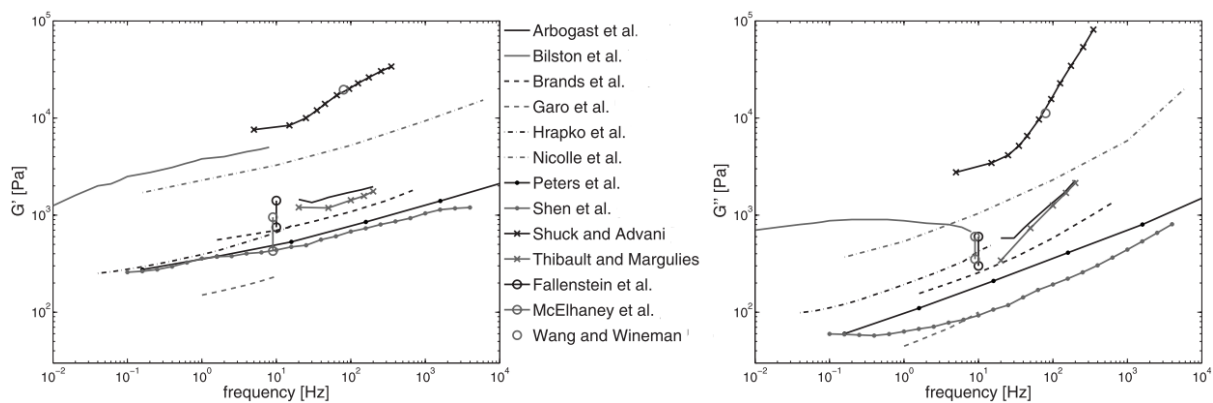


Figure 14: Summary of the linear viscoelastic properties of the brain reported in literature showing the large discrepancy between different experiments, reproduced from (Hrapko *et al.*, 2008)

This is largely to be expected with a problem such as this. Some of the earlier papers that initially kicked off interest in this topic were written more than 20 years before this documents time of writing (Fallenstein, Hulce and Melvin, 1969; Estes, 1970; Shuck and Advani, 1972; Donnelly and Medige, 1997), and in many cases, they were limited by the technology and resources available to them. Although it must be said that in several cases, the results reported by those early papers are still relevant today.

A fundamental problem with the majority of the experiments reported in literature, including most of the older ones and some of the newer ones that focused on other areas of improvement, is that tissue, in particular brain tissue, is highly dependent on the ambient conditions and the age of the tissue (Hrapko *et al.*, 2008), as well as being fundamentally unsuited for the lab apparatus they were using.

Brain tissue has been shown to be highly viscoelastic (Miller and Chinzei, 1997; Prange and Margulies, 2002; Tamura *et al.*, 2008), and this behaviour appears to be nonlinear (Jin *et al.*, 2013). As such it is difficult to infer overall behaviour from the narrow region of strain rates investigated, as well as being similarly difficult to estimate behaviour at an un-investigated strain rate with a flawed understanding of the behaviour. Computational models have predicted strain rates during a blast event of between 226 and 571 s⁻¹ (Singh, 2015) and up to almost 1000 s⁻¹ once cavitation is accounted for (Panzer *et al.*, 2012). Unfortunately the majority of existing lab equipment suitable for testing tissue is only suited to running tests in the quasi-static and very low strain rate regions, as is evident from Table 2. This is reflected in the main body of experimental work in literature, which focusses on this region of low strain rates leaving the higher strain rates unexplored.

A special mention should be made at this point of the Split-Hopkinson pressure bar apparatus, also known as the Kolsky bar, which has been used to mechanically test soft tissue at high strain rates (Saraf *et al.*, 2007; Pervin and Chen, 2009). However, it has a number of limitations which prevent it from being able to test tissue at higher rates without supporting results from other apparatus.

Firstly it is fairly imprecise when being used to test very soft materials such as brain tissue, giving results with a fairly high error region. This was addressed somewhat by (Zhang *et al.*, 2008), which suggested a system of modifications to the original bar design, including special hollow aluminium bars, semiconductor strain gauges and quartz crystal load cells, pulse shaping techniques and annular shaped specimens. However these modifications were only tested on a gel surrogate, not deployed on actual tissue, and represented a large modification to a fairly expensive piece of equipment that could potentially over specialize it, rendering it unsuitable for other materials.

Secondly the Split-Hopkinson bar is limited to a single mode of loading, compression. Again modifications to the setup have been proposed to allow tensile testing such as (Panowicz and Janiszeqski, 2016), and it is believed the system could be modified to allow shear testing as well. However these modifications are largely untested and incompatible with several of the proposed changes by (Zhang *et al.*, 2008), leading to concerns about their accuracy. As well as the existing concern that it would over specialize an expensive piece of equipment.

In the more recent past several attempts have been made to design and prototype custom apparatus to address this lack of equipment suitable to carry out these tests. Several studies (see Table 2) have carried out tests on tissue using custom built apparatus, which have been capable of pushing higher strain rates. However even the highest strain rates achieved by these apparatus were lower than the region we were hoping to test, with a ceiling of 90 s^{-1} in for tensile loading (Rashid, Destrade and Gilchrist, 2014), and the lack of standardization with regards to tissue type and condition, as well as testing conditions and protocols meant there was a need to develop an apparatus that could test in the region we were interested in that would allow us to run our own series of tests where these variables could be controlled.

Table 2: A summary of tissue characterization experiments in literature

	Loading Mode	Strain Rate	Tissue Type
Existing Laboratory Apparatus			
Fallenstein, Hulce & Melvin 1969 (Fallenstein, Hulce and Melvin, 1969)	Shear	9-10 Hz	Human ('cerebral white matter)
Estes & MacElhaney 1970 (Estes, 1970)	Compression	Up to 40 s^{-1}	Human (white matter)
Shuck & Advani 1972 (Shuck and Advani, 1972)	Shear	5-350 Hz	Human (separate white and grey matter)
Brands et al 1999 (Brands, Dave W.A., Bovendeerd, Peter H.M. and Peters, Gerrit W.M., 1999)	Shear	0.1-16 Hz	Porcine (mixed grey and white matter – thalamus)
Bilston et al 2001 (Bilston, Liu and Phan-Thien, 2001)	Shear	Up to 10 Hz	Bovine (Corpus Callosum and Optic Radiation)
Darvish & Crandall 2001 (Darvish and Crandall, 2001)	Shear	0.5-200 Hz	Bovine (mixed grey and white matter)
Miller et al 2002 (Miller and Chinzei, 2002)	Tension	Up to 0.64 s^{-1}	Porcine (mixed grey and white matter)
Franceschini 2006 (Franceschini, 2006)	Tension and Compression	$5.5\text{-}9.3 \cdot 10^{-3} \text{ s}^{-1}$	Human (Corpus Callosum, Thalamus, Medulla Oblongata,

			Frontal Lobe, Occipital Lobe, Parietal Lobe)
Hrapko et al 2006 (Hrapko <i>et al.</i> , 2006)	Compression and Shear	0.04-16 Hz (Shear) 1 s ⁻¹ (Compression)	Porcine (Corona Radiata)
Velardi et al 2006 (Velardi, Fraternali and Angelillo, 2006)	Tension	Approximately 0.01 s ⁻¹	Porcine (grey matter, Corpus Callosum and Corona Radiata)
Feng et al 2013 (Feng <i>et al.</i> , 2013)	Shear	20-30 Hz	Lamb (mixed white and grey matter)
Jin et al 2013 (Jin <i>et al.</i> , 2013)	Tension, Compression and Shear	Up to 30 s ⁻¹	Human (Corpus Callosum, Corona Radiata, Cortex, Thalamus)
Budday et al 2017 (Budday <i>et al.</i> , 2017)	Tension, Compression and Shear	Quasi-static	Human (Corpus Callosum, Corona Radiata, Basal Ganglia and Cortex)
Split-Hopkinson Pressure Bar			
Pervin & Chen 2009 (Pervin and Chen, 2009)	Compression	0.01-3000 s ⁻¹	Bovine (white matter – Corona Radiata, grey matter – Frontal and Parietal Lobe)
Custom Designed Apparatus			
Donnelly & Medige 1997 (Donnelly and Medige, 1997)	Shear	Up to 180 s ⁻¹	Human (mixed white and grey matter)
Arbogast & Margulies 1998 (Arbogast and Margulies, 1998)	Shear	Up to 7.5% strain at 200 Hz	Porcine (brainstem)
Prange & Margulies 2002 (Prange and Margulies, 2002)	Shear	0.42-8.33 s ⁻¹	Porcine (white matter – Corona Radiata and Corpus Callosum & grey matter (thalamus))
Nicolle et al 2005 (Nicolle <i>et al.</i> , 2005)	Shear	0.1-6310 Hz	Porcine (Corona Radiata)
Tamura et al 2008 (Tamura <i>et al.</i> , 2008)	Tension	Up to 25 s ⁻¹	Porcine (mixed grey and white matter)

Rashid & Gilchrist 2012-2014 (Rashid, Destrade and Gilchrist, 2012c, 2012a, 2013, 2014)	Tension, Compression and Shear	Up to 90 s ⁻¹	Porcine (mixed grey and white matter)
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3.2 Aims for the apparatus

In light of the perceived limitations of existing tests, as well as the broad spread of experimental results, it became clear that a new set of tests would be required to accurately determine material properties for brain tissue. These tests would need to be carried out across a range of strain rates not achievable with commercial equipment, and thus would necessitate the design and construction of a new testing apparatus. One which could test at higher rates while minimising or avoiding a number of limitations seen in previous work.

The apparatus was intended to both reinforce the current high rate test results (Tamura *et al.*, 2008; Jin *et al.*, 2013; Rashid, Destrade and Gilchrist, 2014), as well as probe the largely unknown region between the highest non Split-Hopkinson Bar tests (Rashid, Destrade and Gilchrist, 2014), and the lower end of the Split-Hopkinson Bar experimental range (approximately 750 s^{-1}). Therefore our desired strain rate region from the apparatus was between 10 s^{-1} and 750 s^{-1} .

Additionally there has been shown to be a pronounced compression-tension asymmetry in the behaviour of brain tissue (Budday *et al.*, 2017). As such the apparatus was required to operate in both tension and compression in order to investigate this behaviour.

In order to determine material properties in a manner consistent with literature, load and deformation data would need to be acquired for the sample. Specifically the samples deformation would need to be measured as a displacement, while its mechanical response to this deformation would need to be measured as a load. Both would need to be acquired to a high degree of accuracy, a significant challenge, as evident from the wide variety of methods and tools used in attempts to cut the tissue accurately, the high degree of error in reported sample sizes in most literature, as well as being specifically mentioned as a challenge in some papers such as (Velardi, Fraternali and Angelillo, 2006) due to the softness of tissue and the small sample sizes.

Brain tissue is known to be heterogeneous, with many different regions and structures. These structures have been shown to differ significantly in mechanical properties and therefore one of the aims for the proposed tests was to be able to test samples from individual regions. While that obviously presented a challenge for the tissue extraction protocol, in terms of the apparatus it set a high sensitivity requirement. Brain tissue is a soft material and testing very small samples would mean that the signals the apparatus would have to acquire would be very small indeed, fractions

of a newton in some cases. This was exacerbated by the requirement to test on porcine tissue, since pig brains are significantly smaller than human brains, with correspondingly smaller structures. It was estimated that samples could be as small as 4mm, which could result in loads as low as 8 milli-newtons (Franceschini, 2006). The apparatus would be required to read loads this small to a high degree of accuracy.

The final requirements for the apparatus were due to the both hazardous and transient nature of tissue. Since tissue is a potential biohazard it can only be handled in certain labs which adhere to certain safety standards. Additionally, tissue age and dehydration have been shown to affect mechanical properties (Arbogast and Margulies, 1998; Hrapko *et al.*, 2008). Therefore, the apparatus should be portable and easy to clean and disinfect, in order to allow it to be taken into different tissue labs for experiments before being removed safely; this would also help minimise the post mortem time and tissue degradation since potential transport delays could be reduced, or avoided entirely if the apparatus was moved into an autopsy room for example. In order to further reduce tissue degradation, it was decided that the apparatus (and testing protocol) should be capable of running multiple tests in quick succession, so as to avoid a large amount of tissue aging and degradation between the first and final tests.

In summary, the aims for the apparatus were

- To be capable of testing at high strain rates (between 10 s^{-1} and 750 s^{-1})
- To be capable of testing in both tension and compression
- To be capable of testing on very small samples in order to assess the properties of individual regions in the brain
- To be capable of recording accurate deformation data (force and displacement) for such small samples
- The apparatus should be portable, in order to take it into different tissue testing labs and autopsy rooms
- The apparatus should be capable of running tests quickly in order to preserve tissue condition and minimize tissue aging and dehydration.

3.3 Design of the apparatus

3.3.1 Early designs

After deciding what specifications were desired from the apparatus, the first question to answer was how the impulse should be generated. The brain samples were expected to be small, of the order of a few millimetres as they were limited by the size of the various regions in the average porcine brain. Therefore, in order to stretch at a near constant velocity, the acceleration to the desired velocity would have to occur in an extremely small space. This was to ensure that the accelerating portion of the stretch would be a negligible portion of the total stretch applied to the sample.

To achieve this, the impulse would need to either be explosively generated, or initially generated and subsequently applied to the sample once it was already underway. There are multiple ways of generating an impulse when considering such criteria and several designs were hypothesised, one using a dropped weight to generate the impulse (Appendix 1, 10.1.1) and one using a gas powered impactor (Appendix 1, 10.1.2). However both of these designs were eventually rejected in the design stage for a motor based impulse system, which offered a number of advantages in comparison.

- A motor can (depending on the motor) be run both forwards and backwards easily unlike a dropped weight or an impactor. This would allow the apparatus to apply both tensile and compressive loads to a sample without needing a potentially complicated mechanical coupling mechanism to switch the mode of loading.
- A motor based apparatus can be reset easily, without having to lift a potentially heavy weight (Appendix 1, 10.1.1) or re-pressurise a cylinder (Appendix 1, 10.1.2). This would allow for tests to be run at a faster rate, improving the versatility of the apparatus and reducing the potential for tissue degradation between experiments.
- It was felt that any apparatus based around a large impact (such as a dropped weight or a gas-powered impactor) would be comparatively uncontrolled and could produce a high number of vibrations throughout the apparatus from the impact. Considering that our

samples (and therefore our measured signals) were expected to be very small there was concern that the noise generated by other designs might mask the results.

- A motor system takes up considerably less space than a dropped weight or gas impactor, and so an apparatus based around a motor can be miniaturised to a much greater degree than the other two designs, allowing a much more portable device.

Designing a motor-based apparatus presented a new set of challenges. Motors generally do not accelerate explosively enough to reach the speeds required in a sufficiently small space. To offset this, a momentum capture mechanism had to be developed for the relevant system in order to allow the motor to initially accelerate, before coupling to the rest of the system and applying a load to the sample only when the desired motor velocity had been achieved. Motors can broadly be split into two categories, rotational motors and linear motors, each of which requires a different momentum capture method. Designs utilising both a rotational motor (Figure 15) and a linear motor (Figure 16) were developed and can be seen below.

3.3.1.1 The rotary motor design

The rotary motor design allowed the motor to accelerate to its full speed, before being moved into contact with the loading mechanism and coupling via a high friction pad. The rotational motion would then be converted into linear motion by using a toothed gear and rod system in the manner shown below (Figure 15).

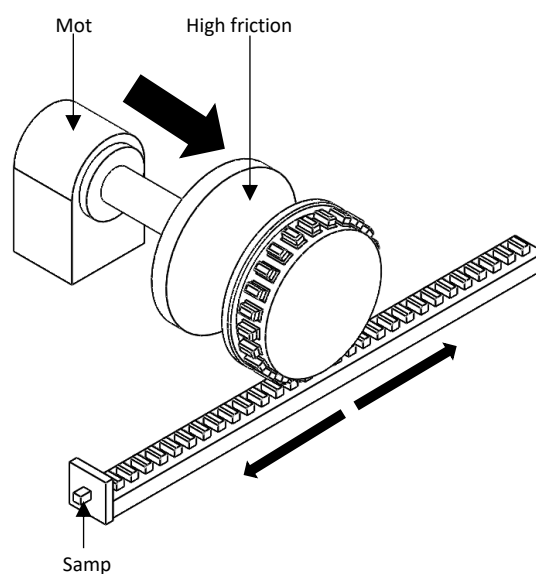


Figure 15: An early design for the apparatus featuring a rotary motor and a high friction pad system to apply load to a sample after the motor was allowed to accelerate

3.3.1.2 The linear motor design

The linear motor design used a hollow cylinder with a catch at the end as a momentum transfer mechanism. The motor would accelerate inside the cylinder before hitting the end, moving the cylinder and applying the load to the sample in the manner shown below (Figure 16).

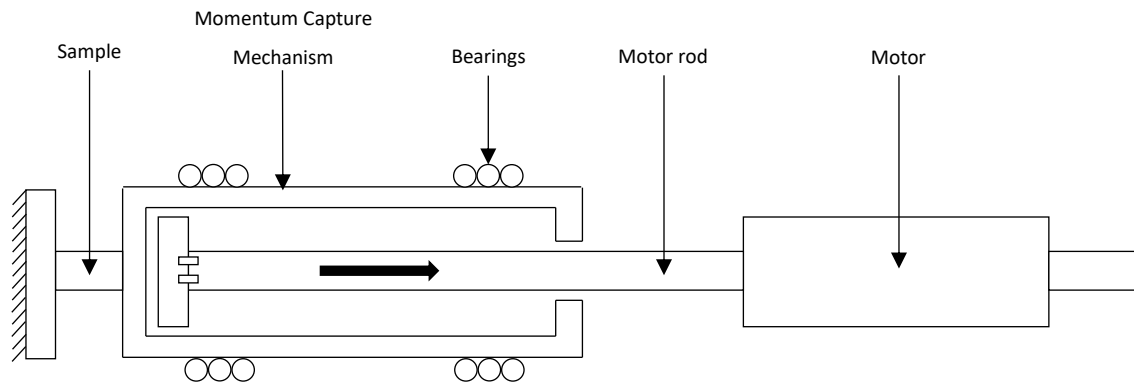


Figure 16: An early iteration of the final design featuring a linear motor and a momentum capture mechanism to apply load to a sample

Both these designs had their advantages. The main benefit for the rotary motor design was that the amount of additional acceleration wasn't limited by the apparatus design. The motor could be spun up to whatever speed desired over whatever time period was necessary before the two parts were mechanically coupled and load applied to the sample. Additionally rotary motors of sufficient power were more commonly available, and the velocity achievable could very easily be increased by use of a gearing system, as long as the power requirements were achievable by the motor.

Conversely high-performance linear motors are significantly harder to come by and a gearing system is significantly harder to implement on a linear model unless the motion is first converted to rotational, at which point using a linear motor over rotary one is pointless. Unless a lever system like in the original dropped weight designs (Appendix 1, 10.1.1) was implemented the speed was limited to the maximum velocity of the motor.

Additionally, in the linear design the acceleration phase is limited by the length of the momentum capture mechanism and the stroke length of the motor. Meaning that the maximum velocity achievable with that design is further limited to the maximum velocity the motor can achieve in that acceleration space, as opposed to its full stroke length.

However, despite these factors the linear motor design was eventually chosen to move forward with over the rotary design for several reasons. Firstly, it was determined that the Quickshaft linear motor could achieve the performance desired, making the design we had viable for our purposes. Additionally the increased simplicity of the design reduced the potential for error and made construction and optimisation significantly easier. For example there was no need to convert rotational motion to linear, removing a coupling step and reducing the number of parts required. Finally, it was felt that the linear motor design had a higher potential for miniaturisation, meaning the apparatus was likely to be more easily portable, which was one of the major requirements.

It is worth mentioning however that the eventual design choice of a linear motor with a cylindrical momentum capture mechanism was made very early on based on estimates of its performance. It was believed that this design would be the most appropriate for our requirements and was used in the final iteration of the design, as can be seen from the CAD model and technical drawing (Figure 17, Figure 18 Figure 20,) and the eventual prototype (Figure 19).

As previously specified, the requirements for the apparatus included simplicity of operation, potential for miniaturization and cost as well as overall performance. None of the designs mentioned above were rejected as fundamentally unfeasible, they were simply believed to be sub-optimal in this specific context, given our parameters and aims for the apparatus. While the linear motor design with a cylindrical momentum capture mechanism was determined to be the best option for our purposes at this early assessment, it is believed that any of the above designs could have made a viable apparatus if given the appropriate design attention.

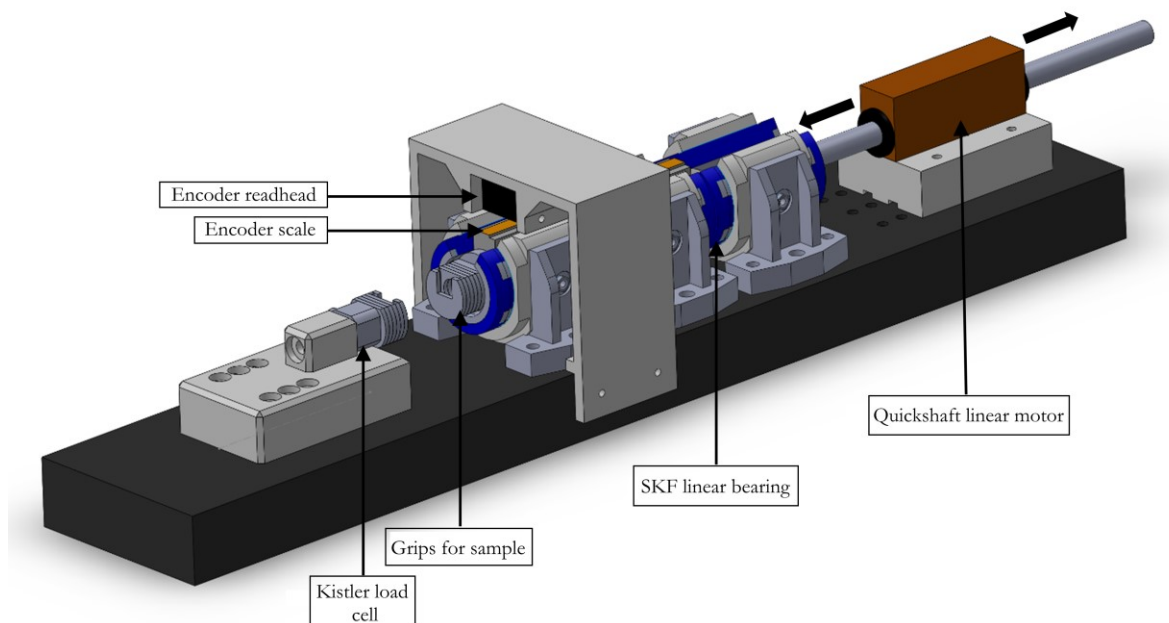


Figure 17: A CAD diagram of the complete apparatus

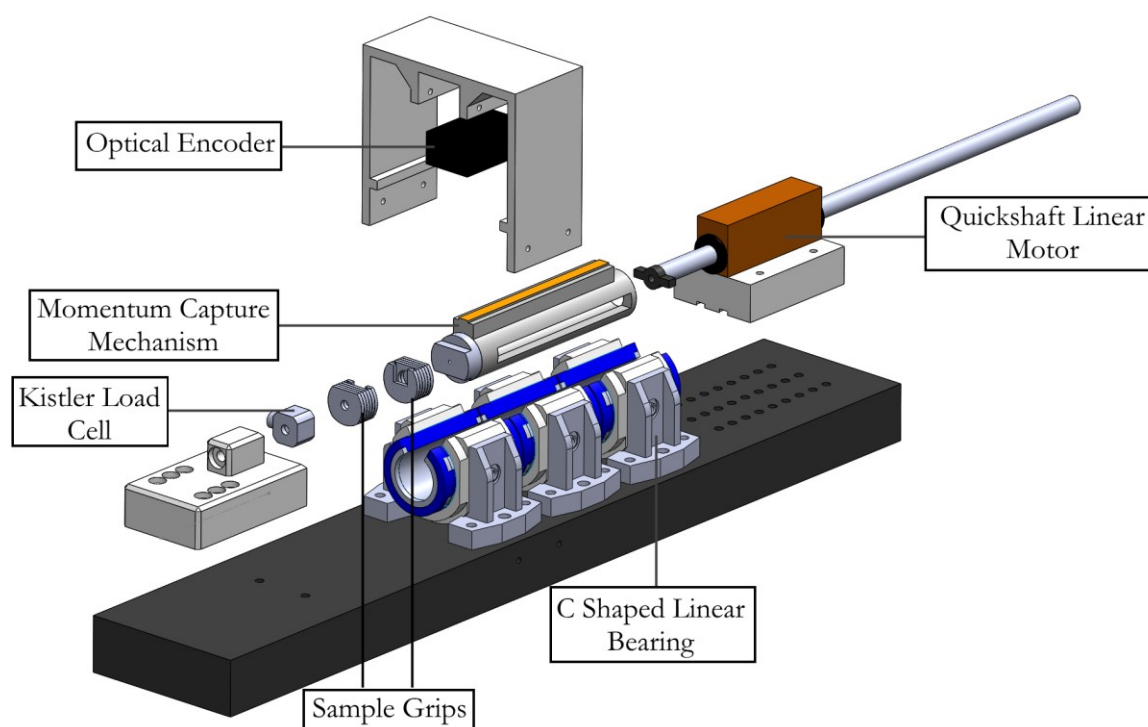


Figure 18: An exploded view of the complete apparatus

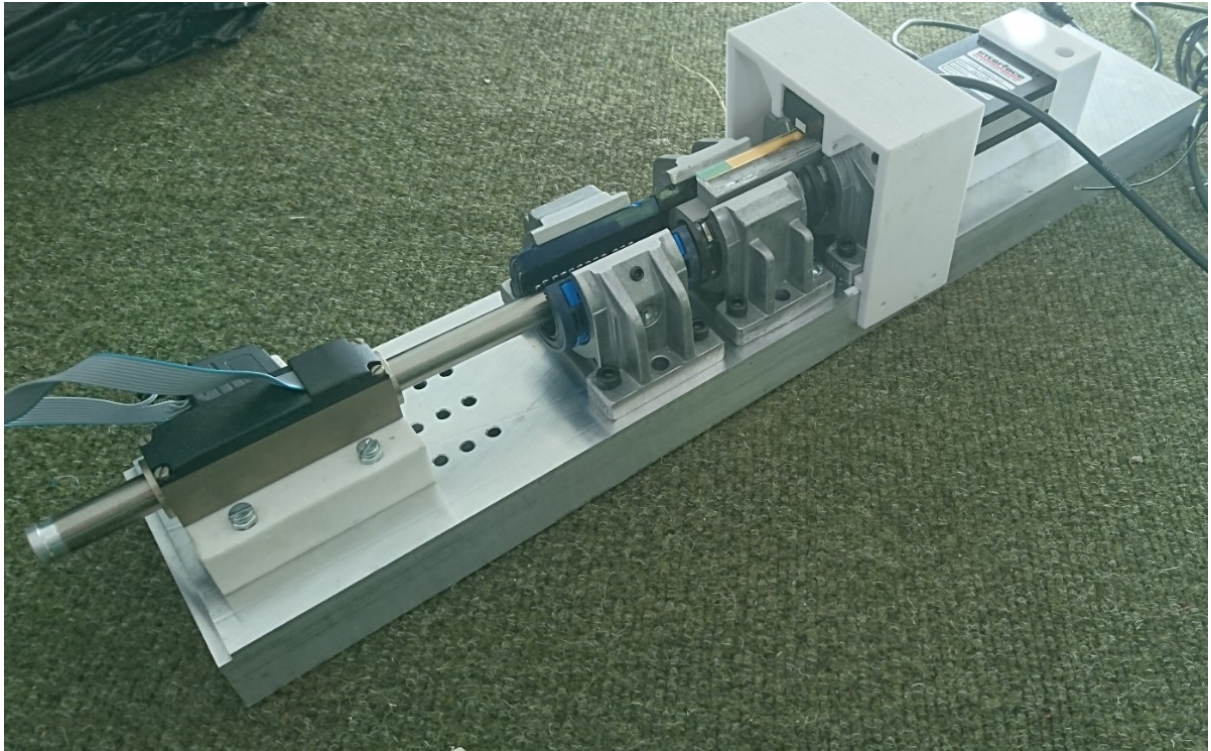


Figure 19: An image of the completed apparatus

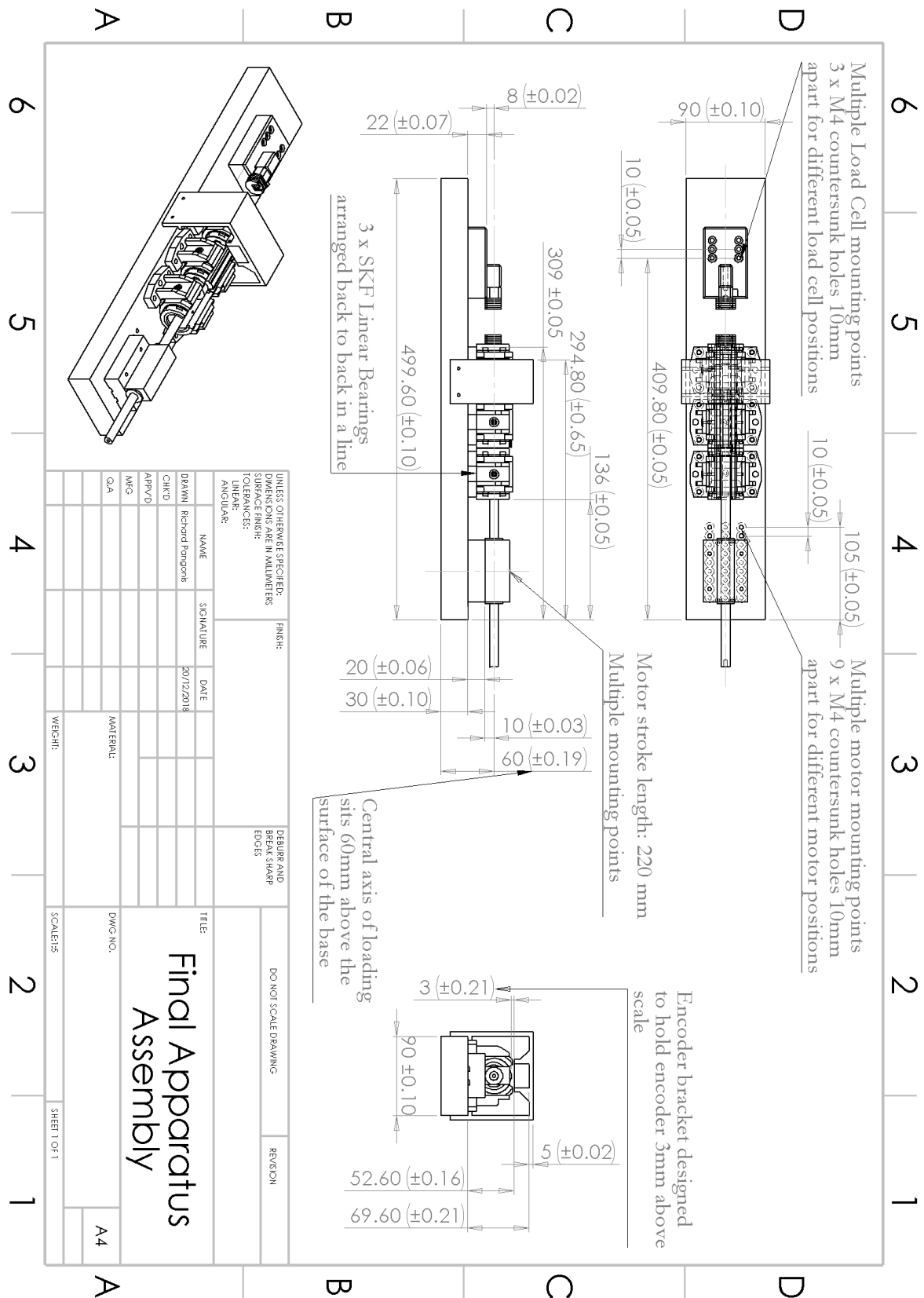


Figure 20: A technical drawing of the final apparatus assembly

3.3.2 Design choices

3.3.2.1 The motor

As previously stated, the choice of the linear motor format was confirmed by the finding of an appropriate motor. The *Quicksaft Linear DC servomotor LM-2070-220-11* was chosen as the motor to power the device. It is a high-performance electromagnetic motor that can achieve impressive speeds in a small space, while still decelerating to zero at the end of the stroke.

The motor can achieve a theoretical peak speed of 2.8 ms^{-1} based on a pyramidal velocity profile according to its datasheet. This peak speed would be reduced in real operation as there would be a load on the motor and it would be required to maintain a velocity rather than hitting a peak. In spite of this, it was estimated that it should be possible to achieve strain rates in excess of 200 s^{-1} using this motor, which was sufficient for our purposes. Its stroke length, which was the main factor in determining the minimum size of the apparatus, was reasonably small at 220 mm. Finally the motor was capable of being run simply in both directions, allowing for both tension and compression testing and it was capable of generating a peak force of 27.6 N. Comfortably in excess of the maximum 2 N requirement expected from literature (Franceschini, 2006).

3.3.2.2 Data output from the device

The apparatus was designed to measure the physical response of tissue to an applied displacement. As such it was required to accurately measure both force and displacement during an experiment with a sufficiently high sample rate to capture high rate behaviour.

Force measurement was accomplished by a load cell. There was a concern that, due to the high rate of testing, the stress wave in the sample would not reach equilibrium during the test and the sample would consequently have different responses on each of its faces. However, it was considered unfeasible to have a secondary load cell attached to the moving side of the sample for several reasons.

- The load cell would add a comparatively large amount of mass to the motor, decreasing the maximum strain rate and making it harder to test at constant velocity. This was a problem even with expensive high-performance load cells, since even when they have

been specifically miniaturized, it proved impossible to find one of sufficiently low mass that was still sensitive enough to measure the expected loads.

- Having a load cell on the moving part would require wires to be attached to it to provide power and record data. This would interfere with the bearings that the momentum capture mechanism had to travel through and was an additional source of drag, further reducing the performance of the motor.
- The load cell would record its own acceleration as force due to its natural inertia, this would be added onto the force recorded from the sample response with no real way of differentiating between the two. It was felt that, under the high accelerations expected from the apparatus this would be significant, adding a high error to the second load cell output.

Since a second load cell was not to be included, this potential error was a cause for concern. However, calculations of the wave speed in tissue gave a longitudinal wave speed of 1500 ms^{-1} and a transverse wave speed of 3 ms^{-1} , both of which were considered fast enough to achieve effective equilibrium in small samples (approx. 5mm).

Finite element simulations were run in LS-DYNA to confirm this, samples were run on a quarter sample in order to reduce computational time. The cylindrical sample size (before quartering) was a cylinder with a 5mm length and 5mm diameter, it was then quartered (Figure 21) and the faces quartered faces were fixed, since in a perfectly aligned cylinder subject to uniaxial tension symmetry can be assumed. It was meshed with an average mesh size of 0.2 mm, with smaller mesh sizes having been shown to not appreciably affect results and the brain material was modelled using a 2 term viscoelastic Ogden model using parameter values from (Kleiven, 2007).

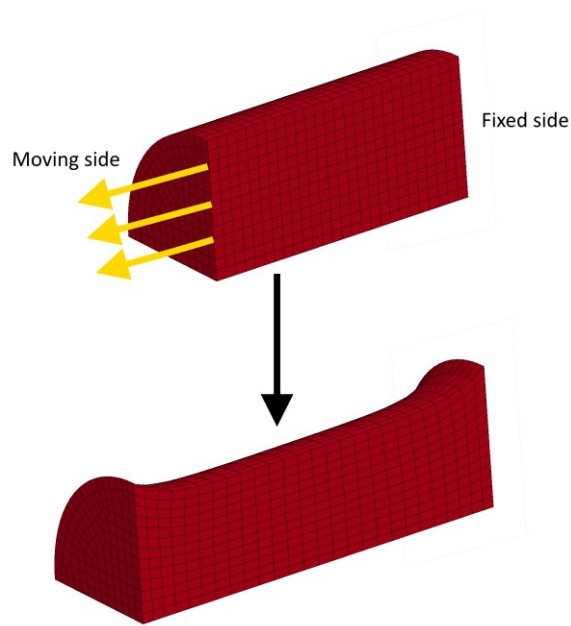


Figure 21: A visualisation of the quarter simulation

The sample was fixed at one side and a velocity profile typical of a high rate experiment was applied to the other side (Figure 22). Analysis of the stress readings from both sides of the sample (Figure 23) showed some difference in the beginning, however during the course of the experiment the differences evened out very quickly to give comparable results past 10% strain at the highest rates, justifying the use of a single load cell in the apparatus.

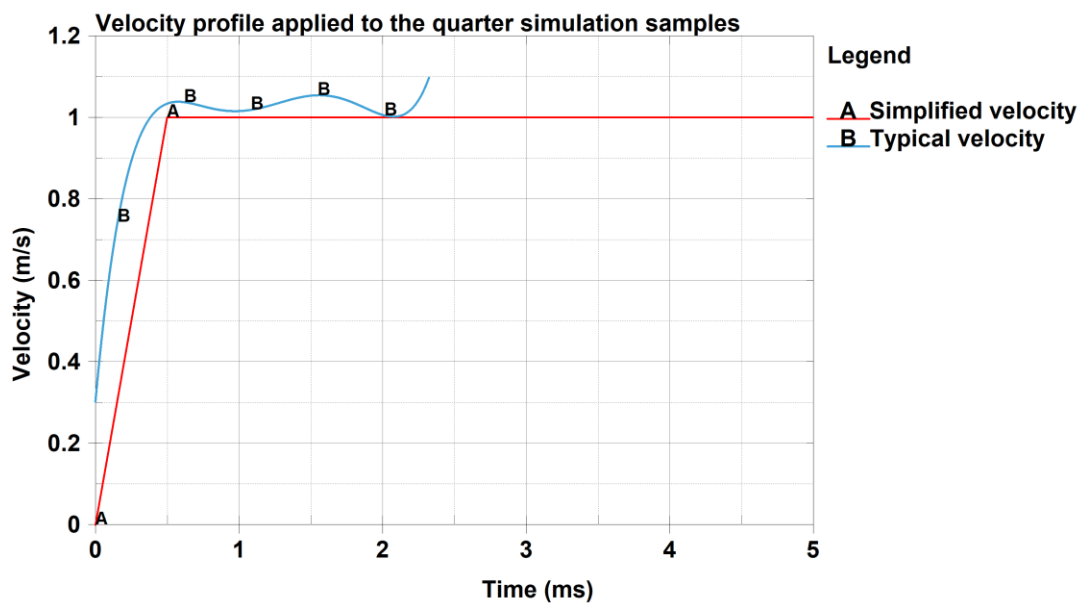


Figure 22: The simplified velocity profile applied to the sample

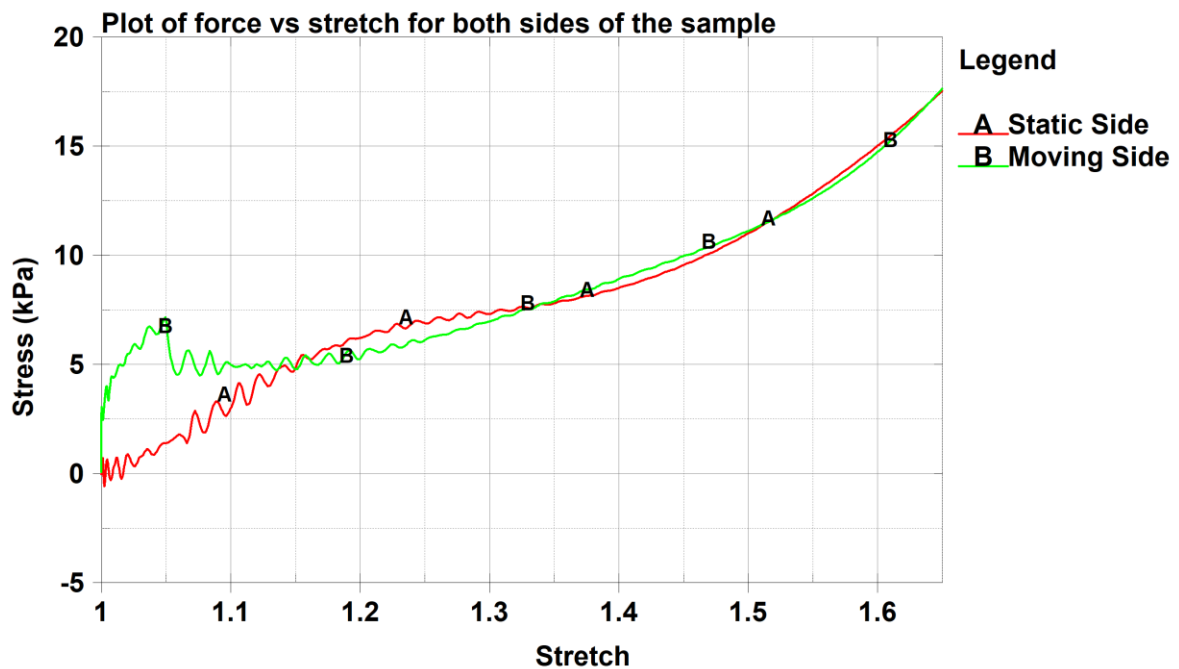


Figure 23: The forces on both sides of the sample compared

3.3.2.3 The load cell

Any load cell used in the apparatus would have to be able to record minute levels of force. Tissue is a very soft material and while its exact properties had yet to be determined, it was expected that the response to displacement would be very small indeed. Results from (Franceschini, 2006) showed upper stresses of approximately 1.5 kPa, which would translate to a load of 0.03 N. Although the tissue response was expected to be viscoelastic, and therefore a higher response than this was expected due to the tests being at higher rate, the load cell would still be required to accurately measure traces with peaks at this order of magnitude.

The initial choice was an *Interface Force ULC-2N* load cell, with a measurement range of 0 to 2 N. This load cell contains a metal internal structure in an S shape, with strain gauges placed on the structure to measure deformation of the S. While it was sufficiently accurate, strain gauges by their nature have a very low output and since we were using the load cell at the low end of its range the output voltage was hidden to a great extent by mains interference (Figure 24).

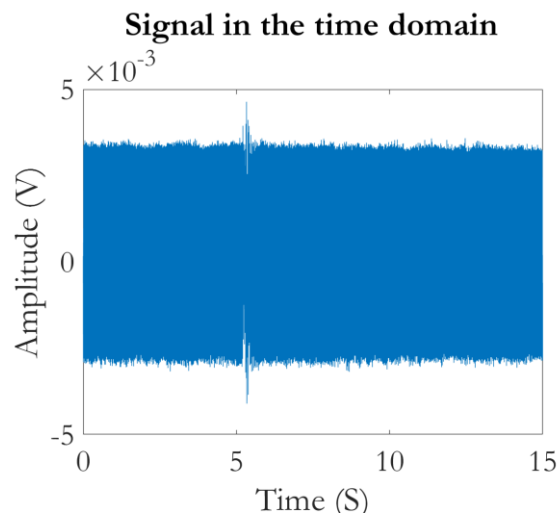


Figure 24: Force readings from an early porcine brain experiment showing a high degree of mains interference

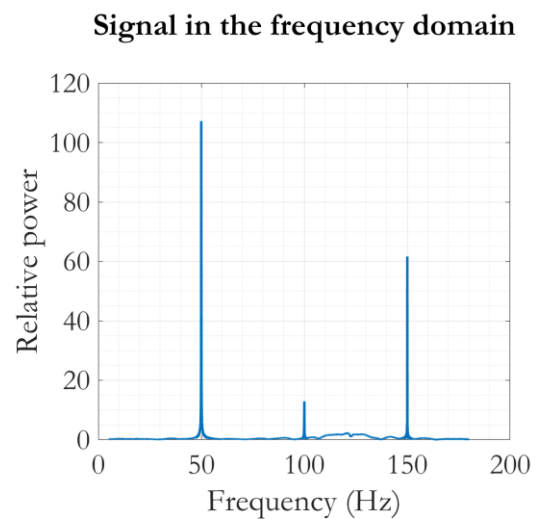


Figure 25: A Fourier analysis of the early porcine brain experiment signal showing high interference at mains frequency and its harmonics

A Fourier analysis of this signal (Figure 25) confirmed that the main frequency component was the 50Hz mains interference (along with its harmonic frequencies). Filtering was an option since the main noise frequency was known, however it was not ideal due to the effective frequency of the tissue response being fairly close to the mains frequency leading to concerns that any filtering in that frequency region could artificially influence the tissue response signal.

Isolating the apparatus from mains power significantly reduced the noise as shown below (Figure 26), which made the signal much cleaner and much more suitable for filtering, since the mains component was largely removed and the dominant noise frequency was significantly higher (Figure 27).

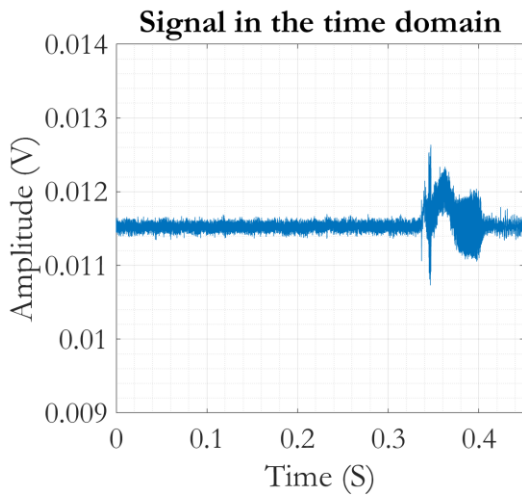


Figure 26: Force readings from a comparable porcine brain experiment showing much lower noise levels as a result of isolating the system from mains power

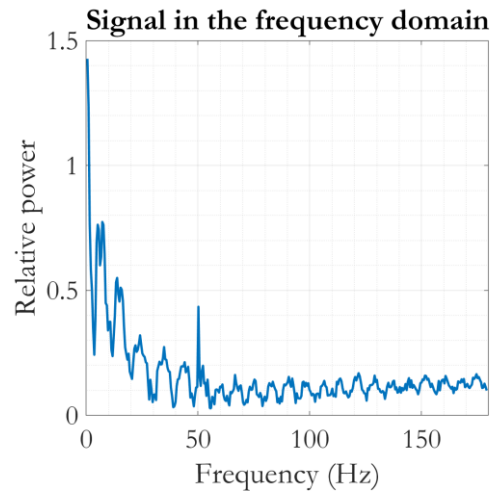


Figure 27: A Fourier analysis of this isolated signal showing a much lower comparative noise peak at the 50Hz mains interference frequency

While isolating the load cell and the datalogger from mains power did largely solve the noise problem, it was still far from an ideal solution. This was mainly due to the impracticality of actually isolating the load cell from the mains. For example, it meant that readings could only be taken from a laptop and not a mains powered desktop computer, additionally the laptop would need to be running on battery power and not being charged via mains power. It can also be seen that the signal in Figure 26 is still quite messy, while the signal is now significantly higher than the noise it is still hard to infer an accurate shape of curve reliably from that type of a signal.

The other problem with isolating the load cell was that the motor was powered by mains power and controlled by a computer, which meant that there was an unbroken connection between mains power and that computer even if it was a laptop running on battery power. This meant that the load cell could not be connected to this computer without connecting it to the mains power interference too.

As Figure 26 shows, it was possible to isolate the load cell and take readings, however this was done in a very inefficient way with one laptop controlling the motor and a second one unplugged from mains recording data from the load cell. This system was also dependent on the user activating both the data recording LabVIEW program and the motor at the same time on both machines. Because of these difficulties it was decided that an alternative solution needed to be found.

A Kistler Type-9712b5 Quartz load cell was selected as a final solution to this. Load cells based on quartz technology output significantly higher voltages for a given load than a strain gauge load cell. For reference, the Kistler load cell outputted 181.4 mV/N while the Interface Force load cell outputted 13.01 mV/N. Since isolating the load cell from the mains was considered impractical the hope was that the increased output magnitude would cause the measured response to ‘rise above’ the interference.

As can be seen in Figure 28 below, the Kistler load cell gave a much greater response to the load. Mains interference is still an issue; however, the signal is much more readable than the Interface Force load cell output, even when isolated from the mains and the mains interference component is relatively insignificant now as can be seen from Figure 29. The ability to read the output of the new load cell even when it was connected to mains power meant it was possible to run the device and the datalogging from a single laptop without worrying about whether it was charging or not, allowing the process of activating the datalogger and the motor to be automated, increasing the usability of the apparatus and reducing human error.

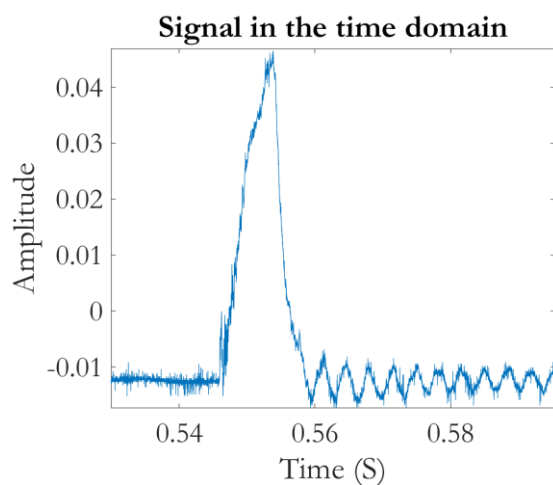


Figure 28: Force readings from a porcine brain experiment showing a greatly improved signal to noise ratio when using a Kistler piezoelectric load cell, even with mains interference

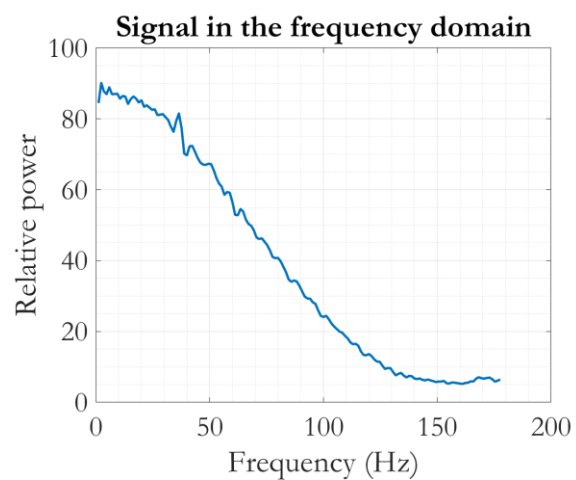


Figure 29: A Fourier analysis of the readings from the Kistler load cell, showing no significant spike at mains frequency

3.3.2.4 Measuring displacement

The Quickshaft linear motor has integrated sensors for tracking its own displacement, these are Hall effect sensors that measure the magnetic field of the motor rod and use that to track

displacement. However, upon comparing their output with high speed video test of the apparatus moving, it was discovered that they were not accurate enough for our purposes. Additionally, the sampling rate was insufficient and the difficulties inherent with syncing the displacement up with load measured by a different datalogger meant that an alternative solution needed to be found.

The first method attempted for tracking displacement was using an accelerometer fixed to the momentum capture mechanism. The acceleration undergone by the momentum capture mechanism would be recorded and integrated twice to give first velocity, and then displacement of the momentum capture mechanism. The accelerometer was considerably lower mass than the load cells under consideration, so the additional weight applied to the motor was not as big an issue as with the second load cell. However any error or drift in the signal was compounded by each integration step, so while the acceleration was measured accurately, the velocity had large amounts of error after the integration and the displacement was essentially unusable.

The second method was using a linear variable differential transducer (LVDT), essentially an electrical resistor with a sliding contact used to measure displacement. This had the advantage of measuring the displacement directly, unlike the accelerometer, and thus avoided the errors inherent in the integration steps. Ultimately though it added too much resistance to the motion of the momentum capture mechanism to be a viable method of measuring displacement.

The final method for recording displacement, and the one that was used in the eventual prototype was an optical encoder, the actual model was RGH41, purchased from Renishaw. An encoder is composed of two components, a read-head and a scale. The scale is a float length of material that is striped, alternating between non-reflective and reflective. The striping pattern is regular with a known thickness, known as the pitch of the scale. The read head contains a laser and an optical receiver and is used to read the scale.

The read head shines a laser onto the scale and records whether the surface is reflective or not. As either the scale or the read head moves the reading will change from reflective (high) to non-reflective (low), giving a measurement of displacement with time. Most encoders have 2 scales and 2 lasers, with the scales 90 degrees out of phase with each other. This allows the encoder to read the direction the relative motion is in by determining which scale is leading the other (Figure 30).

Of the two components, the scale is by far the smaller and lighter of the two and so this was chosen to be the moving component, as it would have the least effect on the motor and the speed applied to loading the sample. The scale was installed on the top of the momentum capture mechanism and a custom bracket was designed and 3d printed to hold the read head exactly 1mm above the scale throughout the motion.

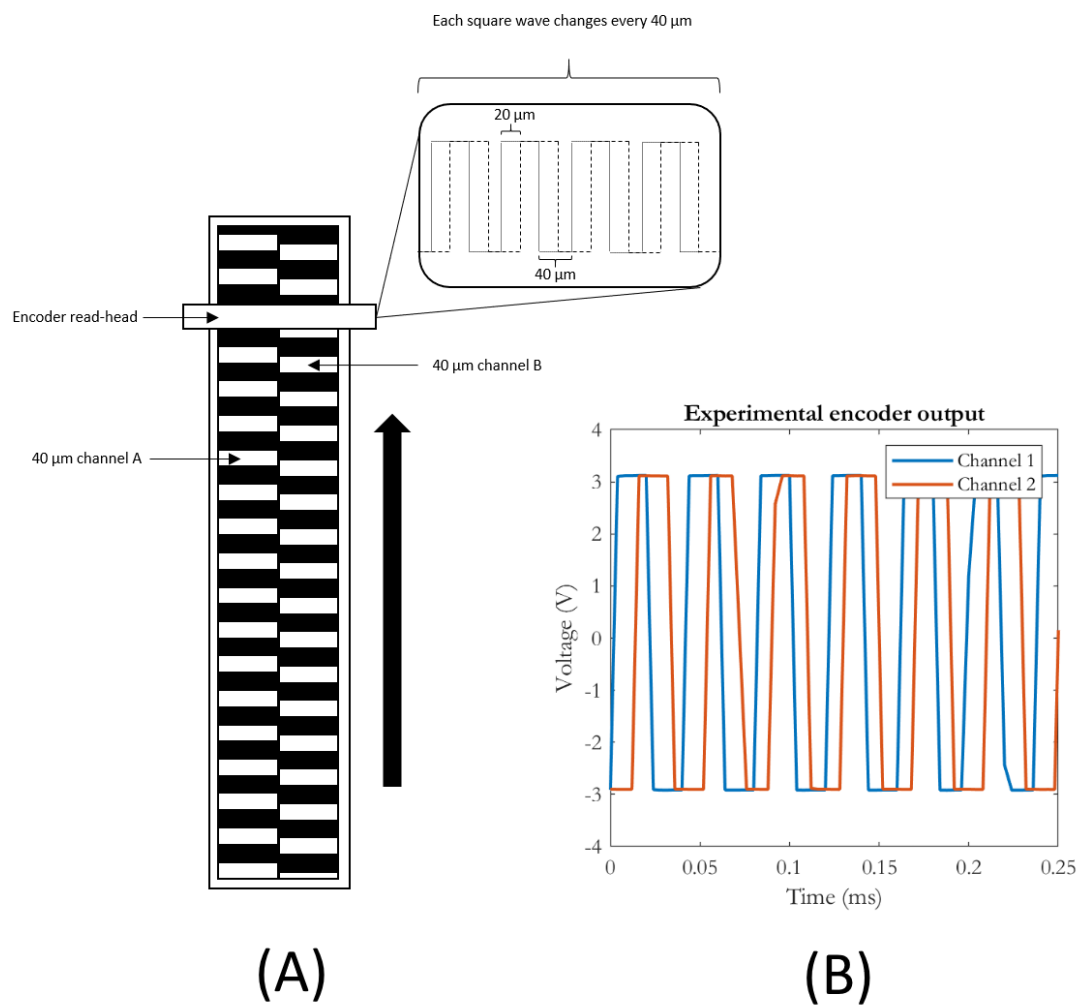


Figure 30: (A) An illustration of the method of operation for an optical encoder, (B) Actual output from an optical encoder when run at a high speed

3.3.2.5 The momentum capture mechanism

The momentum capture mechanism offered a unique challenge in that it needed to be as low mass as possible, so as to minimize the impact it had on the motor speed. While still being strong enough to handle the impacts and high accelerations it would undergo. Additionally it had to be suitably resistant to vibrations and other oscillations so as to keep the apparatus viable.

The initial design was a trolley-based system on a sliding linear stage. However this was rejected after finite element models of the design highlighted a substantial bending moment in the setup due to the loading not being in line with the sample, causing the momentum capture mechanism to flex during operation and introducing excessive vibrations into the readings.

A new momentum capture mechanism was designed based around a single axis of loading. This prevented the bending moment since the force vector now went through the parts centre of gravity. The initial design had four cut-outs to minimize the parts mass and a 3D printed version was created using an Ultimaker-2 printer during early iterations of the device.

Initially the 3D printed version was too weak and flexed too much under the vibrations induced by the device. A second momentum capture mechanism was 3d printed using a Z-Corp 3d printer, which is based on a sintering action rather than laying down layers of plastic, which gives a denser and stronger part. However, it still showed an undesirable level of flexion and the rough surface of the part was adding too much friction and fouling the bearings.

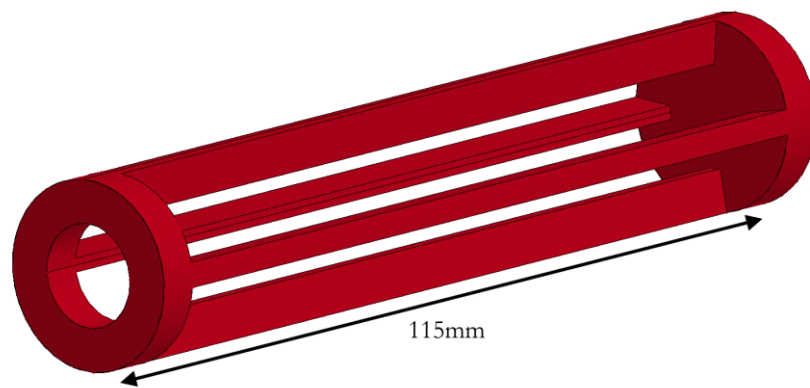


Figure 31: An early design for the momentum capture mechanism

A stronger momentum capture mechanism was designed with two cut-outs to increase its overall strength and machined from aluminium. This did have substantially higher mass than the initial designs. However, this was offset by the reduced friction on the smoother aluminium surface which gave a much more consistent velocity profile. Additionally, the motor proved sufficiently powerful that the additional mass did not significantly affect the velocity.

The momentum capture mechanism was very time consuming to manufacture, therefore it was designed in two parts, with a removable 'cap' that could be manufactured more easily and

replaced to allow for different grip mounting methods, a CAD model (Figure 32) and an engineering drawing (Figure 33) can be seen below. The overall diameter of 24.90 mm was chosen based on 3d printed prototypes in order to fit into the 25 mm linear bearing with minimal friction while still not significantly ‘rattling’ or affecting alignment.

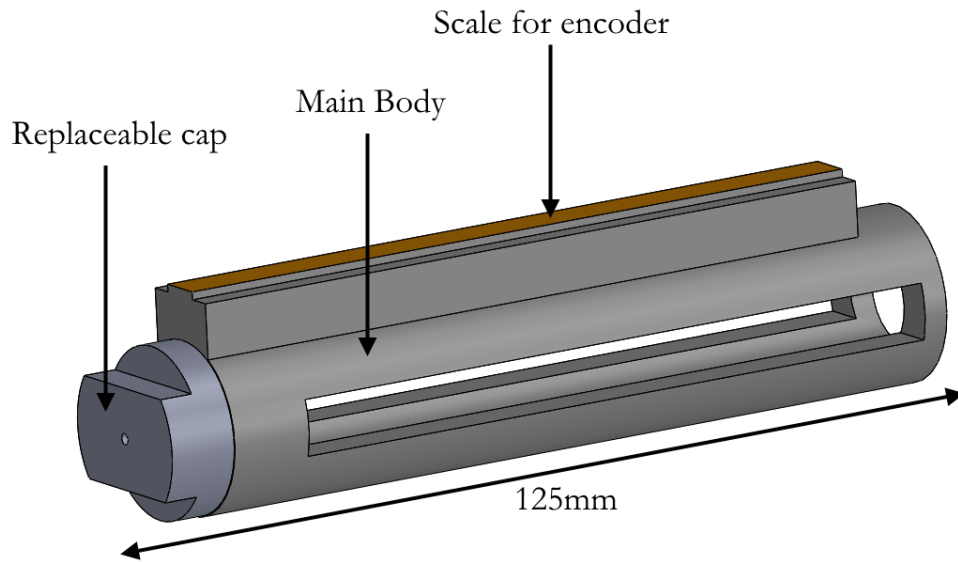


Figure 32: The final momentum capture mechanism design

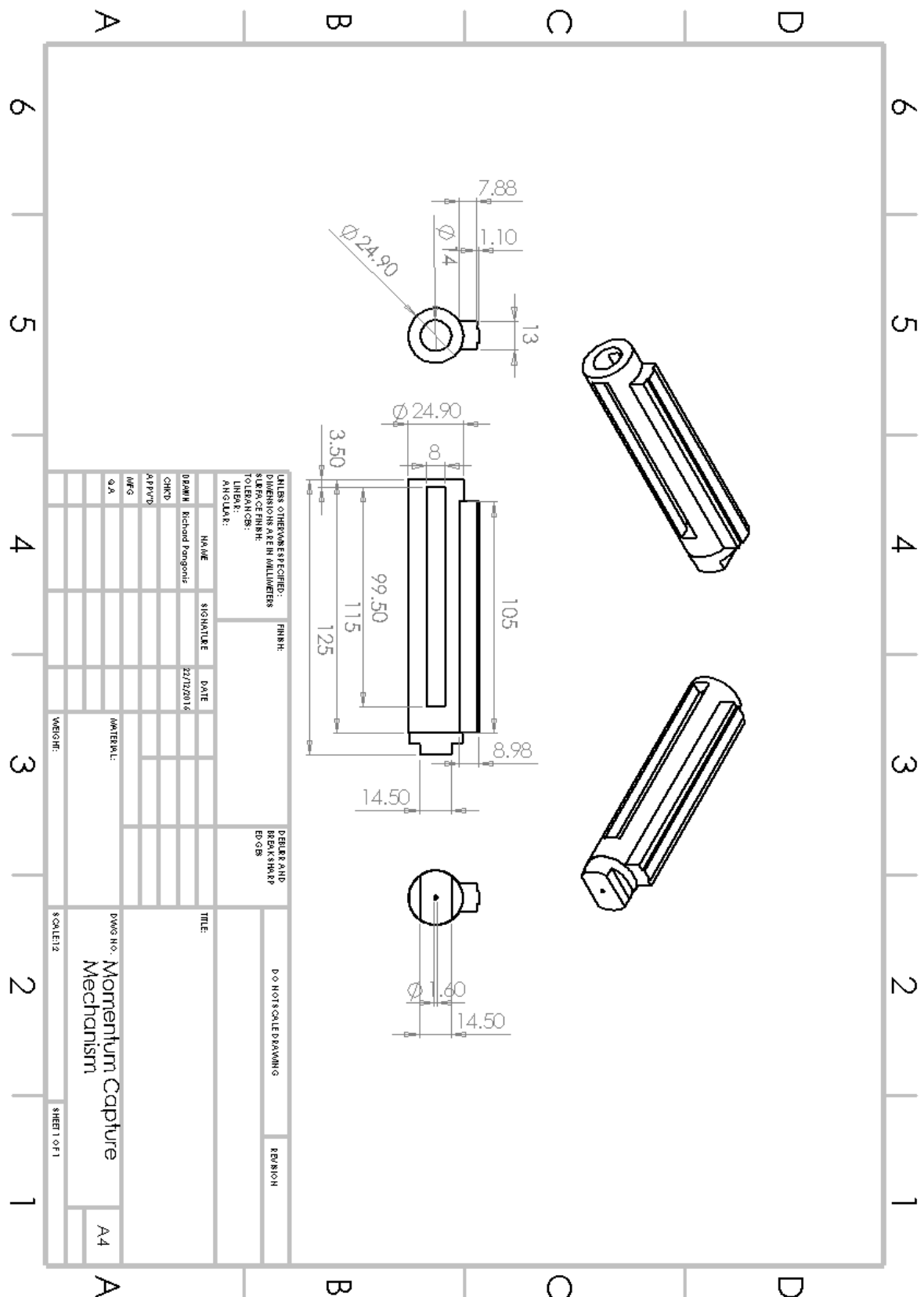


Figure 33: Engineering drawing of the final momentum capture mechanism design

3.3.2.6 Other design considerations

Since everything in the apparatus had to move along the same axis, alignment was a significant concern. The length of the eventual apparatus base (550 mm) meant that even a small error translated into a large discrepancy. For reference, an error in the angle the surface made with a flat plane of just 1 degree would translate to a height difference of 9.6 mm between one side and the other.

The base was machined from high quality tooling plate, which is cut by the supplier specially to sit flat at a high tolerance. Kastal 300 tooling plate was purchased from Smiths metals, which has a thickness tolerance of 0.35mm/m. The length of the apparatus base was kept approximately 150 mm longer than necessary as the design contained multiple fixation points, allowing the components of the apparatus to be moved in order to test different sized samples in both tension and compression while using the full stroke length of the motor.

The axis of loading was determined by the linear bearings used. Due to the design of the encoder and the need to have the scale constantly visible, open C shaped bearings had to be used. Initially two SKF LUCF 25 (25mm bore) were used, however the lack of support across the full range of motion caused some alignment problems at the extreme edges of motion, so a third one had to be added.

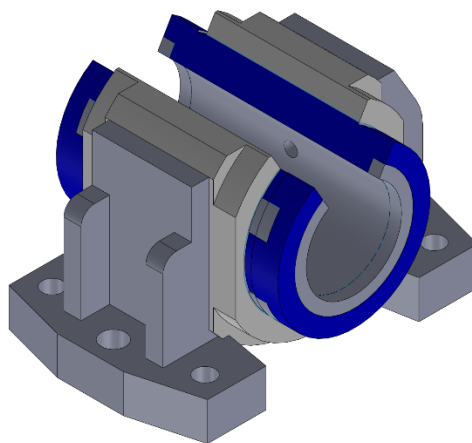


Figure 34: A CAD model of the SKF LUCF-25 linear bearing

Since the motor, load cell and encoder were all different sizes to the bearings, custom brackets had to be manufactured to raise them all to the same axis. Again, these had to be raised within a very tight tolerance as any error in alignment would mean substantial resistance to the motion of

the momentum capture mechanism and a possible bending moment. Custom brackets were 3d printed for all three components using the Z-Corp printer, which can print to a higher precision than the Ultimaker-2 printers.

The final component in the apparatus was the sample grips and the sample testing plates. These were originally 3D printed on an Ultimaker-2. However, while suitable for early experiments the Ultimaker-2 versions were ultimately unsuitable for the application, both because of their mechanical strength and the precision the printers were capable of. While the Z-Corp printer was an option the cost associated with it was considered overkill, particularly since the sample plates were going to be disposable. A second iteration of the grips saw them made out of folded sheet metal, however due to the design the folding process was imperfect, they did not hold the plates tightly enough.

In the final iteration both the plates and the grips are made from 2mm thick extruded acrylic, which is cut to size with a laser cutter. For the grips several shapes need to be stacked up and connected with a cyanoacrylate adhesive.

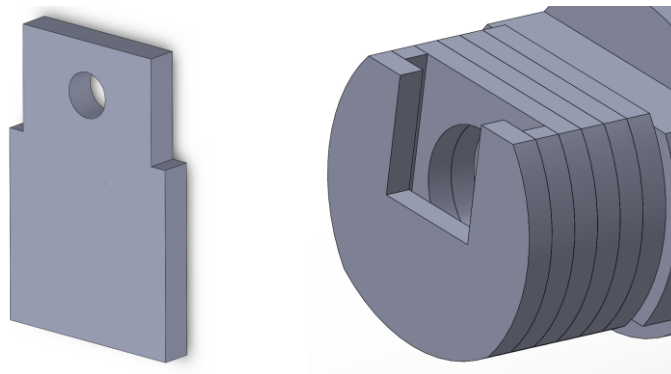


Figure 35: CAD models of the sample plate (left) and the grips (right), made from slices of 2mm thick acrylic

3.3.2.7 Data acquisition

Datalogging presented a challenge because of the high speed of the motor being used and the detailed resolution of the encoder. As shown in Figure 30, while each square wave outputted by the encoder changes every 40 μm , the total signal changes every 20 μm due to the signals being out of phase. Therefore any datalogger used would need a minimum sampling frequency of 1 sample every 20 μm . Considering the motor was expected to travel at speeds up to 2.5 ms^{-1} , this would mean the datalogger would require a sample rate of at least 125 kHz to be able to record the data.

During the earlier design phases an NI 9234 was being used to collect data. This was chosen because it was capable of providing constant current excitation from its channels, in addition to data recording. Back when an accelerometer was being used this was the primary requirement as it was needed to power the accelerometer. However this particular module only has a maximum sample rate of 40 kHz per channel, which cannot be combined into a faster rate in fewer channels.

Attempts were initially made to use this with the apparatus. If the assumption that the apparatus would only travel in one direction during tests was justified, the required sample rate would halve, since only one channel would need to be measured and therefore a resolution of 40 μm , rather than 20, would be needed. Therefore, if the speed was limited to 1.6 ms^{-1} , a sample rate of 40kHz would suffice. Early testing and lower speed (limited to 0.4 ms^{-1} for accuracy) validations were carried out using this datalogger. However high-speed video recordings of tests showed the assumption that the momentum capture mechanism only moved in one direction to be false for stiffer materials such as Ecoflex gel and Armourgel. Additionally, there was the desire to test at higher speeds so other datalogging methods were investigated.

A RIGOL digital oscilloscope was initially used to measure the apparatus displacement at high speeds. With a sampling frequency of 20 MHz its sampling rate was more than sufficient for its purpose. However, it was a large desktop oscilloscope and its size greatly affected the portability of the apparatus. Additionally, it required mains power, rather than being powered by USB and therefore it was unsuitable for use with the Interface Force load cell, which was in operation at the time as described in section 3.2.3.

Picoscope digital oscilloscopes provided a potential solution to the shortcomings of the RIGOL scope. They are small digital oscilloscopes roughly the size of a large smartphone that connect directly to a computer via USB, thereby making it possible to isolate them from the mains. They also have sufficiently high sample rates. Unfortunately the ones on hand had only two channels and so were incapable of measuring both channels of the encoder as well as the load. It also proved difficult to sync up multiple Picoscopes to the same clock and so the data traces from multiple scopes were out of sync. Picoscopes with more channels are available for purchase however it was felt that the increased integration and usability of National Instruments hardware justified the additional cost when purchasing a new datalogger, meaning Picoscopes were eventually passed over.

A National Instruments 9223 datalogger was purchased and installed in the final iteration of the device. This has a maximum sample rate of 1MHz per channel across 4 channels and was more than sufficient for the apparatus. Like both the RIGOL scope and the Picoscopes it was not able to provide constant current excitation. However this was no longer necessary as the encoder, rather than the accelerometer was being used to measure displacement at this point. It was chosen over the cheaper Picoscopes mainly because of the option to integrate it with the LabVIEW programming and data acquisition environment easily. Additionally, it is not hard wired into the apparatus and can be taken out and used for other experiments. Consequently, its increased versatility for a variety of blast experiments ultimately justified the additional cost.

3.4 Prototyping and validating the apparatus

Once the apparatus was assembled, it was necessary to check that the readings it was giving were accurate. The apparatus outputs both force via a load cell, and displacement via an optical encoder. Both of these were checked as detailed below in order to validate the apparatus.

3.4.1 Validating the load cell

Both the Kistler and the Interface Force load cells came with a calibration certificate, giving the conversion factor from output voltage to measured force. Both of these calibrations were validated by suspending a known weight from the load cell and measuring its output.

This method is less reliable than the lab tests used to calibrate the load cells at their manufacturing plants, therefore it was merely used to check if the calibration was approximately correct. If the calibration was sufficiently close to these suspension test results, the calibration conversion factor was deemed trustworthy.

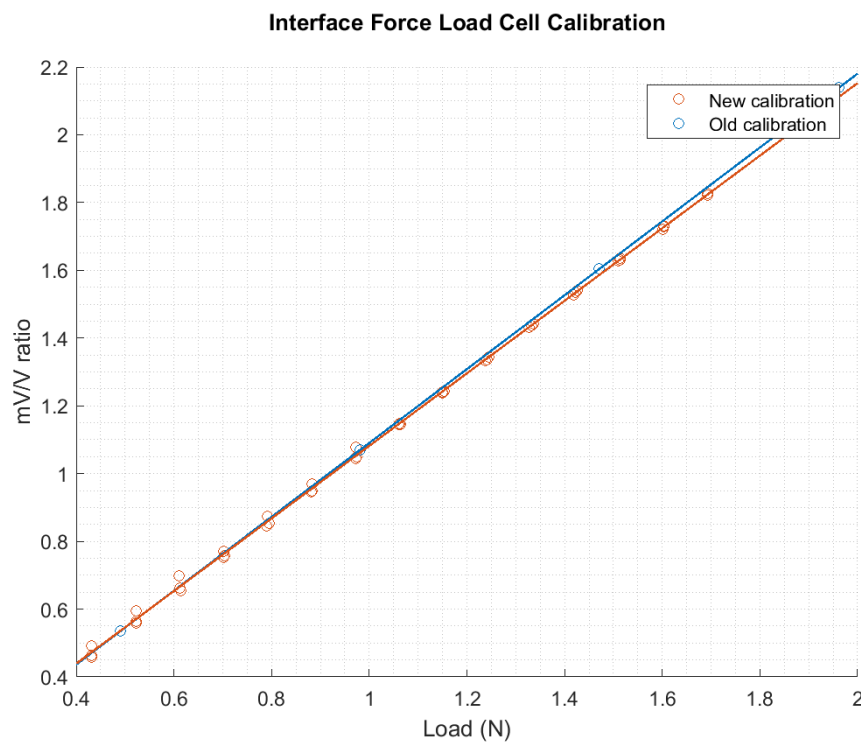


Figure 36: The calibration of the load cell in comparison with the manufacturer's calibration

3.4.2 Validating the encoder

The encoder was validated using high speed video recordings of the experiments to check the recorded displacement against what was actually seen. Experiments were recorded from above

using a Phantom v210 high speed camera and the scene was calibrated by taking an image with a displacement reference (a steel rule) as shown in Figure 37 below.

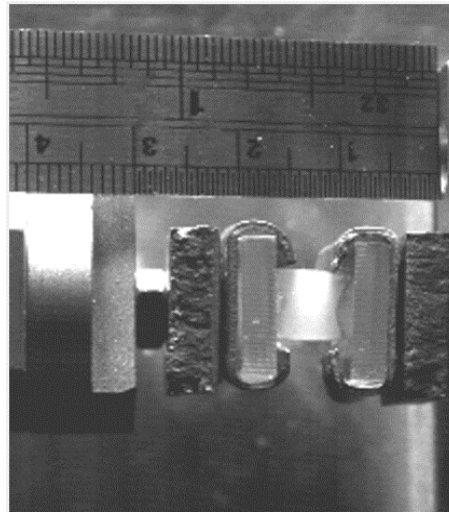


Figure 37: An image from a high-speed video of an Ecoflex gel experiment showing the calibration of the scene

Once the scene was calibrated custom pixel tracking software was used to track the motion of several landmarks on the apparatus throughout the experiment, giving an independent measure of displacement, as shown in Figure 38 below. Like the load cell validation, this was an approximate measurement since there would be a higher error in both the pixel tracking and the calibration than from the encoder itself. However, it was used to check that the encoder was giving out approximately correct data, at which point the higher accuracy of the encoder was assumed to be correct.

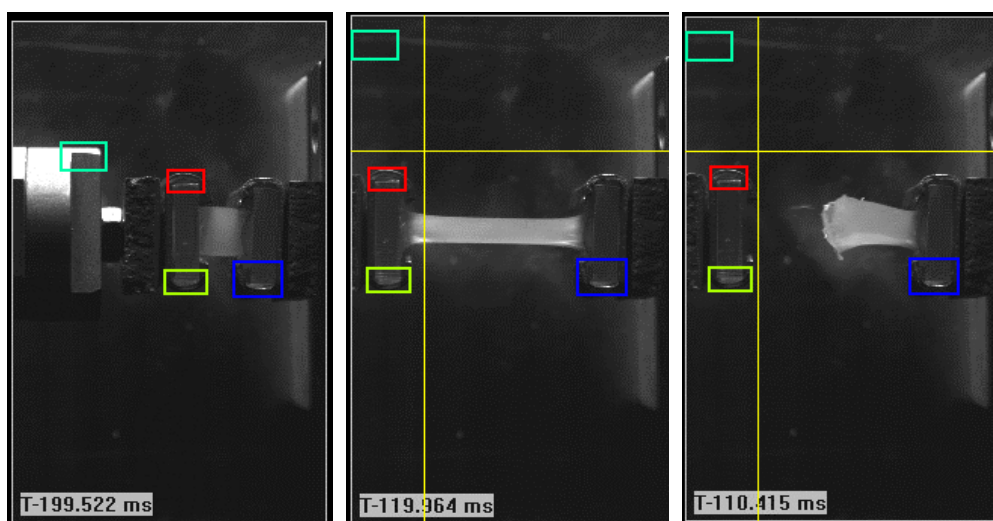


Figure 38: An example of the automatic pixel tracking using high speed video, in the above images the cyan tracking failed when its landmark left the frame

The high-speed video showed that the encoder output could reasonably be assumed to be correct, as can be seen in Figure 39

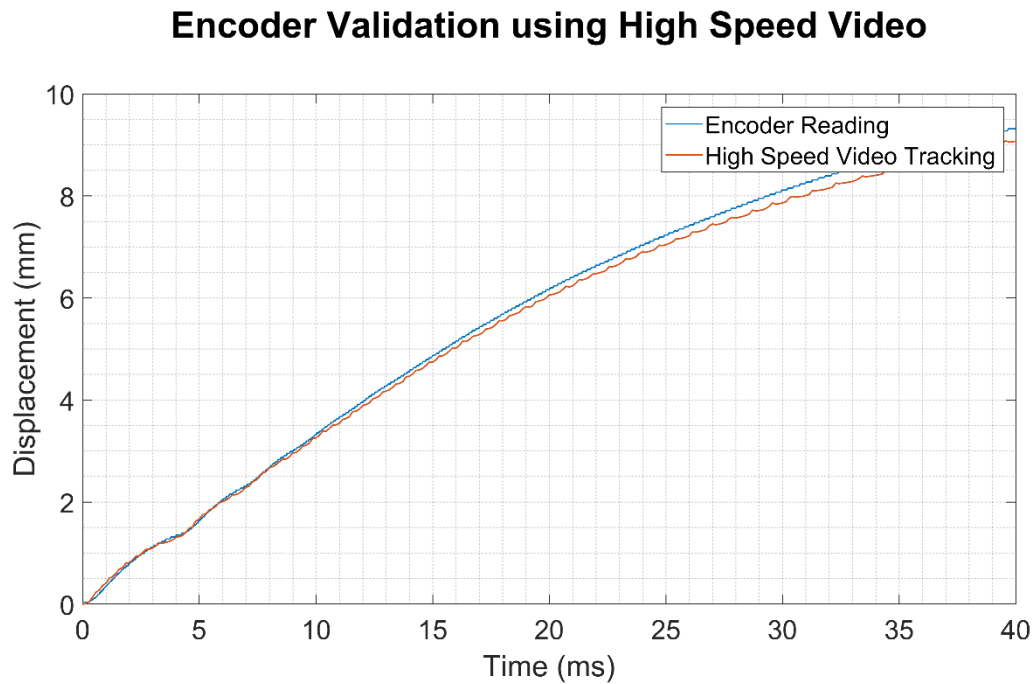


Figure 39: A comparison of the encoder readings against the high-speed video tracking results, showing the encoder to be a suitable measure of displacement

3.4.3 Alignment

Having properly aligned samples is a concern during the experimental work, and great care was taken during the design of the apparatus and the experimental procedure to minimise errors here. However, due to the uncertainties inherent during the manufacture and assembly of the device, such as the degree of uncertainty in the component dimensions and the amount of ‘slack’ space surrounding the momentum capture mechanism in the linear bearing, which is necessary to reduce friction during operation, some errors will still occur. The alignment of both sides of the sample when installed in the device is known to an accuracy of ± 0.1 mm. This was considered negligible however compared to the potential error incurred during the fixing of the samples to the plate, where error in placing the samples in the center of the plates could cause an alignment uncertainty of up to 1mm.

Simulations of experiments of offset samples were run to determine the level to which this error in alignment could affect the results. A typical cylindrical sample (5mm diameter, 5mm length) was meshed (mesh size was 0.2mm) and fixed on one side (Figure 40). The previously used simplified velocity profile typical of high rate experiments was applied to the opposite side of the sample in a normal direction to the faces. For the purposes of this work the material properties of the sample were defined as a 2-term viscoelastic Ogden model with parameter values from (Kleiven, 2007).

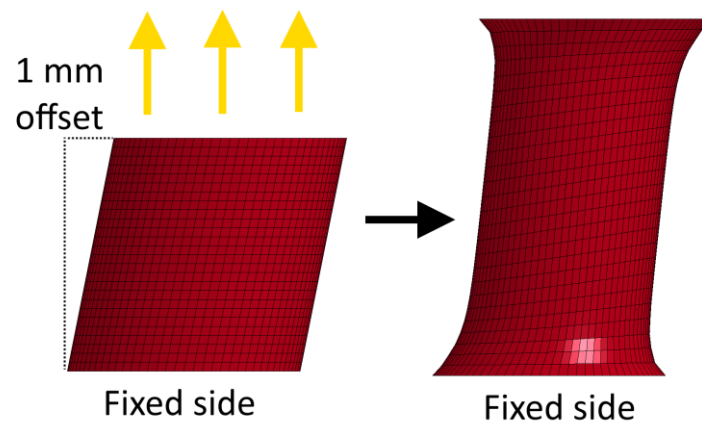


Figure 40: A visualisation of the offset simulation

The simulation showed very little difference between the forces (converted to stress) measured at the static side of the sample for perfectly aligned samples vs samples misaligned by the maximum error of 1mm. The stresses at the static side were compared as that location corresponds to the position of the load cell in the experimental apparatus. Due to the extremely similar results visible in (Figure 41), the potential effects of misalignment were considered to be insignificant.

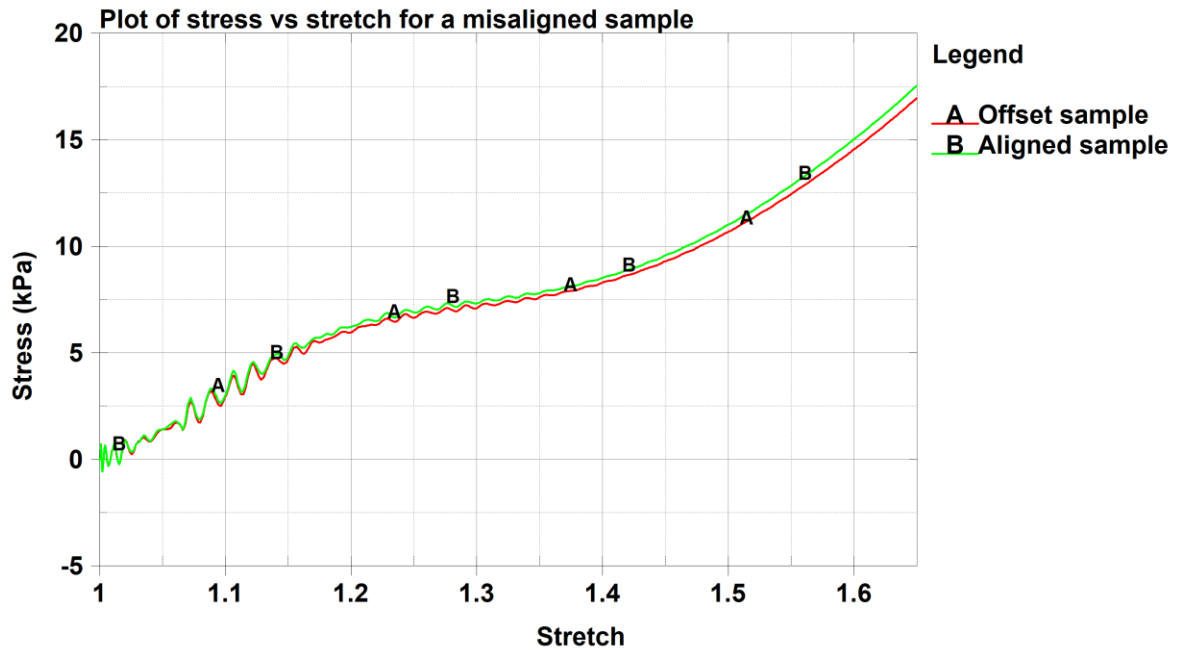


Figure 41: The results of the offset simulation, showing the stress recorded on the static side of the sample for the offset sample vs a perfectly aligned sample

3.4.4 Testing the speed

Once the encoder was validated as a reliable method of measuring displacement, it was possible to use it to measure the speed of the momentum capture mechanism during an experiment, speed which would be applied to the sample and which would, along with sample size, determine overall strain rate.

Unfortunately, due to unforeseen inaccuracy in the motor alignment, it was not possible to use the full stroke length of the motor. This is because the motor rod does not sit truly level in the motor housing. At full extension the rod tilts down slightly, causing it to brush the momentum capture mechanism at its extremity which in turn jars the mechanism due to friction when the motor is triggered, but before the rod has properly accelerated.

One avenue for future work is to redesign the momentum capture mechanism to have a wider channel, as detailed in 3.6 Discussion. However, for the current tests the motor was started at 'position 4000', approximately 2/3 of the way down the momentum capture mechanism, at which point the deflection of the rod was small enough so as to not touch the mechanism.

However this smaller stroke length was an additional factor, along with the mass of the momentum capture mechanism and friction in the bearings that would detract from the maximum motor speed and consequently lower the strain rates achievable. Therefore it became necessary to check the performance the motor was capable of under these conditions.

As shown below in Figure 40 below, even with this smaller stroke length significant speeds were still achieved. The average speed of 1.3 ms^{-1} that Figure 40 displays would correspond to a strain rate of 260 s^{-1} for a 5mm thick sample, which was sufficient for our purposes.

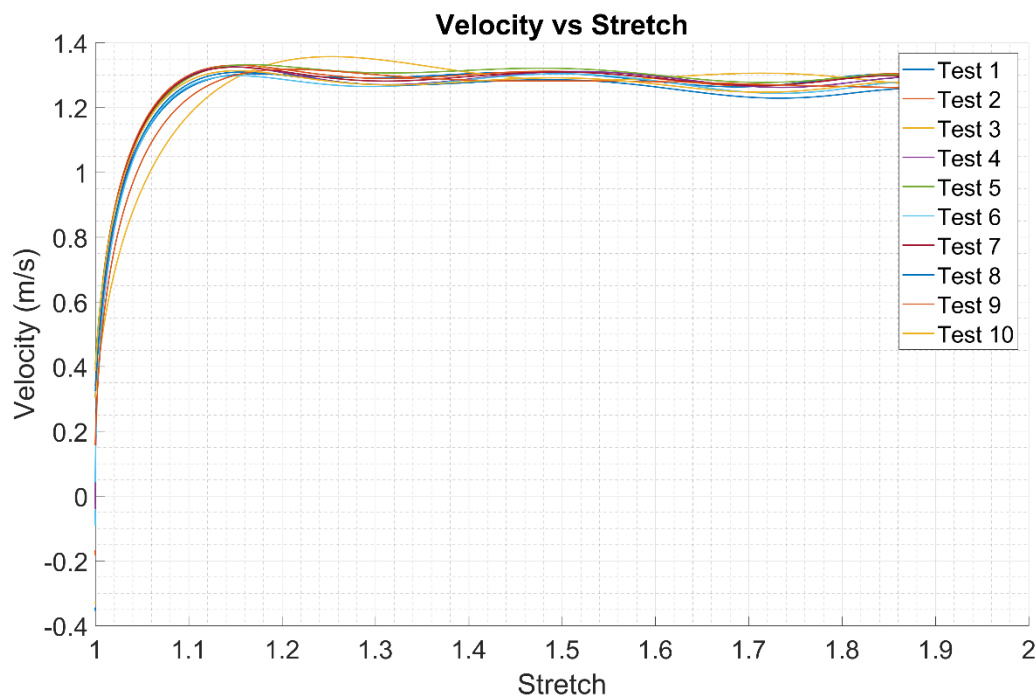


Figure 40: A plot of a series of high-power experiments, showing the maximum velocity of the motor

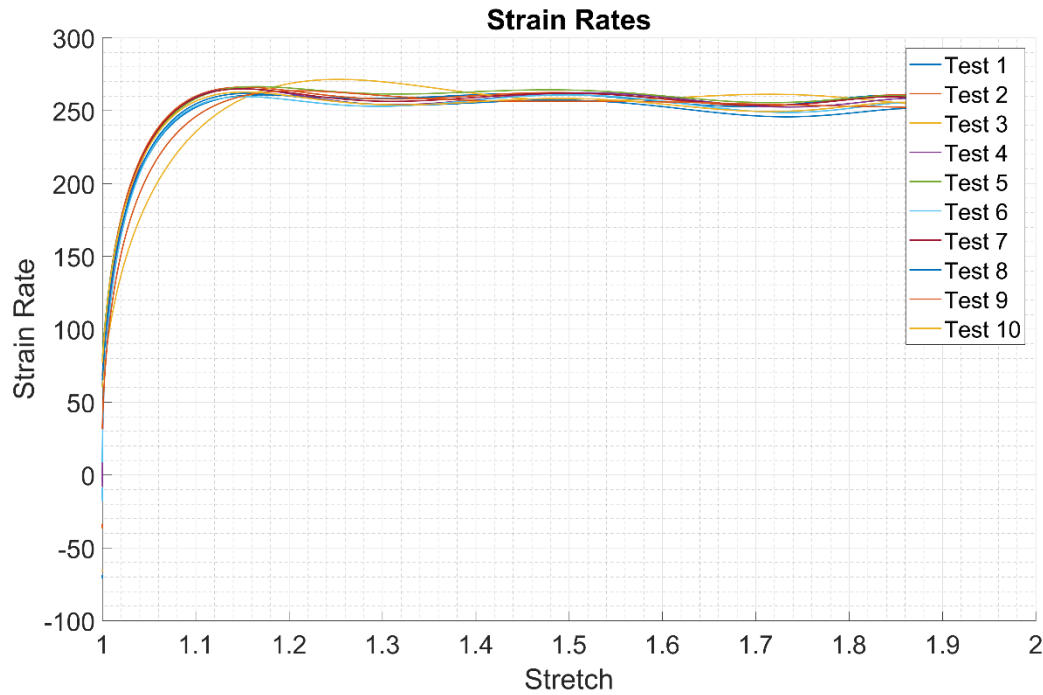


Figure 41: A plot of a series of high-power experiments, showing the maximum strain rate the motor can achieve assuming a 5mm sample

3.4.5 Tests on Armourgel

Once the apparatus outputs were validated in isolation the apparatus as a whole was validated by testing on Armourgel at high speeds. Armourgel is an engineered polymer developed by colleagues in the Department of Mechanical Engineering, Imperial College London. Armourgel is significantly stiffer than tissue, however it was expected to show viscoelastic behaviour in a similar manner. The primary reason Armourgel was chosen was because an extensive and well documented mechanical characterization had been carried out by colleagues (Ghajari, 2016), meaning that the results were trusted and any queries were easily answered. Additionally, since it had been developed and it was in active use by other groups within the same institution samples were readily available.

In order to validate the apparatus in this manner tensile tests were carried out on Armourgel samples of known thickness and length, as shown below in Figure 42. These tests were then replicated in LS-DYNA (Figure 43).

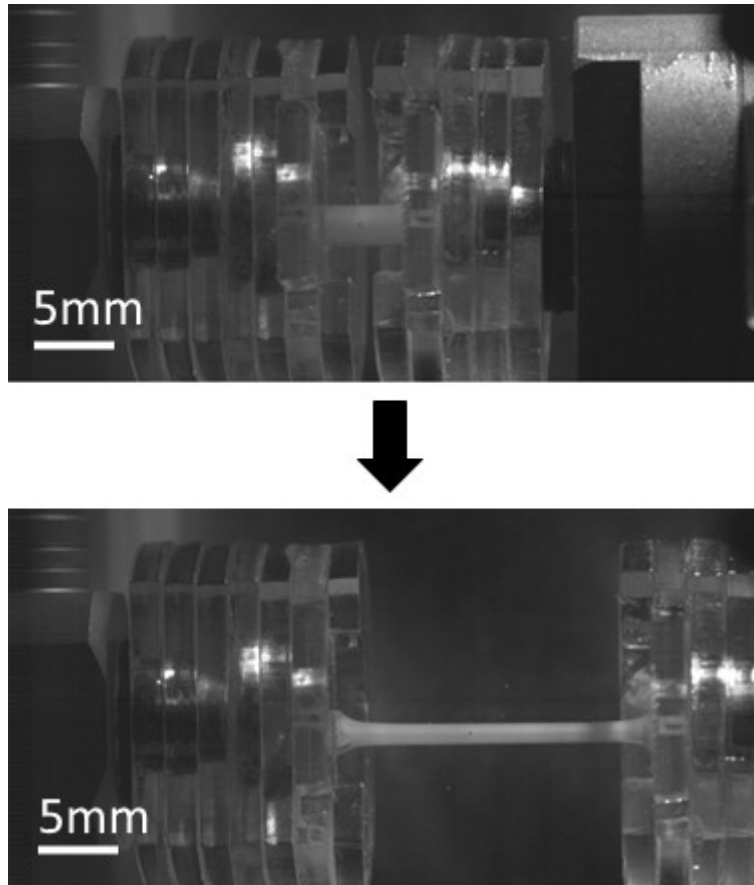


Figure 42: Samples from a high-speed video of an Armourgel experiment

In the LS-DYNA simulations, the material model used was created using properties from the characterization of Armourgel carried out by colleagues. This characterization was carried out independently of the apparatus before it had been constructed using a variety of techniques including Instron testing in both tension and compression, high frequency DMA analysis and drop tower testing. If the apparatus results showed good agreement with the predicted results it could be reasonably taken as validation that the apparatus was producing correct results during these and similar experiments.

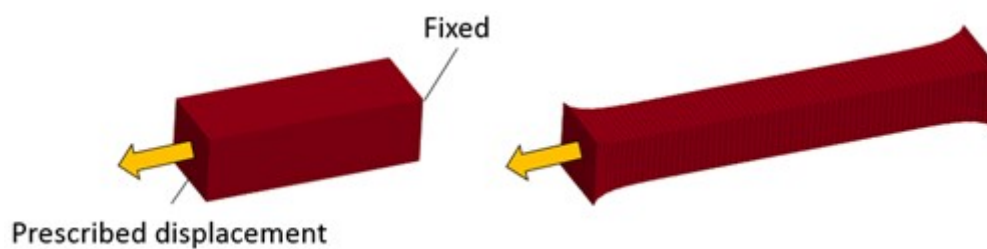


Figure 43: A visualisation of the LS-DYNA simulations of the Armourgel experiments

To cut down on computational time and resources, 5 experiments out of a total of 10 were selected for simulation. The selection criteria were firstly no noted errors with the experiment (such as slight misalignment during fixing, or the sample breaking prematurely at the glue layer), and secondly a smooth even displacement trace that would be easy to simulate and was less likely to give an error in the model.

The displacements for these five experiments were imported into LS-DYNA and applied to one side of the simulated Armourgel sample, with the other side fixed as shown in Figure 43 above. The sample was meshed with 0.1 mm elements and the material properties from the separate characterisation (Ghajari, 2016), summarised below (Table 3), were applied to it. The stress reading for the fixed side, which translates to the side attached to the load cell in the experiments, were then exported and compared to the stress readings recorded during the experiments, as shown in Figure 44 below.

Table 3: Material properties for Armourgel (Ghajari, 2016)

ρ (kg/mm ³)	1×10^{-6}	β_1 (ms ⁻¹)	0.01	G_1 (GPa)	0.00112
Poisson's Ratio	0.49	β_2 (ms ⁻¹)	0.1	G_2 (GPa)	0.00181
μ_1 (GPa)	7.77×10^{-6}	β_3 (ms ⁻¹)	1	G_3 (GPa)	0.01136
μ_2 (GPa)	1×10^{-6}	β_4 (ms ⁻¹)	10	G_4 (GPa)	0.03649
μ_3 (GPa)	-1×10^{-6}	β_5 (ms ⁻¹)	100	G_5 (GPa)	0.02274
α_1	1.037	α_2	5.375	α_3	1

Perfect agreement was not expected since there were too many sources of errors. The LS-DYNA simulation assumed a perfect rectangular shape combined with absolutely perfect alignment and even deformation, while, as with any real-world experiment, the alignments and shape of the samples could only be accurate to within a tolerance and consequently deformation would not be perfectly uniform. However good agreement was still observed, as displayed in Figure 44 with both the magnitude and general shape of the stress readings being accurately replicated by the simulations for a given displacement.

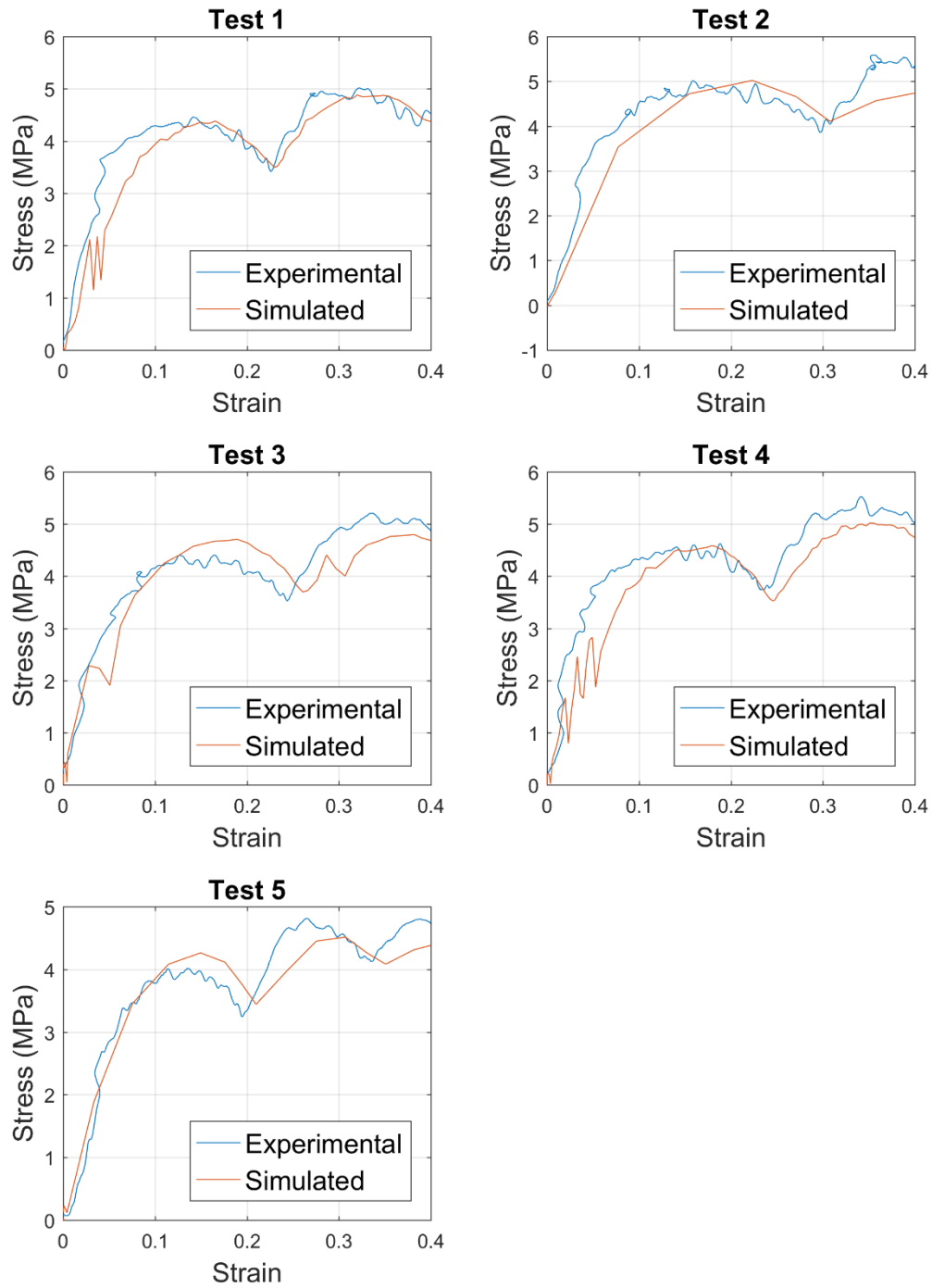


Figure 44: Graphs comparing the experimental and simulated results for Armourgel, used to validate the apparatus

3.5 Reducing noise

The apparatus had been validated and tested with stiff materials and surrogate tissue, and initial steps had been taken, such as changing the load cell to a quartz crystal version, to reduce the effect of noise while testing soft materials such as tissue. However concern about the noise was still an issue, particularly when the extremely small size of the samples expected in the experiment was considered. It was judged that the signal noise present from tissue tests in the apparatus 'default' configuration was sub optimal and would be difficult to obtain accurate curve shapes from, even with filtering, as can be inferred from the orange trace in Figure 46 below.

The main issue was the reaction force when the motor activated. This oscillated through the base and was seen in the load cell, adding this base stress oscillation as noise to the signal. The effect of this was minimal for larger samples of tissue or stiffer materials, since the higher signal magnitude made such a noise source negligible. However for the soft tissue experiments it was too high.

In order to reduce this noise source the load cell was removed from the base and suspended from a separate frame in order to mechanically isolate it from the motor. This reduced the noise problem significantly; however it was still seen as the wave would travel through the table both the base and the frame were sitting on. Foam layers between the base/frame and the table further reduced this effect but did not eliminate it. The best results came from setting the frame on a separate table next to the table with the base on it, the foam layers between the base/frame and their respective tables were retained and the tables had rubber feet. An image of this new setup is shown below in Figure 45.

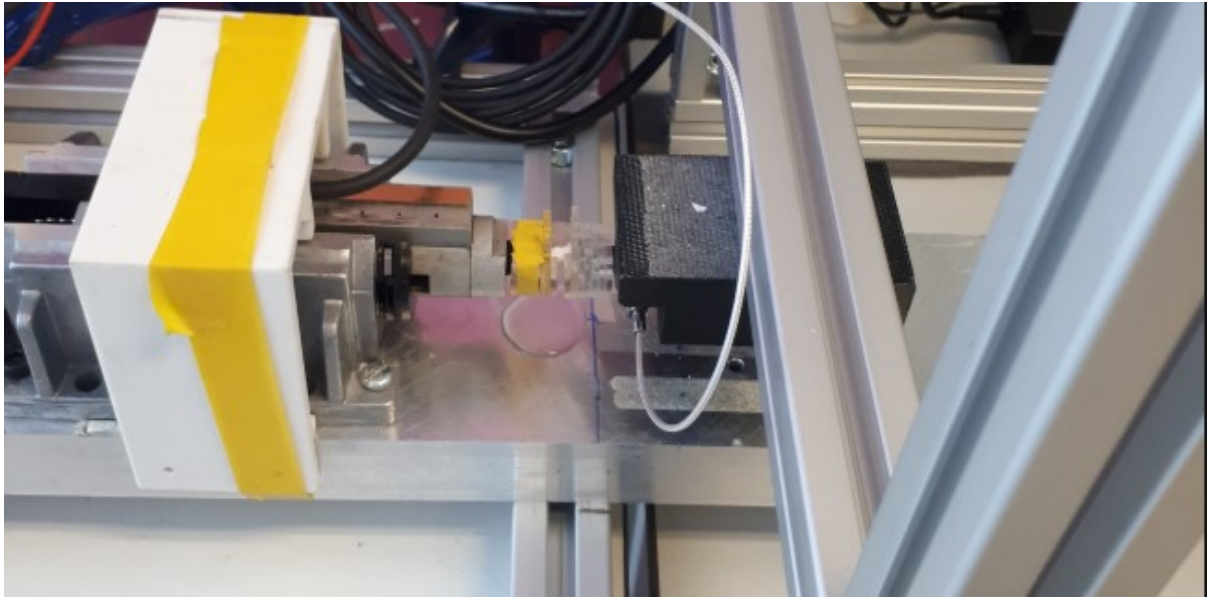


Figure 45: Image of the new apparatus configuration to reduce noise in soft tissue experiments

The greatly extended mechanical path between the motor and the load cell, having to go through a foam layer, a table, the floor, another table and another foam layer served to minimize this effect and greatly improve signal fidelity, as can be seen on the blue trace in Figure 46 below.

Comparison of Different Apparatus Configurations

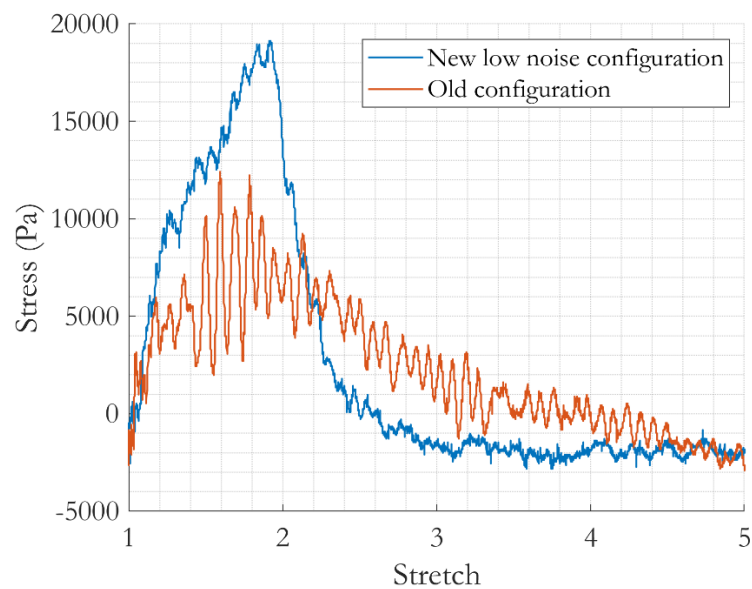


Figure 46: A Comparison of Different Apparatus Configurations, Using Similar Tissue Samples

3.6 Discussion

Through the methods and steps detailed a novel new testing apparatus was designed, prototyped, developed and validated for use with soft tissue and other materials. The apparatus was found to be capable of running mechanical experiments on tissue samples at higher strain rates than any other apparatus found in literature, with the exception of the Split-Hopkinson Pressure Bar which is not optimized for soft tissue and has a comparatively high error. Furthermore, the apparatus is

- Versatile
 - It is capable of testing in either tension or compression at the push of a button, rather than having to reconfigure the device
 - It is sensitive enough to test extremely small samples of soft tissue, allowing samples from individual brain regions to be tested in isolation, rather than a mix of tissue with potentially different mechanical properties.
- Portable, the apparatus is a desktop apparatus and all components can be carried by a single person in a single trip. This allows it to be taken into different labs as well as locations such as autopsy rooms.
- Rapid and streamlined – The apparatus is capable of running multiple tests in quick succession. In the hands of a skilled operator, four or five experiments can be run every minute. This allows tissue or other time sensitive materials to be tested quickly as well as allowing efficient use of experiment or lab time.

The strain rates the apparatus is capable of testing at are lower than the theoretical value, as is almost always the case when a new machine is taken from the drawing board to an actual prototype. However, the machine still comfortably runs in the 1.3 to 1.5 ms⁻¹ range, which translates to strain rates of between 240 and 300 s⁻¹ for a typical (5mm) sample. This is an order of magnitude greater than commercial apparatus, where nothing directly comparable seems to exist at the time of writing, and represents a significant improvement over comparable custom build apparatus found in literature, with the previous leaders (Tamura *et al.*, 2008; Jin *et al.*, 2013; Rashid, Destrade and Gilchrist, 2014) testing at maximums of 25, 30 and 90 s⁻¹ respectively. Since brain tissue has been shown, both in literature as previously stated and in experiments with this

apparatus, to exhibit viscoelastic behaviour, the ability to probe its behaviour at higher strain rates more applicable to impact and blast is paramount.

The apparatus does have some limitations:

- The motor rod does not quite sit flat in its motor housing; this is a consequence of the tolerance of the Quickshaft motor and the error is less than a degree, but it means that the motor rod does not quite run parallel to the momentum capture mechanism and scrapes against the side of it at when extended. This is compensated for by starting the motor approximately two thirds of the way down the momentum capture mechanism where this error is small enough not to touch the sides, however this means that the full stroke length of the motor cannot be used and its maximum rate cannot be achieved.
- The momentum capture mechanism is more reinforced than it needs to be, adding mass which decreases the maximum strain rate, and meaning the full stroke length of the motor cannot be used without contacting the momentum capture mechanism
- The base is thicker than it needs to be and therefore, while still portable, the apparatus is heavier than it could be.
- The electrical components controlling the apparatus are still in a prototype stage, with components soldered onto Veroboard.

Therefore, future work in the short term would be to

- Redesign the momentum capture mechanism with a larger internal channel, increasing the viable stroke length and decreasing the mass of the momentum capture mechanism
- Re-fabricate the base to be 20mm thick rather than 30, cutting down on the weight of the apparatus.
- Have the electronic components fabricated as a printed circuit board (pcb) and incorporated into the apparatus. This would make it more robust since there is less that can be knocked loose and easier to fix since a problem or loose connection could be more easily identified.

In the longer term, the apparatus could be validated more extensively in compression and modifications could be made to allow it to test in shear as well. Additionally, a humidity chamber could be incorporated to allow it to test tissue at conditions closer to *in vivo*, increasing its accuracy. Finally, different motors or methods of generating the impulse could be used with the setup. Since the device only requires a rod to be driven through the momentum capture mechanism to operate, it is not committed exclusively to the Quickshaft motor. The current setup is very portable while still being able to run at very high speeds. However, the datalogging and force/displacement sensors are both capable of recording at higher rates, the motor is the limiting factor. The setup could be used in conjunction with a drop tower or one of the previous designs such as a rotary motor (3.3.1.1), levers (Appendix 1) or gas powered impactors (Appendix 1). These setups would in all likelihood be less portable but represent an alternate configuration of the apparatus that could potentially probe into even higher strain rates.

While the apparatus was designed to be used with tissue, its scope of application is far wider. The device could reasonably be used to test any soft material in tension or compression at high strain rates to a degree of accuracy not found in commercial apparatus under these conditions. In addition to tissue the apparatus has been used to test several gels such as Armourgel, Ecoflex and various concentrations of Sylgard gel. Additionally, the apparatus has been used successfully by colleagues to validate a variety of different silicon-based gels mechanically, testing their performance as surrogates for various biological materials such as brain and lung tissue.

3.7 Dissemination

An earlier iteration of the apparatus presented in this chapter was the subject of a conference paper at the 2016 International Research Council on Biomechanics of Injury (IRCOBI) conference in Malaga, Spain (Pangonis, Ghajari and Sharp, 2016)

4 Experimental methods

4.1 The tissue

12 Adult porcine brains were obtained from Cheale meats, a local slaughterhouse. Porcine tissue was selected as a surrogate for human tissue due to its increased availability and comparable ease of access, as well as its broadly similar overall structure and mechanical properties. This is in line with common practices in literature (Arbogast and Margulies, 1998; Nicolle *et al.*, 2005; Hrapko *et al.*, 2006; Velardi, Fraternali and Angelillo, 2006; Tamura *et al.*, 2008; Rashid, Destrade and Gilchrist, 2014). It should be noted however, that human brain has been shown to be, on average stiffer than porcine brain in several studies (Prange and Margulies, 2002; Jin *et al.*, 2013), as illustrated below in Figure 47, taken from work published by (Prange and Margulies, 2002)

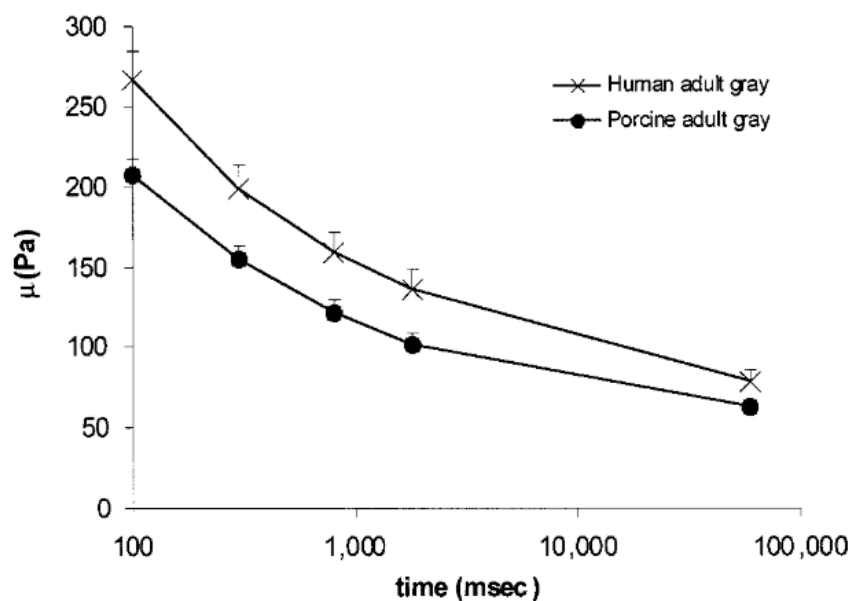


Figure 47: Graph showing the increased stiffness of human tissue (grey matter) compared to porcine, reproduced from (Prange and Margulies, 2002)

The animals were slaughtered first thing in the morning and the brains were immediately transferred to a sealed rigid plastic container, with 2-3 brains per container. Having multiple brains in each container reduced their effective surface area, reducing any 'drying out' effects, while the rigid walls prevented any pre-compression during transport. However, the containers used were sufficiently large so that the brains could be placed into them easily without any pushing or compression necessary, but small enough so that the brains didn't move around very much during transport and did not become isolated from each other. These containers were then placed inside a larger insulated container, along with ice packs to keep the tissue cold for transport. This method of transport preserved the tissue without freezing it, which was confirmed on arrival with no evidence of freezing in any of the brains or the samples that were later cut from them.

Due to the methods used to extract the brains from the skull, the brains were necessarily cut in half along the coronal axis at the slaughterhouse. Due to limitations in the slaughterhouse's equipment this was a necessary step. However, the cuts were very clean in the majority of cases and did not affect the structure. Due to the organic and variable nature of pig brains and skulls a few brains were damaged. However, this was obvious upon a visual inspection and those that exhibited damage from the saw blade were rejected from the sample group.

Every effort was made to minimize the post-mortem time between animal slaughter and tissue testing, and the rate at which the custom apparatus could run experiments greatly assisted with this. Brains were received 2-3 hours post-mortem and all high rate testing was completed at a maximum of 8 hours post-mortem with the vast majority of results, including all the high rate tests, being completed less than 6 hours post-mortem. Particular emphasis was placed on minimizing the post mortem time, to the point where it was a design consideration in the apparatus, as this has been shown to adversely affect tissue properties (Hrapko *et al.*, 2008).

4.2 Methods for cutting the tissue

Porcine brain tissue is very soft and difficult to handle, consequently it is almost impossible to reliably cut samples to a repeatable size and shape without a special procedure and equipment. Various other studies have utilized several methods to cut tissue. Several (Franceschini, 2006; Velardi, Fraternali and Angelillo, 2006; Budday *et al.*, 2017) cut the samples out using a scalpel or similar sharp blade. However, in the studies that specifically reported the difficulty in cutting such soft tissue a high error and variability was also reported in their sample sizes and shapes. (Franceschini, 2006) reported samples varying between 9-15mm long and 5-11mm wide, giving a wide range of aspect ratios (0.9-2.5). This level of variance is assumed in the other studies as well since how they accounted for and overcame such difficulties is not reported.

(Miller and Chinzei, 2002) first used a scalpel to manually cut and smooth slices of brain followed by a sharpened cylinder to cut out cylindrical samples, which presumably gave more consistent dimensions due to the cylinder being a fixed shape and dimensions. However, a 2-3mm variance in diameter across individual samples was reported due to the difficulty inherent in cutting soft tissue, which meant an average thickness had to be used and could lead to inaccurate stress conversions. This method was also used by (Rashid, Destrade and Gilchrist, 2014), presumably with similar limitations.

(Jin *et al.*, 2013) used a specialized construct consisting of a pair of paralleled blades held a fixed distance apart to first cut the brain into 5mm slices and then a second set of paralleled blades to then cut 14mm square samples from these slices. The variance in sample size is not reported but the blade structure is expected to increase the consistency and reliability of the sample sizes verses manual cutting with a scalpel, in a similar vein to using a sharpened cylinder. However there was no method reported to support the brain during cutting so inaccuracies due to tissue deformation would still be expected to occur.

Due to the softness of brain tissue, it deforms significantly when cutting, leading to variance in sample size and shape even when repeatable tools such as sharpened cylinders or paralleled blades are used. (Tamura *et al.*, 2008) cored 14mm diameter samples out of their brains using a sharpened cylinder and unlike (Miller and Chinzei, 2002), they didn't slice their brains first. However, prior to this they placed their brains into a -20°C freezer for approximately 1 hour before cutting in order to partially freeze the surface, creating a 1-2mm layer that was frozen to a

slurry like state 'like a sherbet'. This increased the rigidity of the sample and reduced the deformation during cutting, increasing the accuracy to a reported $\pm 0.2\text{mm}$. However this method, while apparently effective, was not used for these experiments as the freezing process is expected to damage the microstructure of the tissue, affecting the mechanical properties. This is exacerbated in our case since the samples being used are 5mm thick and 5mm in diameter, so even a 1-2mm frozen layer is significant. This is also assuming that the thin layer was truly the extent of the freezing effect as the method for determining the thickness of this 1-2mm layer was not reported, leading to worries that it could affect the properties at deeper levels.

Large variances in sample size are not a problem in themselves. It is possible to account for varying sample size by measuring the size of individual samples and using those results to accurately calculate stress and strain. The majority of these studies do this, and this was also done in our experiments. However, inaccuracy can occur when the samples are not uniform across their length and width. If one side of a sample is larger than another, or the sample is a slightly irregular shape the calculated stress would be inaccurate and would not be uniform throughout. Since the tissue was so soft there was concern that it would be difficult to cut accurately shaped samples reliably, and this was actively reported by (Miller and Chinzei, 2002). It is assumed to affect all similar studies that do not mention a method for overcoming it.

Indeed, the samples deformed under their own weight so much that a sample sitting upright on the benchtop measured on average 19% thinner than when the same sample was adhered to a platen on one side and allowed to hang. This meant that there was a need to develop a repeatable support for the brain tissue, one that could support it across its surface and minimize this deformation, both due to its own weight and due to the cutting tool.

To this end a brain matrix was developed to support the brain and provide fixed cutting widths in the same manner that (Jin *et al.*, 2013) achieved with paralleled blades. A porcine brain atlas was obtained from colleagues in Imperial College Medical school to act as the model for this matrix. The atlas was imported into 3d modelling software Geomagic Wrap and a mesh generated, before being processed, decimated and exported as a stl file. Geomagic Wrap was used for this step due to it being optimized for complex shapes with many faces such as the brain, and it was used to decimate the model to make it suitable for use in software less optimized for this such as Solidworks. The decimated model was in turn imported into Solidworks and subtracted from a solid block to make a CAD mould model. Solidworks was

chosen due to the researchers experience with it and because it was readily on hand at the relevant institution, as well as for its optimization for making moulds and 3d print files. Slits were then added at 5mm spacing to create a brain matrix that could support the brain while cutting slices from it.

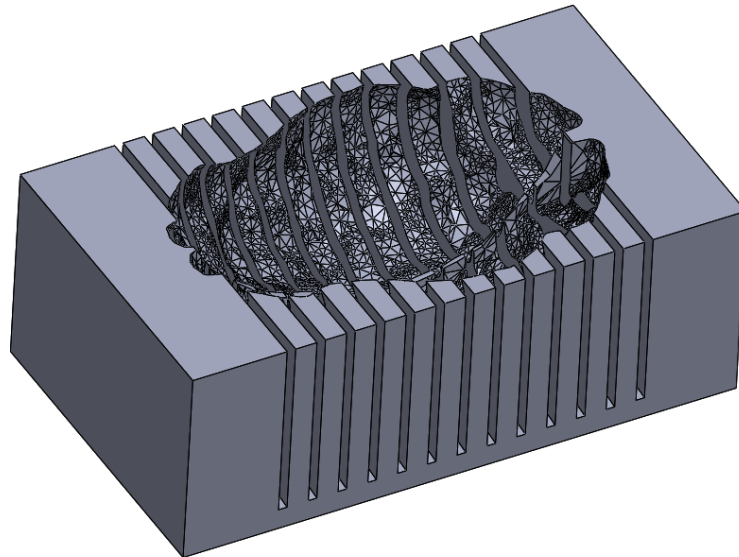


Figure 48: A CAD model of the brain matrix

A Z-Corp 3d printer associated with the Imperial College Advanced Hackspace was used to print a prototype matrix from this CAD model. This 3d printer uses a sintering technique which gives a higher accuracy than the traditional layering method. The final model was sprayed with several coats of tough waterproof varnish to prevent any possibility of organic matter and fluids infiltrating the structure, as well as to make cleaning and disinfecting the matrix after use easier.

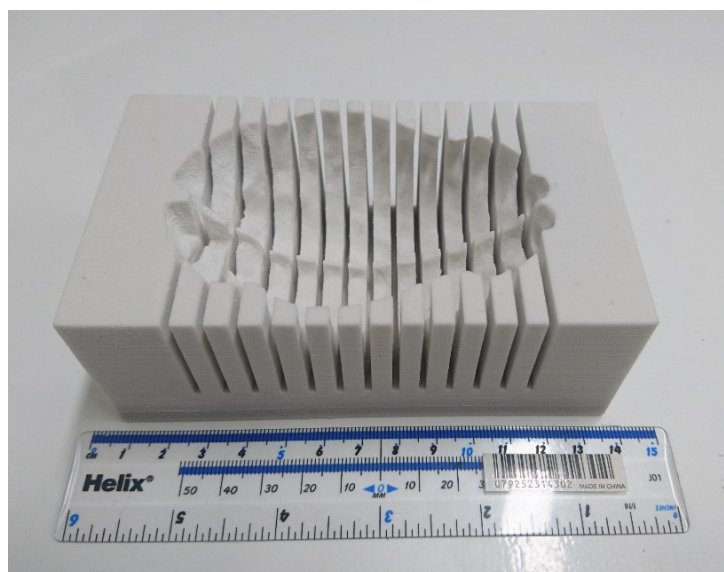


Figure 49: The completed brain matrix

4.3 Preparing the samples

The animals were sacrificed at the slaughterhouse and their brains immediately exhumed and transferred to the insulated container for transport. As previously stated they arrived at the testing facility approximately 2 - 3 hours post-mortem.

PBS solution was sprayed onto the brain matrix and a single brain half was removed from the container and inspected for damage. If none was found it was transferred into the brain matrix, where a steel plate, wetted with PBS solution, was inserted into one of the slits was used to support the halved side.

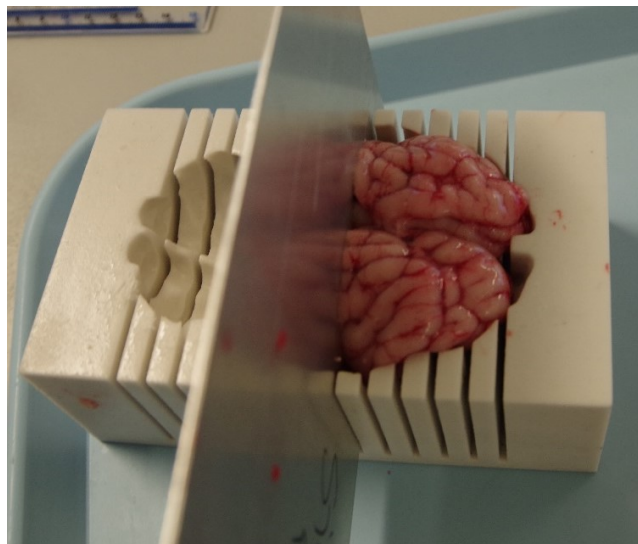


Figure 50: The brain matrix in use

A long microtome blade was also wetted with PBS solution before being lined up with the first slit following the one occupied by the steel plate in the matrix and gently moved back and forth in a slight sawing motion to cut through the brain. Throughout the experiment all tools used to handle the brain were wetted with PBS solution. This was to reduce friction between the brain and the tool, producing a cleaner cut and minimizing the deformation introduced by the tool to the soft brain tissue in line with work done by (Rashid, Destrade and Gilchrist, 2014).

Additionally, this measure helps to minimize any dehydration that might occur if the brain was brought into contact with a dry tool which was of particular concern due to the small size of the samples. This was repeated to give two central slices from the brain half, each 5mm thick (although each sample would be measured individually during testing).

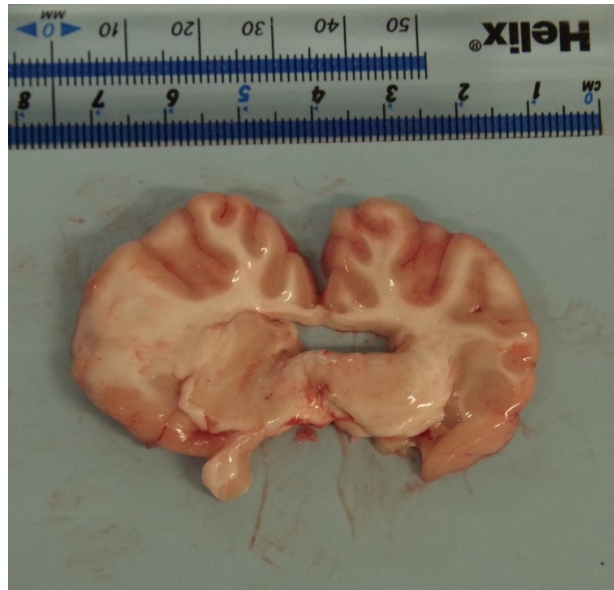


Figure 51: An example of a porcine brain slice

The slices were transferred to a petri dish containing a small amount of PBS solution and a lid was placed on the petri dish. This was to prevent dehydration during the course of the experiment. PBS was used because it mimics the water potential of the cells, thereby maintaining physiological water content, preventing both dehydration and over saturation with water.

A 7mm biopsy punch, again wetted with PBS, was used to extract a cylindrical sample from the central node of the corona radiata. The corona radiata was chosen as a recognizable landmark from which to repeatably extract white matter samples, as evident in the brains anatomical cross section (Figure 52) and the extracted cross section (Figure 51). White matter was chosen as a focus as it has been shown to be preferentially injured during brain trauma (Smith and Meaney, 2000), and it was logical to extrapolate this to blast in the absence of conflicting evidence. The goal was to extract 5mm samples, however a 7mm punch was used for two reasons.

- The 7mm diameter was the external diameter not accounting for blade thickness, the actual cutting diameter was closer to 6.2 mm, while the cutting diameter of the corresponding 5mm punch gave samples closer to 4mm diameter
- It was noticed that the cylindrical brain samples would shrink once they were cut out from the brain. This is hypothesized to be due to the surrounding tissue matrix supporting them to some degree, as it was already shown that brain tissue samples do deform significantly under their own weight.

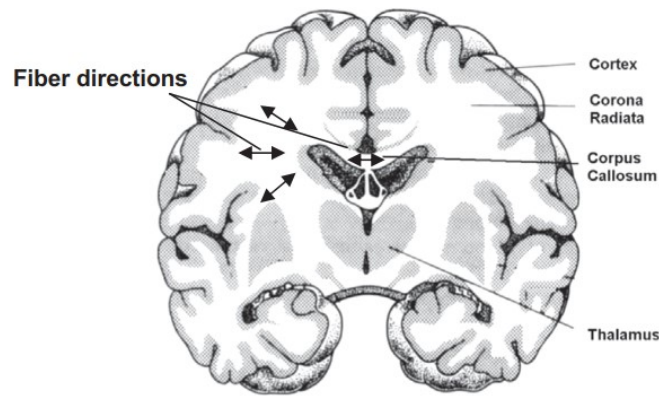


Figure 52: A diagram of a coronal cross section of the brain (Jin *et al.*, 2013)

Because of these reasons it was found that a 7mm punch gave samples which measured close to 5mm in diameter, while still being a small enough punch to extract samples from individual brain regions. A single sample was extracted from the central node of the corona radiata in both hemispheres of the brain, example locations can be seen below in Figure 53. Following the extraction from one hemisphere the brain half was returned to the PBS petri dish while the experiment was run on the sample before being removed again and having a sample taken from its opposite hemisphere in order to minimize tissue drying and degradation during the course of the experiment. It was observed that this cutting method gave good quality samples in a repeatable manner, with an even cylindrical shape, as can be seen with the example sample shown in Figure 54.



Figure 53: A porcine brain slice with samples removed from the central node of the corona radiata

A single dab of Dermabond surgical glue was placed in the centre of a platen and the sample transferred to the platen immediately after cutting. Dermabond is a cyanoacrylate adhesive much like superglue, however as it is a medical grade version its setting process is significantly less exothermic than regular superglue, as well as being significantly less toxic, which was considered beneficial for keeping the tissue as uninfluenced by the glue as possible. Similar medical grade adhesives were used by (Miller and Chinzei, 2002; Rashid, Destrade and Gilchrist, 2014). Many studies (Franceschini, 2006; Jin *et al.*, 2013; Budday *et al.*, 2017) use more common cyanoacrylate adhesives ('superglues') without obtaining the medical variety. This is presumably because it is easier to obtain and there is no real evidence that it would affect the mechanical properties of the tissue. However, since it was possible to obtain a surgical glue such as Dermabond it was used in order to eliminate this as an unknown.

It is also possible to increase the adhesion between the sample and the platen by coating the platen in a layer of masking tape (Rashid, Destrade and Gilchrist, 2014), or sandpaper (Budday *et al.*, 2017), increasing the surface area in contact with the platen during adhesion. However, high speed video analysis of tests showed this to be unnecessary for our experiments. While the samples did often fail at the glue layer rather than in the centre, the adhesion was more than sufficient to stretch the samples to 100% or more before failure, easily capturing the required experimental range we are interested in.

Methods other than adhesive for securing samples are present in literature, however the most common, using a high friction surface, is only suitable for shear and compression, not tension. Mechanical grips were used by (Velardi, Fraternali and Angelillo, 2006) and offer a certain way of removing any chemical or thermal interference in the samples mechanical properties. However, the specimens used in that study were an order of magnitude longer than the ones in this study and this method was impractical for the small sample sizes we were using. Additionally, there was concern that the deformation introduced in soft material by a mechanical grip, as well as the inherent stress in the material created by it would create a non-uniform stress distribution and skew the results. As such an adhesive was considered preferable in this scenario.

One more exotic method for adhering the samples to the platens is by 'quench freezing', as demonstrated by (Tamura *et al.*, 2008). In this method, platens are immersed in liquid nitrogen for approximately 5 minutes before the sample is introduced to the platen, instantly flash freezing the sample to the plate. While again this removes any possibility of chemical

interference in the mechanical properties it has its own issues. Freezing temperatures are known to lyse cells as water expands upon freezing, meaning the microstructure of tissue is likely to be damaged by such a method. Additionally, due to the small size of the samples in question there is no real way to localize this affect to an adhesion layer on both sides and leave the centre untouched. As such it was felt that this method introduced more uncertainty than it eliminated, and an adhesive (Demabond) was used instead.

Once the sample was glued to one platen it was allowed to sit for several seconds before being transferred to a grip in the apparatus. Another platen was likewise prepared with a dab of glue and placed in the opposing grip before the grips were moved together carefully. The grips were moved just enough to allow the opposite side of the sample to adhere to the second plate without any significant compression being applied to the sample. The load cell readout was monitored to prevent significant pre-compression or pretension at this stage. The samples diameter and length were carefully measured with Vernier callipers (again the jaws were wetted with PBS) and their dimensions noted down to accurately calculate stress and strain later. Finally, before the test was run a drop of PBS was applied to the sample.

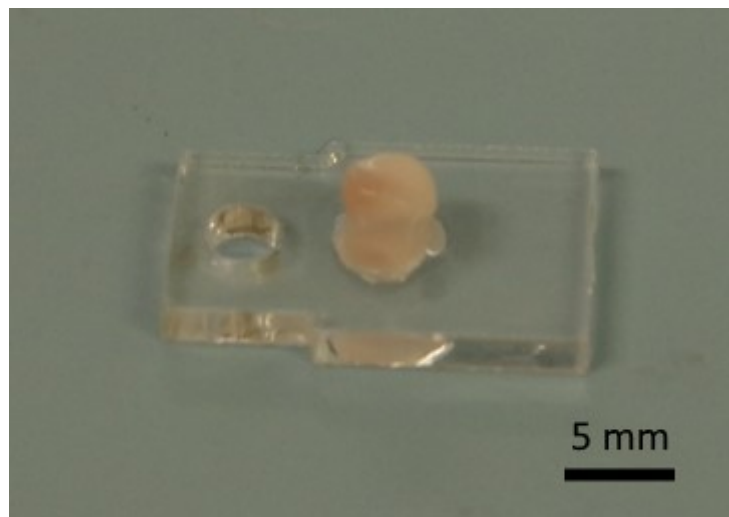


Figure 54: An example sample, attached to a platen with Demabond

4.4 Testing the tissue

Different strain rates were applied to the sample by feeding different levels of power to the motor, where the approximate strain rate each power level corresponded to had previously been characterized. From these tests the displacement of the moving side of the sample was recorded by an optical encoder and the mechanical load the sample experienced was recorded by a piezoelectric load cell in the manner described in chapter 0. Tests were run at 3 different power levels

- High Rate; estimated to produce strain rates of between 200 and 250 s⁻¹ in a 5mm thick sample
- Medium Rate, approximately half the high rate tests, expected to produce strain rates of between 110 and 140 s⁻¹ in a 5mm thick sample
- Low Rate, approximately 1/10th of the high rate power, expected to produce strain rates of around 20 s⁻¹ in a 5mm thick sample

Many of the tests were filmed with a phantom high-speed camera and the footage reviewed before proceeding, there were three main reasons for this

- To confirm that the samples adhered to the platens properly throughout the experiment, making sure the mechanical properties of the tissue, not the glue layer, was being measured
- To confirm that the samples stretched evenly and did not tear/fail visibly before the experimental range was exceeded
- To confirm that the samples and the motor rod were aligned properly so the cylindrical samples stretched along their principal axis.

There were initially concerns about the adhesion method being too weak to hold the samples in place over the course of the experiment. Dermabond is a surgical cyanoacrylate adhesive and had been chosen in line with literature due to its low toxicity and setting temperature, minimizing its effect on the tissue. However, it is significantly weaker than commercial superglue given the low setting times it was allowed in order to reduce tissue drying. Analysis of the high-speed video however showed that, when the glue layer failed, it did so significantly past the maximum strain

level of interest to this experiment. Additionally, it was noted that the deformation was almost entirely in the middle of the sample away from the glue layer, meaning that the mechanical properties of the glue layer could be considered negligible for our purposes.

A number of experiments had to ultimately be eliminated from the final testing group, the primary reason for this was issues with alignment, uneven stretching, not reaching the desired stretch before glue failure or excessive glue running along the side of the sample as seen in the high-speed video. Further to this stress values were taken for every 0.05 stretch increment up to 1.35 for each strain rate set. If at any point the stress value for a sample was a statistical outlier (more than 2 standard deviations away from the mean for its set) that curve was eliminated as an outlier.

4.5 The data range

The stretch of the tissue was calculated by dividing the displacement outputted from the encoder by the tissue samples initial length, thereby calculating the strain, and adding 1 to the result to convert it into stretch. Stretch was used as opposed to strain throughout this work as the mathematical model described in chapter 6 uses stretch over strain in its simplest form.

For the purposes of filtering, an experimental stretch range of 1 to 1.4 was used. This range was selected because analysis of the data showed that many samples showed signs of artefacts past this point, particularly at the higher rates, as can be seen below in

Figure 55 with the dips in the gradients of several curves at points past 1.4 stretch. This effect could be due to the beginnings of tissue damage or failure although this was not broadly observed on the high-speed video. It could however be occurring on a microscopic level.

Unfortunately, since this could not be seen on the high-speed video it was impossible to confirm or reject this hypothesis. It should be noted however that this effect was also observed in results from (Velardi, Fraternali and Angelillo, 2006), where similar tests were carried out with a completely different apparatus, meaning that this artefact was unlikely to be due to the apparatus exclusively. Since the artefact was unaccounted for however, only the region before the artefact typically occurred was analysed, this is consistent with the stretch regions analysed in comparable

literature (Franceschini, 2006; Tamura *et al.*, 2008; Rashid, Destrade and Gilchrist, 2014; Budday *et al.*, 2017).

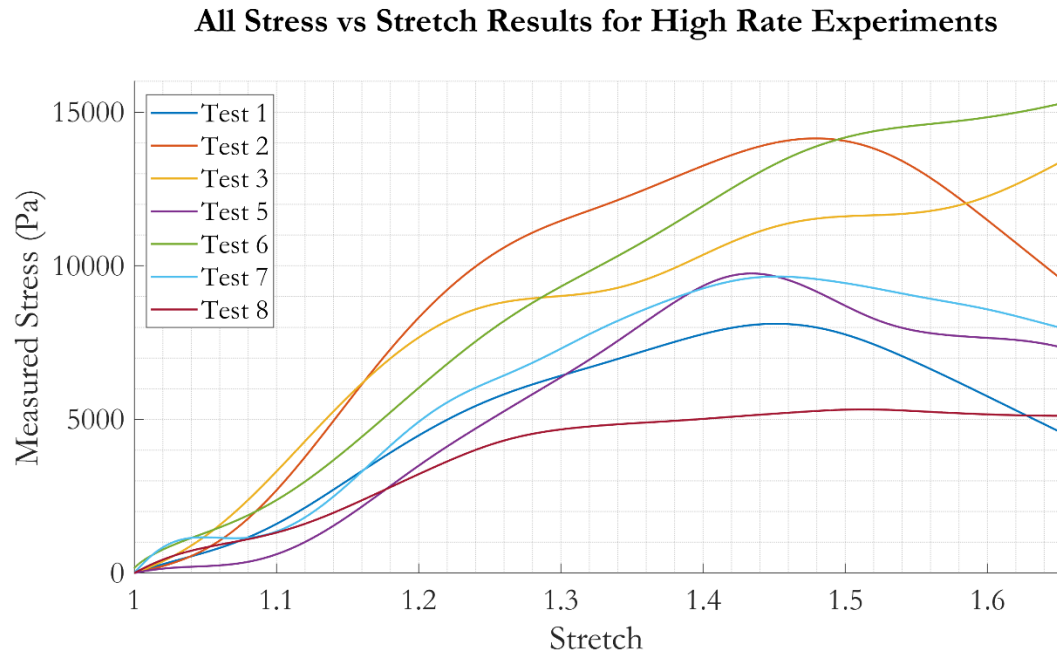


Figure 55 : Graph of all high rate filtered test results, showing artefacts beyond 1.3 stretch

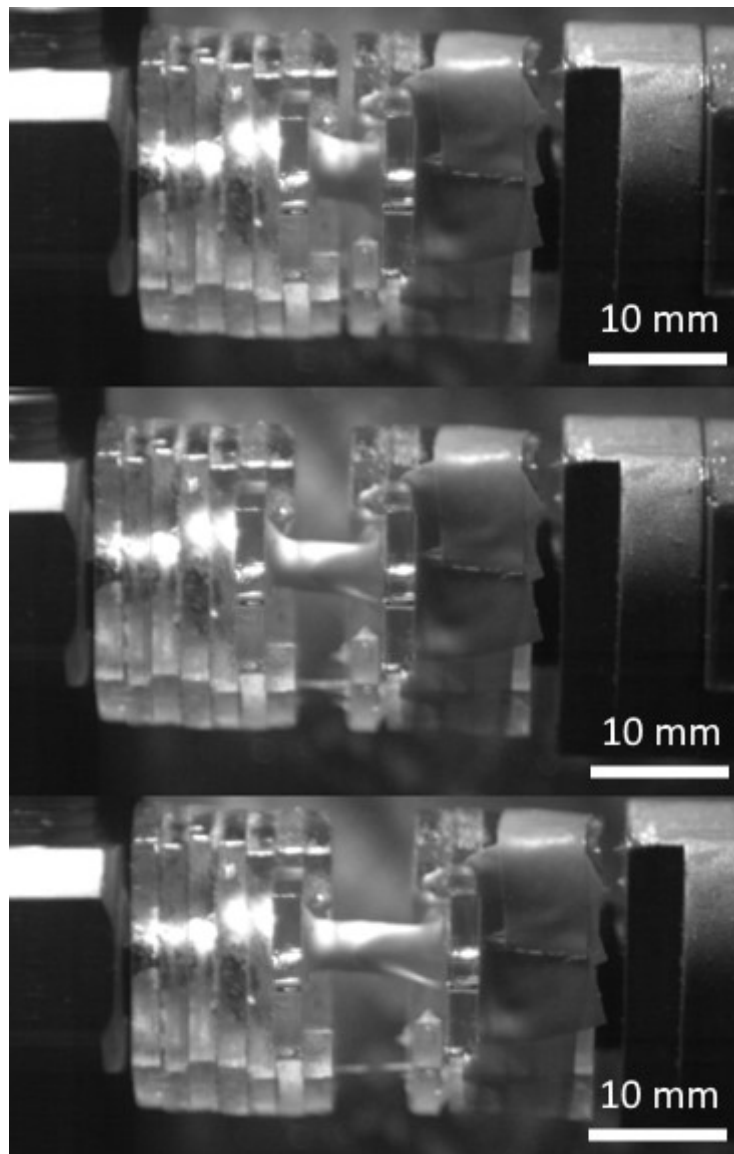


Figure 56: High speed video footage showing even stretch across a high stretch range

4.6 Strain rates achieved

Strain rates during the experiment were determined by fitting a 6th order polynomial curve to the recorded displacement, and then differentiating the resulting equation and dividing the resulting polynomial constants by the samples initial length. In keeping with the speed tests done during the apparatus validation stage, the strain rates throughout the experiments were very consistent and relatively constant once the full velocity had been achieved, although it was observed that higher velocities were achieved with tissue, which is significantly less stiff and therefore offers less resistance than Ecoflex.

As can be seen below, the high strain rate tests were carried out at strain rates of between 190 and 250 s⁻¹ (Figure 57). The medium strain rates ranged between 90 and 140 s⁻¹ (Figure 58) and the low strain rate tests were run between 13 and 22 s⁻¹ (Figure 59). This represented a good spread of strain rates, with the low rate experiments offering insight into low rate behaviour, while still being dynamic strain rates. The medium rate data on average higher, but still comparable to 90 s⁻¹, which is the highest tensile strain rates reported in literature (Rashid, Destrade and Gilchrist, 2014). The high rate tests represent a significant improvement over maximum rates in literature, representing a 2-3 fold increase in rate while using a comparable apparatus.

In total a large spread of rates between 13 and 250 s⁻¹ were carried out, which represents a considerably greater range than currently exists in literature. This is especially valuable considering the range of tissue, apparatus and testing conditions present in literature. Testing across an extensive range of strain rates in the same series of tests, and thus keeping all these variables constant was expected to give a much more complete characterization than currently available. Additionally the overarching goal of these experiments is to come up with a set of values that work for all strain rates and the variety represented here will allow any hypothesis to be tested across a wide and previously unavailable range of strain rates.

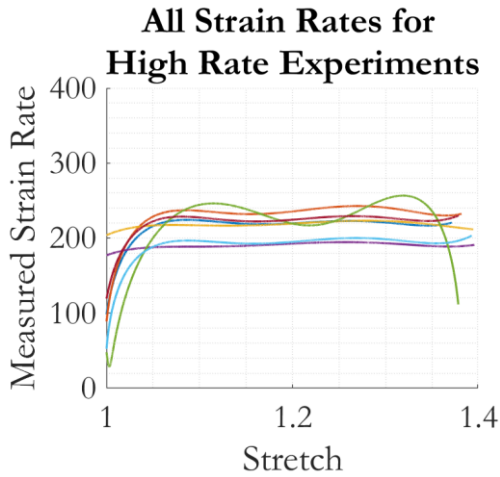


Figure 57: Strain rates achieved during the high rate tests

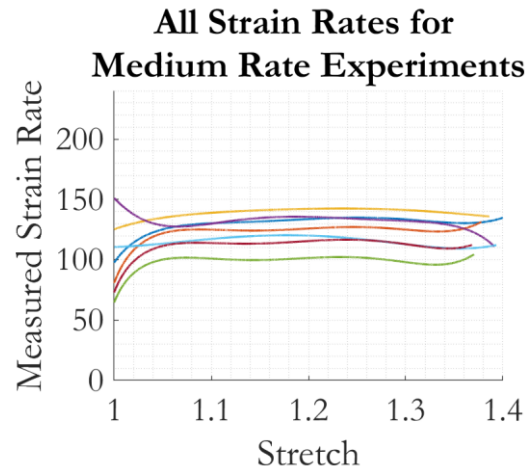


Figure 58: Strain rates achieved during the medium rate tests

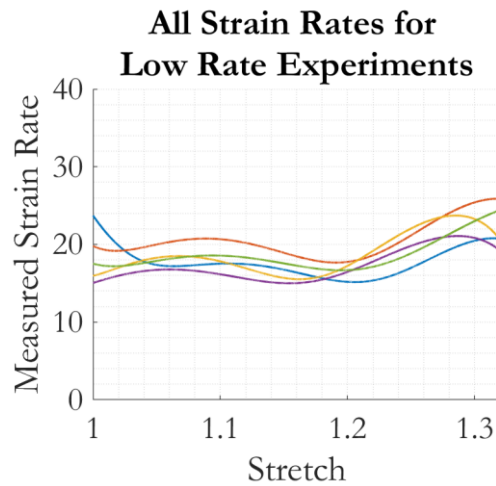


Figure 59: Strain rates achieved during the low rate tests

As can be seen, particularly in the high rate tests, there is still some acceleration phase visible at the start of the experiments. This is, to some extent, unavoidable however due to it being a physical system subject to inertia. Regardless, the target velocity is achieved in less than 10% strain (1.1 stretch), since the average sample thickness during these experiments is 4.7mm, this corresponds to the full acceleration (up to 1.4 m/s in some experiments) taking place across a distance less than 0.5mm. While this is obviously not ideal it was the smallest distance that was possible given the resources available and the effect it was expected to have on the overall results was not significant, since the rate which the apparatus can accelerate greatly minimizes its effect.

4.7 Potential gauge length effects

The gauge length of 5mm was largely dictated by the size of the porcine brains used in the experiments. The gauge length of 5mm was chosen as it was felt it was the largest size it was possible to get consistently. It should be noted however that the glue affixing each side of the sample will constrain the tissue in a way that is not representative of the in vivo conditions. In the previous LS-DYNA simulations this constraint has been modelled by a constraint in both x and y at both ends of the sample (the tension was applied in the z axis), leading to a sample that necked in the centre (Figure 60).

In order to investigate the effect of this glue constraint a quartered simulation was run without this constraint and the forces on the static side (where the load cell is situated in the apparatus) compared to the constrained sample quarter simulations previously reported (Figure 61), all other conditions were kept constant, with the same 0.2mm mesh size, material properties from (Kleiven, 2007) and simplified high rate velocity profile applied to the sample (Figure 22).

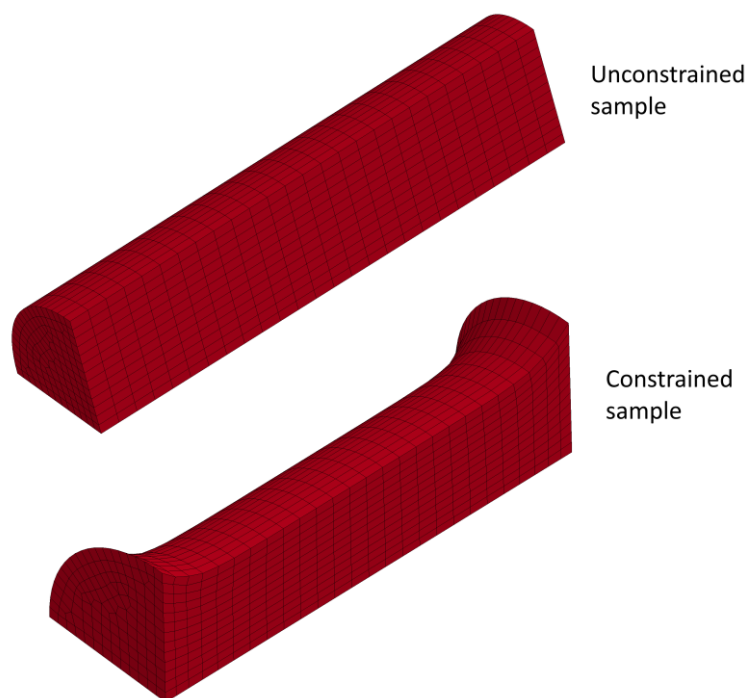


Figure 60: A visualisation of a simulated deformed unconstrained sample vs a sample constrained by the glue layer

It can be seen below in Figure 61 that the forces recorded from the unconstrained sample, which could represent a sample deforming in vivo or in the centre of a larger gauge appear lower than in the 5mm constrained sample. This suggests that the results achieved in this study may be an

overestimate, however it should be noted that a true in vivo sample will be under external constraints from surrounding tissue in a way impossible to model with the apparatus and so the unconstrained example isn't necessarily true to in vivo conditions either. This is a potential limitation of this work and one which is unavoidable in this sort of experimental work due to the necessity of a glue layer or similar adhesion method. The difference at the extreme end of the experimental range (stretch of 1.4) corresponds to a difference of about 15%.

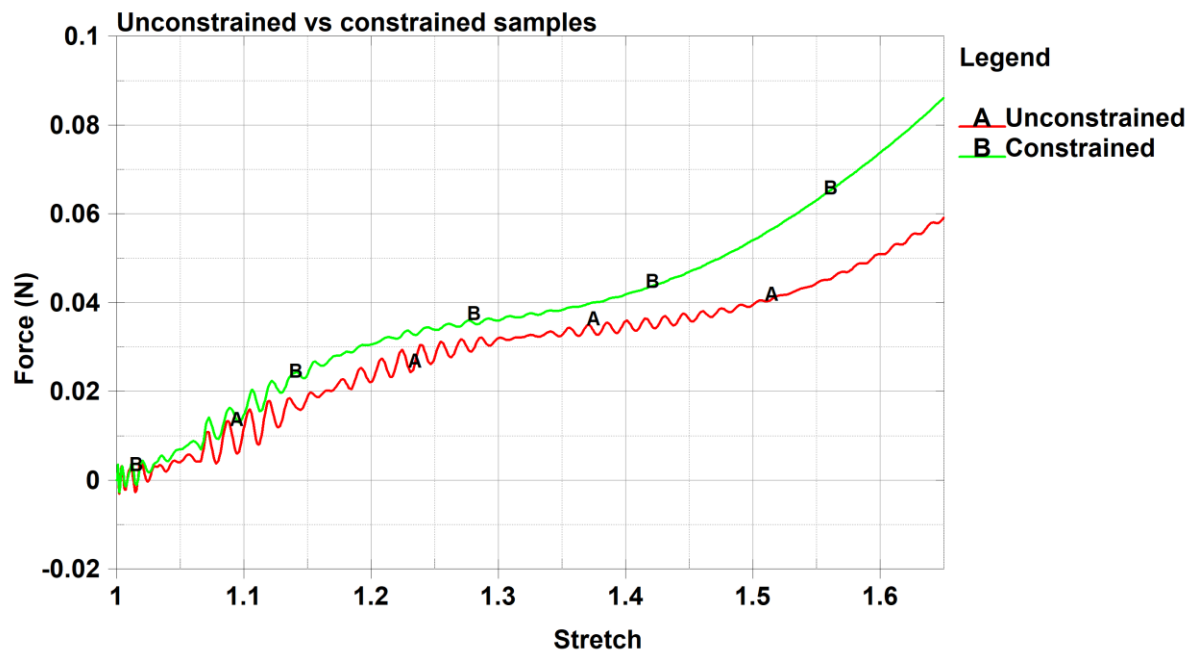


Figure 61: The forces on the static side of the unconstrained sample, compared with the constrained sample

4.8 Filtering

4.8.1 Filter design and cut-off frequency

In order to filter high frequency noise from the data, a 6th order low pass Butterworth filter was implemented in MATLAB. Using the experimental stretch range of 1.4, the timescales the experiments took place over were observed and can be seen below in Table 4. The timescale is simply the time taken for the total stretch to occur, and the signal frequency is the corresponding frequency. This was taken as the ‘rough’ frequency of the signal, since any signals of significantly higher frequency were expected to be experimental noise, either electrical or from vibrations or stress waves in the apparatus.

Table 4: Timescales for the different experimental rates

STRAIN RATE	TIMESCALE FOR 1.3 STRETCH	SIGNAL FREQUENCY	INITIAL FILTER CUTOFF FREQUENCY
HIGH RATE	1.5×10^{-3} s	666 Hz	1332 Hz
MEDIUM RATE	3×10^{-3} s	333 Hz	666 Hz
LOW RATE	1.5×10^{-2} s	66 Hz	132 Hz

The start point for cut-off frequencies was initially chosen to be twice the signal frequency over the 1.3 stretch range. The frequency was initially doubled to keep the cut-off frequency high, in order to minimize the effect of the filter on the actual signal. The cut-off frequency was further refined by carrying out a Fourier analysis on the acquired signals, searching for any noise spikes in the frequency domain between the signal frequency and the initial cut-off frequency that would need to be eliminated.

The Fourier analysis showed no significant consistent peaks that needed to be accounted for in the low rate (Figure 70) and medium rate (Figure 69) experiments, however the high rate tests (Figure 68) showed a consistent noise peak at approximately 1300 Hz. To account for this, the cut-off frequency for the high rate tests was reduced to 1000 Hz, which still acts on a timescale significantly shorter than the experimental range and so is not expected to affect the

experimental results unduly, although this was verified by visual inspection. The difference between the 1332 Hz cut-off frequency and the 1000 Hz cut-off frequency can be seen in Figure 66 and Figure 67. The cut-off frequencies for the medium and low rate tests were similarly determined to be the upper end of the suitable range.

Other papers have used filters with much higher cut-off frequencies, such as 16 kHz used by (Rashid, Destrade and Gilchrist, 2014). However, these cut-off frequencies were not practical for our experiments, where the noise appeared to be of much lower frequency. A comparison of the different filter cut-off frequency effects can be seen in Figure 62 to Figure 67 below. It is hypothesized that the much larger samples used by (Rashid, Destrade and Gilchrist, 2014) would have generated a much larger signal. (Rashid, Destrade and Gilchrist, 2014) used a 15mm diameter sample, compared with our average sample size of 5mm, meaning that for the same stress the response measured by the load cell would be larger by a factor of 9. Assuming the noise magnitude did not increase proportionally, this would be sufficient to 'lift the signal' out of the noise to a much greater degree, meaning the lower frequency noise in our signal would not need to be filtered in a response such as theirs.

Filter Example at 16000 Hz Cutoff Frequency

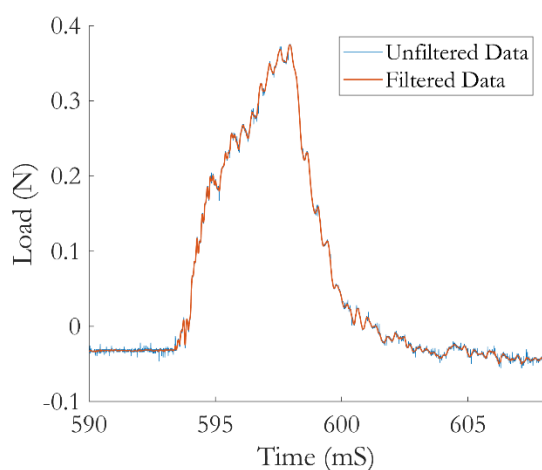


Figure 62: Filter example at 16000 Hz (porcine test)

Filter Example at 10000 Hz Cutoff Frequency

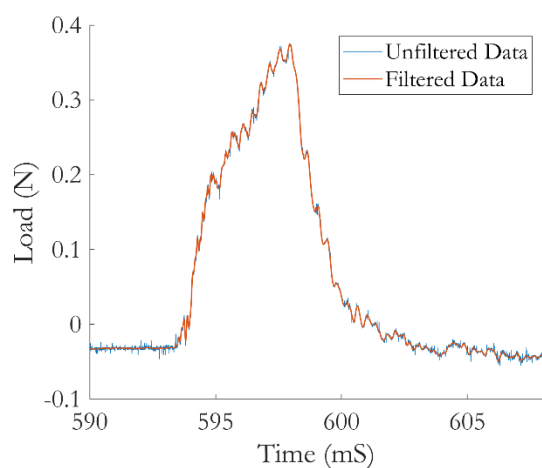


Figure 63: Filter example at 10000 Hz (porcine test)

Filter Example at 5000 Hz Cutoff Frequency

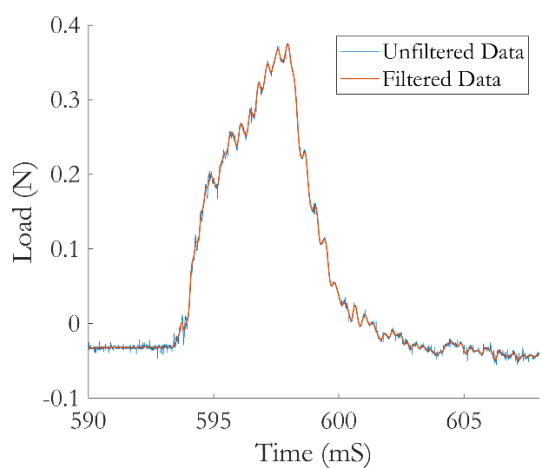


Figure 64: Filter example at 5000 Hz (porcine test)

Filter Example at 2500 Hz Cutoff Frequency

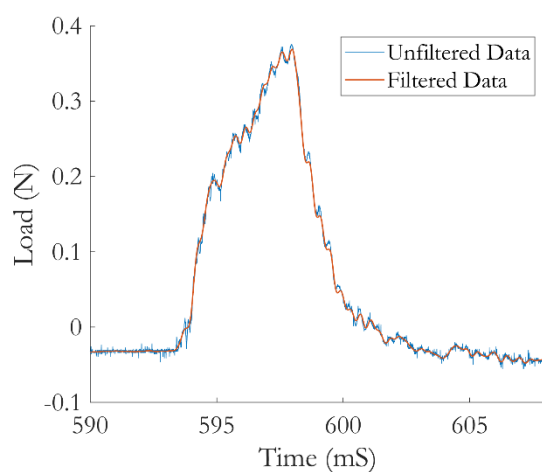


Figure 65: Filter example at 2500 Hz (porcine test)

Filter Example at 1332 Hz Cutoff Frequency

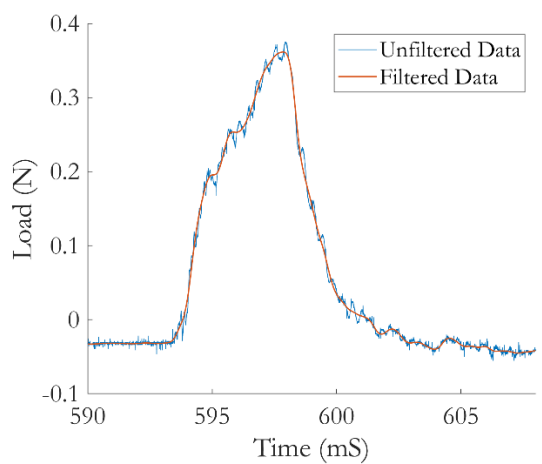


Figure 66: Filter example at 1332 Hz (porcine test)

Filter Example at 1000 Hz Cutoff Frequency

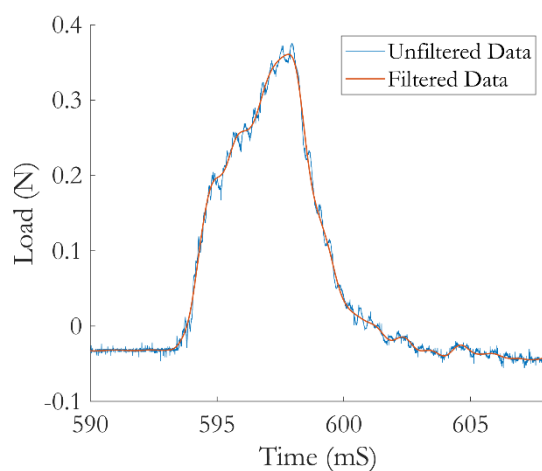


Figure 67: Filter example at 1000 Hz (porcine test)

Fourier Analysis of the High Rate Experiments

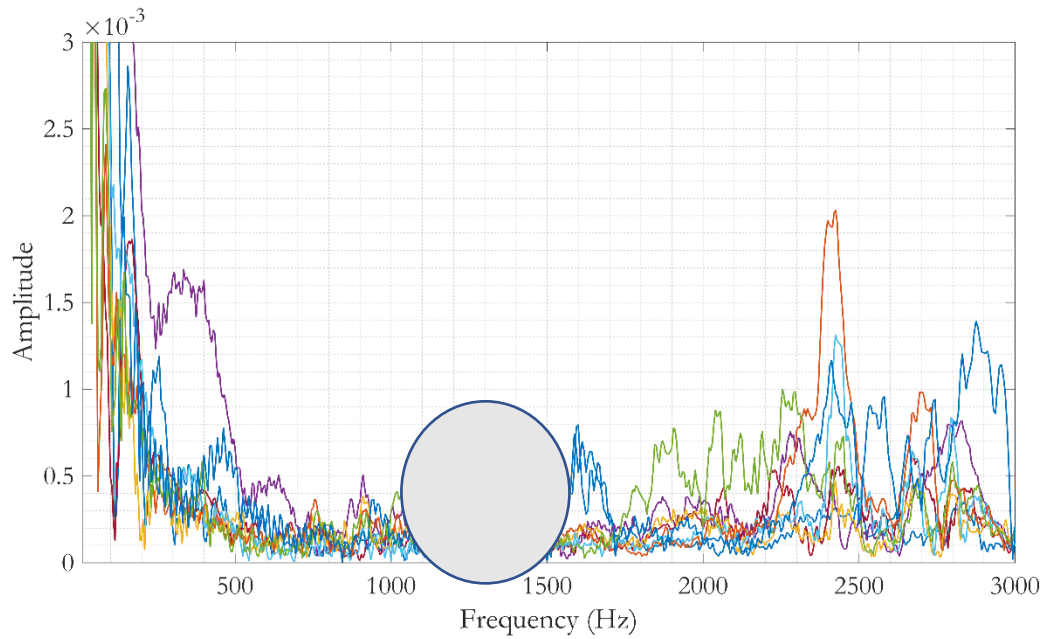


Figure 68: A Fourier analysis of the high rate experiments

Fourier Analysis of the Medium Rate Experiments

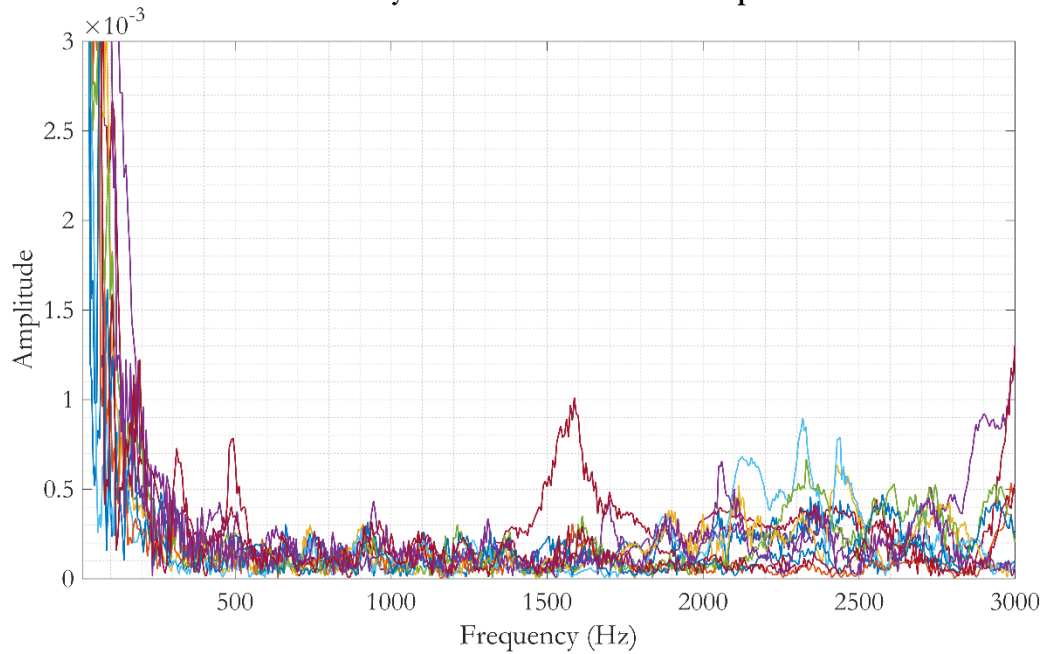


Figure 69: A Fourier analysis of the medium rate tests

Fourier Analysis of the Low Rate Experiments

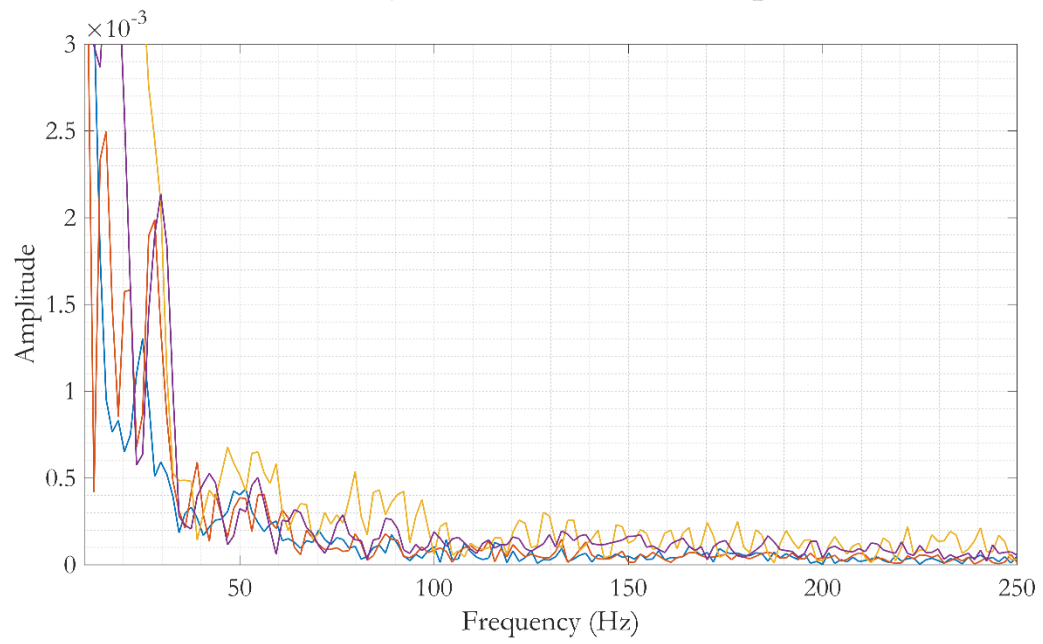


Figure 70: A Fourier analysis of the low rate experiments

4.8.2 Filter validation

Once the cut-off frequencies for the filters had been determined the filters were applied to sample traces (with the induced delay compensated for) and visually inspected to ensure there was no significant divergence from the signal induced by the filtering. Filter examples for high rate (Figure 71), medium rate (Figure 72) and low rate (Figure 73) can be seen below.

High Rate Filter Example at 1000 Hz Cutoff Frequency

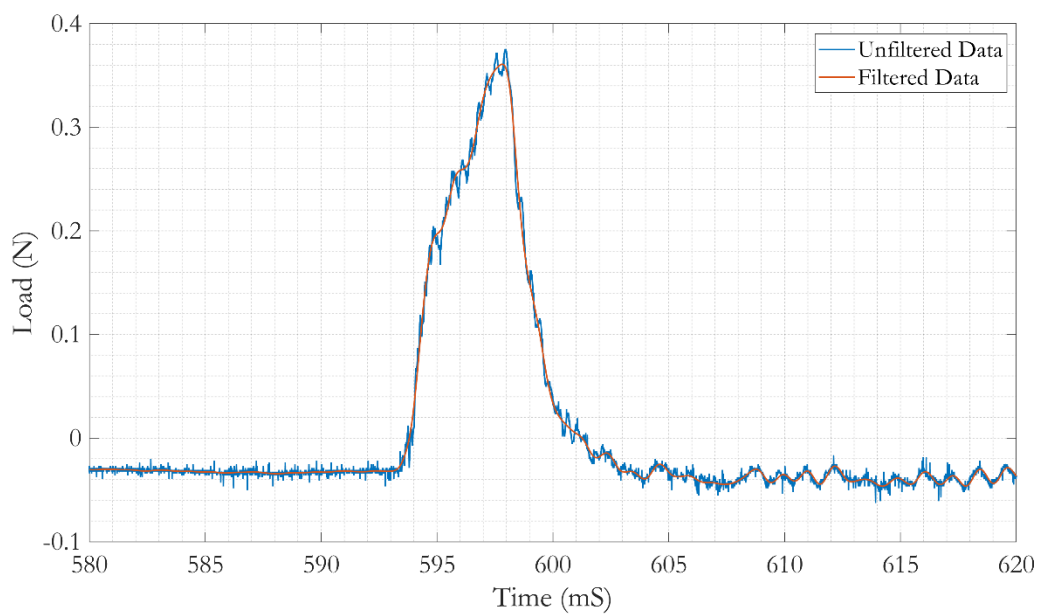


Figure 71: A high rate filtering example

Medium Rate Filter Example at 666 Hz Cutoff Frequency

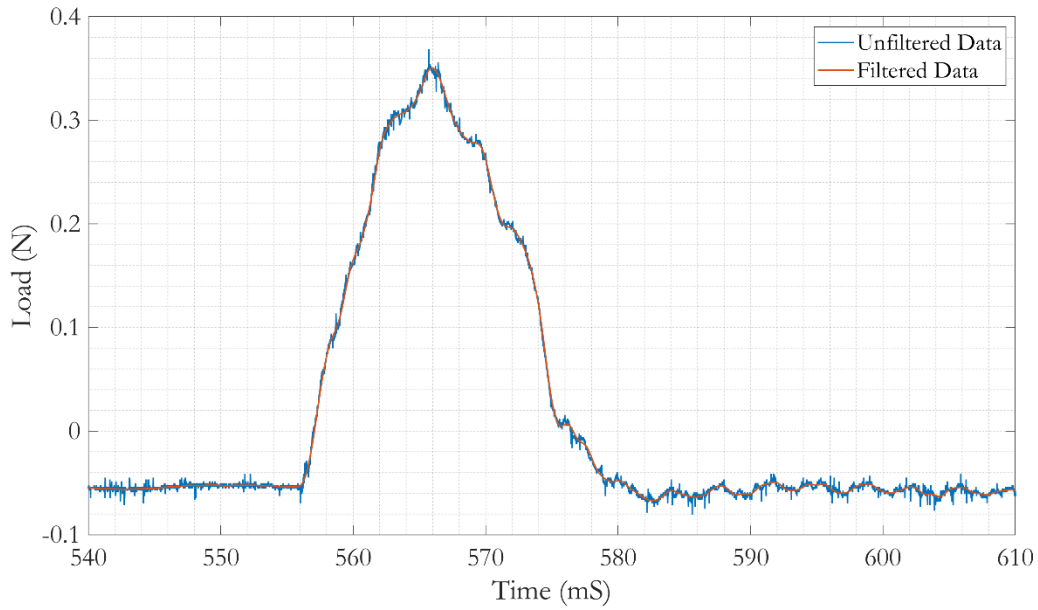


Figure 72: A medium rate filtering example

Low Rate Filter Example at 132 Hz Cutoff Frequency

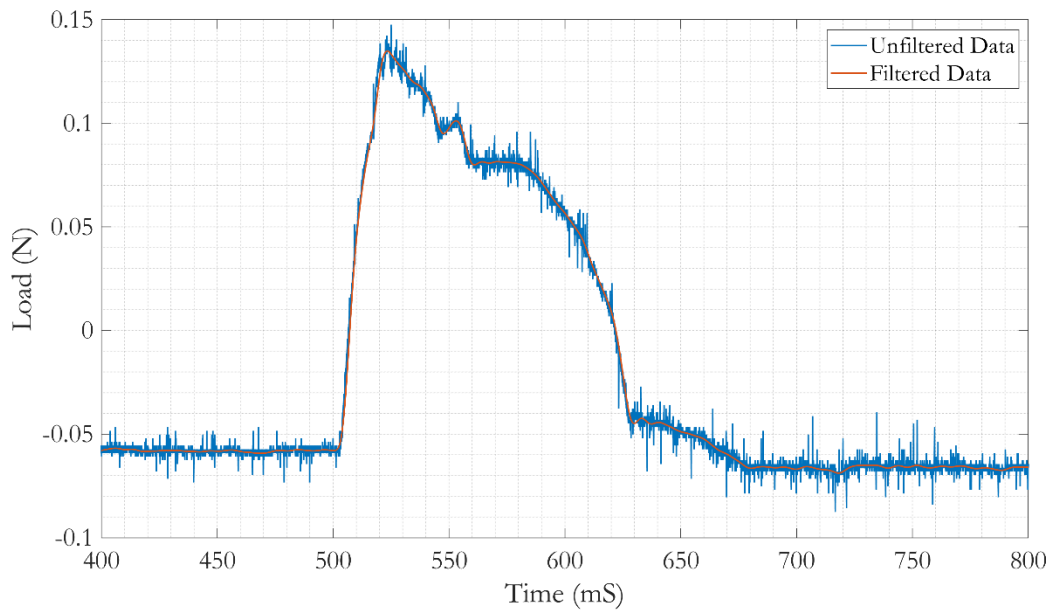


Figure 73: A low rate filtering example

As can be seen from the above examples, the filtered trace shows strong agreement with the unfiltered trace, there are no noticeable artefacts from the filtering process and the choices of cut-off frequency seem to have effectively filtered out the high frequency noise without affecting the magnitude or shape of the acquired signal to any significant degree.

5 Experimental results

5.1 Introduction

There are significantly fewer examples in literature of brain tissue testing in tension at high strain rates than in either shear or compression, with only (Tamura *et al.*, 2008; Jin *et al.*, 2013; Rashid, Destrade and Gilchrist, 2014) testing in tension at rates significantly above quasi-static. Of these, the highest reported strain rate was (Rashid, Destrade and Gilchrist, 2014) where a maximum rate of 90 s^{-1} was achieved. All three of these experiments showed strain rate dependence in the tissues mechanical response to loading, indicating viscoelasticity.

The goal of the experiments reported below was to use the custom developed apparatus described previously to test brain tissue in tension at several rates, with a maximum rate in the region of 250 s^{-1} . This was intended to validate the hypothesis that brain tissue is viscoelastic. Since the maximum strain rate is considerably higher than previously achieved the difference in the mechanical response of the tissue is expected to be greater, making the viscoelastic effect clearer.

The methodology and filtering techniques are first discussed, then the results are reported and the differences between the low and high rates evaluated statistically, before being summarized and discussed. If viscoelasticity was evident as hypothesized, it would validate the inclusion of a viscoelastic component in the mathematical model for brain behaviour.

It should be noted that there is an expected level of variability in result such as these due to the natural variation across individuals' biological samples, which is expected in biomechanics

studies such as these. The goal of this work is to determine an average set of mechanical properties, although this variation will still exist.

5.2 Results

The filtered stress-stretch curves for each strain rate set were linearly interpolated across 1000 linearly spaced datapoints between stretch values of 1 and 1.4 (the slightly higher maximum stretch was used to ensure that the range of 1-1.3 was acquired since, due to an artefact of the data processing code, the end of the signal will be trimmed off during the interpolation. These interpolated curves were then averaged (mean value) at each datapoint and an average curve was generated. The high, medium and low rate experimental results can be seen below in Figure 74, Figure 75 and Figure 76. The 3 average curves, along with their standard deviations can be seen plotted together in Figure 77

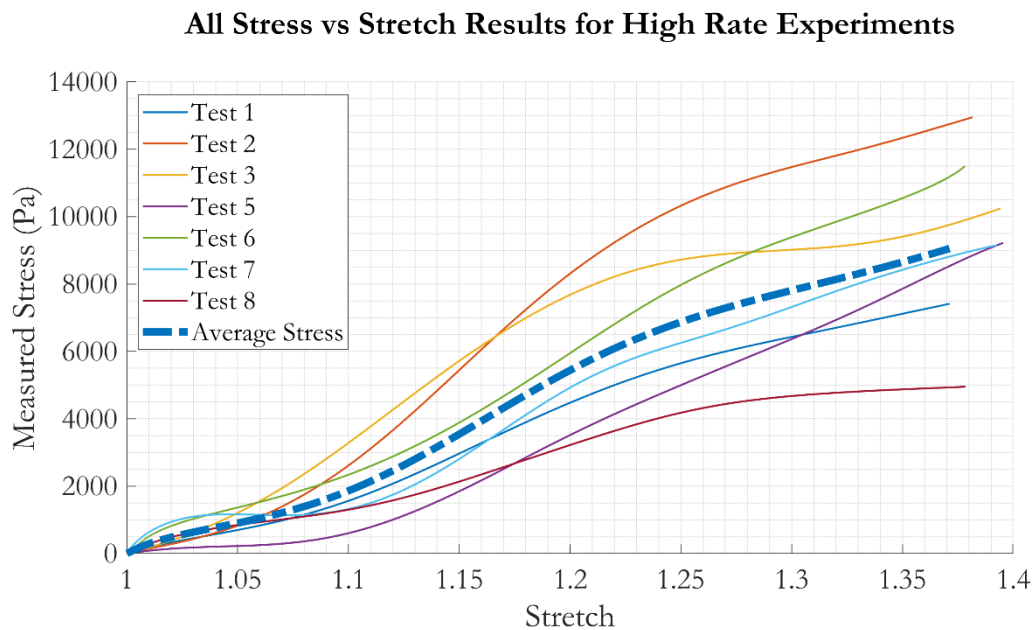


Figure 74: A graph of all the filtered high rate experimental results

All Stress vs Stretch Results for Medium Rate Experiments

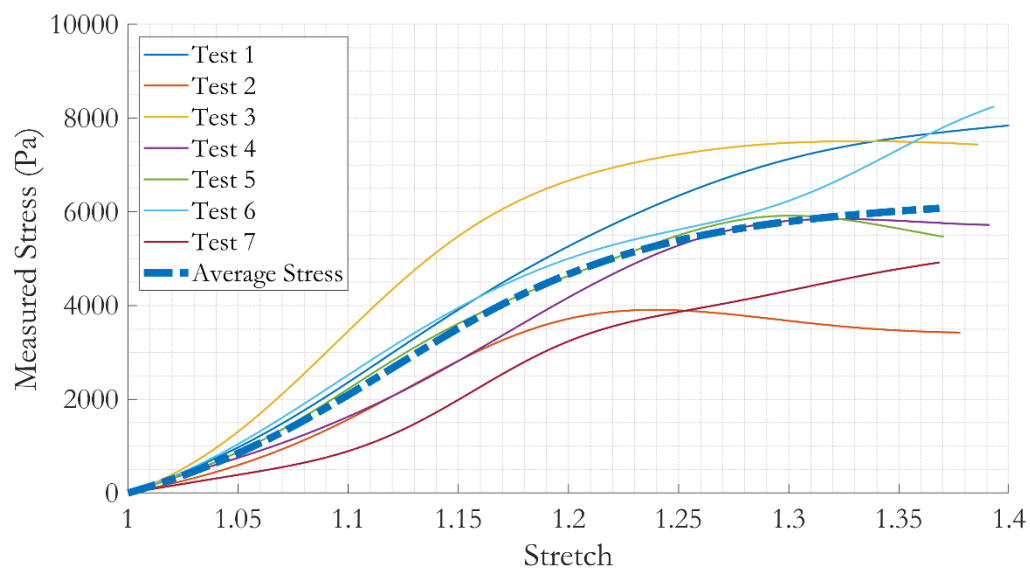


Figure 75: A graph of all the filtered medium rate experimental results

All Stress vs Stretch Results for Low Rate Experiments

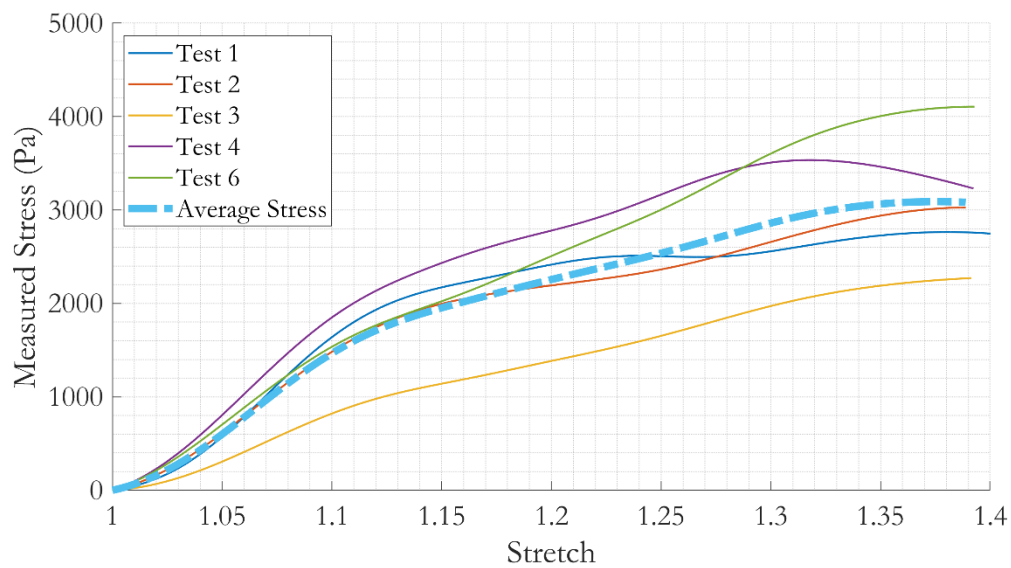


Figure 76: A graph of all the filtered low rate experimental results

Average Stress vs Stretch Results

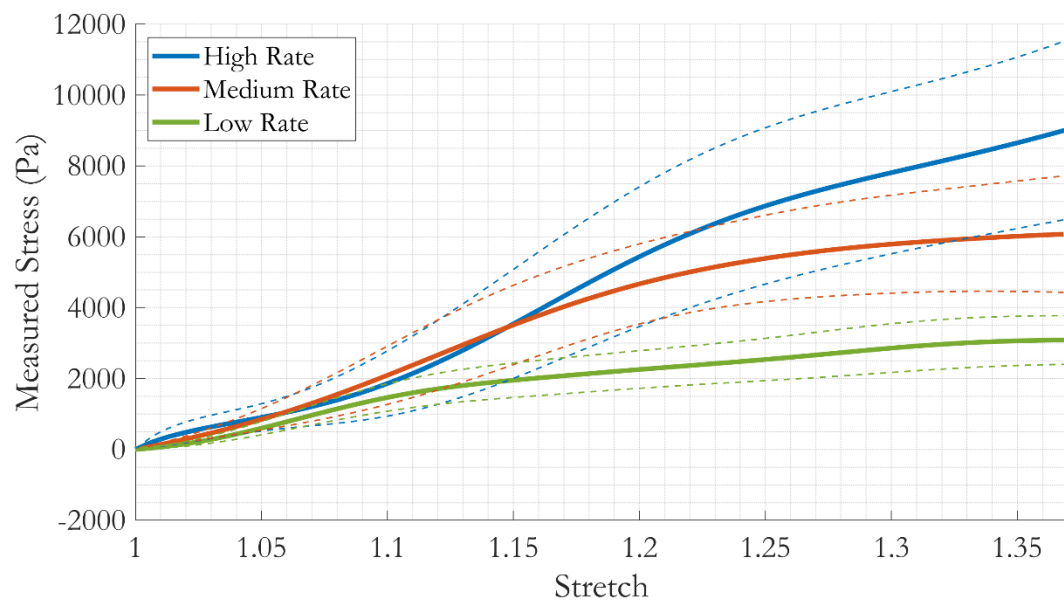


Figure 77: Average stress - stretch curves for high, medium and low rate, with standard deviation shown with dotted lines

5.3 Statistical significance

Using the low rate experiments as a baseline, statistical tests were carried out to determine what percentile result the observed stresses would be, assuming there was no underlying rate dependency in the mechanical properties of tissue.

The differences between the curves were determined at the maximum stretch in the experimental range, a stretch value of 1.35 (a little less than 1.4 since the ends of the traces get snapped slightly by the filtering process). As can be inferred from Figure 77, the values were generally higher for the high rate test than for the medium rate tests, and similarly higher for the medium rate tests than the low rate tests. The statistical tests were designed to determine the probability that this increase was due to some underlying cause and not simply down to the variance in the results.

2 sample T tests were carried out to compare the high rate set with the medium rate set, the high rate set with the low rate set and the medium rate set with the low rate set. The test determines the probability (p value) that the null hypothesis, in this case set A = set B, is true. A P threshold value of 0.05, corresponding to a 5% chance that the two sets have no underlying differences, was chosen in line with the most common standard in literature and the default in many scientific software packages such as MATLAB.

Table 5: Probabilities that the different strain rate sets had no underlying mechanical difference

T Test		
High Rate vs Medium Rate	High Rate vs Low Rate	Medium Rate vs Low Rate
P = 0.03524	P = 0.00057	P = 0.00174
t = 2.4244	t = 5.7877	t = 4.4305
df = 10.2514	df = 7.3240	df = 8.7891

As can be seen in Table 5, $P < 0.05$ for all three cases, meaning that the null hypothesis can be rejected in every case and a difference due to strain rate can be inferred.

5.4 Discussion

As can be inferred from Figure 77, brain tissue was shown to exhibit a strong strain rate dependence, with the high rate tests resulting in a significantly greater mechanical response to deformation, indicating a ‘stiffer’ material. At the maximum end of the experimental range (a stretch of 1.3), the average high rate stress (7810 Pa) was almost three times the average low rate stress (2860 Pa). This is in line with other experiments carried out in literature, (Rashid, Destrade and Gilchrist, 2014), who showed a stress at 90 s^{-1} to be twice as high as that found at 30 s^{-1} at 1.3 stretch. Similarly (Jin *et al.*, 2013) reported a six fold increase in recorded stress between 0.5 s^{-1} and 30 s^{-1} , although this was at 1.5 stretch. (Miller and Chinzei, 2002) also reported a 50% increase in stress at a stretch of 1.5 between 0.0064 s^{-1} and 0.64 s^{-1} . While none of these results are directly comparable, since they all test different brain tissue from different animals and different brain regions, the overall trend of strain rate dependence should still be noted. Additionally the tests were all carried out at different strain rates to different stretch values under a variety of test conditions (Table 6). The results presented here are within the same range.

Table 6: Summary of literature results compared with our own

Experiment	Stress (Pa)	Strain rate (s^{-1})	Stretch at measurement
(Rashid, Destrade and Gilchrist, 2014)	3000, 4200, 6000	30,60,90	1.3
(Jin <i>et al.</i> , 2013)	2000, 4000, 12000	0.5, 5, 30	1.5
(Tamura <i>et al.</i> , 2008)	2400, 4000, 6500	0.9, 4.3, 25	1.3
(Miller and Chinzei, 2002)	120, 180	0.0064, 0.64	1.2
(Franceschini, 2006)	750 (approximate)	Between 5.5×10^{-3} and 9.3×10^{-3}	1.3
Our results	2860, 5793, 7810	20, 125, 250	1.3

The statistical analysis backs up the rate dependence, since it shows that there is no statistical evidence for such an underlying rate dependence. This provides a strong basis for assuming

viscoelastic behaviour and supports the addition of a viscoelastic component to the hyperelastic Ogden model.

It should be noted that during an impact stretches in the brain are expected to reach as high as 1.6 in extreme cases (Ghajari, Hellyer and Sharp, 2017), and here a stretch range of 1-1.3 was used as previously discussed. This is because the aim of this research is to characterize the behaviour of brain tissue before tissue damage, hence data at stretches higher than this, when signs of damage were being shown in the stress-stretch curves, would not be relevant to the current analysis. An experimental stretch range of 1.3 is also reasonably consistent with existing tensile tests in literature (Franceschini, 2006; Velardi, Fraternali and Angelillo, 2006; Tamura *et al.*, 2008; Rashid, Destrade and Gilchrist, 2014; Budday *et al.*, 2017), with those that go higher (Velardi, Fraternali and Angelillo, 2006) also showing this damage effect in their reported data.

The acquired signals are noisy and need to be put through a filtering process with a necessarily low cut-off frequency as previously described. It is hypothesized that this is due to the smaller sample size than with comparable literature, meaning the acquired signal would be smaller and thus the noise would be comparatively larger. One potential solution to this problem would be to test on human brain rather than porcine. Since a human's brain is larger the internal structures are also larger, meaning that larger samples could be taken without mixing brain tissue types within the sample and therefore larger signals could be acquired. However, for porcine tissue this noise is believed to be a limitation of the apparatus. Several methods for reducing noise such as using a special quartz crystal load cell, introducing a gel layer between the apparatus base and the load cell and isolating the entire system from mains power were employed to reduce the noise to the observed level. Redesigning the apparatus and using different materials in its construction could potentially further reduce the noise, though this would likely be at the expense of its portability.

5.5 Conclusion

The results show a strong rate dependence in the mechanical behaviour of brain tissue, and this is backed up by the T tests showing this conclusion to be valid from a statistical point of view. This is in agreement with work done by (Miller and Chinzei, 2002; Jin *et al.*, 2013; Rashid,

Destrade and Gilchrist, 2014) The tests carried out support the hypothesis that brain tissue is a viscoelastic material and supports the inclusion of a viscoelastic component in the hyperelastic Ogden model.

These results could be extended mainly by increasing the size of the dataset in order to make the statistical tests more valid and to give a better indication of the average behaviour at all 3 rates. In addition tests could be carried out in the sagittal plane, rather than the coronal, meaning the axis of stretching would line up with the general axon direction in the tissue. Anisotropy in brain tissue white matter is still a debated topic and the apparatus is well suited to investigating it. Finally the tests could be extended to human tissue, since that is the tissue that it is aiming to model. Additionally human tissue is expected to be stiffer, based on results by (Prange and Margulies, 2002; Jin *et al.*, 2013) as well as allowing for larger sample sizes, which would reduce the effect of noise on the signal.

5.6 Dissemination

- 1) A summary of the results presented in this chapter was presented at the BioMedEng18 conference in 2018 at Imperial College London and a short paper was published in the conference proceedings (Pangonis and Ghajari, 2018).
- 2) A manuscript reporting these results and the relevant methods has been submitted to *Acta Biomaterialia* and is currently under review

6 The mathematical foundation for the hyper-viscoelastic model

Since LS-Dyna has been used to validate the results being produced throughout this experiment, its equations were used as a basis for the model being developed. Much like in LS-DYNA, the model is broken down into two parts, with the first part being an Ogden hyperelastic model to account for the hyperelastic behaviour of the tissue, and the second part being a convolution integral to model viscoelasticity.

6.1 The hyperelastic component

As shown in the LS-DYNA manual (MAT_077_0), which is based on work published in (Ogden, 1997), the strain energy function of a hyperelastic material can be modelled as

$$W^* = \sum_{i=1}^3 \sum_{j=1}^n \frac{\mu_j}{\alpha_j} (\lambda_i^{\alpha_j} - 1) + K(J - 1 - \ln(J))$$

Equation 11: Ogden strain energy function

where λ represents the principle stretches, μ and α are constants, K is the bulk modulus and J is the volume ratio:

$$J = \lambda_1 \lambda_2 \lambda_3$$

Equation 12: The volume ratio

In Equation 11 the asterisk (*) indicates that volumetric effects have been eliminated from the principle stretches, λ_j^* . Note that in many publications the symbol employed for strain energy W is often replaced by Ψ .

6.1.1 Simplifying the strain energy function for an incompressible material

As detailed in (Holzapfel, 2000), in the case of incompressible materials

$$J = 1$$

Equation 13: The volume ratio for incompressible materials

Therefore, in the incompressible case, the second term in the strain energy function disappears as shown below:

$$W^* = \sum_{i=1}^3 \sum_{j=1}^n \frac{\mu_j}{\alpha_j} (\lambda_i^{*\alpha_j} - 1) + K(1 - 1 - \ln(1))$$

$$W^* = \sum_{i=1}^3 \sum_{j=1}^n \frac{\mu_j}{\alpha_j} (\lambda_i^{*\alpha_j} - 1) + K(1 - 1 - 0)$$

$$W^* = \sum_{i=1}^3 \sum_{j=1}^n \frac{\mu_j}{\alpha_j} (\lambda_i^{*\alpha_j} - 1) + K(0)$$

$$W^* = \sum_{i=1}^3 \sum_{j=1}^n \frac{\mu_j}{\alpha_j} (\lambda_i^{*\alpha_j} - 1)$$

Equation 14: The strain energy function for an incompressible case

This equation can be applied in 3 dimensions (and therefore 3 principle stretches) and expanded to give

$$W^* = \sum_{j=1}^n \frac{\mu_j}{\alpha_j} (\lambda_1^{*\alpha_j} + \lambda_2^{*\alpha_j} + \lambda_3^{*\alpha_j} - 3)$$

Equation 15: The expanded strain energy function for 3 dimensions

6.1.2 Simplifying the strain energy function for a 2 term Ogden model in uniaxial tension

As shown in (Holzapfel, 2000), any two of these principle stretches can be expressed in terms of the final one. Using the volume ratio (Equation 12) and setting it equal to 1 as in the case of an incompressible material (Equation 13), we can infer Equation 16 below.

$$\lambda_1 \lambda_2 \lambda_3 = 1$$

Equation 16: The principle stretches for incompressible materials

In the case of uniaxial tension, such as in the experiments being run in chapter 4, where the direction of uniaxial tension is taken as the direction of the first principle stretch, there is symmetry in the 2nd and 3rd principle stretches.

$$\lambda_2 = \lambda_3$$

Equation 17: The 2nd and 3rd principle stretches for uniaxial tension

By substituting Equation 17 into Equation 16, the 2nd and 3rd principle stretches can now be written in terms of the 1st principle stretch.

$$\lambda_1 \lambda_2^2 = 1$$

$$\lambda_2^2 = \frac{1}{\lambda_1}$$

$$\lambda_2 = \sqrt{\frac{1}{\lambda_1}}$$

$$\lambda_2 = \lambda_1^{-\frac{1}{2}}$$

Equation 18: The 2nd principle stretch in terms of the 1st principle stretch

Using Equation 17, we can also infer the 3rd principle stretch.

$$\lambda_3 = \lambda_1^{-\frac{1}{2}}$$

Equation 19: The 3rd principle stretch in terms of the 1st principle stretch

Equation 18 and Equation 19 can now be used to write the simplified strain energy function, Equation 14, in terms of only the 1st principle stretch and the constant groups α and μ

$$W^* = \sum_{j=1}^n \frac{\mu_j}{\alpha_j} \left(\lambda_1^{*\alpha_j} + \lambda_1^{*-\frac{1}{2}\alpha_j} + \lambda_1^{*-\frac{1}{2}\alpha_j} - 3 \right)$$

$$W^* = \sum_{j=1}^n \frac{\mu_j}{\alpha_j} \left(\lambda_1^{*\alpha_j} + 2\lambda_1^{*-\frac{\alpha_j}{2}} - 3 \right)$$

Equation 20: The expanded strain energy function in terms of the 1st principle stretch

For a 2 term Ogden model ($n = 2$) Equation 20 can be further expanded.

$$W^* = \frac{\mu_1}{\alpha_1} \left(\lambda_1^{*\alpha_1} + 2\lambda_1^{*-\frac{\alpha_1}{2}} - 3 \right) + \frac{\mu_2}{\alpha_2} \left(\lambda_1^{*\alpha_2} + 2\lambda_1^{*-\frac{\alpha_2}{2}} - 3 \right)$$

Equation 21: The strain energy function for an incompressible 2 term Ogden model in uniaxial tension

6.1.3 Finding the 1st Piola-Kirchoff stress tensor

Stress can be measured in several ways, the most common one is using the Cauchy stress or ‘true’ stress. Alternatively, the 1st and 2nd Piola-Kirchoff stresses are often used.

The 1st Piola-Kirchoff stress is defined as the force in the current configuration acting on the original area. It is a useful quantity to calculate for this purpose since it acts on the reference configuration (initial shape) of the sample. For our samples this is a simple cylinder with easily measurable dimensions. This is preferable to calculations that reference the deformed configuration during the experiment, which is a significantly more complicated shape mathematically.

Additionally, integrating the 1st Piola-Kirchoff stress across the initial cross-sectional area of the side of the sample in contact with the load cell gives the load that the load cell is measuring directly, meaning that the theoretical forces can be directly compared to those recorded in the experiment.

The 1st Piola-Kirchoff stress tensor is defined as (Holzapfel, 2000)

$$P_a = \frac{\partial W^*}{\partial \lambda_a}$$

Equation 22: The 1st Piola-Kirchoff stress

As the experiment is in uniaxial tension, the relevant 1st Piola-Kirchoff stress is that for the 1st principle stretch λ_1 , since we already have the equation for strain energy (W^*) in terms of λ_1 (Equation 21) we can carry out the differentiation.

$$P_1 = \frac{\partial W^*}{\partial \lambda_1}$$

$$W^* = \frac{\mu_1}{\alpha_1} \left(\lambda_1^{*\alpha_1} + 2\lambda_1^{*-\frac{\alpha_1}{2}} - 3 \right) + \frac{\mu_2}{\alpha_2} \left(\lambda_1^{*\alpha_2} + 2\lambda_1^{*-\frac{\alpha_2}{2}} - 3 \right)$$

$$\frac{\partial W^*}{\partial \lambda_1} = \frac{\mu_1}{\alpha_1} \left(\alpha_1 \lambda_1^{*[(\alpha)_1-1]} - \alpha_1 \lambda_1^{*-(\frac{\alpha_1}{2}+1)} \right) + \frac{\mu_2}{\alpha_2} \left(\alpha_2 \lambda_1^{*[(\alpha)_2-1]} - \alpha_2 \lambda_1^{*-(\frac{\alpha_2}{2}+1)} \right)$$

$$\frac{\partial W^*}{\partial \lambda_1} = \mu_1 \left(\lambda_1^{*[(\alpha)_1-1]} - \lambda_1^{*-(\frac{\alpha_1}{2}+1)} \right) + \mu_2 \left(\lambda_1^{*[(\alpha)_2-1]} - \lambda_1^{*-(\frac{\alpha_2}{2}+1)} \right)$$

Equation 23: The differentiation of the strain energy function

Therefore, the stress in the sample due to Ogden hyperelasticity behaviour (not including viscoelastic rate effects at this stage, for a 2 term Ogden model) can be modelled using the below equation for the 1st Piola-Kirchoff stress.

$$P_1 = \mu_1 \left(\lambda_1^{*[(\alpha)_1-1]} - \lambda_1^{*-(\frac{\alpha_1}{2}+1)} \right) + \mu_2 \left(\lambda_1^{*[(\alpha)_2-1]} - \lambda_1^{*-(\frac{\alpha_2}{2}+1)} \right)$$

Equation 24: The 1st Piola-Kirchoff stress for a 2 term Ogden model

Or, more generally, for an Ogden model with n terms.

$$P_1 = \frac{\partial W^*}{\partial \lambda_1} = \sum_{i=1}^n \mu_i \left(\lambda_1^{*[(\alpha)_i-1]} - \lambda_1^{*-(\frac{\alpha_i}{2}+1)} \right)$$

Equation 25: The 1st Piola-Kirchoff stress for an n term Ogden model

For the sake of clarity, in the future we shall refer to P_1 as P_∞ . This is to represent zero rate effects in this component of the stress, or the theoretical scenario where the body deformed to the new configuration in an infinite amount of time, meaning any rate effects would go to zero.

6.2 The viscoelastic component

In LS-Dyna, rate effects (viscoelasticity) are modelled using a convolution integral (Equation 26, below). This is in line with work published by (Christensen, 1980). In this model there are two components to the stress, the hyperelastic component as previously detailed, modelled by a two term Ogden model, and the viscoelastic component, modelled by this convolution integral. The sum of the two components represents the overall stress.

$$\sigma_{ij} = \int_0^t g_{ijkl}(t - \tau) \frac{\partial \varepsilon_{kl}}{\partial \tau} d\tau$$

Equation 26: The convolution integral for rate effects calculating Cauchy stress

where σ_{ij} represents the Cauchy stress, g_{ijkl} is the relaxation function, which can be expanded to a Prony series of viscoelastic constants, ε is the strain, t is the current time and τ is a previous point in time.

However, in the case of uniaxial tension, where only 1 dimension is considered, this can be simplified to

$$\sigma = \int_0^t g_i(t - \tau) \frac{\partial \varepsilon}{\partial \tau} d\tau$$

Equation 27: The one-dimensional convolution integral for computing Cauchy stress

The hyperelastic component previously calculated (Equation 25) gives the 1st Piola-Kirchoff stress in the material. In order to combine the viscoelastic and hyperelastic components together, the Cauchy stress calculated by Equation 27 must first be converted to the 1st Piola-Kirchoff so the two can be summed together. It can be converted using the following formula (Holzapfel, 2000).

$$P_a = J \lambda_a^{-1} \sigma_a$$

Equation 28: The relationship between Cauchy stress and the 1st Piola-Kirchoff stress

For incompressible materials $J = 1$ (Equation 13), so the convolution integral for the 1st Piola-Kirchoff stress can be written as

$$P = \frac{1}{\lambda} \int_0^t g_i(t - \tau) \frac{\partial \varepsilon}{\partial \tau} d\tau$$

Equation 29: The convolution integral representing rate effects for the 1st Piola-Kirchoff stress

where g is given by the Prony series

$$g(t) = \sum_{i=1}^n G_i e^{-\beta_i t}$$

Equation 30: The Prony series for the relaxation function

In Equation 30 above, G_i represents shear relaxation moduli and β_i are decay constants given by

$$\beta_i = \frac{1}{\tau_i}$$

Equation 31: The equation for the decay constants

In Equation 31 above, τ_i represents the time period the shear modulus G_i applies to. Note that it is different to the time constant τ found in the convolution integral in Equation 26 and Equation 29.

6.3 Combining hyperelasticity and viscoelasticity

The overall 1st Piola-Kirchoff stress in the sample can be modelled by summing the hyperelastic component for P_∞ (Equation 25) and the viscoelastic component (Equation 29), in line with the methods and formulas used in LS-DYNA.

$$P_{tot} = P_\infty + \frac{1}{\lambda} \int_0^t \frac{g_i(t - \tau) \partial \varepsilon}{\partial \tau} d\tau$$

Equation 32: The full equation for the 1st Piola-Kirchoff stress in the sample

The 1st Piola-Kirchoff Stress can be calculated using Equation 32 above. This can then be integrated across the initial cross-sectional area of the sample to theoretically calculate the force recorded by the load cell for a given stretch. This can then be compared with actual experimental results and an optimisation loop can be used to calculate the material constants.

6.4 Solving analytically

6.4.1 Making the equation solvable

In order to solve the equation analytically the expression under the integral needs to be put in terms of τ , since g is already a function of τ ($t - \tau$) all that remains is the strain ε . During an experiment the strain varies with time, however the equipment outputs an array of datapoints rather than a mathematical curve. In order to put the equation into an analytical format, a curve must be fit to the strain.

6.4.2 Fitting a polynomial

This was achieved by fitting a polynomial curve to the displacement output of the apparatus. This was achieved with the MATLAB *fit* command, additionally, the curve fitting was limited by fixing the final term to 0 (since the strain will start from 0 in the experiment). This was then scaled to strain ε by dividing all the terms by the sample thickness. It could further be converted to stretch λ by changing the final term from 0 to 1.

In order to determine a suitable polynomial to fit to the displacement curve, several different orders were tried. Across a sample of 15 experiments on porcine brain tissue, the displacement curves were trimmed to a reasonable experimental range (40% strain) and different orders of polynomial were fitted to the curve. The mean cumulative square difference between the fitted and experimental curves was then calculated and used as a metric for how close a match the polynomial gave. The average mean cumulative square difference across the 15 experiments is shown below in Table 7.

Table 7: A comparison of different orders of polynomial to be fitted to the measured displacement

Number of terms in the Polynomial	Mean cumulative square difference between the fitted curve and the measured curve
2	0.664
3	0.110
4	0.091
5	0.059
6	0.051
7	0.052
8	0.053

As can be seen, further increasing the order of the polynomial gives a reduced benefit as the order is increased. As the higher the polynomial order is, the more complex the analytical equation becomes, this assessment was used to determine the minimum order required for good accuracy in the curve matching. The data suggested this was a 6th order polynomial, since further increasing the order gave no real increase in accuracy. The suitability of the polynomial was further confirmed by plotting it against the measured stretch from the encoder and visually confirming it was a good match, as can be seen below in Figure 78.

Measured vs Fitted Stretch for a 6th Order Polynomial

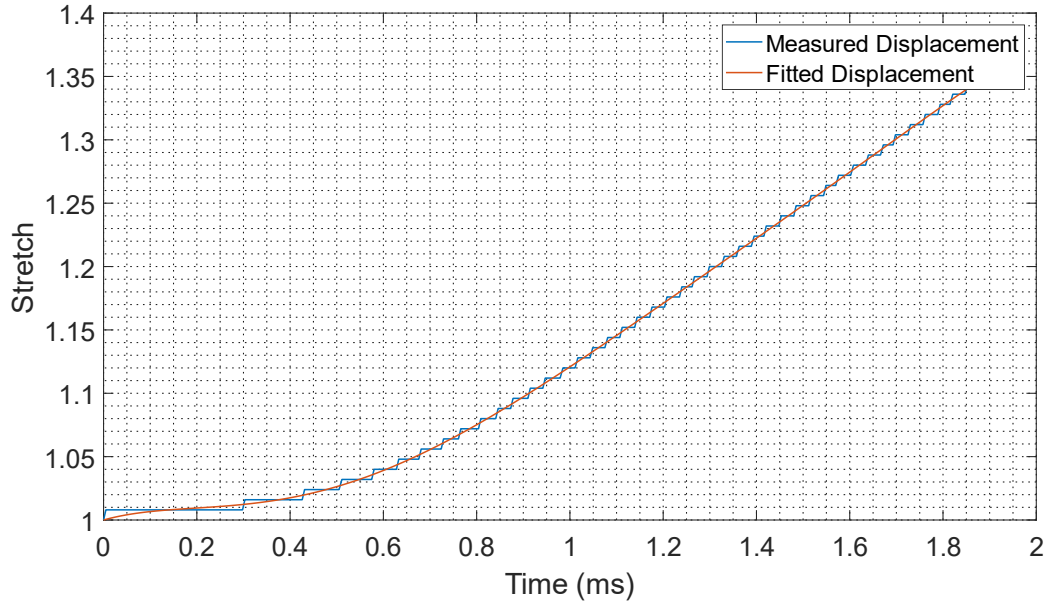


Figure 78: A comparison of the measured stretch vs fitted stretch using a 6th order polynomial

6.4.3 Solving the equation

Using the determined 6th order polynomial the λ and ε in Equation 32 could be substituted, writing the entire equation in terms of t (and τ , however τ changes to t values during the integral). It is then possible to solve the integration, expanding the equation to give a full analytical solution for P_{tot} . The equation was solved and simplified using Wolfram Mathematica and is given in (Appendix 2, 10.2).

6.4.4 Validating the equation

Once the expanded analytical equation had been determined, it needed to be validated. This was done using LS-DYNA in a similar manner to the custom apparatus. A 4mm diameter cylinder, 5mm thick was generated, meshed with 0.6 mm elements and given ‘average’ material properties for brain tissue taken from (Kleiven, 2007), (Table 8, Table 9). 0.6 mm elements were used in place of 0.2 mm elements due to a subsequent sensitivity analysis showing that such a fine mesh was unnecessary for such a simple mode of loading.

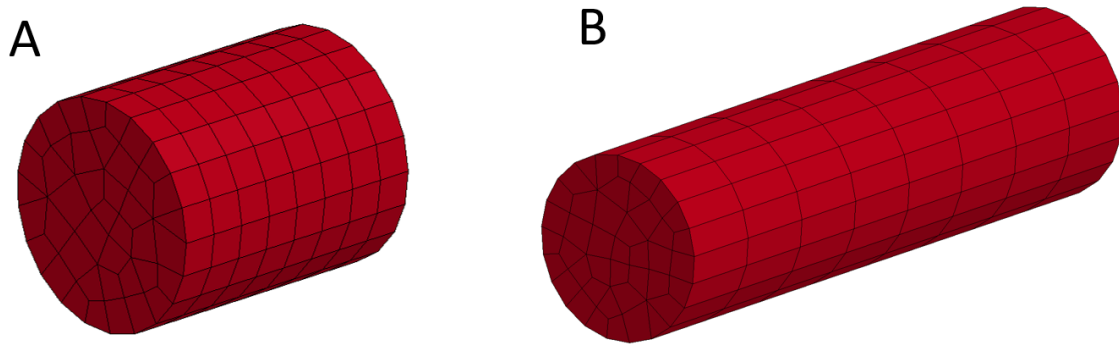


Figure 79: An image of the LS-DYNA model used for validating the analytical equation in both its undeformed configuration (A) and its deformed configuration (B)

The model was then subjected to constant velocity deformation, both ‘high’ rate, at 2 ms^{-1} and ‘low’ rate, at 0.2 ms^{-1} , up to a total stretch of 150%. These motions were similarly fed into the analytical equation and the results compared, as shown below in Figure 80 and Figure 81.

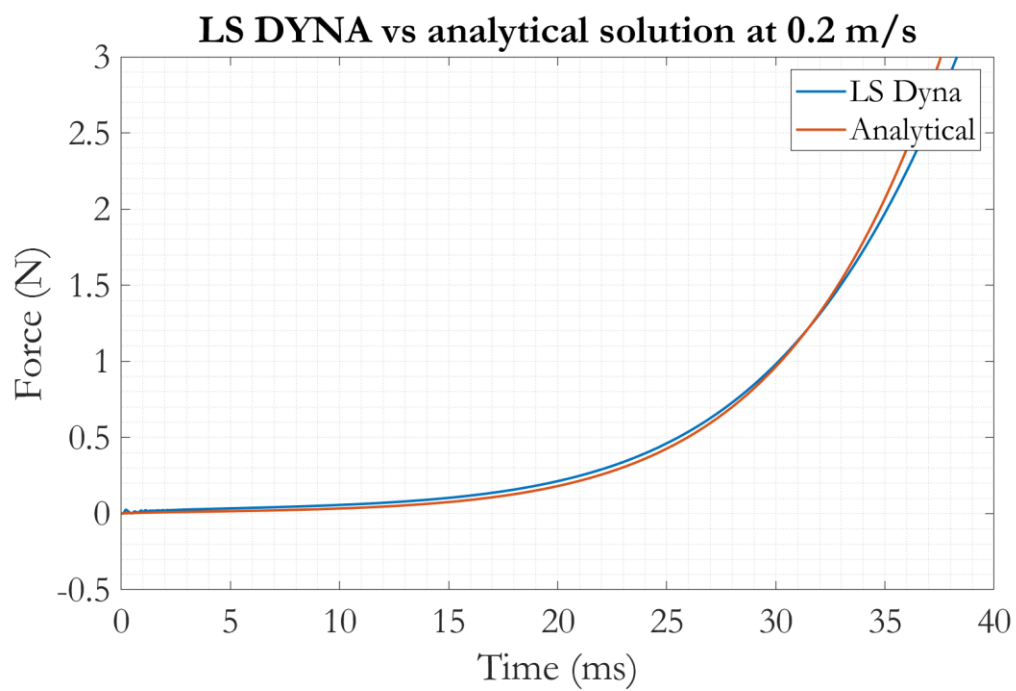


Figure 80: A LS-DYNA simulation compared to the analytical solution at low rate

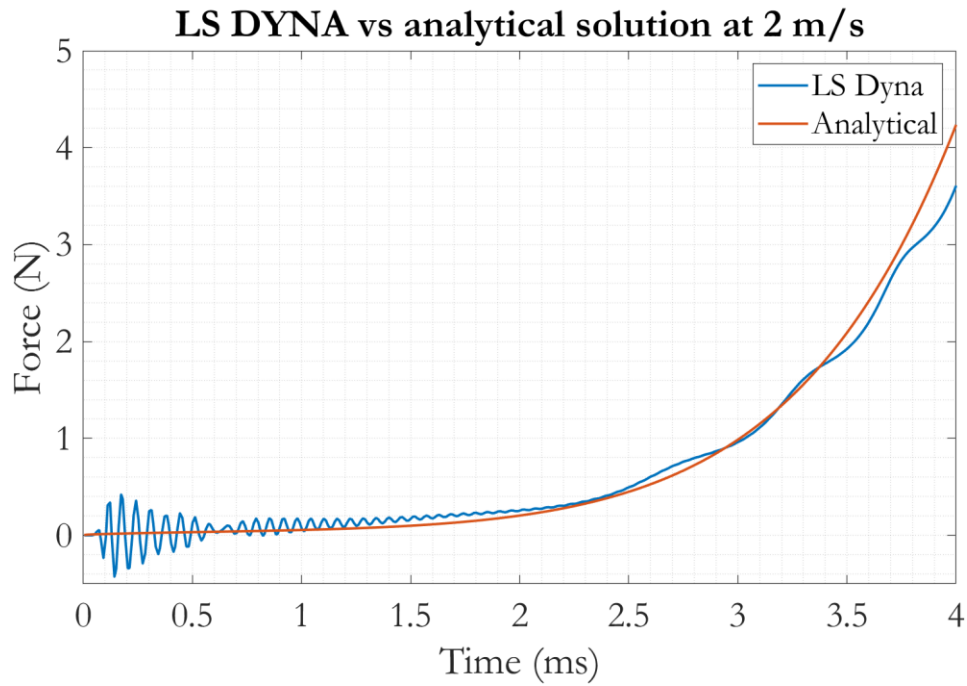


Figure 81: A LS-DYNA simulation compared to the analytical solution at high rate

The model showed strong agreement with LS-DYNA at both rates, disregarding the vibrations in LS-DYNA at the beginning of the high rate simulation. These came about because a constant velocity was instantly applied to the sample at $t = 0$, meaning the solver interpreted with a very high acceleration, which is unrepresentative of the real world. The analytical solution was additionally significantly more efficient than the LS-DYNA simulation, taking only 0.03 seconds to run, as opposed to between 4 and 5 seconds for the simulation. The increase in efficiency is particularly noteworthy as such simulations will be run many times to determine the material constants of the tissue through curve fitting.

7 Determining the viscoelastic constants

7.1 Determining constants from experimental data

The overarching goal of these experiments was to experimentally determine the material constants for brain tissue, specifically white matter as that was the tissue type experimented upon. It has been shown in literature that an Ogden model, either one term (Budday *et al.*, 2017) or two term (Kleiven, 2007; Ghajari, Hellyer and Sharp, 2017), summed with a viscoelastic component is a suitable mathematical model for modelling the mechanical behaviour of brain tissue. This viscoelastic Ogden model can be manipulated to give the first Piola Kirchhoff stress tensor ($\mathbf{P}$) as a function of stretch (λ) and a series of material specific constants ($\mu_1, \mu_2, \alpha_1, \alpha_2, \beta_1, \beta_2, \beta_3, \beta_4, \beta_5, \beta_6, G_1, G_2, G_3, G_4, G_5$ and G_6) as detailed in the mathematical model chapter.

The goal of this work is to determine values for these constants experimentally, specifically the viscoelastic constants G_1, G_2, G_3, G_4, G_5 and G_6 , since the experiments are being carried out at rates not investigated previously in literature where the viscoelastic component is expected to play a much greater role. Additionally, the quasi static and low rate strain rate regions have been more extensively investigated in literature, with experiments in tension, compression and shear significantly more readily available (Table 2). Additionally, the nature of high rate experiments means that the quasi static experiments are generally more accurate. Therefore it was judged that the hyperelastic component of the equation could be taken from literature, allowing the focus of this work to be on the viscoelastic components.

7.2 Ogden variants

There are a few variants for the (non-viscoelastic) Ogden model, for example, (Budday *et al.*, 2017) used a one term Ogden model with the form

$$\Psi^{Ogd} = \frac{2\mu}{\alpha^2(\lambda_1^\alpha + \lambda_2^\alpha + \lambda_3^\alpha - 3)}$$

Equation 33: Variant of the Ogden model used by (Budday *et al.*, 2017)

While the two term model developed by the mathematical model chapter starts with the model implemented in LS-DYNA, based off Ogden's original 1984 work published in (Ogden, 1997)

$$\Psi^{Ogd} = \sum_{j=1}^n \frac{\mu_j}{\alpha_j} (\lambda_1^{\alpha_j} + \lambda_2^{\alpha_j} + \lambda_3^{\alpha_j} - 3)$$

Equation 34: The original Ogden model as published by Ogden (Ogden, 1997) and used in the LS-DYNA FE modelling package

These two models are very similar, however there is one important difference (aside from the number of terms used in the model). The model used by (Budday *et al.*, 2017) divides the function by α^2 , while the model developed in the mathematical model chapter divides the function by α . This difference allows the α values used by (Budday *et al.*, 2017) to be negative, while still yielding a positive strain energy function. According to (Budday *et al.*, 2017) a negative α value more accurately represents the tension-compression mechanical asymmetry in brain tissue, causing the stresses to be higher in compression, which is the observed behaviour. This is opposed to a positive α , which causes the compression stresses to be lower than tension, an effect which is not observed.

While the same symbol is used for α in both cases, they are fundamentally different since, in the (Budday *et al.*, 2017) equation, α is squared in only one instance, rather than across the equation. Additionally, the (Budday *et al.*, 2017) version of α does not conform to several rules for α , such as (Holzapfel, 2000)

$$2\mu = \sum_{p=1}^N \mu_p \alpha_p$$

With $\mu_p \alpha_p > 0$

Due to its ability to account for tension-compression asymmetry better, according to (Budday *et al.*, 2017), the model used by (Budday *et al.*, 2017) would arguably be more accurate. However, the model developed in the mathematical model chapter is the one widely recognized across literature and furthermore is implemented in commercially available FE modelling suites such as LS-DYNA, meaning that any constants extracted for that model could be directly plugged into simulations. As such, the 2 term Ogden model detailed in the mathematical model chapter was used in the data analysis of these experiments.

7.3 Determining the constants

The 2 term viscoelastic Ogden model was used by (Kleiven, 2007) in a computational model to reconstruct head impacts recorded in American football games for the NFL, and their values were used as a starting point for this work. (Kleiven, 2007) fit curves to data from (Franceschini, 2006) and (Franceschini *et al.*, 2006) in order to obtain values for the Ogden hyperelastic constants (μ_1 , μ_2 , α_1 and α_2). The data published by (Franceschini, 2006; Franceschini *et al.*, 2006) was obtained from cyclic tension-compression experiments at quasi-static rates. Therefore it can be assumed that the hyperelastic Ogden component of the model dominated the behaviour and the viscoelastic component had negligible effect. As our goal with these experiments was to obtain values for the viscoelastic constants, the hyperelastic constants reported here were not further investigated and were used without modification.

Table 8: (Kleiven, 2007) average values for Ogden hyperelastic constants

μ_1 (Pa)	μ_2 (Pa)	α_1	α_2
53.8	-120.4	10.1	-12.9

For the viscoelastic constants, it is necessary to determine a ratio linking them all together in order to extract values from our experimental results. This is because the overall behaviour is a

compound effect from several constants (G_1 to G_6) and can be achieved analytically with multiple different values. It is possible, for example, to achieve a good match in a single experiment by taking G_1 to G_5 down to negligible values and bringing G_6 up to an unrealistically high number. However such a set of constants would only be applicable to that particular experiment and would not give a good match when applied to others. However only one set of these values will be true across multiple strain rates and multiple experiments.

For the viscoelastic constants, it is expected that the relaxation moduli follow an exponential decay curve. This was demonstrated by (Nicolle *et al.*, 2005) where the longer timescale G modulus was directly measured with a rotating rheometer, and shorter timescale G modulus values was reconstructed from higher frequency measurements using their custom shear testing apparatus, as shown below in Figure 82. (Kleiven, 2007) fitted a 6 term Prony series to this data, fixing the β values to a logarithmic scale in order to find G_1 to G_6 . The results are reported below in Figure 82. These values were used as a basis for our curve fitting work and they defined the ratio we expected the G values to have, relative to each other.

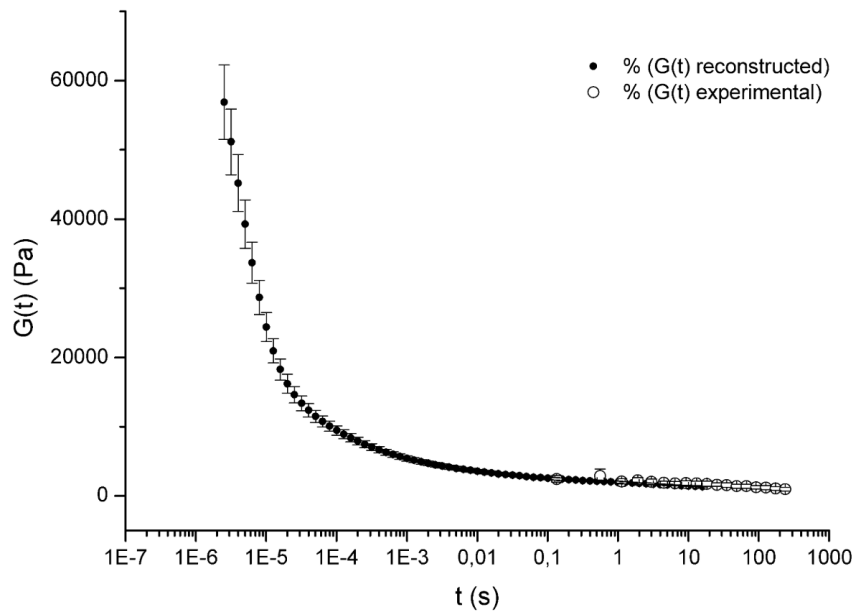


Figure 82: Shear relaxation modulus, taken from (Nicolle *et al.*, 2005)

Table 9: Viscoelastic constant values reported by (Kleiven, 2007), taken from (Nicolle *et al.*, 2005)

t_1 (s)	10^{-6}	β_1 (s $^{-1}$)	10^6	G_1 (Pa)	160000
t_2 (s)	10^{-5}	β_2 (s $^{-1}$)	10^5	G_2 (Pa)	39000
t_3 (s)	10^{-4}	β_3 (s $^{-1}$)	10^4	G_3 (Pa)	3100
t_4 (s)	10^{-3}	β_4 (s $^{-1}$)	10^3	G_4 (Pa)	4000
t_5 (s)	10^{-2}	β_5 (s $^{-1}$)	10^2	G_5 (Pa)	50
t_6 (s)	10^{-1}	β_6 (s $^{-1}$)	10	G_6 (Pa)	1500

(Kleiven, 2007) postulated that the G values found from fitting the Prony series to data from (Nicolle *et al.*, 2005) were smaller than realistic due to the post mortem time and preconditioning that the tissue was subjected to, and estimated that the values should be doubled for average results, giving final (average) G values that we used as a starting point.

Table 10: (Kleiven, 2007) G Values used as a starting point for the curve fitting

G_1 (Pa)	G_2 (Pa)	G_3 (Pa)	G_4 (Pa)	G_5 (Pa)	G_6 (Pa)
320000	78000	6200	8000	100	3000

A typical high rate experiment run by our custom apparatus takes a few milliseconds, or over a timescale of 10^{-3} . As such it was chosen to base the ratio around G_4 , with G_4 being the variable that was changed by the curve fitting algorithm, and the other G values were modified by constants K

$$G_i \rightarrow K_i G_4$$

where

$$K_i = \frac{G_i}{G_4}$$

This ratio was determined from initial G values, which were taken from (Kleiven, 2007)

Table 11: The multipliers linking each G value to G4

K_1	K_2	K_3	K_4	K_5	K_6
40	9.75	0.775	1	0.0125	0.375

7.4 Comparison of experimental results with literature predictions

Although the apparatus had been validated against Armourgel and the experimental results had been checked against literature experimental results for overall magnitude, a more complete comparison was needed.

The viscoelastic Ogden model had been integrated for a 6th order polynomial as detailed in Chapter 6, leaving the 1st Piola-Kirchoff stress solvable as a function of time t , the material constants a , β , μ and g , and the stretch polynomial constants C .

Material constants for the viscoelastic Ogden equation used in this study were taken from (Kleiven, 2007), as previously detailed and reported in Table 8 and Table 9.

A 6th order polynomial was fitted to the recorded stretch curve for each individual experiment and the resulting C values used alongside the constants from (Kleiven, 2007) and the time vector to calculate a predicted analytical stress for the given recorded stretch. This was not expected to be exact since the constants used by (Kleiven, 2007) were drawn from different sources, both of which were limited to much lower strain values, as well as different testing conditions. However the predictions were expected to be of the same order of magnitude as the experimental results, since the constants used were not expected to be radically different from the ones that would suit our data. This preliminary comparison served to test the derived mathematical formula (Figure 83, Figure 84 and Figure 85), as well as act as another validation step for the apparatus.

Experimental vs Kleiven Predictions at High Rate

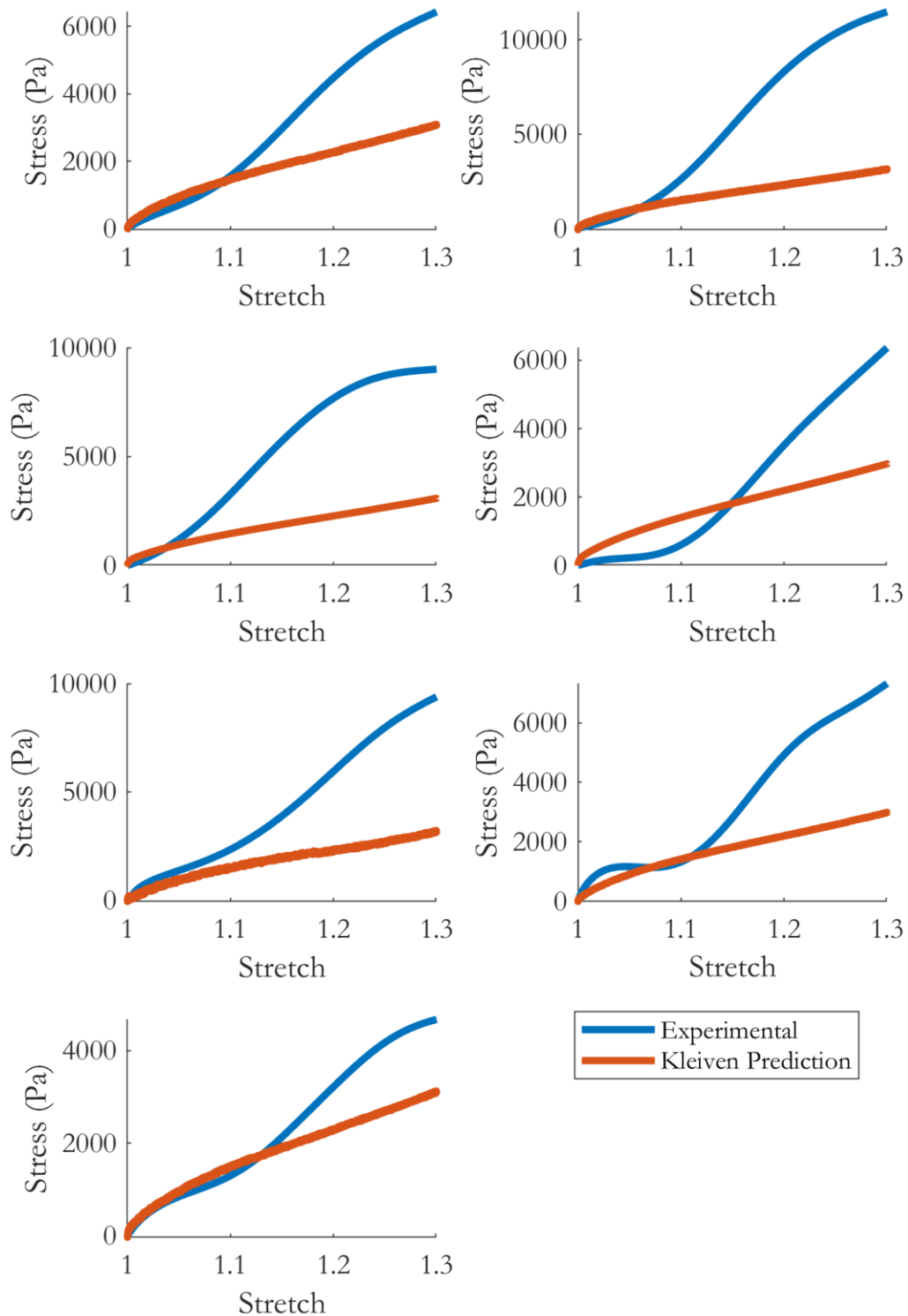


Figure 83: Analytical vs Experimental results for all high rate tests using material constants from (Kleiven, 2007)

Experimental vs Kleiven Predictions at Medium Rate

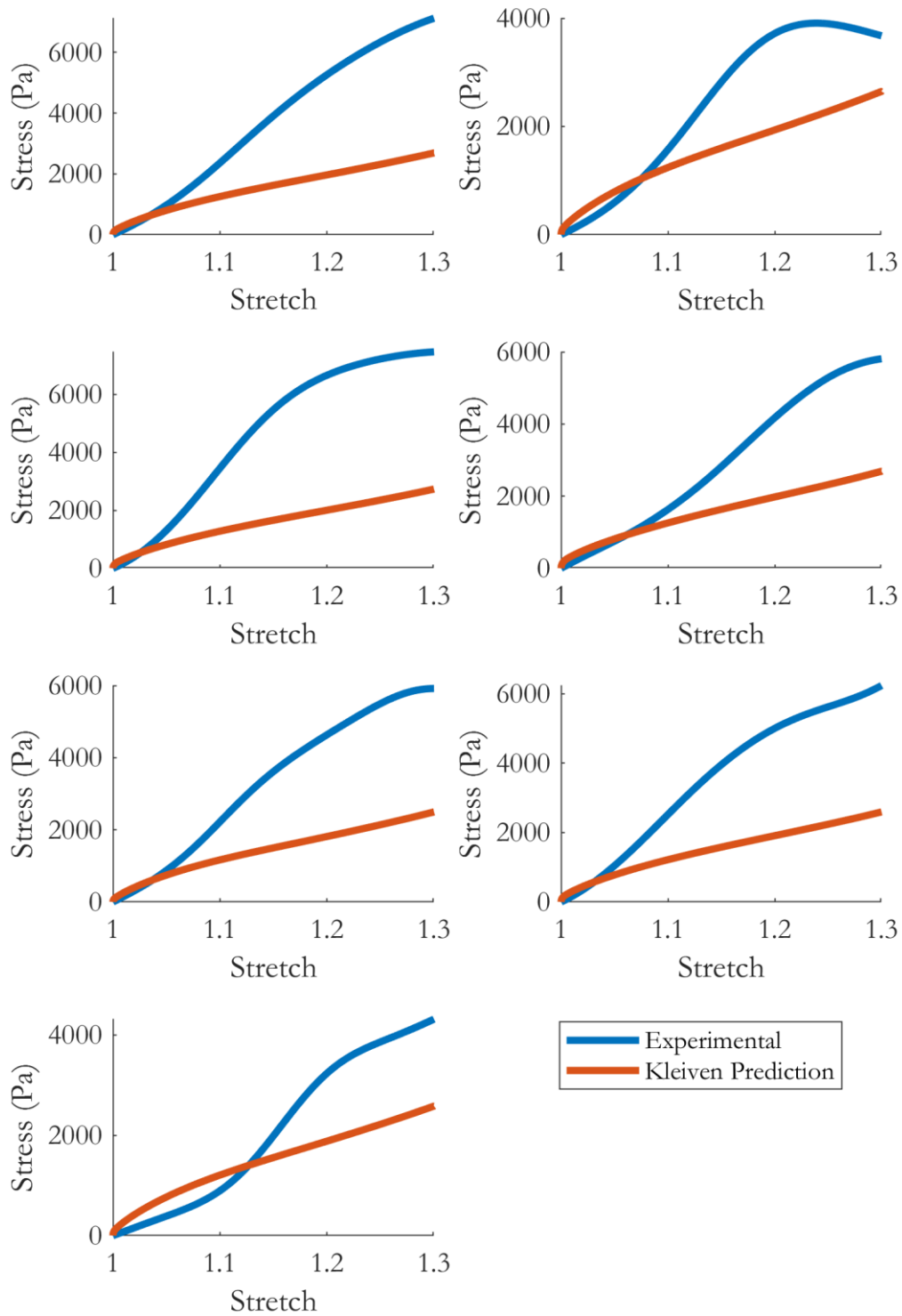


Figure 84: Analytical vs Experimental results for all medium rate tests using material constants from (Kleiven, 2007)

Experimental vs Kleiven Predictions at Low Rate

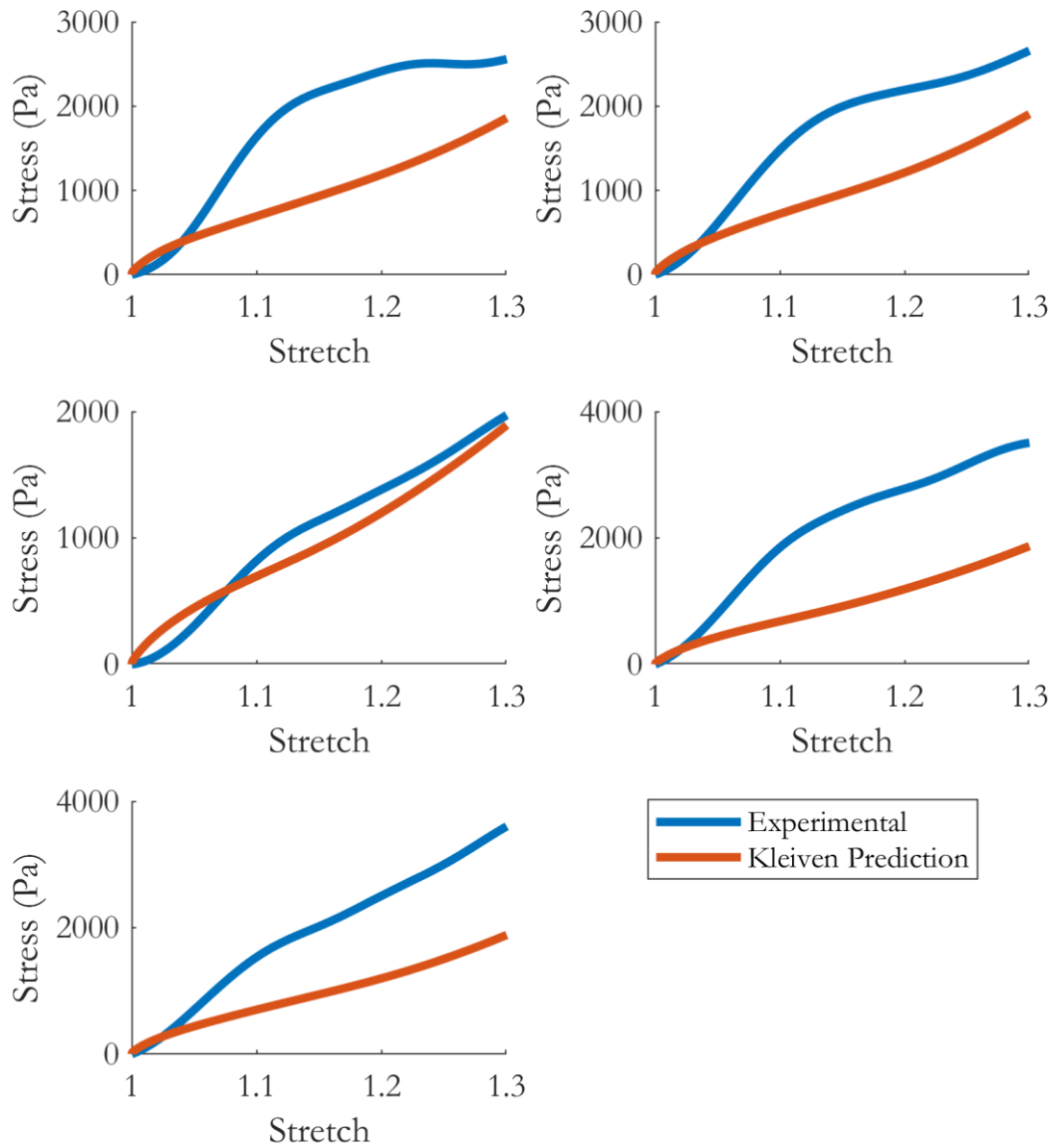


Figure 85: Analytical vs Experimental results for all low rate tests using material constants from (Kleiven, 2007)

It can be seen that the analytical prediction using constants from (Kleiven, 2007) is a reasonable match for the experimental results in terms of orders of magnitude. However it can also be seen that the experimental results are almost universally ‘stiffer’ than the Kleiven predictions, with the highest discrepancies occurring at the high rate tests (Figure 83) and the smallest discrepancies at the low rate (Figure 85). This indicates that the viscoelastic constants may be a bit too low for this experimental data, since they are not playing as large a part as the results indicate they should

and the effect greatly increases with strain rate, indicating that the error is primarily with the viscoelastic component.

7.5 Results

7.5.1 Curve fitting

The experiments were filtered and trimmed as described in the results chapter, then a curve was fitted to them using the analytical solution to the viscoelastic Ogden model described in section 6 and reported in (Appendix 2, 10.2). The curve was fitted using the MATLAB command *lsqnonlin* using the constant G_4 as the changing variable. As previously described, the other G values were based on G_4 with a multiplier, in order to reduce the equation to one unknown variable.

The results of the curve fitting for all three rates, along with the respective Kleiven predictions and the separated Ogden and viscoelastic components in the curves can be seen below in Figure 86, Figure 87 and Figure 88. It can be seen that the analytical prediction with the new G values offers a substantially better fit than the Kleiven predictions in all cases, supporting the use of the G values as the variable for curve fitting. It can also be noted that the viscoelastic components, shown in green in the graphs below, are always substantially higher than the Ogden components (shown in purple) meaning that, according to this model, the brain tissue behaviour is dominated by viscoelasticity even at the lower rates. This has implications for impact and blast modelling, since these almost always involve high strain rates in the brain equal to or higher than the high rate tests in these experiments, underlining the importance of accurate viscoelastic properties for such modelling applications.

It can be seen in the curve fitting results below (Figure 86, Figure 87, Figure 88), particularly in the high rate results (Figure 86) that the analytical results do not always qualitatively conform to the experimental results. It is believed this is due to the imperfect nature of real-world experiments vs the idealised analytical model. One consistent feature of this discrepancy at the high rates is that there appears to be a slight ‘delay’ before the expected loading behaviour is observed, which could be due to a delay in stress transmission through the tissue, although this is speculation. Alternatively the discrepancy could be a limitation of the model and its analytical solution. One potential avenue of future research could be to investigate this model more thoroughly at high rates and to investigate other models to better represent this trend.

Analytical vs Experimental Results At High Rate

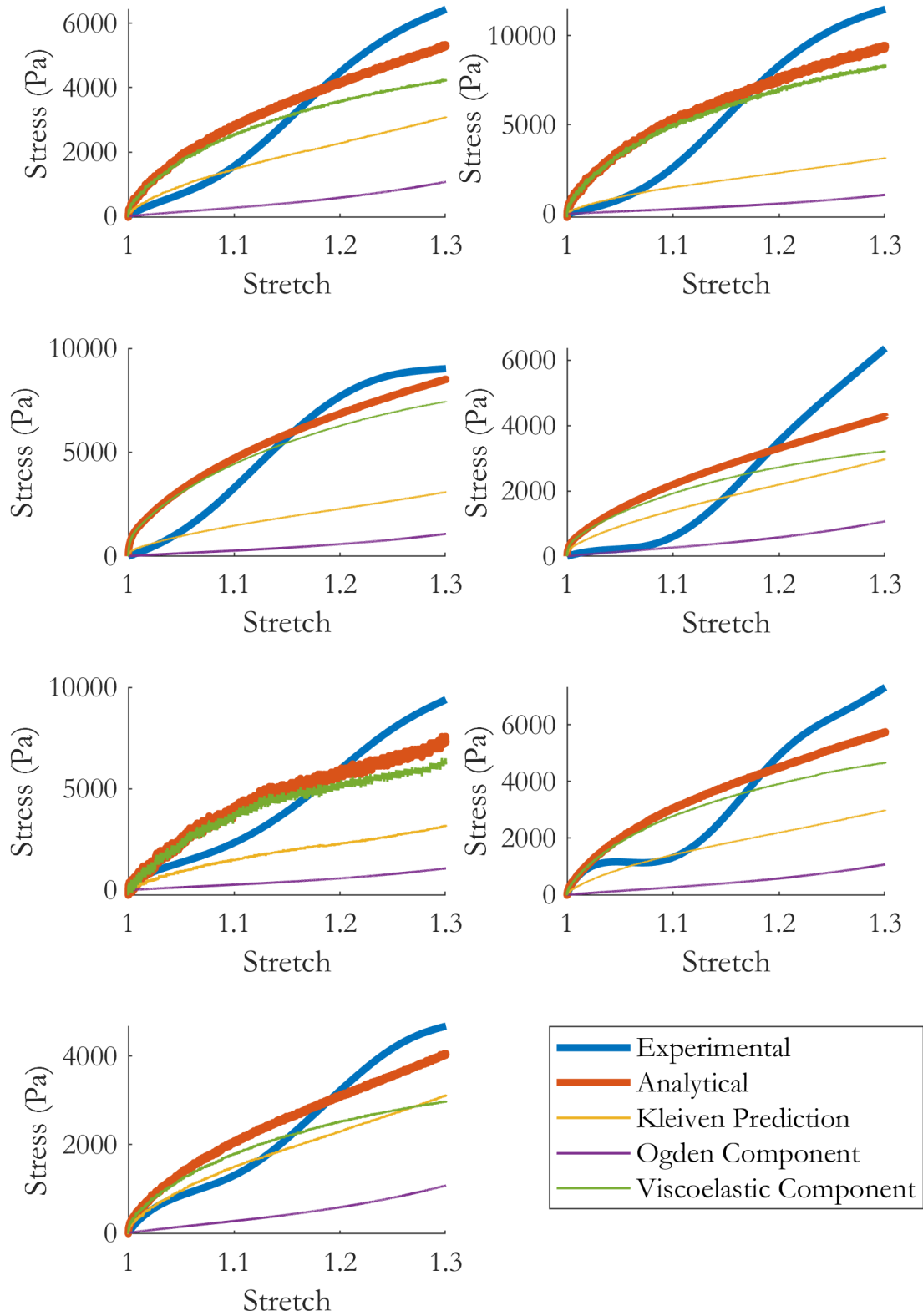


Figure 86: All Curve Fitting Results for High Rate

Analytical vs Experimental Results at Medium Rate

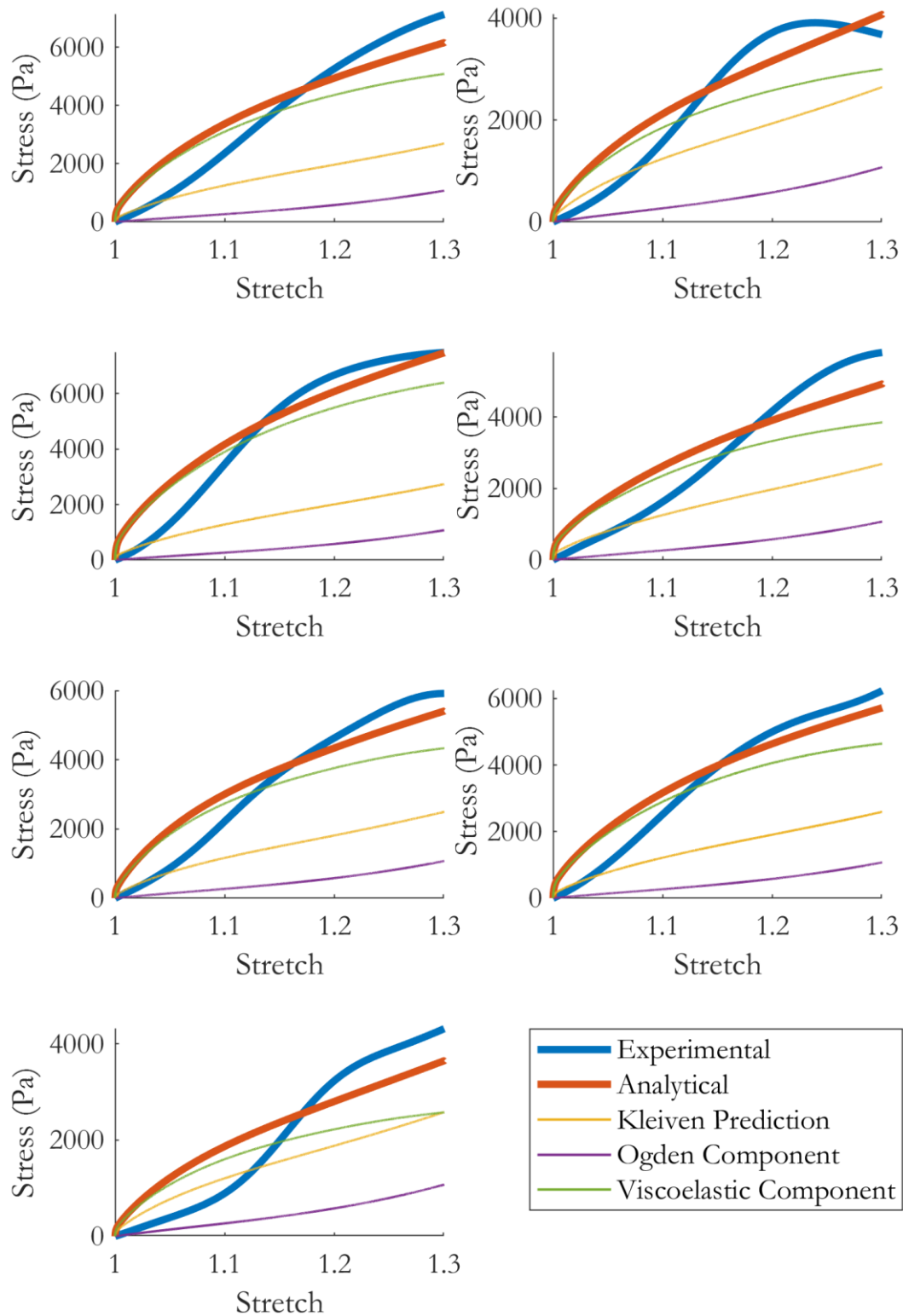


Figure 87: All Curve Fitting Results for Medium Rate

Analytical vs Experimental Results at Low Rate

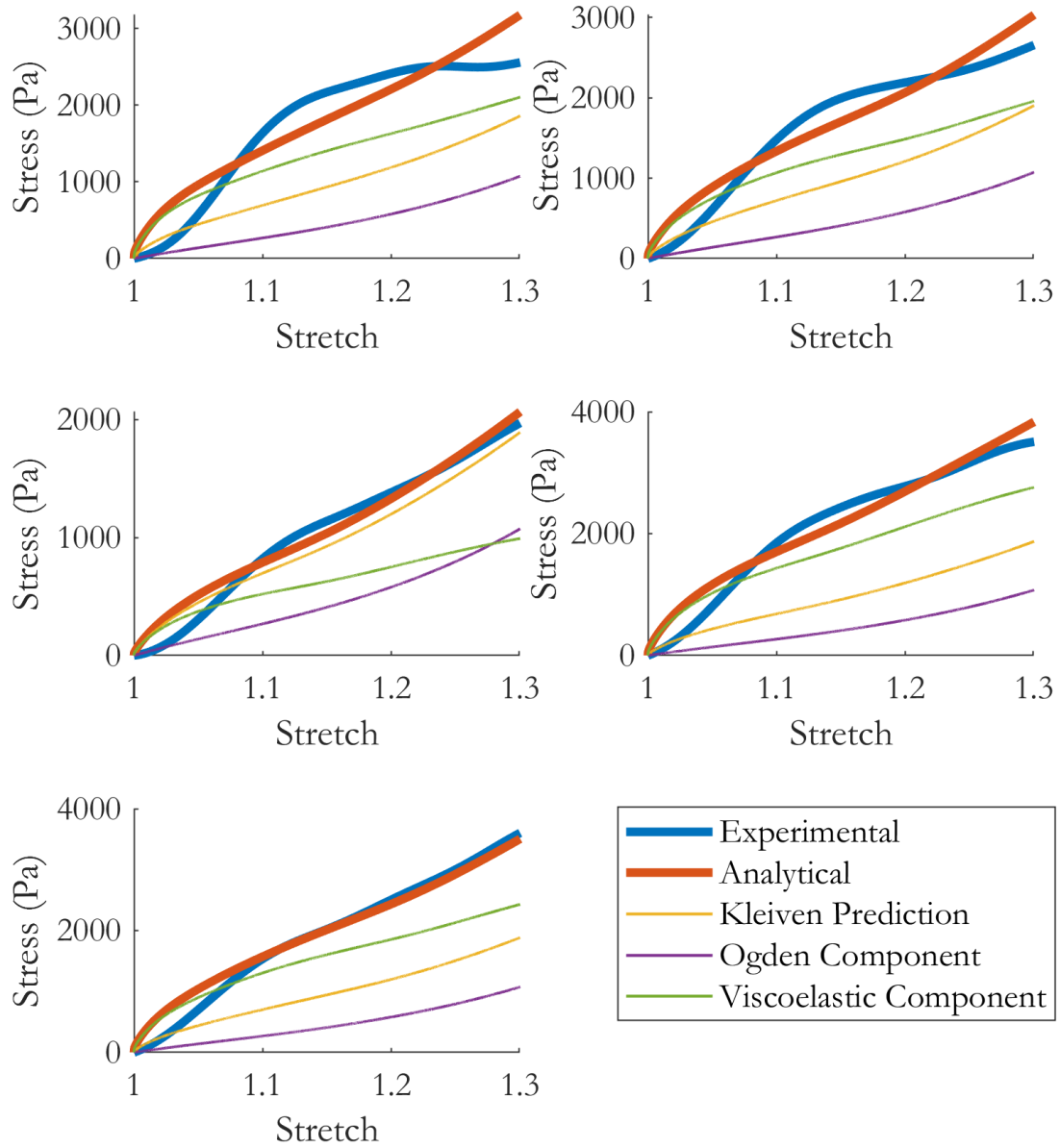


Figure 88: All Curve Fitting Results for Low Rate

7.5.2 G values

The curve fitting algorithm previously described finds the optimal G_4 value that makes the analytical prediction match the experimental results, and those curves can be seen above in Figure 86, Figure 87 and Figure 88. These G_4 values, and the appropriately scaled G_1 , G_2 , G_3 , G_5 , and G_6 values, are the desired output of these experiments. In order to validate the viscoelastic Ogden model for all strain rates with a single set of constants, these extracted G values should be similar for all strain rates measured. Since the strain rates investigated range over a factor of 10, it is judged that this is a sufficient range to infer the validity of these extracted G values for all strain rates, should there be no significant differences or trends over this range

The results for high, medium and low rate are reported below in Table 12, Table 13 and Table 14, respectively. It should be noted that while all G values have been reported for completeness, G_4 is the only variable that was determined by curve fitting, all the others are simply G_4 multiplied by the same fixed ratio, reported previously in Table 11.

Table 12: Curve fitting G values for all high rate tests

Test	G_1 (Pa)	G_2 (Pa)	G_3 (Pa)	G_4 (Pa)	G_5 (Pa)	G_6 (Pa)
1	673036	164053	13040	16826	210	6310
2	1283747	312913	24873	32094	401	12035
3	1182893	288330	22919	29572	370	11090
4	541319	131946	10488	13533	169	5075
5	970973	236675	18813	24274	303	9103
6	776706	189322	15049	19418	243	7282
7	467656	113991	9061	11691	146	4384
Average	842333	205319	16320	21058	263	7897

Table 13: Curve fitting G values for all medium rate tests

Test	G ₁ (Pa)	G ₂ (Pa)	G ₃ (Pa)	G ₄ (Pa)	G ₅ (Pa)	G ₆ (Pa)
1	1006038	245222	19492	25151	314	9432
2	609777	148633	11814	15244	191	5717
3	1232127	300331	23872	30803	385	11551
4	763269	186047	14788	19082	239	7156
5	976368	237990	18917	24409	305	9153
6	978103	238413	18951	24453	306	9170
7	546468	133201	10588	13662	171	5123
Average	873164	212834	16918	21829	273	8186

Table 14: Curve fitting G values for all low rate tests

Test	G ₁ (Pa)	G ₂ (Pa)	G ₃ (Pa)	G ₄ (Pa)	G ₅ (Pa)	G ₆ (Pa)
1	857154	208931	16607	21429	268	8036
2	754103	183812	14611	18853	236	7070
3	388036	94584	7518	9701	121	3638
4	1107416	269933	21456	27685	346	10382
5	959570	233895	18592	23989	300	8996
Average	813256	198231	15757	20331	254	7624

7.6 Analysis

The goal of these experiments is to validate the viscoelastic Ogden model detailed in the mathematical model chapter for use in describing tissue behaviour across all strain rates, and whether this is successful to determine values for the constants used by the model. In order to truly validate the model it should be possible to determine a set of constants that are true for all experiments, as the rate dependent stiffness differences should be accounted for by the viscoelastic component of the model and is the reason for including it. It is believed that this

represents substantial improvement over current leading methods for accounting for viscoelasticity, such as (Rashid, Destrade and Gilchrist, 2014) who used different μ and α values for different strain rates that could be looked up by way of a table. The advantage of this method is its comparative simplicity, with one equation and one set of values to describe tissue behaviour. Additionally using this system strain rates can be modelled mathematically and computationally without having to experimentally determine the constant values for that strain rate prior to modelling, as the constants will not change across strain rates.

As the G values should be the same across all strain rates, ideally there would not be much variation between the determined constants for the different experimental rates. As can be seen in the box plot below (Figure 89) there is no obvious trend where the rate the experiments were carried out at determines the G values, as the three sets of data don't appear to be significantly different. As can be seen the distributions are very similar, with much of their regions overlapping with each other, indicating no strong difference between the rates. It should also be noted that there is no obvious (simple) trend in the results, since the central one has the highest average value (indicated by the red line). This means that there is not a trend observed where G values decrease or increase with rate, as would be expected if they were rate dependent.

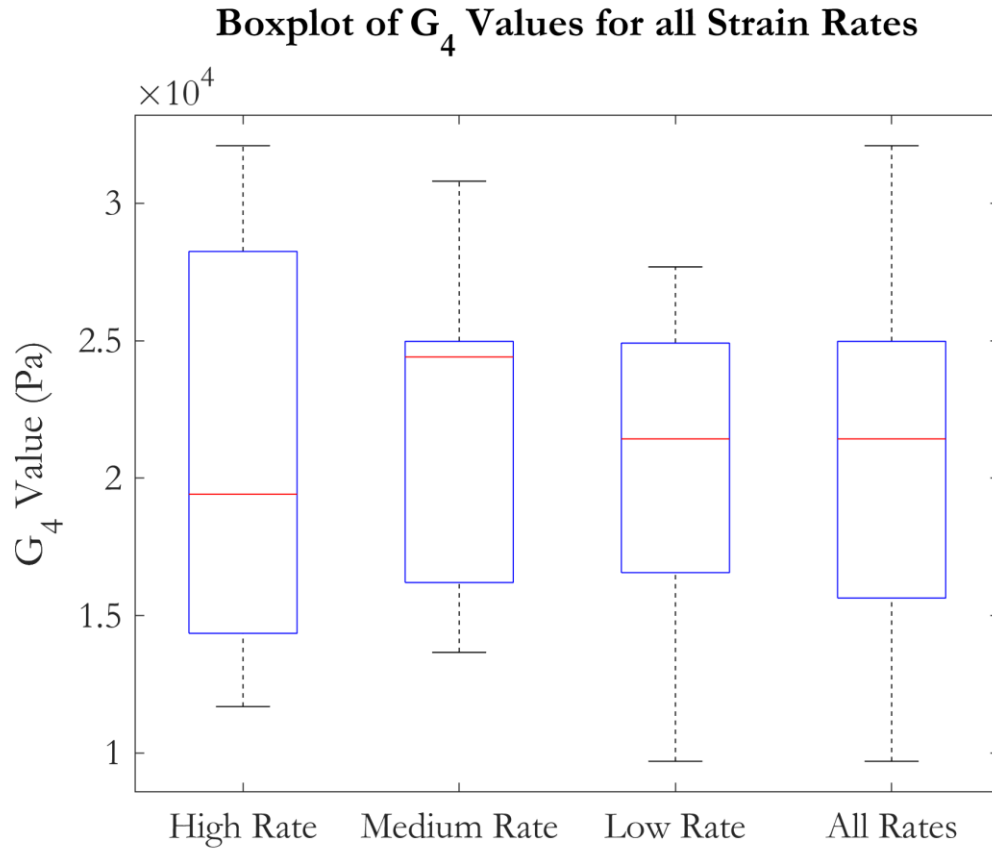


Figure 89: Box plot showing the distribution of each set of experiments

7.6.1 Statistical significance

2 tailed T tests were used to determine if there was a statistical difference between the results for the high medium and low rate, with both sets being equal used as the null hypothesis. A P value of less than 0.05 would indicate a statistical difference, as that threshold is the most widely used standard in scientific literature and is consistent with previous T tests in this work. This would correspond to a 5% chance the observed differences would occur by chance. As can be seen in the statistical results below (Table 15) there is no statistical difference ($P < 0.05$) between any of the 3 rates measured. Indeed, the smallest P value (0.7041) corresponds to a 70% chance that the datasets have no underlying difference, strongly supporting the use of the viscoelastic Ogden model with a single set of G values. Furthermore, it supports combining the results into one large dataset, and a single overall average to be taken to apply for all strain rates, as has been done below in Table 16.

Table 15: P value results for statistical tests between the rate experiments

	High Rate vs Medium Rate	High Rate vs Low Rate	Medium Rate vs Low Rate
P value	0.8410	0.8675	0.7041
t value	-0.2053	0.1714	0.3934
df	11.3049	9.5124	8.1401

Table 16: Average G results for all 3 rates combined

G₁ (Pa)	G₂ (Pa)	G₃ (Pa)	G₄ (Pa)	G₅ (Pa)	G₆ (Pa)
846040	206222	16392	21151	264	7932

7.7 Discussion

Due to the experimental advantages previously stated over other experiments in literature, especially the greater range of strain rates, it is believed that these results represent the most complete viscoelastic characterisation of white matter in tension currently available.

The use of the Ogden model to model the hyperelastic component falls in line with the current prevalent theories in brain tissue modelling and, as shown by Budday et al (Budday *et al.*, 2017), can accurately describe both tension and compression without recalibration, justifying the extrapolation of these results to compressive loading as well.

The addition of a viscoelastic component to the Ogden model is also supported by literature and is supported by many FE modelling packages such as LS-DYNA, where the viscoelastic Ogden model is an inbuilt function. The viscoelastic Ogden model is superior to other methods because it allows a single set of parameters to model behaviour across all strain rates, rather than having to recalibrate between tension and compression as shown by Budday et al (Budday *et al.*, 2017), or requiring the parameter values to be changed depending on the strain rate, which must be looked up from an experimentally determined table, as was the approach by Rashid et al (Rashid, Destrade and Gilchrist, 2014).

As previously stated, it is believed that this represents the most comprehensive characterisation of white matter viscoelasticity in tension. The determined viscoelastic constants are equally applicable to all strain rates tested, as reported in the Analysis section and shown in the boxplot of all strain rates (Figure 89). Considering the experimental strain rates varied over more than a factor of 10 this greatly supports the hypothesis that these viscoelastic constants are applicable across all strain rates, and they have been experimentally validated to a much higher rate than before. Combined with the close match between the experimental stress results and the predicted stress results using the new values, this work supports the use of a viscoelastic 2 term Ogden model, using hyperelastic constants from Kleiven et al (Kleiven, 2007) and the viscoelastic constants determined in this thesis for use in the modelling of head injury biomechanics, particularly in scenarios where high strain rates are expected.

7.8 Dissemination

Manuscript in preparation

8 Conclusions and future work

Over the course of this PhD thesis, a new testing apparatus was developed to test brain tissue mechanically in tension. The apparatus was successfully used to test porcine white matter brain tissue harvested from the central node of the corona radiata perpendicular to the coronal plane. To the author's knowledge, this represents the most complete tensile characterisation of white matter, including significantly higher strain rates than previously achieved in a comparable experiment in literature, as can be seen from Table 2 in the literature review.

8.1 The apparatus

The apparatus featured several novelties and improvements over existing technology available in literature or commercially, namely

- A high motor speed that could be applied to a sample at a relatively constant level, enabling higher strain rate testing than comparable apparatus.
- The apparatus can be used to test in both tension and compression, with the potential for shear testing as well with a simple grip modification. Significantly more versatile than many existing apparatuses that run comparable tests, since these have only been reported to be used in a single mode of loading.
- The apparatus is a desktop size and portable, allowing it to be transported easily into separate labs and other facilities such as an autopsy room. Especially valuable since mechanical testing labs often do not have clearance for tissue testing and those that

do are often limited. The ability to take the apparatus into an autopsy room is expected to allow the post-mortem time between tests to be cut down significantly.

- The apparatus can run multiple tissue tests in quick succession, with each experiment taking a very short amount of time. This allows many tests to be run and the effects of tissue degradation and drying out while in the rig are minimized.

8.2 The experiments

These experiments had several advantages over the majority of the experiments in literature, including

- Significantly higher strain rates (250 s^{-1}) than previously achieved in comparable experiments.
- Tissue from a single region/structure in the brain (the corona radiata), rather than a mix of tissue that contained differing amounts of each tissue type between samples.
- Tissue was tested up to and beyond the maximum strains seen in impact and blast scenarios within the brain, which oscillatory tests (that make up the majority of experiments in literature) rarely go up to.
- Tissue was tested in tension, the most underrepresented mode of loading in literature.

8.3 The determination of viscoelastic constants

A new method for analysing the data and extracting material constants was implemented. The process of fitting a 6th order polynomial to the displacement curve and using that displacement in an analytical equation to solve for the predicted stress is an approach previously unseen in

literature and significantly less computationally intensive than reverse FE modelling, which is currently the most common method for calculating predicted stress from a recorded displacement. With the inverse FE method, a new FE simulation has to be run for every iteration of the optimisation loop, which compared to this analytical method requires substantially more time and power, which in turn can limit studies utilising it.

8.4 Future work

This thesis endeavours to answer some important questions with relation to brain biomechanics, and it is believed that it does so. However, as is often the case in such scenarios it also raises more questions.

The apparatus developed during the course of this work has application beyond the scope of this thesis, as it represents an easy and portable way to test extremely soft materials like brain tissue with all the advantages over current existing apparatus that were previously stated.

The scope of this thesis only extends to testing white matter in tension. While it should be noted that the work by Budday et al (Budday *et al.*, 2017) indicates that this would also be valid in compression due to the use of an Ogden model, this has not been verified experimentally for these values or for the viscoelastic component. Therefore a similar characterisation of white matter in compression using the same apparatus at similar strain rates would be the next logical step. This would further reinforce the use of a viscoelastic Ogden model with these values to model head injury biomechanics, as a combination of compressive, tensile and shear loading is expected in almost all scenarios.

This thesis focussed on characterising white matter, specifically the corona radiata although, in lieu of more complete data, this mechanical model could be extended to the more general ‘white matter’ in the brain. This was chosen because white matter was expected to exhibit more viscoelasticity than grey matter, as indicated by (Jin *et al.*, 2013), which was the most poorly understood aspect of the brains mechanical behaviour. However this work could be extended to different regions of the brain, which consists of many regions and tissues, each of which is expected to have different mechanical properties. Extending this experimental protocol to grey matter as well as white, or even further specialising into other tissue types and regions in order to

build up a more complete picture of the brain as a whole would also be a logical extension of this work. Building up from this, the work could be further extended to characterise human tissue rather than the porcine tissue presented in this thesis. Porcine tissue is commonly used in literature due to its increased availability and ease of access (see Table 2), as well as its broadly comparable structure and mechanical properties to human tissue. However, several studies (Prange and Margulies, 2002; Jin *et al.*, 2013) have shown human tissue to be stiffer on average than porcine tissue, and so a subsequent characterisation of human tissue in the same manner as presented for porcine tissue would increase the accuracy of the constitutive model presented in this thesis.

Mechanical anisotropy is also a hotly debated topic in brain biomechanics. Due to the structure of the brain, particularly the white matter where bundles of axons exist almost in parallel to each other in many regions, it seems logical that the mechanical properties should differ as the angle of loading varies from parallel to perpendicular to the general axon direction. Mechanical anisotropy was reported by Hrapko *et al* in 2008 (Hrapko *et al.*, 2008) but investigated more thoroughly and not seen in the recent work by Budday *et al* (Budday *et al.*, 2017). It should be noted however that Budday *et al* only experimented on brain tissue at quasi-static strain rates. The existence of mechanical anisotropy at high strain rates such as those applicable to blast or impact scenarios has not been adequately investigated in the opinion of the author, and it is another avenue of future research the apparatus developed would be well suited to.

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10 Appendix

10.1 Appendix 1, Early designs for the apparatus

10.1.1 The dropped weight design

The dropped weight design utilised a set of L shaped levers to increase the strain rate applied to the sample, in the manner shown below (Figure 90)

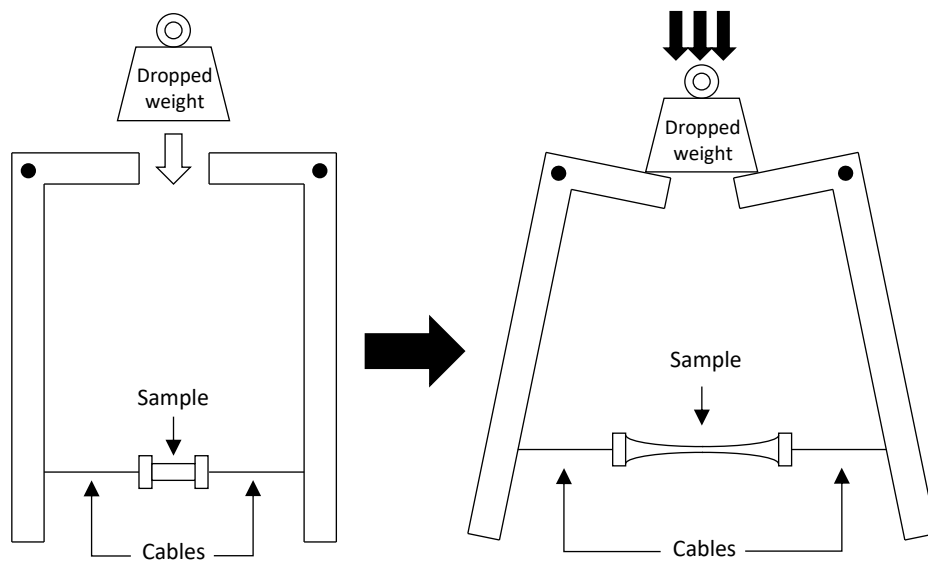


Figure 90: An early design for the apparatus utilising a dropped weight to apply load to a sample

The aim was to run a test at constant velocity, or as close to as possible. Practically this meant that the load velocity needed to be firstly built up before applying load to the sample, and secondly that the power applied by the apparatus should be sufficiently large so the additional resistance offered by the sample when the load was applied did not slow down the strain rate to any meaningful degree.

In the case of the dropped weight design this was relatively simple. A weight allowed to accelerate from a height before hitting the lever system would achieve sufficient speed before applying load to the sample. The weight would need to be of sufficient mass would need to be used in order to reduce any resistance from either the response of the sample or the inertia of the apparatus to a negligible degree, however considering the expected response of the tissue was approximately 2N (Franceschini, 2006), this would be easily achievable given a well-designed and

lubricated apparatus. Tensile loading could be applied with a mechanical coupling to convert the impulse from a push to a pull.

This method was advantageous in that high strain rates could be achieved with a relatively low impactor velocity by using levers in the mechanical coupling to multiply the velocity, as shown in (Figure 90). However, as mentioned in chapter 0, there was concern that such an impact would induce a large number of vibrations into the system, which could potentially mask the small signals we were hoping to acquire. Additionally, the dropped weight system is inherently larger and heavier than the other designs, since it needs space and guide rails for the weight to drop and has the added mass of the weight to consider. These drawbacks eventually led to this design being discarded in favour of the motor design, however it has promise, particularly for extremely high rate testing, which it is well suited for due to the L shaped lever system which greatly increases the maximum strain rate achievable.

10.1.2 The gas impactor design

The gas impactor design utilised a gas powered impactor to apply an impulse to a sample (compression), or to a plate attached to a sample in the manner shown in (Figure 91) below for tensile tests. The advantage of a gas-powered impactor was that it can explosively generate power at a much higher rate than any of the other designs, meaning it could accelerate to the required velocity in a very small space.

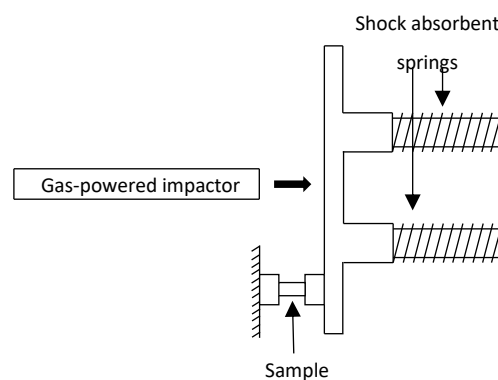


Figure 91: An early design for the apparatus utilising a gas-powered impactor to apply load to a sample

Unfortunately, despite the small space requirements for the acceleration, the need for a gas cylinder and the associated apparatus for the impactor meant that any apparatus using this design was still likely to be larger and heavier than a motor driven system. Additionally, there was

concern that such a heavy impact could induce excessive vibrations in the system, in the same manner as the dropped weight design. These perceived drawbacks offset the power advantage this design had and eventually resulted in it being dropped in this early stage in favour of a motor design. Like the dropped weight design however, the gas impactor design was simply considered sub-optimal for our purposes as opposed to fundamentally flawed or unworkable.

10.1.3 Summery

While both the above methods appeared viable and would allow a comparatively high strain rate to be applied to the sample, ultimately a motor was selected as the impulse source for the device. There were several reasons for this

- A motor can (depending on the motor) be run both forwards and backwards easily unlike a dropped weight or an impactor. This allows the apparatus to apply both tensile and compressive loads to a sample without needing an additional coupling mechanism to switch the mode of loading.
- A motor-based apparatus can be reset easily, without having to lift a particularly heavy weight or re-pressurise a cylinder. This would allow for tests to be run at a faster rate which would help with preventing tissue degradation.
- It was felt that any apparatus based around a large impact would produce a high number of vibrations. Considering that our samples (and therefore our measured signals) were expected to be very small there was concern that the noise generated by other designs might mask the results
- A motor driven apparatus can be miniaturised to a much greater degree than the above two designs, allowing a much more portable device.

10.2 Appendix 2, General solution to the mathematical model for a 6th order polynomial

Below is the general solution to the mathematical model presented in chapter 6, solved using Wolfram Mathematica. The solution is presented in plain text (10.2.1), traditional form (10.2.2) and finally MATLAB code (10.2.3) for convenience. The solution is presented since finding its solution was computationally intensive and it is hoped that the solution here will aid any researchers hoping to utilise this method.

10.2.1 The general solution to the mathematical model for a 6th order polynomial, presented in plain text

$$\begin{aligned}
 P = & 1/(t (c6+t (c5+t (c4+t (c3+t (c2+c1 t))))+1) (-u1 (t (c6+t (c5+t (c4+t (c3+t (c2+c1 t))))+1)^{-a1/2}+u1 (t (c6+t (c5+t (c4+t (c3+t (c2+c1 t))))+1)^{a1}+((720 c1-b1 (120 c2+b1 (c6 b1^3-2 c5 b1^2+6 c4 b1-24 c3))) E^{(-b1 t) g1}/b1^6+((720 c1-b2 (120 c2+b2 (c6 b2^3-2 c5 b2^2+6 c4 b2-24 c3))) E^{(-b2 t) g2}/b2^6+((720 c1-b3 (120 c2+b3 (c6 b3^3-2 c5 b3^2+6 c4 b3-24 c3))) E^{(-b3 t) g3}/b3^6+((720 c1-b4 (120 c2+b4 (c6 b4^3-2 c5 b4^2+6 c4 b4-24 c3))) E^{(-b4 t) g4}/b4^6+((720 c1-b5 (120 c2+b5 (c6 b5^3-2 c5 b5^2+6 c4 b5-24 c3))) E^{(-b5 t) g5}/b5^6+((720 c1-b6 (120 c2+b6 (c6 b6^3-2 c5 b6^2+6 c4 b6-24 c3))) E^{(-b6 t) g6}/b6^6+1/b1^6 g1 (6 c1 (b1 t (b1 t (b1 t (b1 t (b1 t-5)+20)-60)+120)-120)+b1 (5 c2 (b1 t (b1 t (b1 t (b1 t-4)+12)-24)+24)+b1 (4 c3 (b1 t (b1 t (b1 t-3)+6)-6)+b1 (b1 (2 b1 t c5-2 c5+b1 c6)+3 c4 (b1 t (b1 t-2)+2)))))+1/b2^6 g2 (6 c1 (b2 t (b2 t (b2 t (b2 t (b2 t-5)+20)-60)+120)-120)+b2 (5 c2 (b2 t (b2 t (b2 t (b2 t-4)+12)-24)+24)+b2 (4 c3 (b2 t (b2 t (b2 t-3)+6)-6)+b2 (b2 (2 b2 t c5-2 c5+b2 c6)+3 c4 (b2 t (b2 t-2)+2)))))+1/b3^6 g3 (6 c1 (b3 t (b3 t (b3 t (b3 t (b3 t-5)+20)-60)+120)-120)+b3 (5 c2 (b3 t (b3 t (b3 t (b3 t-4)+12)-24)+24)+b3 (4 c3 (b3 t (b3 t (b3 t-3)+6)-6)+b3 (b3 (2 b3 t c5-2 c5+b3 c6)+3 c4 (b3 t (b3 t-2)+2)))))+1/b4^6 g4 (6 c1 (b4 t (b4 t (b4 t (b4 t (b4 t-5)+20)-60)+120)-120)+b4 (5 c2 (b4 t (b4 t (b4 t (b4 t-4)+12)-24)+24)+b4 (4 c3 (b4 t (b4 t (b4 t-3)+6)-6)+b4 (b4 (2 b4 t c5-2 c5+b4 c6)+3 c4 (b4 t (b4 t-2)+2)))))+1/b5^6 g5 (6 c1 (b5 t (b5 t (b5 t (b5 t (b5 t-5)+20)-60)+120)-120)+b5 (5 c2 (b5 t (b5 t (b5 t (b5 t-4)+12)-24)+24)+b5 (4 c3 (b5 t (b5 t (b5 t-3)+6)-6)+b5 (b5 (2 b5 t c5-2 c5+b5 c6)+3 c4 (b5 t (b5 t-2)+2)))))+1/b6^6 g6 (6 c1 (b6 t (b6 t (b6 t (b6 t (b6 t-5)+20)-60)+120)-120)+b6 (5 c2 (b6 t (b6 t (b6 t (b6 t-4)+12)-24)+24)+b6 (4 c3 (b6 t (b6 t (b6 t-3)+6)-6)+b6 (b6 (2 b6 t c5-2 c5+b6 c6)+3 c4 (b6 t (b6 t-2)+2))))))
 \end{aligned}$$

10.2.2 The general solution to the mathematical model for a 6th order polynomial, presented in traditional format

$$\begin{aligned}
& \frac{1}{t \left(c_6 + t \left(c_5 + t \left(c_4 + t \left(c_3 + t \left(c_2 + c_1 t \right) \right) \right) \right) \right) + 1} \left(-u_1 \left(t \left(c_6 + t \left(c_5 + t \left(c_4 + t \left(c_3 + t \left(c_2 + c_1 t \right) \right) \right) \right) \right) + 1 \right)^{-\frac{a_1}{2}} + \right. \\
& u_1 \left(t \left(c_6 + t \left(c_5 + t \left(c_4 + t \left(c_3 + t \left(c_2 + c_1 t \right) \right) \right) \right) \right) + 1 \right)^{a_1} + \\
& \frac{\left(720 c_1 - b_1 \left(120 c_2 + b_1 \left(c_6 b_1^3 - 2 c_5 b_1^2 + 6 c_4 b_1 - 24 c_3 \right) \right) \right) E^{-b_1 t} g_1}{b_1^6} + \\
& \frac{\left(720 c_1 - b_2 \left(120 c_2 + b_2 \left(c_6 b_2^3 - 2 c_5 b_2^2 + 6 c_4 b_2 - 24 c_3 \right) \right) \right) E^{-b_2 t} g_2}{b_2^6} + \\
& \frac{\left(720 c_1 - b_3 \left(120 c_2 + b_3 \left(c_6 b_3^3 - 2 c_5 b_3^2 + 6 c_4 b_3 - 24 c_3 \right) \right) \right) E^{-b_3 t} g_3}{b_3^6} + \\
& \frac{\left(720 c_1 - b_4 \left(120 c_2 + b_4 \left(c_6 b_4^3 - 2 c_5 b_4^2 + 6 c_4 b_4 - 24 c_3 \right) \right) \right) E^{-b_4 t} g_4}{b_4^6} + \\
& \frac{\left(720 c_1 - b_5 \left(120 c_2 + b_5 \left(c_6 b_5^3 - 2 c_5 b_5^2 + 6 c_4 b_5 - 24 c_3 \right) \right) \right) E^{-b_5 t} g_5}{b_5^6} + \\
& \frac{\left(720 c_1 - b_6 \left(120 c_2 + b_6 \left(c_6 b_6^3 - 2 c_5 b_6^2 + 6 c_4 b_6 - 24 c_3 \right) \right) \right) E^{-b_6 t} g_6}{b_6^6} + \frac{1}{b_1^6 g_1} \left(6 c_1 (b_1 t (b_1 t (b_1 t (b_1 t (b_1 t - 5) + \right. \\
& 20) - 60) + 120) - 120) + b_1 \left(5 c_2 (b_1 t (b_1 t (b_1 t (b_1 t - 4) + 12) - 24) + 24) + \right. \\
& b_1 \left(4 c_3 (b_1 t (b_1 t (b_1 t - 3) + 6) - 6) + b_1 (b_1 (2 b_1 t c_5 - 2 c_5 + b_1 c_6) + 3 c_4 (b_1 t (b_1 t - 2) + \right. \\
& 2)) \right) \left. \right) + \frac{1}{b_2^6 g_2} \left(6 c_1 (b_2 t (b_2 t (b_2 t (b_2 t (b_2 t - 5) + 20) - 60) + 120) - 120) + \right. \\
& b_2 \left(5 c_2 (b_2 t (b_2 t (b_2 t (b_2 t - 4) + 12) - 24) + 24) + b_2 \left(4 c_3 (b_2 t (b_2 t (b_2 t - 3) + 6) - 6) + \right. \right. \\
& b_2 (b_2 (2 b_2 t c_5 - 2 c_5 + b_2 c_6) + 3 c_4 (b_2 t (b_2 t - 2) + 2)) \left. \right) \left. \right) + \\
& \frac{1}{b_3^6 g_3} \left(6 c_1 (b_3 t (b_3 t (b_3 t (b_3 t (b_3 t - 5) + 20) - 60) + 120) - 120) + \right. \\
& b_3 \left(5 c_2 (b_3 t (b_3 t (b_3 t (b_3 t - 4) + 12) - 24) + 24) + b_3 \left(4 c_3 (b_3 t (b_3 t (b_3 t - 3) + 6) - 6) + \right. \right. \\
& b_3 (b_3 (2 b_3 t c_5 - 2 c_5 + b_3 c_6) + 3 c_4 (b_3 t (b_3 t - 2) + 2)) \left. \right) \left. \right) + \\
& \frac{1}{b_4^6 g_4} \left(6 c_1 (b_4 t (b_4 t (b_4 t (b_4 t (b_4 t - 5) + 20) - 60) + 120) - 120) + \right. \\
& b_4 \left(5 c_2 (b_4 t (b_4 t (b_4 t (b_4 t - 4) + 12) - 24) + 24) + b_4 \left(4 c_3 (b_4 t (b_4 t (b_4 t - 3) + 6) - 6) + \right. \right. \\
& b_4 (b_4 (2 b_4 t c_5 - 2 c_5 + b_4 c_6) + 3 c_4 (b_4 t (b_4 t - 2) + 2)) \left. \right) \left. \right) +
\end{aligned}$$

$$\begin{aligned}
& \frac{1}{b_5^6 g_5} \left(6 c_1 (b_5 t (b_5 t (b_5 t (b_5 t (b_5 t - 5) + 20) - 60) + 120) - 120) + \right. \\
& b_5 \left(5 c_2 (b_5 t (b_5 t (b_5 t (b_5 t - 4) + 12) - 24) + 24) + b_5 \left(4 c_3 (b_5 t (b_5 t (b_5 t - 3) + 6) - 6) + \right. \right. \\
& \left. \left. b_5 (b_5 (2 b_5 t c_5 - 2 c_5 + b_5 c_6) + 3 c_4 (b_5 t (b_5 t - 2) + 2)) \right) \right) \Bigg) + \\
& \frac{1}{b_6^6 g_6} \left(6 c_1 (b_6 t (b_6 t (b_6 t (b_6 t (b_6 t - 5) + 20) - 60) + 120) - 120) + \right. \\
& b_6 \left(5 c_2 (b_6 t (b_6 t (b_6 t (b_6 t - 4) + 12) - 24) + 24) + b_6 \left(4 c_3 (b_6 t (b_6 t (b_6 t - 3) + 6) - 6) + \right. \right. \\
& \left. \left. b_6 (b_6 (2 b_6 t c_5 - 2 c_5 + b_6 c_6) + 3 c_4 (b_6 t (b_6 t - 2) + 2)) \right) \right) \Bigg)
\end{aligned}$$

10.2.3 The general solution to the mathematical model for a 6th order polynomial, presented in MATLAB code

```
P=(1+t.*(c6+t.*(c5+t.*(c4+t.*(c3+t.*(c2+c1.*t)))))).^(-1).*(b1.^(-6) ...
.*(720.*c1+(-1).*b1.*(120.*c2+b1.*((-24).*c3+6.*b1.*c4+(-2).* ...
b1.^2.*c5+b1.^3.*c6))).*exp(1).^((-1).*b1.*t).*g1+b2.^(-6).*(720.* ...
c1+(-1).*b2.*(120.*c2+b2.*((-24).*c3+6.*b2.*c4+(-2).*b2.^2.*c5+ ...
b2.^3.*c6))).*exp(1).^((-1).*b2.*t).*g2+b3.^(-6).*(720.*c1+(-1).* ...
b3.*(120.*c2+b3.*((-24).*c3+6.*b3.*c4+(-2).*b3.^2.*c5+b3.^3.*c6))) ...
.*exp(1).^((-1).*b3.*t).*g3+b4.^(-6).*(720.*c1+(-1).*b4.*(120.*c2+ ...
b4.*((-24).*c3+6.*b4.*c4+(-2).*b4.^2.*c5+b4.^3.*c6))).*exp(1).^((-1). ...
.*b4.*t).*g4+b5.^(-6).*(720.*c1+(-1).*b5.*(120.*c2+b5.*((-24).* ...
c3+6.*b5.*c4+(-2).*b5.^2.*c5+b5.^3.*c6))).*exp(1).^((-1).*b5.*t).* ...
g5+b6.^(-6).*(720.*c1+(-1).*b6.*(120.*c2+b6.*((-24).*c3+6.*b6.*c4+ ...
(-2).*b6.^2.*c5+b6.^3.*c6))).*exp(1).^((-1).*b6.*t).*g6+b1.^(-6).* ...
g1.*(6.*c1.*((-120)+b1.*t.*(120+b1.*t.*((-60)+b1.*t.*(20+b1.*t.*(( ...
-5)+b1.*t)))))+b1.*(5.*c2.*(24+b1.*t.*((-24)+b1.*t.*(12+b1.*t.*(( ...
-4)+b1.*t)))))+b1.*(4.*c3.*((-6)+b1.*t.*(6+b1.*t.*((-3)+b1.*t)))+ ...
b1.*(b1.*((-2).*c5+b1.*c6+2.*b1.*c5.*t)+3.*c4.*(2+b1.*t.*((-2)+ ...
b1.*t)))))+b2.^(-6).*g2.*(6.*c1.*((-120)+b2.*t.*(120+b2.*t.*(( ...
-60)+b2.*t.*(20+b2.*t.*((-5)+b2.*t)))))+b2.*(5.*c2.*(24+b2.*t.*(( ...
-24)+b2.*t.*(12+b2.*t.*((-4)+b2.*t)))))+b2.*(4.*c3.*((-6)+b2.*t.*( ...
6+b2.*t.*((-3)+b2.*t)))+b2.*(b2.*((-2).*c5+b2.*c6+2.*b2.*c5.*t)+ ...
3.*c4.*(2+b2.*t.*((-2)+b2.*t)))))+b3.^(-6).*g3.*(6.*c1.*((-120)+ ...
b3.*t.*(120+b3.*t.*((-60)+b3.*t.*(20+b3.*t.*((-5)+b3.*t)))))+b3.*( ...
5.*c2.*(24+b3.*t.*((-24)+b3.*t.*(12+b3.*t.*((-4)+b3.*t)))))+b3.*( ...
4.*c3.*((-6)+b3.*t.*(6+b3.*t.*((-3)+b3.*t)))+b3.*(b3.*((-2).*c5+ ...
b3.*c6+2.*b3.*c5.*t)+3.*c4.*(2+b3.*t.*((-2)+b3.*t)))))+b4.^(-6).* ...
g4.*(6.*c1.*((-120)+b4.*t.*(120+b4.*t.*((-60)+b4.*t.*(20+b4.*t.*(( ...
-5)+b4.*t)))))+b4.*(5.*c2.*(24+b4.*t.*((-24)+b4.*t.*(12+b4.*t.*(( ...
-4)+b4.*t)))))+b4.*(4.*c3.*((-6)+b4.*t.*(6+b4.*t.*((-3)+b4.*t)))+ ...
b4.*(b4.*((-2).*c5+b4.*c6+2.*b4.*c5.*t)+3.*c4.*(2+b4.*t.*((-2)+ ...
b4.*t)))))+b5.^(-6).*g5.*(6.*c1.*((-120)+b5.*t.*(120+b5.*t.*(( ...
-60)+b5.*t.*(20+b5.*t.*((-5)+b5.*t)))))+b5.*(5.*c2.*(24+b5.*t.*(( ...
-24)+b5.*t.*(12+b5.*t.*((-4)+b5.*t)))))+b5.*(4.*c3.*((-6)+b5.*t.*( ...
6+b5.*t.*((-3)+b5.*t)))+b5.*(b5.*((-2).*c5+b5.*c6+2.*b5.*c5.*t)+ ...
3.*c4.*(2+b5.*t.*((-2)+b5.*t)))))+b6.^(-6).*g6.*(6.*c1.*((-120)+ ...
b6.*t.*(120+b6.*t.*((-60)+b6.*t.*(20+b6.*t.*((-5)+b6.*t)))))+b6.*( ...
5.*c2.*(24+b6.*t.*((-24)+b6.*t.*(12+b6.*t.*((-4)+b6.*t)))))+b6.*( ...
4.*c3.*((-6)+b6.*t.*(6+b6.*t.*((-3)+b6.*t)))+b6.*(b6.*((-2).*c5+ ...
```

```

b6.*c6+2.*b6.*c5.*t)+3.*c4.*(2+b6.*t.*((-2)+b6.*t))))))+(-1).*(1+ ...
t.*(c6+t.*(c5+t.*(c4+t.*(c3+t.*(c2+c1.*t)))))).^((-1/2).*a1).*u1+( ...
1+t.*(c6+t.*(c5+t.*(c4+t.*(c3+t.*(c2+c1.*t)))))).^a1.*u1);

```