Using Statistics, Computational Modelling and Artificial Intelligence Methods to Study and Strengthen the Link between Kinematic Impacts and mTBIs

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Abstract

Mild traumatic brain injuries (mTBIs) are frequently occurring, yet poorly understood, injuries in sports (e.g., ice hockey) and other physical recreation activities where head impacts occur. Helmets are essential pieces of equipment used to protect participants’ heads from mTBIs. Evaluating the performance of helmets to prevent mTBIs using simulations on anatomically accurate computational head finite element models is critically important for advancing the development of safer helmets. Advancing the level of detail in, and access to, such models, and their continued validation through state-of-the-art brain imaging methods and traditional head injury assessment procedures, is also essential to improve safety. The significant research contributions in this thesis involve evaluating the decrease in blunt impact-induced brain axon fiber tract strains that various helmets provide by studying outputs of existing finite element brain models and implementing open-source artificial intelligence technology to create a novel pipeline for predicting such strains.

Keywords

Artificial Intelligence; Axon Fiber Tract; Biomechanics; Concussion; Diffuse Axonal Injury; Finite Element Brain Model; Gradient Boosting Machines; Helmets; Injury Metrics; Mild Traumatic Brain Injuries; Sports Injuries
Instances of concussions in sports such as ice hockey are often underreported. The mechanisms of how concussions occur are also not fully understood. Concussions are currently thought to be caused by direct or indirect impacts to the head or upper body that cause damage to the tissues that make up the brain. Using laboratory experiments and simulating impacts with detailed computer models to evaluate the effect that an impact has on the brain are important steps in learning how concussions are caused from different types of impacts and how they can be treated most effectively. Improving the quality and level of detail of such models through methods such as brain imaging and concussion metric baseline testing is of high importance for the field of brain injury research. The best way to prevent concussions in sports and other physical recreation activities where head and upper body impacts may occur is by wearing a helmet. Developing helmets that protect not just against focal injuries such as fractures or gashes, but also against tissue injuries such as concussions, is imperative to increase the safety of activities where head or upper body impacts may occur. In this research, laboratory tests were paired with computer model simulations to evaluate the relationship between impact type and severity and concussion metrics. These computer model simulations were also used to evaluate the ability of different helmets to protect against concussions. Lastly, with the goal of increasing the speed of solving individual head impact computer model simulations, artificial intelligence was implemented to use the results from existing simulations to be able to predict the output of new head impact cases. This artificial intelligence concussion prediction pipeline presents many advantages over running individual computer models for each head impact case, but most notably everything in the pipeline is open source. Being open source allows anyone with an interest in concussions and other brain injuries to explore the relation between impacts and concussions and brain injuries without the need to purchase specific software licences or have access to high performance research computers.
Co-Authorship Statement

Chapter 2 ("A Detailed Review of the Regions, Functional Mapping, Roles and Responsibilities of the Human Brain") was supported by research completed by Emilie Potts and Yanir Levy. Chapter 3 ("Evaluating Three Types of Simple Artificial Intelligence Algorithms to Instantaneously Predict Brain Strain-based Injury Metrics Based on Head Impact Kinematics") was co-authored by Dr. Haojie Mao, Kalish Gunasekaran and Oliver Ma, with data collected and methodology developed by Yanir Levy and edits provided by Dr. George Knopf and Dr. Katarina Grolinger. Chapter 4 ("Quantifying the Effect of a Helmet in the Reduction of Blunt Impact-induced Brain Axon Fiber Tract Strain using an Advanced Finite Element Model of the Head") was supported by work completed by Yanir Levy, Kewei Bian, Sakib Ul Islam and Dr. Haojie Mao. Chapter 5 ("Selection, Development and Implementation of an Artificial Intelligence Pipeline for the Prediction of Blunt Impact-induced Brain Axon Fiber Tract Strain") was supported by work done by Kalish Gunasekaran.
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Chapter 1

1 Introduction

1.1 Chapter Abstract

*Ice hockey is a popular sport worldwide. This chapter aims to introduce readers to a commonly occurring, yet under reported and poorly understood, injury to which ice hockey players and referees are exposed: the mild traumatic brain injury (mTBI). The anatomy of the head and the current biomechanical explanation for various types of mTBIs is outlined, as well as protective tools used to mitigate and prevent mTBIs that may occur during sports such as ice hockey as well as other physical recreation activities where head and upper body impacts may occur. A literature review covering the rates of occurrence of mTBIs in various ice hockey leagues provides a glimpse into the importance and rationale behind conducting brain injury prevention research. Lastly, the scope of the research conducted in this thesis is defined, and the outline of the thesis detailing the key points of each of the subsequent chapters is provided.*

1.2 Injuries in Ice Hockey

Ice hockey is the most popular winter sport in Canada with over 500,000 players registered in Canada and 1.5 million players registered worldwide [1]. Ice hockey is the fastest team sport played in the world and involves both finesse and controlled aggression. It is also considered to be one of the roughest and most physical of all sports. A fundamental component of ice hockey is intentional and unintentional blunt impacts. These impacts can be between two or more players or referees, between a player or referee and the ice surface, or between a player or referee and an element of the playing area such as the hockey net, an open door, the surrounding rink boards and glass or the hockey puck. These impacts, whether or not they are intentional, can be the cause of injuries to participants. Common musculoskeletal injuries associated with blunt impacts in ice hockey include knee injuries, injuries to the shoulder, injuries to the groin and back injuries [2]. These injuries, while sometimes debilitating, can be diagnosed and treated
through means of rest and recovery programs, medication, physical therapy and, in the worst cases, surgery. Another common injury associated with playing ice hockey is a mTBI. mTBIs are different than the previously listed musculoskeletal injuries in that they are not as well understood and that the recommended treatment for them at this time is symptom and pain management, as opposed to a direct or specific treatment that remedies the issue.

The Canadian Journal of Public Health has called mTBIs a “silent epidemic” in Canada [3]. Instances of mTBIs have increased by 9.6% per year across all ages in Canada between 2005 and 2014 [4]. Historically, ice hockey participants that suffered mTBIs were provided with remarkably little information on how to prevent and understand the possible short- and long-term implications of their injuries [5]. Although mTBI prevention and treatment methods have improved substantially in the past two decades, the needs for improved diagnostic and injury spotting methods, a better understanding of the complicated biomechanics that can explain mTBI occurrence and improved injury prevention and rehabilitation tools are crucial to decrease the rate of mTBI occurrence in ice hockey, improve mTBI patient outcomes and decrease post-injury recovery time.

1.3 What is a mTBI?

The brain and its tissue are primarily composed of glial, endothelial and neuronal cells [6]. Glial cells are cells that maintain the environments of other cells and provide them with chemical and physical supports. Endothelial cells form thin layers of cells that line blood vessels and regulate the exchanges between the surrounding tissue and the blood supplied to the brain. Endothelial cells also coordinate the development and growth of connective tissue cells that surround the blood vessels in the brain. Neuronal cells are electrically excitable cells that communicate with other cells in the form of connections called synapses. Each neuronal cell, or neuron, is connected to other neurons through axons. Axon fibers are thin, snake like connectors that carry electrical signals between neurons. Some axons are protected by myelin sheaths, a fatty substance that acts as a form of insulation and protection from damage. These axons make up what is known as white matter in the brain. Axon fibers, serving as connectors and communication
facilitators, are critical for the regulation and management of a human’s brain and body. Damage to their function or structure may occur because of a mTBI.

A mTBI is usually caused by either an indirect or direct blunt impact to the head or upper body, in which there may be damage or significant strain in the tissues and cells of the brain [7]. There are several different types of injury mechanisms that can result in a mTBI, each with their own biomechanical explanation. Examples of these injury mechanisms include coup contrecoup injuries, focal brain tissue injuries and bruising, and diffuse axonal injury (DAI). DAI as an injury mechanism causing a mTBI is of particular interest to researchers, as this injury type can be caused by both direct and indirect impacts, both of which occur frequently in ice hockey. This thesis will focus on mTBIs that damage axon fibers through the means of DAI.

DAI is caused by the shearing or tearing of the axon fibers in the brain. This occurs when, for example, dynamic forces are applied to the brain as in scenarios of a blunt impact. The principal mechanical force associated with DAI is rotational forces acting on the brain due to unrestricted head movement in the instant after injury [8]. The associated inertial loading of the brain that comes with these rotational forces induces dynamic shear, tensile and compressive strains within the tissue leading to dynamic tissue deformation [8]. The size of the human brain plays an important role in the development of DAI because of the substantial mass effects during injury that result in high strains between regions of tissue [8]. Under routine daily activity, brain tissue is ductile and compliant in stretching and recovers easily to its original geometry [8]. Under impact or severe dynamic shearing conditions where strain is rapidly applied, brain tissue acts in a significantly stiffer manner, making it somewhat brittle [8]. Tensile elongation of brain tissue, or rapid uniaxial stretching, is thought to be the root cause of damage in the axonal cytoskeleton [8]. Under these conditions, brain tissue and axon fibers act as viscoelastic materials, meaning they exhibit a time-dependent strain property [8]. Therefore, the severity of DAI is dependent on both the magnitude of strain and rate of strain during conditions causing brain trauma, and subsequently the severity of the mTBI [8].
1.3.1 Anatomy of the Head: How is the Brain Protected from Injury?

The brain is the central organ in the human head and is protected from injury by several layers of various tissues, fluid-filled spaces and bone. Working from the inside of the head to the outside, the brain is enclosed in the pia mater, the subarachnoid space, the arachnoid mater and the dura mater, the skull and then the skin [9]. These layers of tissue, or meninges, offer protection against brain injuries in different ways [9].

The pia mater is the innermost layer which is closest to the brain and brain tissue [9]. The pia mater is composed of two layers, each following the contours of the sulci and gyri [9]. The outer layer of the pia is called the epipal layer, and it contains collagen fibers [9]. The inner layer, called the intima pia, contains elastic and reticular fibers [9]. The epipal layer has mesothelial cells that connect to the arachnoid mater, the second to inner layer, by the arachnoid trabeculae [9]. The intima pia is attaches to the outermost layer of neural brain tissue on the inside, through what is known as the glial membrane [9]. The cerebral pia mater forms sheaths around the blood vessels that enter and exit the brain, and this sheathing creates an interstitial fluid-filled space called the perivascular or Virchow-Robin space, between the vessel walls and the pia [9].

The second to most inner space is the subarachnoid space. It is a cerebrospinal fluid-filled space that exists between the arachnoid mater and the pia mater [9]. This space is continuous between the brain and spinal cord, so cerebrospinal fluid flows between the two through what is known as the foramen magnum [9]. The primary functions of the cerebrospinal fluid are to cushion the brain and spinal cord from dynamic forces and trauma, and to supply them with nutrients and remove waste [9]. In addition to the cerebrospinal fluid, the major arteries of the brain run through the subarachnoid space [9]. In addition, projecting into this space are arachnoid trabeculae, which are strands of arachnoid mater connective tissue [9].

Moving outwards, the next layer is the arachnoid mater [9]. This layer is an avascular membrane, and it is involved in cerebrospinal fluid metabolism in conjunction with the subarachnoid space [9]. The arachnoid does not follow the contours of the sulci and gyri,
but rather bridges over them [9]. It is generally a thin, lucent membrane, but also has varying appearances in different locations in the cranium [9]. The structure of the arachnoid mater consists of a superficial mesothelial layer below the dura, a central layer composed of cells conjoined by several junction proteins, and lastly a deep layer of less tightly packed cells with collagen fibers [9].

The outermost layer is the dura mater [9]. The dura mater is composed of two layers, known as the periosteal layer and the meningeal layer [9]. The periosteal layer consists of fibroblasts and osteoblasts, with a large amount of extracellular collagen existing in its intracellular space, which helps give strength to this portion of the dura [9]. The meningeal layer is the inner layer of the two that make up the dura [9]. The two layers are mostly fused, only separating to form venous sinuses and dural reflections, the latter of which refer to places where two meningeal layers, face to face, descend into the cranial cavity to form the septa [9]. The two layers that make up the dura create a thick, dense, fibrous membrane that is inelastic in nature [9].

Lastly, the skull is made of thick bone that encloses the previously discussed layers or meninges of tissue and space. The skull is made of three layers: the innermost and outermost layers made of dense cortical bone and the central layer made of porous trabecular bone [10]. The cranium is the set of bones that makes up the protective layer of bone for the brain. The skull is surrounded by the skin, which protects it from dirt, dust and small debris that could cause infection or other injury.

These layers of tissues, fluid-filled spaces and bone work together to protect the brain and mitigate mTBI occurrence and severity. However, if the dynamic shear-inducing forces from an impact are too great, injuries of various types, including DAI, will occur.

1.3.2 Focal versus Diffuse Head and Brain Injuries
An important distinction that is often not made clear to the public is the difference between focal and diffuse brain injuries. These injuries affect the brain in vastly different ways. Impacts can cause one, both or neither of these types of injuries. Both types of injuries can result from violent blows or jolts to the head or to the body [11]. A focal
brain injury is caused when an object, such as an ice hockey puck, affects the intracranial tissues. Results of a focal brain injury may include external bleeding and bruising, skull fracture, intracranial hematoma or blood clots [11]. Diffuse injuries such as DAI, on the other hand, may not show local physical damage such as bruised tissues or blood clots [11]. Victims of suspected DAI or other diffuse mTBIs are evaluated using scales such as the Glasgow Coma Scale (GCS) [11]. The GCS evaluates eye opening, verbal response and motor response on a scale [11]. Traumatic brain injury patients with a GCS score of 13 to 15 are classified to have a mild impact. This includes most TBI patients [11]. A patient with a GCS of nine to twelve is considered to have a moderate TBI, while a patient with a GCS below eight is classified as having a severe TBI [11]. The full GCS scoring system is shown in Table 1.
Table 1: GCS Rating System [11]

<table>
<thead>
<tr>
<th>Scoring Criteria</th>
<th>Scale</th>
<th>Description of Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eye Opening</td>
<td>4</td>
<td>Spontaneous</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>To Voice</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>To Pain</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>None</td>
</tr>
<tr>
<td>Verbal Response</td>
<td>5</td>
<td>Normal Conversation</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>Oriented Conversation</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Words, but not Coherent</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>No Words, Only Sounds</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>None</td>
</tr>
<tr>
<td>Motor Response</td>
<td>6</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>Localized to Pain</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>Withdraws to Pain</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Decorticate Posture</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Decerebrate</td>
</tr>
</tbody>
</table>

During clinical diagnoses, DAI can manifest itself in a spectrum of neurological dysfunctions [11]. DAI can present itself at various levels, from clinically insignificant to a comatose state, depending on the injury [11].

Another useful scale for the diagnosis of DAI and other brain-specific injuries is the Adams Diffuse Axonal Injury Classification. This classification utilizes pathophysiological lesions in the white matter tracts and clinical presentation [11]. Lesions in the white matter tracts of the brain leading to the disconnection or malfunction of the connection of neurons are the primary cause of DAI [11]. The Adams Diffuse Axonal Injury Classification is shown in Table 2.
Table 2: The Adams Diffuse Axonal Injury Classification [11]

<table>
<thead>
<tr>
<th>Grade Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>A mild DAI with microscopic white matter changes in the cerebral cortex, corpus callosum and brainstem</td>
</tr>
<tr>
<td>2</td>
<td>A moderate DAI with gross focal lesions in the corpus callosum</td>
</tr>
<tr>
<td>3</td>
<td>A severe DAI with finding as Grade 2 and additional focal lesions in the brainstem</td>
</tr>
</tbody>
</table>

Both the GCS and the Adams Diffuse Axonal Injury Classification are used in the diagnosis and evaluation of patients with suspected mTBI or DAI [11]. Although most severe focal brain injuries cause some form of diffuse injury, it is not always a guarantee. An impact that does not cause a physically apparent focal injury may still cause a mTBI or, in more severe cases, a DAI. Utilizing protective devices such as helmets can help prevent both focal and diffuse brain injuries.

1.3.3 Helmets for Protecting the Brain from Injury in Ice Hockey

The most common tool used for head protection in ice hockey, in other sports and in non-sports activities is a helmet. The first prototype ice hockey helmet was presented in 1927 [12], [13]. They were used in play sporadically from the late 1920s until 1968, when National Hockey League player Bill Masterton died due to a severe internal brain injury suffered while hitting his head on the ice during play [12], [13]. Helmets were mandated for players in the National Hockey League in 1979, and for on ice officials in 1988, although it was not until 2006 when the last official not wearing a helmet began doing so due to exemptions granted by the league for legacy employees [12], [13].

The majority of modern ice hockey helmets have a similar construction: an adjustable plastic rigid outer shell made of a material such as high-density polyethylene plastic or polycarbonate combined with an inner layer made of expanded polypropylene or vinyl nitrile liner, or some other sort of impact cushioning material such as a plastic cylinder...
array [14]. The outer shell provides a firm barrier between external objects contacting the head, and the inner layer provides impact absorption protection and cushions the head from the force of impacts. Modern helmets of this construction are excellent at providing protection from focal injuries but struggle to provide protection against dynamic shear-inducing impact forces, which are the main forces involved in causing mTBIs or DAI [7].

Modern helmets have been studied extensively in laboratory research and through the use of finite element modelling and computerized impact simulation. Metrics for rating a helmet’s ability to reduce mTBI occurrence have been developed, such as Hockey STAR [15]. Additionally, head impact injury metrics including the Gadd Severity Index (GSI), the Head Injury Criteria (HIC), the Generalized Acceleration Model for Brain Injury Threshold (GAMBIT), the Brain Injury Criteria (BrIC), the Universal Brain Injury Criterion (UBrIC), the Diffuse Axonal Multi-Axis General Equation (DAMAGE), average maximum principal strain (MPS) and cumulative strain damage measure (CSDM) have been calculated using laboratory testing on helmeted dummy head and neck models [7]. Kraus et al. (1970) demonstrated that a properly designed ice hockey helmet, including tested foams and solid construction, can reduce head injuries from 8.3 per 100 games to 3.8 per 100 games [16]. This study compared helmeted and non-helmeted players and proved that the use of helmets in the sport of ice hockey for head injury reduction is warranted [16]. The overwhelming consensus from this and other related research is that helmets can protect the brain and reduce the rate and severity of both focal and diffuse injuries in ice hockey and other sports and physical recreation activities. As discussed in Section 1.4, the number of brain injuries resulting from playing ice hockey is increasing, only reinforcing the importance of developing better helmets that excel at reducing dynamic shear-inducing forces from impacts [3], [17].

### 1.4 Prevalence of mTBIs in Ice Hockey

Several research studies have discussed the prevalence of mTBIs in ice hockey. The studies defined below provide mTBI incidence rates in terms of exposures, which are defined as one player participating in an ice hockey game or practice, unless otherwise specified. Marar et al. (2012) conducted a study that found that an estimated 300,000
sports-related concussions occur annually in the United States, and that among individuals 15 to 24 years of age, sports are second only to motor vehicle crashes as the leading cause of concussions. In the same study, it was found that for every 1,000 exposures, 0.54 concussion occurred in high school ice hockey in the United States [18]. In collegiate ice hockey in the U.S., Flik et al. (2017) found in game situations there was an average of 4.9 injuries per 1,000 exposures, with a breakdown of 13.8 per 1,000 exposures in games situations and 2.2 per 1,000 exposures in practice situations [19], [20]. Wennberg and Tator (2008) found that there were 1.04 to 1.81 injuries per 1,000 exposures in the National Hockey League in the seasons spanning from 1997 to 2008, depending on the season [21]. Williamson and Goodman (2006) studied rates of concussion occurrence in the British Columbia Amateur Hockey Association, and found that concussions are considerably underreported, and that rates can be as high as 24.3 injuries per 1,000 player hours during games only [22]. Kontos et al. (2016) conducted work that studied 397 youth ice hockey players from Western Pennsylvania, Boston, Massachusetts, and Birmingham, Alabama during the youth ice hockey seasons spanning from 2012 to 2014 and found a rate of 1.58 injuries per 1,000 exposures combining games and practices, broken down to 2.49 injuries per 1,000 exposures in games and 1.04 injuries per 1,000 exposures in practices [23]. Agel and Harvey (2007) found a rate of 0.72 injuries per 1,000 exposures for men and 0.82 injuries per 1,000 exposures for women from the season starting in 2000 to the season ending in 2007 [24]. This study only tracked mTBIs occurring during games. Schick and Meeuwisse (2017) reported 9.19 injuries per 1,000 exposures for males and 7.77 injuries per 1,000 exposures for female athletes in Canada Western Universities Athletic Association play across one varsity season for six male and six female teams [25]. In addition to games and practices, this study also tracked mTBIs occurring in weight training sessions. Echlin et al. (2010) found a rate of 21.5 injuries per 1,000 exposures in a fourth-tier male junior ice hockey season from 2009 to 2010 [26]. A study completed from 1984 to 2013 on a Swedish elite series ice hockey team by Pauelsen et al. (2017) yielded an incidence rate of 1.06 injuries per 1,000 exposures for the entire period [27]. This study only tracked mTBIs occurring during games. These studies show that although the rates of mTBI are varied depending
on the time period, level, age and gender of the participants, mTBIs have occurred and are still occurring at high levels in ice hockey. Therefore, conducting research into decreasing the rate of occurrence and severity of mTBIs in ice hockey participants is essential to making the game safer and more enjoyable for all.

1.5 Research Rationale

This thesis will relate three major fields of active research in engineering and the medical sciences: soft tissue biomechanics and their behaviour under load, computational modelling of the human body and brain, and artificial intelligence (AI). Uniting these three areas of active research will provide a unique perspective on how impacts to the head and upper body can cause mTBI, DAI and other injuries. Subsequently, the damage caused by these impacts can be traced back to the cognitive function of each of the parcellated axon fiber tracts through the neuroscience research summarized in this thesis, allowing readers to understand the full timeline from initial injury-causing impact all the way through to short- and long-term effects on the brain. The benefits of wearing a helmet are also quantified through a finite element comparison of impact studies conducted on dummy models wearing and not wearing a helmet. This provides readers with an in-depth understanding of the improvement in safety that helmets provide while playing ice hockey. Axon fiber tracts are examined individually in this analysis and the improved level of protection that each of the parcellated tracts is provided through the use of a helmet is quantified. Lastly, a novel pipeline for predicting the strain in each axon fiber tract using AI is presented, allowing readers a unique perspective on how to utilize the outputs of large, computationally expensive, and slow finite element models. This pipeline is entirely open source, expanding access beyond the laboratory environment where previously this was impossible due to licensing and computing power requirements. Individuals or organizations with an interest in mTBIs, particularly those affected by or recovering from mTBIs, can now access more detailed information about the direct relation between impacts and how their brains and their axon fiber tracts are affected.
1.6 Research Scope

Scope definition was driven by work completed by previous members of Dr. Mao’s research group. This thesis is based on the novel head and brain finite element model that was developed by Dr. Mao’s research group. Such model is called the Brain Axon Fiber Tract Global Human Bodies Models Consortium (GHBMC) Model and is referred to in this thesis as the Brain Axon Fiber Tract GHBMC Model. The Brain Axon Fiber Tract GHBMC Model, which is discussed at length in Chapter 4, was developed from the Global Human Bodies Models Consortium Model, which is referred to in this thesis as the base GHBMC Model. The Brain Axon Fiber Tract GHBMC Model was particularly important to the scope definition as this model and its output results are focal points of this thesis. The selection of parcellated axon fiber tracts was completed within this model, leading to the neuroscience and cognitive function research completed in Chapter 2. Finite element models of the brain served as the basis for the scope of work completed in Chapters 3 and 4. The scope was further defined by the blunt impact data provided by Bauer Hockey Ltd. This data was used as inputs for the work completed in Chapters 3, 4 and 5. Available computational resources and workstation memory limitations also contributed to scope definition for the work completed in Chapters 4 and 5. For example, memory limitations on the available workstations led to the decision to divide data by impact direction and by axon fiber tract, resulting in many smaller impact databases as opposed to one large database, which was the original goal. For Chapter 5, it was determined to focus the scope of work on the applied aspect of the AI algorithms, even though the theory and logic behind each algorithm was summarized in this thesis. Furthermore, the work in Chapter 5 was restricted to PyTorch machine learning framework implementations of multi-in single-out algorithms, as opposed to other implementations of artificial intelligence packages that require the use of TensorFlow or Keras software libraries. This allowed for a fair comparison between algorithms and decreased the total implementation cost of the various algorithms that were evaluated.
1.7 Thesis Outline

This thesis contains six chapters. Chapter 1 contains the introduction, relevant statistics to mTBI risk in ice hockey, rationale and purpose for conducting research. Chapter 2 contains an in-depth review of 33 parcellated axon fiber tracts, their locations, cognitive functions and possible symptoms and risks if impact-induced damage occurs. Chapter 3 establishes a relationship between various kinematic input variables and two measures of brain tissue strain, MPS and CSDM, and determines which of these kinematic input variables is best for predicting brain tissue behaviour during impacts. Chapter 4 compares the base GHBMC Model and Brain Axon Fiber Tract GHBMC Model, a novel version developed by members of Dr. Mao’s research group. Chapter 4 also details work done using laboratory testing on dummy head and neck models and quantifies the benefit that wearing a helmet has on reducing brain axon fiber tract strain during an impact. Chapter 5 details a novel prediction pipeline that uses AI to output brain axon fiber tract strains and bypass the finite element modelling process, which was previously essential to obtaining brain axon fiber tract strain results. Lastly, Chapter 6 contains conclusions that were drawn from the results of the work conducted in this thesis, a summary of research, and areas of future work including novelty, significance and the overall impact of the research completed for this thesis.
Chapter 2

2 A Detailed Review of the Regions, Functional Mapping, Roles and Responsibilities of the Human Brain

2.1 Chapter Abstract

The human brain is a multifunctional organ, critical for controlling several systems in the human body. The relationship between the different areas of the brain and their functions has been a focal area of research for scientists for at least the last century. Using anatomical references, the brain has been parcellated into 33 different critical axon fiber tracts, each with distinct purposes. In this chapter, the location, functionality and other important aspects of each of these axon fiber tracts are summarized, with possible symptoms and disorders occurring because of blunt impact-induced damage also noted. Medical imaging scans of each axon fiber tract such as those from diffusion magnetic resonance imaging tractography are provided, along with the matching axon fiber tracts shown in the Brain Axon Fiber Tract GHBMC Model. Lastly, a summary is provided, detailing general disorder categories for which each of the 33 axon fiber tracts is responsible.

2.2 Physiological, Anatomical and Functional Overview of Key Axon Fiber Tracts in the Brain

Axon fiber tracts are an area of particular interest for mTBI and DAI researchers, as axon fibers are what gets sheared or damaged due to the dynamic forces acting upon them during an impact. This chapter contains an overview detailing 33 key parcellated brain axon fiber tracts, including where they are located within the brain, descriptions of the purpose and function of each tract, and what each tract is responsible for. Additionally, if a tract is damaged, possible short- and long-term symptoms of damage are explored based on available studies from existing literature.

The 33 parcellated brain axon fiber tracts outlined in this chapter span throughout the frontal lobes, parietal lobes, temporal lobes, occipital lobes, brain stem and cerebellum.
Figure 1: Overview of Key Brain Regions [28]

Figure 1 shows the key regions of the human brain. Each of these regions contain axon fiber tracts that are outlined in the subsequent sections.

A useful way to specify and localize parcellated areas of the brain is through Brodmann areas. Brodmann areas are regions of the cerebral cortex defined by their neuropsychological functions. The concept was originally developed by Korbinian Brodmann in 1909 and is still universally used for locating and identifying brain areas [29]. Brodmann areas are frequently referred to in this chapter, so a map of the human brain with Brodmann areas located is shown in Figure 2 below for reference.
Figure 2: Brodmann Areas, as defined in 1909 [30]

Key regions of the brain that house the axon fiber tracts being studied were developed into the Brain Axon Fiber Tract GHBMC Model, which is discussed in Chapter 4. This finite element model is an advanced version of the base GHBMC Model that features added axon fiber tracts in addition to the tissue regions in the brain. Locations of important axon fiber tracts are communicated visually through magnetic resonance imaging (MRI) scans, diffusion tensor imaging and fiber tractography or other clinical
images in each section below. Additionally, the equivalent axon fiber tract is shown in
the Brain Axon Fiber Tract GHBMC Model for reference. The dura mater, or dura, is the
outermost layer of connective tissue that makes up the meninges of the brain, and it
surrounds and protects the brain and spinal cord. This is used as a reference for the
outline of the brain in the Brain Axon Fiber Tract GHBMC Model.

2.2.1 Arcuate Fasciculus

The arcuate fasciculus is a short association fiber bundle, which is located in the parietal,
temporal and frontal regions of the brain. This white matter tract arcs around the end of
the Sylvian fissure to connect Wernicke’s area to Broca’s area, which is the main purpose
of the tract [31], [32]. Figures 3 and 4 outline the location of the arcuate fasciculus in the
brain and in the Brain Axon Fiber Tract GHBMC Model.

![Figure 3: Location of the Arcuate Fasciculus in the Human Brain [33]](image)
Wernicke’s area was first described in 1874 by German neurologist Carl Wernicke [34]. Since then, it has become an anatomical label usually applied to the left posterior superior temporal gyrus and adjacent supramarginal gyrus. This area was thought to be critical for speech perception and word comprehension. However, recent evidence has shown it supports retrieval of phonological forms (mental representations of phoneme sequences), which are used for speech output and short-term memory tasks. Focal damage to this region produces phonemic paraphasia without impairing word comprehension, i.e., conduction aphasia. Recent neuroimaging investigations have shown that Wernicke’s area, which is anatomically defined, is not part of the broadly dispersed temporal, parietal and frontal network supporting language comprehension [35]. Broca’s area is involved in speech function and is located in the frontal part of the left hemisphere of the brain. It was discovered in 1861 by French surgeon Paul Broca, who found that this area serves a vital role in the generation of articulate speech [36]. Because of its inherent neuronal arrangement, Broca's area may be involved in syntactic comprehension of language as opposed to the dorsolateral prefrontal cortex from which it evolved, or the sensory-motor activities of the cortex from which it is descended [37].

**Figure 4: Location of the Arcuate Fasciculus in the Brain Axon Fiber Tract**

**GHBMC Model**
The arcuate fasciculus is an indirect pathway that consists of two main segments. The first segment is the anterior section, which links Broca’s area with the inferior parietal lobes. The second segment is the posterior segment, which links the inferior parietal lobes with Wernicke’s area. These indirectly connecting segments are shown in Figure 3. The arcuate fasciculus connects and spans areas that are relevant to language function, short-term memory tasks and speech. In aphasia literature, it has been considered that a speech repetition defect represents the main aspect of conduction aphasia. Conduction aphasia has frequently been interpreted as a language impairment due to lesions of the arcuate fasciculus that disconnect receptive language areas from expressive ones [38]. These lesions could be caused by impacts causing tissue strain in the arcuate fasciculus, which may cause speech and language disorders and short-term memory disorders, and possibly reading and writing deficiencies [39].

2.2.2 Cingulum Bundle

The cingulum bundle is a major intrahemispheric or cortex-cortex white matter tract that connects the frontal, parietal and temporal lobes together. It is located above the corpus callosum and under the cingulate cortex. Its location is shown in Figure 5 relative to the rest of the brain, and Figure 6 shows the location of cingulum bundle in the Brain Axon Fiber Tract GHBMC Model.
The cingulum bundle is not a unitary pathway, and it is comprised of both short and long sagittal association fibers. Furthermore, additional cingulum fibers extend throughout the tract to connect with cortical and subcortical sites [41]. Numerous short cortico-cortical connections also contribute to the complexity of the cingulum bundle.
association fibers, or U-fibers, connect the medial portions of the frontal, parietal and temporal lobes via its sagittal connections [41]. This is reflected in Figure 6. Consequently, few, if any, connections extend the entire length of the tract [41], [42].

The cingulum bundle is made up five subregions, all of which are responsible for separate tasks, as outlined by Wu et al. (2016) [42]. These subregions, labelled I to V, are shown in Figure 7.
Figure 7: Spatial Relationship of the Subcomponents on the Human Connectome Project (HCP-488) Template. (A) A Complete Schematic Map of the Five Segments. (B) Depicting Five Segments of CB on the HCP-488 Template T1 Sagittal View. (C) Axial View [42].
The lowest subdivision of the CB-I expands into the orbital-frontal cortex and bends tightly around the genu of the corpus callosum [42]. It circles the corpus callosum and extends from the subrostral regions to the precuneus and spleen [42]. The CB-I is closest to the midline in all the segments [42]. The CB-I controls reactions to unpleasant stimuli, modifies depressive mood states, and mediates the connection between cognitive function and verbal performance memory [42]. The superior frontal gyrus' medial aspect is reached by the CB-II, which curves around the spleen and extends anteriorly above the corpus callosum [42]. Despite their overlaps, the caudal section of the CB-II is slightly more medial than the CB-V and the body section of the CB-II extends along the bottom of the CB-III [42]. The CB-II enables path integration and constant input about position and orientation during movement [42]. The medial aspect of the SFG connects the CB-III to the precuneus and superior parietal lobule [42]. The CB-III is the largest of the fiber bundles in the cingulum bundle system and is found in all hemispheres [42]. Performance in attention-demanding cognitive tasks is governed by the CB-III [42]. The CB-IV is the smallest fiber tract in the cingulum bundle system [42]. It is situated superficially lateral to the CB-III [42]. The CB-IV is a relatively minor subcomponent from the superior parietal lobes and precuneus to the frontal region [42]. The medial temporal lobes give rise to the CB-V, the para-hippocampal cingulum, which spreads out to the occipital lobes [42]. Studies on the early diagnosis of Alzheimer's disease have focused on the CB-V, which is also significant in the relationship between different cognitive tasks like attention-shifting and spatial navigation [42]. The CB-V is a control pathway, as it supports memory and executive functions [42]. Overall, the cingulum bundle is responsible for executive control, emotion, pain and episodic memory in the brain.

2.2.3 Corpus Callosum

The corpus callosum is the largest white matter tract in the brain, spanning parts of the frontal, parietal, temporal and occipital lobes. The location of the corpus callosum is shown in a highlighted MRI in Figure 8, and the corpus callosum position is shown in the Brain Axon Fiber Tract GHBMC Model in Figure 9.
The corpus callosum plays a crucial functional role in interhemispheric connections by connecting the cortical regions of the left and right cerebral hemispheres. Additionally, it is crucial for integrating data and modulating complicated activities [44]. Increased callosal thickness during typical childhood development is correlated with intelligence,
processing speed and problem-solving skills, whereas weakened corpus callosum integrity has been found to contribute to a decline in cognitive function in aging adults [44]. An increasing body of research suggests that neurodevelopmental illnesses like autism, schizophrenia and attention-deficit disorder may share cognitive and behavioural problems with minor anatomical alterations in the corpus callosum [44]. Additionally, it has been proposed that aberrant corpus callosal development may contribute to deficiencies in executive function and social cognition. The transfer of somatosensory information and learning processes between the two sides of the cerebral cortex are inhibited by damage to the corpus callosum, which largely obstructs communication between the right and left cerebral hemispheres [44]. Visual, stereognostic and somatosensory information may still be lateralized if the corpus callosum is damaged. In addition, damage may impede ipsilateral sensory-motor functions. Language and speech lateralization, which are restricted to the left and right hemispheres of the brain, can cause issues such as difficulty naming items held in the left hand since those names are sent to the right hemisphere of the brain [44]. This is called Split-Brain syndrome. In some cases where the corpus callosum is so severely injured that the brain fully separates into two hemispheres, significant memory impairment can occur. When compared to a control group, corpus callosum damage can also result in a significant decline in verbal and auditory word learning, orientation, attention, computation, delayed memory and other visuospatial skills [45]. Lesions of any part of the corpus callosum may lead to the loss of contact between the bilateral hemispheres, and subsequently lead to the development of mental disorders such as pseudobulbar palsy, as well as speech and movement ataxia [45].

2.2.4 Cortico-Ponto-Cerebellar Pathway

The cortico-ponto-cerebellar pathway (CPC) is a white matter fiber tract and is the largest component of the corticofugal fiber system of the human brain central nervous system [46]. Figure 10 shows a two-dimensional rendering of the fibers that make up the CPC, and Figure 11 shows the position of the CPC in the Brain Axon Fiber Tract GHBMC Model.
Figure 10: 2-D Rendering of the CPC Using a Combined Constrained Spherical Deconvolution Technique and Probabilistic Streamline Tractography in a Representative Subject. Left Regions of Interest are shown in Blue, and Right Regions of Interest are shown in Red [47]

Figure 11: Location of the CPC in the Brain Axon Fiber Tract GHBMC Model

The CPC forms the largest group of fibers in the basis pontis [46]. The ponto-cerebellar fibers cross the midline to enter the cerebellum via the middle cerebellar peduncle, and the cortico-pontine fibers, which go to the pontine nuclei, make up the two neuron chains
that make up the CPC fibers [46]. The cerebellum receives most of its information from the cerebral cortex via the CPC pathways, which connect various cortical regions with the cerebellum to regulate and coordinate movement [46]. These fibers originate from motor and nonmotor (associative and limbic) areas of the cerebral cortex [46]. Almost all these fibers cross the midline in the basal pons and terminate in the contralateral half of the cerebellum [46].

The CPC was parcellated into four main subtracts by Kamali et al. (2010) [46]. These tracts were called the frondo-ponto-cerebellar (FPC) tract, parieto-ponto-cerebellar tract (PPC), occipito-ponto-cerebellar tract (OPC), and the temporo-ponto-cerebellar (TPC) tract [46]. The FPC travels from the orbitofrontal and prefrontal cortical areas [46]. The FPC fibers descend through the anterior limb of the internal capsule, genu and the anterior one-third portion of the posterior limb of internal capsule (PLIC) [46]. The FPC fibers continue through the ventro-medial region of the cerebral peduncle and proceed caudally up to the level of the pons, where they decussate and enter the cerebellum through the opposing middle cerebellar peduncle [46].

The premotor, primary motor, primary sensory and posterior parietal cortices are among the cortical regions that give rise to the PPC and are posterior to the precentral sulcus and prior to the parieto-occipital sulcus [46]. The PPC fibers descend side by side with the corticospinal tract (CST, see Section 2.2.6) in the centrum semiovale, and then within the posterior two-third portion of the PLIC and the most anterior portion of the retrolenticular portion of the internal capsule [46]. These fibers descend to the basis pontis, where they intersect latero-lateral fibers, passing via the lateral part of the middle portion of the cerebral peduncle either laterally to the CST or medially to the CST [46].

The OPC originates from the occipital cortex posterior to the parieto-occipital [46]. These fibers continue their route caudally through the crus cerebri's dorso-lateral region, which is encircled by the CST ventrally and the TPC dorsally, after descending through the PLIC's most posterior section and the retrolenticular region of the internal capsule [46]. The OPC fibers remain in this position down to the basis pontis, where they cross to the opposing side of the pons and enter the cerebellum through the contralateral MCP [46].
The inferior branch of the uncinate fasciculus and the temporal horn of the lateral ventricle are reached via the inferior branch of the TPC tract, which emerges from the apex of the anterior-inferior temporal lobes [46]. It continues to ascend further in the temporal lobes to the highest axial level of the mesencephalon [46]. The TPC tract then descends at the posterior margin of the crus cerebri, dorso-lateral to the OPC and the CST, and is encircled ventrally by the OPC tract, reaching the level of the pons [46]. At this level, it crosses to the other side and goes through the contralateral MCP into the cerebellum [46].

These four divisions are shown in detail in Figure 12.

Figure 12: Transverse DTI Colour-coded Map and Concordant T2-weighted MRIs for Mapping the FPC (Red), PPC (Yellow), OPC (Green), TPC (Orange), and CST (Pink) [46]

These subetracts span significant portions of the brain, and as a result the CPC is essential for major inputs of the cerebellum from the cerebellar cortex [47]. The CPC links different cortical areas responsible for the coordination and regulation of movement [47]. There is some debate over whether the CPC has a role in processing higher levels of cognitive information [47]. Damage to subetracts or the entirety of the CPC is associated with ataxic neurodegenerative diseases, multiple system atrophy, pure cerebellar
syndrome, Parkinson’s disease, attention-deficit hyperactivity disorder, progressive ataxia, atrophy, dysmetria, dysarthric speech or tremors [47].

2.2.5 Corona-Radiata-Frontal Tract and Corona-Radiata-Parietal Tract

The corona-radiata-frontal tract (CRF) and corona-radiata-parietal tract (CRP) make up a broad fan-shaped array of white matter fibers that converge inferiorly into the internal capsule [48]. This array is called the corona-radiata (CR), which is shown in the sketch in Figure 13. The position of the CR in the Brain Axon Fiber Tract GHBMC Model is shown in Figure 14.

Figure 13: Dissection Showing the Course of the Cerebrospinal Fibers, including the Corona-radiata [49]
The fibers of the corona-radiata cross between the transversely oriented commissural fibers that meet at the corpus callosum [48]. The coronal fibers lie between the longitudinal fibers of the cingulum bundle and superior fronto-occipital fasciculus medially and superior longitudinal fasciculus (SLF) laterally [48]. The cerebral cortex is connected to the thalamus and brainstem in both directions by the corona-radiata [48]. The CR is responsible for connecting several regions of the brain together. In the front of the brain, the CR is responsible for thalamic connection to the frontal lobes and the frontopontine motor fibers that pass through the frontal limb of the internal capsule [48].
The CR is also responsible for the thalamic connections to the frontal parietal lobes and the cortinuclear motor projections that pass through the genu [48]. Closer to the rear of the brain, the CR is responsible for the thalamic connections to the central parietal and occipitotemporal lobes, and the corticospinal, corticopontine and corticotegmental motor fibers that pass through the posterior limb of the internal capsule [48]. The CR oversees distributing motor and sensory information, and injury to this region results in loss of motor function, muscular weakness, hand weakness or ipsilateral hemiparesis [50]. CR damage is also associated with facial and upper or lower limb weaknesses and visual field deficits [50]. Another condition attributed to CR damage is dysarthria, which results in unclear or difficult articulation of speech [50]. Severe motor and sensory deficits such as faciobrachial or brachicrural motor weakness, or hemihypesthesia, are also possible [50]. Hemihypesthesia is a reduction in tactile sensitivity [50]. Additionally, it was shown that damage to the CR disrupted voluntary emotional expression by cutting off the functional connectivity between the frontal cortex and brain stem [51].

### 2.2.6 Corticospinal Tract

The CST is a white matter motor pathway which starts at the cerebral cortex and terminates on lower motor neurons and interneurons in the spinal cord [52]. Figure 15 shows the CST of a healthy 45-year-old male, and Figure 16 shows the location of the CST in the Brain Axon Fiber Tract GHBMC Model.
Figure 15: Diffusion Tensor Tractographies for the CST in a Healthy 45-year-old Male [53]

Figure 16: Location of the CST in the Brain Axon Fiber Tract GHBMC Model

The CST originates from the precentral motor cortex and descends through the CR and posterior one-third portion of the PLIC side by side to the PPC tract [46]. The CST continues to descend in the cerebral peduncle surrounded side by side with the PPC and
dorso-laterally by the OPC and TPC tracts [46]. This descent occurs downwards to the
level of the pons where the CPC pathways cross to the other side [46]. The CPC fibers
cease to exist in the medulla and spinal cord, where the CST tract continues caudally and
terminates in the grey matter of the spinal cord [46].

In a study done by Kamali et al. (2016), four of the five study subjects were observed to
have the PPC tract passing through the most lateral portion of the crus cerebri (which is
lateral to the CST) [46]. Additionally, it was found in that study that the CST passed
through the more medial and dorsal areas than the PPC in the crus cerebri [46].
Therefore, it was found that the CST was surrounded by the PPC laterally in the crus
cerebri, PLIC and centrum semiovale [46]. In one subject in the study, the CST passed
through the most lateral segment of the middle one-third portion of the crus cerebri [46].
For this subject, in the crus cerebri and higher levels, like the PLIC and the centrum
semiovale, the PPC tract traveled medially to the CST [46].

The CST is the most important major neuronal pathway for motor function in the human
brain [54]. After a brain injury, the CST is recognized to be crucial for recovering from
motor weakness, especially when it comes to the hands' fine motor skills [54]. The CPC
enables people to control their walking because the lateral CST regulates the distal
muscle, which is employed for fine movement, and modifies gait patterns in response to
external cues [55]. The CST covers between 75% and 90% of fibers that cross at the
medulla [56]. The anterior CST innervates proximal muscles, such as the neck, trunk and
proximal upper extremities [57], [58]. Severe motor weakness can be caused throughout
the body by even the tiniest CST lesions at the brainstem [55]. The inability to do fine
motor tasks with the hands and fingers and poor overall motor function may also result
from CST damage [55]. Residual weakness on one side of the body may also occur with
damage to the CST [55], [59]. Damage to the CST leads to functional reorganization in
the ipsilateral and contralateral sensorimotor cortices [59]. Lang and Schieber (2004)
demonstrated that CST injury decreased the selectivity of finger muscle activation during
individuated finger abduction/adduction motions, resulting in decreased independence of
these movements [55].
2.2.7 External Capsule

The external capsule is a series of white matter tracts organized in a thin sheet within the brain [60]. The location of the external capsule is shown in Figure 17, and within the Brain Axon Fiber Tract GHBMC Model in Figure 18.

Figure 17: Location of the External Capsule, Emphasized in Orange [49]
The external capsule lies lateral to the putamen and medial to the claustrum [60]. The insular folds cover a major portion of the association fibers that make up the external capsule and connect the cerebral cortex to the striatum [60]. Fibers in the medial aspect are derived from the inferior fronto-occipital fasciculus and cross over the foot of the CR [60]. As it reaches the rostral end of the corpus striatum, the uncinate fasciculus supplies fibers to the anterior section of the external capsule [60]. The inferior longitudinal fasciculus is essentially where the posterior fibers originate. Such fibers make up most of the external capsule [60]. Some frontal lobe fibers pass through the external capsule and reach the substantia nigra and tegmentum of the mesencephalon nuclei [60]. The external capsule is a route for cholinergic fibers from the basal forebrain to the cerebral cortex [60].

Isolated lesions of the external capsule are rare [60]. In general, white matter damage occurring in the external capsule is most typically associated with executive dysfunction in the cognitive profile [61]. Changes in white matter in the external capsule due to aging have been reported specifically within the external capsule and associated with executive dysfunction [61].
2.2.8 Extreme Capsule

The extreme capsule is a thin series of white matter association fibers that span the brain horizontally. The location of the extreme capsule on a population-averaged template is shown in Figure 19, and within the Brain Axon Fiber Tract GHBMC Model in Figure 20.

Figure 19: Tractography Showing the Location of the Extreme Capsule on a Population-averaged Template [33]
Figure 20: Location of the Extreme Capsule in the Brain Axon Fiber Tract GHBMC Model

The extreme capsule lies between the claustrum medially and the insula laterally [60]. It spans from the inferior frontal cortex (Broca’s area) through the middle part of the superior temporal gyrus into the inferior parietal lobule (the angular gyrus/Geschwind’s territory), adjacent to the middle longitudinal fascicle [60]. The extreme capsule is important in language processing, and specifically language expression [60].

Similar to the external capsule, a small number of isolated lesions can have a significant effect on the extreme capsule but are rare [60]. Lesions that occur on the left side of the extreme capsule can cause language impairment [60]. In the event of causal lesions to one side of the extreme capsule, the other side may develop mild-to-moderate paralysis, a condition called contralateral hemiparesis [60]. Extreme capsule hemorrhaging may affect the striatum and cause anterograde and retrograde axonal degeneration [60]. The striatum is the input module to the basal ganglia, a neuronal circuit necessary for voluntary movement control [62]. The striatum is also responsible for social rewards, which are events or objects that elicit learning and produce positive emotions [62].

Language and how people process calls, vocalizations and auditory object recognition are heavily influenced by the extreme capsule [63]. There is proof that electrical stimulation
of the extreme capsule causes a disorder known as semantic paraphasias, which causes a speaker to swap one word for another in a sentence [63]. Several speech and language conditions may be developed if damage to the extreme capsule occurs, as it is an essential pathway in connecting the frontal and temporal regions [64], [65]. The extreme capsule also has a role in linking the inferior frontal gyrus (Broca’s area), the middle part of the superior temporal gyrus (Wernicke’s area) and the inferior parietal lobule (the angular gyrus) [64], [65]. This involvement and presence in many areas of the brain that are relevant to language suggests that the extreme capsule has a prominent role in language and speech functions [64], [65].

2.2.9 Internal Capsule

The internal capsule is a projection tract within the human brain, meaning it is a long tract that connects cortical and subcortical centers [60]. Nearly all information that reaches the cerebral hemispheres travels through projection tracts in the brain [60]. The location of the PLIC in a sketch of the human brain is shown in Figure 21, and in the Brain Axon Fiber Tract GHBMC Model in Figure 22. Figure 22 does not show the PLIC, which is discussed in Section 2.2.10 and shown in Figures 23 and 24.
Figure 21: Cross Section View of the Brain, Showing Location of the Internal Capsule [49]

Figure 22: Location of the Internal Capsule in the Brain Axon Fiber Tract GHBMC Model
The internal capsule is a subcortical white matter structure which lies in the inferomedial portion of each cerebral hemisphere [66]. It is a two-way tract that acts as the route through which information is sent to and received from the cerebral cortex [66]. The internal capsule is a V-shaped structure on transverse brain slices, with its apex pointing medially [66]. The cerebral hemispheres are connected to subcortical regions, the brainstem and the spinal cord by myelinated ascending and descending fiber networks that travel past the basal ganglia [66]. It splits the putamen and globus pallidus from the caudate nucleus and thalamus as it moves through the basal ganglia tissues [66]. The internal capsule's fibers are arranged in a radiating pattern called the CR above the superior border of the lentiform nucleus [66].

The internal capsule is made up of tightly packed CR fibers that move caudally. As the fibers continue past the basal ganglia, they become even more tightly packed, forming the basis pedunculi at the midbrain [66]. The number of descending axonal tracts that terminate in the thalamus and other brainstem nuclei reduces as the axons from the internal capsule move down the brain [66]. There are different ascending and descending axonal tracts in each part of the internal capsule, and each one serves a vital purpose [66].

The internal capsule is traditionally divided into five smaller tracts of axons, each with critical functions [60]. These five smaller tracts are the anterior limb (ALIC), the genu, the PLIC, the retrolenticular segment and the sublenticular segment [60]. Five major sections of fiber projections pass through the various divisions of the internal capsule [60]. These fiber projections connect the cortex to the brain's lower regions and the spinal cord [60]. These fiber projections are the thalamocortical projection, the corticothalamic projection, the corticopontine projection, the corticobulbar projection and the corticospina projection [60]. This section will focus on the ALIC and the genu [60]. Section 2.2.10 will discuss the PLIC, the retrolenticular division and the sublenticular division [60].

The ALIC contains several fiber bundles. Examples of these include the anterior thalamic radiation, the superolateral division of the medial forebrain bundle, the fronto-pontine motor tracts and the anterior thalamic fibers [60]. These fibers are mostly horizontal on
an axial plane [60]. Bundles in the ALIC are responsible for mediating reward seeking and euphoric feelings, and also states such as those of sadness and psychic pain [60]. Damage to the ALIC has been associated with deficits in storage and retrieval of verbal memory and decreases in motor initiation [60]. Arnold’s bundle, another related fiber bundle, is involved with anhedonia and depression [60]. It has also been connected to the treatment of psychiatric diseases, severe anxiety, panic disorders and obsessive-compulsive disorders [60]. Damage can also lead to conjugate eye deviation toward the site of the lesion [60].

Most of the motor fibers in the genu are corticobulbar, with a small number of anterior and inferior thalamic fibers also travelling through this region [60]. The location of the genu is at the apex of the pallidal part of the lentiform nucleus [66]. The ALIC and posterior limbs join at a right angle to form the genu [66]. The corticobulbar tract fibers and superior thalamic radiation fibers are two of the tracts that pass through the genu [66]. Corticobulbar tract fibers originate from the primary motor cortex, premotor cortex and supplementary motor areas (SMA) [66]. They terminate at the appropriate cranial nerve nuclei within the brainstem [66]. Dysarthria, dysphagia and faciolingual weakness are brought on by contralateral motor impairments in the head or neck and face muscles that result from genu injury [60]. Bilateral injury to thalamofrontal fibers can cause abulia, somnolence and cognitive impairment [60]. Clumsy-hand dysarthria presents with difficulty articulating speech and weakness in the hands and results from damage to the genu or the ALIC [66]. Additionally, the muscles of the face and neck, as well as the movement of the facial musculature, mastication and swallowing, are all controlled by corticobulbar motor fibers [66].

2.2.10 Posterior Limb of Internal Capsule

The PLIC is a fiber bundle that travels through the thalamus medially and the lenticular nuclei laterally [60]. The location of the PLIC in a healthy volunteer is shown in Figure 23 in an MRI of the brain, and in the Brain Axon Fiber Tract GHBMC Model in Figure 24.
The PLIC is split into three equal parts, each of which makes up a separate section of the tract. The anterior third of the PLIC, just behind the genu, carries superior thalamic fibers that link the ventral and lateral thalamic nuclei (thalamocortical sensory fibers) to the frontal and parietal cortices [60]. The middle third of the PLIC is comprised of fibers forming the CST [60]. The posterior thalamic fibers that connect the pulvinar and lateral...
geniculate bodies of the thalamus to the posterior parietal and occipital cortices are found in the posterior third of the PLIC [60]. Through this region of the PLIC, the third-order sensory fibers from the posterolateral nucleus of the thalamus travel until they reach the somesthetic area in the postcentral gyrus of the cerebral cortex [60].

The retrolenticular division of the internal capsule mostly contains fibers that make up the optic radiation [66]. Portions of the optic radiation also travel through the sublenticular segment of the internal capsule [66]. The optic radiation transmits visual information from the retina to the visual cortex [66]. Damage to this division may lead to homonymous hemianopia, superior quadrantanopia or inferior quadrantanopia [66]. Homonymous hemianopsia is a condition in which a person sees only half of the visual world of each eye. Inferior and superior quadrantanopia results in vision loss where roughly a quarter of a person’s vision is blacked out or blocked.

The optic radiation, also known as the geniculocalcarine tract, is contained in the retrolenticular division of the PLIC [60]. The fibers that make up the optic radiation come from the superior colliculi and lateral geniculate bodies of the thalamus, and they go backward to the occipital cortex [60]. The optic radiation is comprised of two main sets of fibers [60]. These two groups are the inferior fibers, which travel around the temporal horn of the lateral ventricle to the primary visual cortex, and the superior fibers, which travel posteriorly toward the primary visual cortex (also called Meyer’s loop) [60]. A precise visuotopic order is maintained by the optic radiation. Superior fibers represent the superior half of the visual field, whereas inferior fibers contain information from the inferior half [60].

The location of the sublenticular segment of the internal capsule is below the lentiform nucleus [66]. This division contains auditory radiation fibers which travel from the medial geniculate body and terminate in the transverse temporal gyri of Heschl [66]. The sublenticular segment contains auditory radiation fibers. Lesions in the sublenticular limb may create auditory and hearing deficits [66].
The sublenticular division of the posterior PLIC is where fibers from the lateral lemniscus pass via the inferior colliculi on their way to the medial geniculate bodies [60]. This pathway is part of the lemniscal pathway of auditory processing [60]. Auditory stimuli are connected to limbic system nuclei via a non-lemniscal channel that leaves the medial geniculate body for more advanced, complicated auditory processing [60]. The acoustic radiation fibers facilitate speech and nonspeech recognition with the left hemisphere of the brain responsible for speech sound recognition [60]. Defects in the acoustic radiation may lead to cortical deafness, auditory agnosia and sound agnosia [60].

2.2.11 Inferior Longitudinal Fasciculus

The inferior longitudinal fasciculus (ILF) is an axon fiber tract that connects the temporal and occipital lobes in the brain. The location of the ILF is shown in diffusion tensor tractography image in Figure 25, while the location of the ILF in the Brain Axon Fiber Tract GHBMC Model is shown in Figure 26.

![Diffusion Tensor Tractography of ILF Subcomponents in an Individual](image)

**Figure 25**: Diffusion Tensor Tractography of ILF Subcomponents in an Individual. Top Row: A Coronal View of the Whole Course of Each Segment (From the Occipital Terminations). Lower Row: A Sagittal View of a Tractographic Reconstruction of the Four ILF Subcomponents on the Right Side and Only Three Segments on the Left Side [68].
The ILF is a white matter tract, located in the temporoparietal region, which is made primarily of long fibers [60]. These fibers originate in the fusiform gyri, inferior frontal gyri, superior temporal gyri and middle temporal gyri. They then project to the cuneus, lingual gyrus and lateral occipital lobes [60]. These fibers make up the occipitotemporal connection [60]. The parahippocampal gyrus and the uncus are connected to the more posterior visual association areas via short fibers [60]. Additionally, these short fibers link the inferior parietal lobes and the intraparietal sulcus to the primary, secondary and associate visual areas [60].

The right portion of the ILF has been linked to the analysis of faces, and it plays an important role in visual memory and visually evoked emotions [60]. The study of colours, shapes and forms that enables word, object and colour recognition is critical in the left section of the ILF [60]. Through its connections to other crucial language routes, such as the extreme capsule, the ILF also plays a crucial role in language processing [60].

Lesions or damage to the ILF can disrupt the flow of information between visual areas, limbic regions and memory regions [60]. Prosopagnosia, visual object agnosia, alexia, contralateral hemiachromatopsia, a decline in recent visual memory and hypoemotionality may also result from these lesions or damage [60]. The disease of
having trouble recognizing faces, known as prosopagnosia, is more strongly associated with the right than the left hemisphere of the brain [60]. Visual object agnosia is a term for a problem identifying objects that are presented visually and is more strongly associated with the left hemisphere of the brain [60]. Alexia is the difficulty of recognizing written words, which is seen in conjunction with additional splenial lesions [60]. Contralateral hemiachromatopsia refers to disorders in colour recognition [60]. Hypoemotionality refers to deficits in visually evoked emotions [60]. For patients with semantic dementia, the ILF offers a decoy and alternate path to ventral semantic processing that may be changed [60]. There is some evidence, such as a study by Corrivetti et al. (2017), which shows that the portion of the ILF that is responsible for the usually right hemisphere dominant network of facial recognition can reorganize itself within the left hemisphere [69]. This indicates that if damage were to occur, the left and right ILF parts could cover each other's customary roles [69]. Herbet et al. (2018) studied and confirmed that the left portion of the ILF is involved in lexical access, which suggests that the information shared by this tract can be rerouted along alternative pathways when damage occurs [70]. The ILF is still an area of intense research, with most of the current hypotheses and findings in terms of the results of damage and subsequent rehabilitation options proposed needing experimental confirmation [68].

2.2.12 Intracerebellar Input and the Purkinje Tract

The tract representing the intracerebellar input and the Purkinje tract make up a network of fibers that receive input from and output to the cerebellar cortex [71]. This fiber tract is essential for intracerebellar input and information transfer [71]. This fiber tract is shown in the diffuse tensor imaging of a mouse brain in Figure 27, and in the Brain Axon Fiber Tract GHBMC Model in Figure 28.
Figure 27: Axial Views of Tractography Pathways of the Cerebellum in a Mouse Brain, Aged 8 Months. Mean Diffusion Weighted Image Shown in Figure 27b. The Small Rectangle Insertion in Figure 27a is a Sagittal Slice with Yellow Lines Indicating the Level of Axial Slices. Ten Percent of the Total Reconstructed Tractography Pathways Are Shown in Figure 27c, and 50% in Figure 27d, for Visualization Purposes. White Arrows Point to Red Pathways That Likely Correspond to Parallel Fibers. Light Blue Arrows Point to Green Pathways in the White Matter Between the Red Pathways [71].
Purkinje fibers, a large portion of this tract, are a type of GABAergic neurons. GABAergic neurons transmit signals through the use of the amino acid neurotransmitter called GABA, or γ-Aminobutyric acid [72]. GABA’s main role in the human nervous system is reducing neuronal excitability in the central nervous system [72]. Massive, intricately branching, flat dendritic trees are what distinguish Purkinje fibers, which have the capacity to process substantial amounts of information and learn by remodeling their dendrites [73]. Both the brain and other parts of the body, such as the heart, include these kinds of cells. A single long axon fiber from a Purkinje fiber also creates an inhibitory projection that travels to the cerebellar nuclei [73]. In the cerebellar cortex, the dendritic Purkinje fibers' plane is parallel to the tissue folds [73]. Parallel fibers pass through the distal dendritic trees of many Purkinje cells, forming weak synapses [73]. There are a few hundred synapses made by a single fiber, known as a climbing fiber, which connect to the soma and proximal dendrites [73]. The ten or so axons from an inferior olivary cell that make up a climbing fiber mean that different Purkinje fibers receive the same input [73]. The Purkinje cells' bodies make up the middle layer of the cerebellar cortex's three layers, whereas some inhibitory cells, such as basket cells, and their dendritic trees with parallel fibers make up the outer molecular layer [73].
In particular, the capacity to fine-tune and rectify a movement that is already underway is facilitated by the Purkinje tract in the brain [73]. The dendritic trees of the Purkinje fibers are thought to be critical to this process [73]. This is explained by the fact that complex inputs from parallel fibers are received by the dendritic trees and combined into a signal that depicts what the Purkinje cells believe the current motion should be [73]. It is thought that the ascending fibers are the biological counterpart of an error signal that can replace or modify the initial signal [73]. The total output is subsequently sent to the ventrolateral nucleus of the thalamus through the deep cerebellar nuclei, where it feeds into the motor cortex's ongoing operations and ideally smooths out any motion errors [73]. The outputs of Purkinje cell travel to various regions of the motor cortex, and signals from parallel and climbing fibers travel to regions of the cortex that overlap [73]. As a result, both the cerebellum and the cerebrum include sizable portions of the information contained in this circuit [73].

Throughout their lifespan, Purkinje cells continue to go through the long-term potentiation and depression processes that help create their dendritic trees [73]. As the relationship between the inputs and the Purkinje cell's impact on motor activity grows more precise over time, this process aids in motor coordination [73]. Injuries to the cerebellum typically result in motor coordination issues, such as ataxia without loss of strength [73]. Purkinje fiber tracts have also been associated with autism and Alzheimer’s disease [71]. Additionally, injury may cause the white matter volume to decrease, axonal pathways to become disrupted, surrounding mossy fibers to be harmed, and aberrant fibers to or from the cerebellum to exist [71].

2.2.13 Intracerebellar Parallel Tract and the Cerebellum

The intracerebellar parallel tract, like the intracerebellar input and Purkinje tract discussed in Section 2.2.12, is a cerebellum-based tract. This tract is shown in Figures 29a and 29b, and Figure 30 shows the location of the intracerebellar parallel tract in the Brain Axon Fiber Tract GHBMC Model.
Figure 29: Axial (A) and Coronal (B) Plane Images of the Cerebellum Showing Dendritic Tree Structure [74]

Figure 30: Location of the Intracerebellar Parallel Tract in the Brain Axon Fiber Tract GHBMC Model

The intracerebellar parallel tract and cerebellum are in charge of both motor and non-motor processes [74]. This tract oversees maintaining the posture of the antigravitational muscles, as well as controlling muscle tone and axial limb movements [74]. Additionally, this region has strong connections to the brainstem nuclei and vestibular nuclei, enabling crucial head and eye movement coordination [74]. This region receives input from the brain via the pontine nuclei for non-motor processes [74]. Non-motor processes like
cognition, language, emotion processing and modulation are just a few examples of what this region of the brain controls [74]. Specific areas in this tract that process cognitive and emotional information have been discovered through functional MRI investigations [74]. The intracerebellar parallel tract is present in both the left and right hemispheres of the brain, and the portions of the tract present on either side are responsible for different processes [74]. For example, visuospatial abilities appear to be more lateralized to the left cerebellar hemisphere, as opposed to language, which is lateralized to the right posterior hemisphere [74].

2.2.14 Inferior Frontal-Occipito Fasciculus

The inferior frontal-occipito fasciculus (IFOF), also known as the inferior occipito-frontal fasciculus, is a large white matter tract located in the cerebrum [75]. It is located through the center of the brain, medially to the ILF [60]. The IFOF on a population-averaged template is shown in Figure 31, and in the Brain Axon Fiber Tract GHBMC Model in Figure 32.

![Image of brain showing IFOF](image.png)

Figure 31: Tractography Showing the IFOF on a Population-averaged Template [33]
The IFOF plays a critical role in semantic language processing, goal-oriented behaviour and visual switching tasks [75]. Given its breadth and vast coverage, it is also possible that the IFOF participates in additional functional networks inside the human cerebrum [75]. The IFOF connects the frontal eye fields, ventrolateral and dorsolateral prefrontal cortex, posterior temporal cortex and the occipital lobes [60]. The fusiform gyrus is a portion of the link to the occipital lobes, whereas the middle and inferior gyri are a part of the connection to the posterior temporal cortex [60]. Both frontal and parieto-occipital connections of the IFOF are complex as they fan out to reach different areas [60]. The IFOF is divided into five subdivisions, frequently labelled I to V [60], [76].

The IFOF-I refers to the polar part of the frontal lobes, and approximately corresponds to Brodmann area 10 [76]. Numerous facets of complex cognitive processes, including social cognition, attention, multitasking and episodic memory, are connected to it [76]. Additionally, it has been hypothesized that Brodmann area 10's white matter connections may have a significant impact on modern human cognitively distinctive functions; however, this has to be proven with further research [76].

Damage or developmental differences to the part of the IFOF labelled as the IFOF-II is linked to obsessive compulsive disorder (OCD) [76]. In a study by Garibotto et al.
(2010), patterns of directionality and organization of the major fiber bundles in 15 OCD patients were studied, and significant changes were revealed in the anatomical connectivity of the orbito-frontal cortex of the frontal lobes with the parietal and occipital cortices along the IFOF-II [77]. White matter tracts linking with the frontal lobes have been linked to cognitive impairments in OCD patients, including a lack of cognitive-behavioural flexibility, executive function deficiencies and changes in decision-making [76].

The fibers of the IFOF-III run through the extreme capsule and the external capsule. The IFOF-III is important as it is the main structural pathway for semantic processing of language [76]. Studies on the neural connection of semantic memory have revealed that the inferior frontal gyrus, the posterior lateral temporal region, the anterior temporal cortex and the temporo-parietal junction make up a distributed left-lateralized association [76]. The IFOF-III also functions as an independent second fiber link for the language network in the brain and as a ventral stream that connects the occipital, parietal and posterior temporal regions to Broca's area [76].

The superior frontal gyrus and the middle frontal gyrus components of the IFOF, making up the IFOF-IV and IFOF-V, are not always included as parts of the IFOF in studies [76]. The IFOF-IV and the IFOF-V may take part in the semantic processing of language, visual conceptualization and recognition [76]. It should be noted that further clinical analysis will be needed to confirm this hypothesis [76].

The IFOF is also responsible connecting the temporo-parieto-occipital cortex to the prefrontal cortex [76]. The parieto-occipital junction, intraparietal sulcus, angular gyrus, Wernicke's area on the caudal superior temporal gyrus, superior temporal sulcus and middle temporo-occipital gyrus are all included in the multimodal region known as the temporo-parieto-occipital cortex [76]. This connection provides a link between the multimodal association cortex, the frontal eye fields and the prefrontal cortex [76].

The IFOF allows for higher visual processing via the ventral processing stream which connects the more lateral and ventral occipitotemporal areas with the frontal areas to
facilitate recognition of objects, places, colours, faces and words [60]. It is also associated with ventral language semantic pathways [60].

Isolated lesions of the IFOF are rare, as most commonly lesions to the IFOF occur simultaneously with other tracts due to its centralized position within the brain [60]. Associated lesions in the occipitoparietal (also known as the dorsal stream) and the occipitotemporal lobes (also known as the ventral stream) may cause deficits in visuospatial processing including oculomotor apraxia, optic ataxia and akinetopsia [60]. Oculomotor apraxia refers to the loss of volitional saccades, usually accompanied by lesions in the posterior parietal lobes [60]. Optic ataxia refers to diseases like Balint syndrome that make it difficult to reach for items correctly utilizing vision input [60]. The term "akinetopsia" describes a lack of motion perception [60]. Additionally, there may be a problem with spatial relations due to trouble judging depth, size, orientation and shape [60]. Visual agnosia and poor visual memory are usually associated with ventral occipitotemporal stream lesions, including topographagnosia. Topographagnosia refers to the inability to remember places and previous routes [60]. Lesions in the right IFOF are also associated with nonverbal semantic deficits, although the integrity of both right and left IFOF is important in the ventral semantic processing [60]. Damage to the left IFOF has been reported in aphasia [60]. Aphasia is a kind of language disorder, which is defined by damage in areas of the brain that control language expression and comprehension [60].

2.2.15 Middle Cerebellar Peduncle

The middle cerebellar peduncle is a paired axon fiber tract that contains afferent white matter projection fibers [78], [79]. It is also known as the brachium pontis [78]. Figure 33 shows the location of the paired middle cerebellar peduncles, and Figure 34 shows the location of the middle cerebellar peduncle tract in the Brain Axon Fiber Tract GHBMC Model.
Figure 33: Anatomy of the Middle Cerebellar Peduncles. Figure 33A Shows the Pontine Crossing Fibers (Red and Pink Long Arrows) Originating from the Contralateral Pontine Nuclei and Conforming the Middle Cerebellar Peduncles [80]. Figures 33B and C Show Diffusion Tensor Imaging Tractography of the Bilateral Transverse and Sagittal Middle Cerebellar Peduncles, respectively [80].

Figure 34: Location of the Middle Cerebellar Peduncle in the Brain Axon Fiber Tract GHBMC Model

The middle cerebellar peduncle is the largest afferent system of the cerebellum [81]. Its white matter projection fibers primarily consist of pontocerebellar tract fibers originating and coming from the contralateral pontine nuclei [81]. The fibers of the middle cerebellar peduncle connect the pons to the cerebellum [82]. Additionally, the middle cerebellar peduncle contains an intracerebellar segment known as the middle cerebellar peduncle.
radiation and a cisternal segment [82]. The rostral and lateral surfaces of the peduncle's first half are included in this cisternal segment, which begins lateral to the approximate origin of the trigeminal nerve (cranial nerve V) [82]. The middle cerebellar peduncle's rostral surface runs in the cerebellomesencephalic fissure, where it serves as the lateral portion of the fissure's inner wall [82]. The posterior and anterior walls of the inner aspect of the fissure are made up, respectively, of the lingula and the dorsal surface of the superior cerebellar peduncles [82]. Between the two limbs of the V-shaped cerebellopontine fissure is the lateral surface of the middle cerebellar peduncle [82]. The pontocerebellar fibers that limit the cerebellar lobules that contain the cerebellomesencephalic and pontocerebellar fissures are where the intracerebellar segment begins [82]. The middle cerebellar peduncle connects and enters the cerebellum on the lateral side of the large peduncolar mass, which is formed by the three cerebellar peduncles that connect the brainstem and cerebellum [82].

Damage in the middle cerebellar peduncle can cause a variety of symptoms and conditions [82]. On the side where the lesion is, ataxia, hypotonia and dysmetria may result from lesions of the middle cerebellar peduncle [82]. Ataxia from the middle cerebellar peduncle may cause issues with coordination, balance and speech [82]. Hypotonia refers to decreased muscle tone, which is tied to motor issues and issues with effective speech [82]. The inability to manage distance, speed and the range of motion required to carry out smoothly coordinated movements can be brought on by dysmetria from the middle cerebellar peduncle [82]. When the inferior cerebellar peduncle, a subcomponent of the middle cerebellar peduncle, is injured, individuals may experience symptoms like truncal ataxia, stumbling gait and a propensity to fall to the side of the lesion [82]. Truncal ataxia is a movement disorder characterized by erratic starts and pauses, side deviations and unevenly spaced or lengthened steps. These signs and symptoms, which include momentary disequilibrium, or unsteadiness or imbalance, are comparable to those brought on by damaged-induced lesions of the flocculonodular lobes [82]. Even though the dentate nucleus is close by and is typically not regarded as a component of the middle cerebellar peduncle, it does wrap around that area of the brain [82]. If the dentate nucleus is damaged, equilibrium disturbances, intention tremor,
dyskinesia and dystonia can occur [82]. Intention tremor is characterized by involuntary or rhythmic muscle contractions or oscillations that occur during purposeful, voluntary movement. Dyskinesia episodes are involuntary or erratic writing movements in the legs, arms, face or trunk, whereas dystonia is a disorder that is characterized by involuntary muscle contractions that cause slow repetitive movements or abnormal postures. Lesions and damage of another subsection of the middle cerebellar peduncle, called the superior cerebellar peduncle, induce similar symptoms, although they are usually mild and transient in case of partial sectioning of the peduncle [82]. Overall damage or general deterioration to the middle cerebellar peduncle may also cause difficulty walking and speaking clearly, vertigo or facial weakness [79].

2.2.16 Middle Longitudinal Fasciculus

The middle longitudinal fasciculus (MdLF) is a lengthy associative white matter subcortical axon pathway which connects the superior temporal gyrus to the angular gyrus [83], [84]. A reconstruction of the MdLF is shown in Figure 35, and Figure 36 shows its location in the Brain Axon Fiber Tract GHBMC Model.
Figure 35: Reconstruction of the Left and Right MdLF based on the Fractional Anisotropy Colour-coding System (Left and Right Panel) and Projection of the Reconstructed Tracts on Anatomical 3-D Tensor Imaging (Middle Panel): Axial (Upper Left), Coronal (Upper Right) and Sagittal (Bottom) Planes [84]

Figure 36: Location of the Middle Longitudinal Fasciculus in the Brain Axon Fiber Tract GHBMC Model

There has been significant debate in the neuroscience research community about the MdLF's role in the brain as neither electrical stimulation trials during awake surgery nor
lesion models like post-operative bundle resection have produced any conclusive findings [83]. The MdLF has been strongly linked to involvement in language, attention or auditory functions [83]. The MdLF and its sub-segments appear to be the closest white matter pathways to the primary auditory cortex and acoustic radiations from an anatomical perspective [83].

The MdLF participates in both dorsal and ventral routes involved in language processing [85]. The dorsal route is composed of the SLF-III, the arcuate fasciculus and the MdLF [85]. Pseudoword repetition contrasted with real word repetition indicates activations in the dorsal premotor cortex, inferior frontal gyrus and anterior section of the superior temporal gyrus [85]. The MdLF connects these areas via entering the arcuate fasciculus in the superior temporal gyrus's posterior region. The arcuate fasciculus then passes through the parietal lobes’ white matter and arrives at the premotor cortex [85]. The ventral route is associated with sentence comprehension [85]. It is made up of the MdLF, the extreme capsule and the inferior parietal lobule [85].

It is believed that auditory function is divided into parallel streams that encode auditory information such as the "what" (occurring in the ventral stream) and the "where," the "when", and the "how" (occurring in the dorsal stream) [83], [84]. These parallel streams are structured at the level of the superior temporal gyrus [83], [84]. The MdLF fibers that encircle these regions may facilitate the exchange of auditory information with the superior parietal lobule and superior lateral occipital cortex [83], [84].

The posterior-MdLF may also be related to the encoding of the “where” and the “what” in terms of auditory information [83], [84]. In order to decode the direction of sound-source movements, it has been demonstrated that the posterior auditory belt, which is located at the planum temporale, functionally correlates with the lateral occipital cortex [83]. This plays an important role in supporting auditory motion perception, particularly in the right hemisphere of the brain [83]. Additionally, the anatomical connection between the posterior segment of the MdLF and the acoustic radiation in the temporal lobes, as well as the terminations of the posterior segment of the MdLF, arcuate fasciculus, SLF and IFOF within the parieto-occipital areas, raise the possibility that the
posterior segment of the MdLF plays a role in the processing of auditory information [83]. Therefore, the posterior segment of the MdLF may also be involved in the learning of the verbal stimuli [83].

Connections in the MdLF between the superior temporal gyrus and parietal lobes suggests that the MdLF has a role in facilitating speech processing, possibly through changes in attentional biases [83].

The strong connection between both primary and secondary auditory areas in the superior temporal gyrus and secondary visual areas in the occipital lobes also support that the MdLF has a role in visual-auditory integration processes [83].

It is believed that the anterior region of the secondary auditory cortex processes the characteristics of an auditory object that are independent of either spatial position or attention, including the anterior superior temporal gyrus and planum polare [83]. The successful encoding of cross-modal associations between common auditory and visual objects involves higher-order occipital and temporal cortices [83]. Congruent memory traces are mostly produced by the lateral occipital cortex, whereas incongruent memory traces are primarily produced by the superior temporal gyrus and superior temporal sulcus [83]. It is hypothesized that this network between the visual ventral network and the auditory cortices is crucial for memory-dependent perceptual representations of the auditory world [83].

The lateral occipital cortex may be an important hub common to each of the MdLF sections in each hemisphere of the brain [83]. A potential essential site for the storage of multisensory memory representations with semantically congruent elements has recently been discovered in this significant region [83]. It has also been demonstrated that the activation of the lateral occipital cortex contributes to the development of perceptual cross-modal associations, which are necessary to produce congruent audio-verbal memories [83].

The higher-order occipital cortex and the lateral temporal cortex, respectively, have been proposed to encode the predominantly perceptual links in congruent memories and the
mainly conceptual relationships in incongruent memories [83]. In this network, the antero-ventral portion of the MdLF may be essential for the retrieval of memories that are coherent and have previously been organized into categories linked with visual information [83].

2.2.17 Frontostriatal Tract

The frontostriatal tract, also known as the frontal-striatal tract or the striato-frontal tract, is a series of five key neural pathways that connect regions in the frontal lobes with the basal ganglia and striatum. The frontal-striatal tract is shown in red and green in Figure 37, and in the Brain Axon Fiber Tract GHBMC Model in Figure 38.

**Figure 37:** Coronal (C) and Sagittal (B) Plane Rendering of the Superior and Inferior Frontostriatal Tracts Generated from Probabilistic Diffusion Tensor Atlas [86]
The frontostriatal tract consists of five major routes that leave the prefrontal cortex, pass via the globus pallidus and substantia nigra, go to the striatum, and then link to the thalamus [87]. There is a closed loop link that travels back to the frontal cortex [87]. There are also open loop connections that are projections to and from other cortical and subcortical structures [87]. These projections that travel from cortex to subcortical structures are progressively connected to smaller areas as they continue [87]. It is consistent with their functional segregation that each of the biological circuits that make up the frontostriatal tract has been preserved as a mostly distinct anatomical structure. This implies that each tract addresses a function on its own [87].

Within each biological circuit, there are two component pathways [87]. The first component pathway is a direct connection that exists between the striatum and the globus pallidus interna/substantia nigra complex [87]. The second pathway connects the striatum to the globus pallidus externa, then to the subthalamic nucleus and back to the globus pallidus interna/substantia nigra [87]. It is an indirect pathway [87]. Both direct and indirect biological circuits control and direct input to the thalamus [87]. Direct and indirect pathways control circuit activities in response to different inputs [87]. Both sets of pathways in the biological circuits are present in each hemisphere of the brain [87].
These five biological circuits are the motor circuit, the oculomotor circuit, the dorsolateral prefrontal circuit, the lateral orbitofrontal circuit and the anterior cingulate circuit [87].

The motor circuit originates from axons in the SMA, premotor cortex, motor cortex and somatosensory cortex [87]. These areas project to the putamen in a topographical pattern [87]. The putamen in turn projects to specific portions of the globus pallidus externa, interna and substantia nigra pars reticularis [87]. The centromedian, ventral anterior and ventrolateral thalamic nuclei, which project back to the motor cortex, are connected to the globus pallidus [87].

The oculomotor biological circuit originates in the frontal eye field (Brodmann area 8) and posterior parietal cortex [87]. The caudate nucleus body, dorsomedial globus pallidus and ventrolateral substantia nigra are the next destinations for these fibers [87]. The fibers reach the mediodorsal thalamic nuclei and subsequently terminate the closed loop by projecting back to the frontal eye field [87].

The dorsolateral prefrontal biological circuit begins in Brodmann areas 9 and 10, on the lateral surface of the anterior frontal lobes [87]. This biological circuit projects to the dorsolateral head of the caudate nucleus [87]. As the direct channel, axons extend from this place to the lateral section of the mediodorsal globus pallidus interna and the rostrolateral substantia nigra pars reticulata [87]. The fibers from the basal ganglia travel to parvocellular portions of the ventral anterior and mediodorsal thalamus [87]. The purpose of the mediodorsal thalamus is to route fibers back to the origin of the biological circuit in the dorsolateral frontal cortex [87].

The lateral orbitofrontal circuit starts in Brodmann areas 10 and 11 and sends fibers to the ventromedial caudate nucleus [87]. This area of the caudate connects axons to the rostromedial substantia nigra pars reticulata and the middle section of the mediodorsal globus pallidus interna [87]. The ventral anterior and mediodorsal thalamus are connected by fibers from the substantia nigra and the globus pallidus [87]. Fibers from the thalamus that extend back to the orbitofrontal cortex then close the circuit [87]. The rectus gyrus
and the medial orbital gyrus of Brodmann area 11 are the origins of a medial split of the orbitofrontal circuit [87]. The projections travel to the medial ventral pallidum, medial portions of the accumbens and the mediodorsal thalamic nucleus [87].

The anterior cingulate circuit starts in the anterior cingulate cortex (Brodmann area 24) [87]. The ventral striatum, which contains the nucleus accumbens, ventral putamen, ventromedial caudate and olfactory tubercle, is where the axons are projected [87]. This region is known as the limbic striatum [87]. The rostromedial globus pallidus interna, ventral pallidum and rostroventral substantia nigra receive projections from the ventral striatum [87]. The ventral pallidum links to the ventral anterior nucleus of the thalamus [87]. Projections from the ventral anterior thalamus back to the anterior cingulate cortex complete the anterior cingulate biological circuit [87]. Limbic system connections involve both the anterior cingulate and medial frontal regions [87].

Abnormal thalamic inhibition can result from dysfunction in the direct circuit portion of each of these biological circuits [88]. Dysfunction in the indirect circuit portion leads to disinhibition and thalamic overactivity [88]. The frontostriatal circuit's function is still not completely understood, but it may be critical for habit development, action selection or reinforcement learning, motor learning and sequential motor control and the execution of well-learned automated motor plans [88]. Damage is also associated with cognitive impairments, visuospatial processing, executive functioning and motor speed [88]. Long term disorders attributed to the damage within the frontostriatal system include schizophrenia, impulsive disorders, drug addiction, Parkinson’s disease and Tourette’s syndrome [88].

2.2.18 Superior Longitudinal Fasciculus

The SLF is a vast bundle of white matter tracts that is present in each of the cerebral hemispheres in the brain. It connects the parietal, occipital and temporal lobes with the ipsilateral frontal cortices. This tract is shown in the sketches in Figure 39, and in the Brain Axon Fiber Tract GHBMC Model in Figure 40.
The SLF is made up of four main subcomponents, labelled I to IV [60]. The horizontal fibers that connect the superior parietal lobes to the frontal and opercular areas are labelled the SLF-I [60]. The fibers that connect the angular gyrus to the superior parietal lobes are designated SLF-II [60]. The fibers that connect the superior parietal lobes to the supramarginal gyrus are designated the SLF-III [60]. The fibers sometimes denoted the
SLF-IV connect the superior parietal lobes to the superior temporal gyrus and are frequently referred to as the arcuate fasciculus (see Section 2.2.1) [60]. This is the bundle that connects the superior temporal gyrus and the ventrolateral prefrontal cortex together [60].

The SLF facilitates the structure and function of a bi-directional biological neural network that is needed for several important cognitive processes [60]. These include attention, memory, emotions and language [60]. The SLF links frontal brain regions that control cognitive activities like attention and working memory with higher and lower order audio processing [60].

Functional deficits due to damage in the SLF depend heavily on which part of the SLF is damaged, as it is a large tract that connects several areas of the brain [89]. Damage to the SLF in the left hemisphere can cause language disorders such as impaired repetition, fluent aphasia, anomia and speech arrest [89]. Fluent aphasia, also known as Wernicke aphasia or receptive aphasia, is a communication disorder that causes people to say phrases that sound fluent but lack any meaning. Anomia refers to the inability to name objects. Speech arrest is defined as the complete stoppage or interruption of number counting or continuous speech while talking, characterized by no jaw, facial, tongue or oral movements. This condition is a primary manifestation of partial seizure disorder. Damage to the SLF in the right hemisphere may result in spatial-attention network deficits such as left hemi-spatial neglect [89]. Ideational apraxia, defined as the inability to execute a sequence of actions in a complex learned motor acts despite understanding verbal commands, is thought to occur due to SLF damage in the region beneath the supramarginal gyrus of either parietal lobes [89]. Depressive disorder can result from lesions in the SLF in the insular region [89].

Damage to the SLF was found to cause difficulty in writing and picture correspondence, sentence writing, skillful movement of the hand and calculation [89]. Since the frontal lobes’ motor region controls writing, memories of written words may travel through the white matter pathways, including the SLF, from the temporal lobes to the frontal lobes of the hand area [89]. Dysgraphia could develop from damage to the SLF in the inferior
parietal lobes, which would prevent word pictures from being sent from the posterior inferior temporal lobes to the parietal or frontal lobes [89]. Dysgraphia is a condition defined by impaired letter writing by hand [89]. This relation suggests that the left SLF-pathways are closely associated with writing [89].

2.2.19 Thalamo-Frontal Tract

The thalamo-frontal tract is the axon fiber tract which receives output from the basal ganglia and the cerebellum, forming a pathway with a bidirectional connection to the frontal cortex [90]. An MRI image of a representative patient’s brain with the location of the thalamo-frontal tract in the human brain is shown in Figure 41, and the location of the thalamo-frontal tract in the Brain Axon Fiber Tract GHBMC Model is shown in Figure 42.

Figure 41: Location of the Thalamo-frontal Tact in the Human Brain in Different Planes: Axial (a), Coronal (b), and Sagittal (c) [91]
The thalamo-frontal tract is responsible for the control and execution of two major functions in the brain: language and executive function. With regards to language, this tract involves a large number of cortical areas and subcortical structures [90]. Strain-induced or other types of damage that occurs in the ventral lateral, ventral anterior, intralaminar and mediodorsal thalamic nuclei consistently leads to language disturbances [90]. The thalamo-frontal tract controls language and is adversely affected by damage to the frontal cortex, basal ganglia or cerebellum, which are all involved in language processing in the brain [90]. The thalamo-frontal tract contains thalamic nuclei that connect to the frontal cortex and receive the basal ganglia and cerebellum's output [90].

The thalamic reticular nucleus, which mediates the quick and early processing inhibitory system, and the chemical messenger dopamine, whose precise control is crucial for cognitive functions, monitor this bi-directional circuit [90]. The lateral frontal cortex also includes Broca’s area, which is associated with language [90]. Broca’s area (Brodmann areas 44 and 45) is also directly involved in speech production. During silent speech, Broca’s area 44 is also active [90].

There are certain premotor cortices that are connected to the thalamo-frontal tract and are related to language [90]. An example of these areas includes Brodmann area 6 in the
brain, which is found behind and largely dorsal to Brodmann areas 44 and 45 [90]. At its most dorsal extent, Brodmann area 6 gives way to the SMA [90]. The SMA is situated within the dorsal and medial part of Brodmann area 6 [90]. The cingulate motor areas are located on the cingulate gyrus below the SMA [90]. An important area found below and anterior to the medial premotor cortices is the anterior cingulate cortex [90]. The allocation of attentional resources and vocalization within an emotional context are both crucial processes for language, and both depend on the anterior cingulate cortex [90].

Dorsolateral prefrontal regions (Brodmann areas 46 and 9) are located in front of and above lateral Brodmann areas 44 and 45. They play complementary roles in cognitive processes and are important for linguistic tasks that require retaining information in working memory [90]. Through corticocortical connections and shared nuclei in the thalamus, Brodmann areas 46 and 9 and the anterior cingulate cortex have substantial connections with nearby premotor cortices, particularly the dorsal and medial areas [90]. These prefrontal and premotor cortices’ major thalamic nuclei are closely connected to the basal ganglia, and the cerebellum's output is distributed throughout these nuclei at various locations [90]. This occurs all within the thalamo-frontal tract [90]. The thalamo-frontal tract language route is intricate and complex, and injury caused by strain or other factors to any part of these regions may have a range of effects on language. The link between a damaged thalamo-frontal tract and surrounding regions and executive dysfunction was evaluated in Pulsipher et al. (2009) [92]. Twenty children with juvenile myoclonic epilepsy were evaluated compared to control groups using quantitative MRI and measures of executive abilities through tests such as the Delis-Kaplan Executive Function System and the Behavior Rating Inventory of Executive Function [92]. The results of this study showed that children with developmental damage to their thalamo-frontal area led to executive dysfunction [92]. In the evaluation completed, the test group did not perform with purposeful, goal-directed activities and were not able to synthesize information as well as the control group [92]. They struggled with skills such as the planning and execution of strategies [92]. Damage to the thalamo-frontal tract has also been linked to issues with concept formation, abstract reasoning, mental flexibility and cognitive speed [92].
2.2.20 Thalamo-Occipital Tract

The thalamo-occipital tract encompasses the thalamo-occipital pathway and is the primary axon fiber tract that connects the thalamus to the occipital lobes [93]. An MRI image of a representative patient’s brain with the location of the thalamo-occipital tract in the human brain is shown in Figure 43, and the location of the thalamo-occipital tract in the Brain Axon Fiber Tract GHBMC Model is shown in Figure 44.

Figure 43: Location of the Thalamo-occipital Tract in the Human Brain in Different Planes: Axial (Left), Coronal (Center) and Sagittal (Right) [91]

Figure 44: Location of the Thalamo-occipital Tract in the Brain Axon Fiber Tract GHBMC Model
The thalamus, one end of the thalamo-occipital tract, is an important relay that receives signals and pulses from receptors in different sensory organs and sends signals or pulses away from the central nervous system to the primary sensory cortex [93]. The main sensory cortex receives sensory data from the peripheral sensory receptors through the thalamic nuclei under normal circumstances [93]. The lateral geniculate nucleus, sometimes referred to as the "visual" thalamic relay, is one instance of this information transfer [93]. It primarily transmits visual signals to the primary visual cortex [93]. Another portion of this tract is the medial geniculate nucleus, which serves as a link between the inferior colliculus and the primary auditory cortex [93]. It is the "auditory" thalamic relay [93]. The connection between the ventral posterior nuclei, the "somatosensory" thalamic relay that receives tactile signals and sends them to the primary somatosensory cortex, is a third example of signal transfer in the tract [93].

The transmission of feedback signals between the thalamus and the sensory cortex or the association cortex via the thalamo-occipital tract also enables the regulation of input signals [93]. It is hypothesized in Qin et al. (2013) that non-visual signals may bypass their traditional sensory pathway and get biologically rewired into the “visual” thalamus and end up travelling to the primary visual cortex [93].

Studies completed in animals have shown that the thalamo-occipital tract may also be able to carry auditory inputs if the brain is deprived of peripheral visual input at an early age [93]. Tactile and auditory inputs may also be conveyed to the visual cortex via the thalamo-occipital tract. This has been confirmed in normal adult animals and humans through studies [93].

The thalamo-occipital tract is also a key component in a possible link between isolated rapid eye movement (REM), sleep behaviour disorder (iRBD), cognitive impairments and chronic traumatic encephalopathy (CTE). Probable rapid eye movement sleep behaviour disorder (pRBD) is a parasomnia linked to synucleinopathy in which the absence of REM sleep muscle atonia causes motor activity during REM sleep, including dream enactment [94]. mTBIs are associated with an increased risk of pRBD [94]. Furthermore, pRBD is often observed in CTE, as outlined in the study conducted by Adams et al. (2020) [94].
Byun et al. (2020) conducted a study that investigated whether the thalamo-occipital tract functional connectivity was at all correlated to higher levels of cognitive dysfunction in patients with iRBD using resting-state functional MRI [95]. Thirty-seven patients with iRBD underwent resting-state MRIs and a comprehensive neuropsychological assessment [95]. Functional connectivity in the thalamus and occipital regions was evaluated using seed-to-voxel analysis comparing test patients to control patients [95]. Patients with iRBD were found to have cognitive decline in constructional recall and word list recognition [95]. There was increased functional connectivity between the thalamus and occipital regions, meaning increased activity within the thalamo-occipital tract [95]. Enhancement of the activity in the thalamo-occipital tract functional connectivity levels may reflect a compensatory mechanism for cognitive impairment in iRBD [95]. In summary, patients with REM sleep behaviour disorders or related conditions and increased levels of thalamo-occipital tract activity may develop CTE later in their lives [95].

2.2.21 Thalamo-Parietal Tract

The thalamo-parietal tract is the main axon fiber tract that connects the thalamus and the parietal lobes of the brain. An MRI image of a representative patient’s brain is shown in Figure 45, and the location of the tract in the Brain Axon Fiber Tract GHBMC Model is shown in Figure 46.

Figure 45: Location of the Thalamo-parietal Tract in the Human Brain in Different Planes: Axial (Left), Coronal (Center) and Sagittal (Right) [91]
The thalamus is a major area for corticosubcortical connectivity from the parietal lobes [96]. The thalamo-parietal tract primarily connects the dorso-lateral nuclei to the posterior associative cortex [96]. It was shown in vivo in Behrens et al. (2003) and Traynor et al. (2010) that within the thalamus there is an area that corresponds to the lateral posterior nucleus and the anterior and lateral pulvinar, which is the most prominent target for posterior parietal areas [97], [98]. The anterior parietal somatosensory regions are mostly connected to a zone ventrolateral to this area, notably the region that contains the ventral posterolateral and ventral posterior nuclei [96]. This was originally described in a study involving monkeys, particularly for Brodmann areas 1 and 3b [96]. Additionally, Brodmann area 3a has a significant number of connections with thalamic nuclei associated with motor processing, such as the ventral lateral and the medial dorsal, as well as the intralaminar nuclei [96].

The thalamo-parietal tract is heavily connected and involved in central and pain relief [99]. Certain injuries in the parietal lobes have been discovered to temporarily change the equilibrium of the bilateral biological thalamo-parietal circuits in the brain and may even fully eliminate central pain by affecting the output to the anterior cingulate cortex [99].
Additionally, there are instances that show how some lesions that impact the bilateral balance of the bidirectional biological thalamo-parietal circuits may relieve pain in people with thalamic central pain syndrome, which is most likely a bilateral functional plasticity disorder [99]. Thalamic central pain syndrome is caused when there are disruptions in the pathways that link the sensory cortex and the sensory thalamus, while functional plasticity is the brain's ability to move functions from a damaged area of the brain to other undamaged areas.

The thalamo-parietal tract has also been found to be important in working memory and the relaying of peripheral sensory information to the somatosensory cortex in the parietal lobes [100]. Symptoms of strain-induced or other types of damage include central imbalance, spontaneous pain or nociception and central disinhibition [99], [100].

2.2.22 Uncinate Fasciculus

The uncinate fasciculus is a bidirectional, long-range white matter tract that connects the lateral orbitofrontal cortex and Brodmann area 10 with the anterior temporal lobes [101]. A sketch of the uncinate fasciculus on the lateral surface of the left cerebral hemisphere is shown in Figure 47, and in the Brain Axon Fiber Tract GHBMC Model in Figure 48.

Figure 47: Location of the Uncinate Fasciculus on the Lateral Surface of Left Cerebral Hemisphere [49]
In the inferolateral frontal lobes, the uncinate fasciculus is located inferior to the IFOF and wraps around and into the anterior pole of the temporal lobes [60]. It also provides fibers to the parahippocampal gyrus, the uncus and the amygdala [60]. It is larger in the right hemisphere, indicating greater right-sided fronto-temporal connectivity [60]. The uncinate fasciculus' fibers arch forward medially to the insula and laterally to the lenticular nucleus as it enters the external capsule [60]. The uncinate fasciculus is traditionally broken into three parts. The first is a dorsal or temporal segment, the second is a middle or insular segment, and the third is a ventral or frontal extension segment [101].

The UF is involved with retrieval of past information, both semantic and episodic memory [60]. It is also important in encoding and storage of social and emotional concepts [60]. Damage to the right UF results in impaired retrieval of episodic memory including autobiographical and event-related memories, while damage to the left UF results in impaired retrieval of semantic memory including knowledge of concepts and facts [60]. Right UF damage also disrupts emotional empathy making patients apathic and indifferent to how other people feel [60].
The uncinate fasciculus is involved in several disorders, including anxiety, schizophrenia, psychopathy, epilepsy and frontotemporal dementia [101]. For anxiety, it was expected that the uncinate fasciculus, as a white matter tract that connects limbic regions to orbitofrontal cortices, would be structurally impaired in anxiety disorders [101]. However, in a review of existing Diffuse Tensor Imaging (DTI) literature, it was found the uncinate fasciculus plays either a small or non-existent role in anxiety disorders [101]. For schizophrenia, the results of the conducted literature review on relevant DTI studies measuring changes in uncinate fractional anisotropy values in schizophrenics are contradictory [101]. It is hypothesized that dysfunction of the uncinate fasciculus correlates with specific symptoms of schizophrenia, including a lack of emotional expression and a lack of social engagement [101]. Craig et al. (2009) studied the relationship between uncinate fasciculus damage and psychopathy and antisocial personality disorder and found that the volume of the uncinate fasciculus tract had a negative correlation with antisocial behaviour [102]. Additionally, it was discovered that in comparison to control subjects, members of the antisocial personality disorder test group had dramatically increased mean diffusivity and decreased fractional anisotropy in their right uncinate fasciculus [102]. Temporal lobe epilepsy, especially in the left hemisphere, is strongly associated with decreased white matter integrity in the uncinate fasciculus [101]. Epilepsy literature also has suggested that the uncinate fasciculus may have non-mnemonic functions, as there is a subgroup of grand mal temporal lobe seizures known as “uncinate fits” [101]. These are named because the seizure focus is on the uncus, specifically on the medial surface of the anterior temporal lobes at the anterior end of the parahippocampal gyrus [101]. Uncinate fits are also associated with emotional and sexual arousal, olfactory and gustatory hallucinations, and involuntary movement of the face and mouth, including spitting, depressive symptoms and intense anxiety [101]. Lastly, frontotemporal dementias are not directly caused by uncinate fasciculus dysfunction, but early cell loss from this illness in the front temporal lobes and orbital regions of the frontal lobes is what causes uncinate fasciculus failure [101]. This condition has allowed researchers to clarify that the uncinate fasciculus is more linked to
semantic retrieval rather than speech output, and possibly social-emotional abnormalities [101].

The uncinate fasciculus also is connected to important roles in episodic memory, language retrieval and social-emotional processing, all of which can be affected by strain-based or other types of damage [101]. The creation of associations that motivate behaviour, learning through feedback, rewards and punishments, as well as value-based updating of stored representations, are all aspects of episodic memory to which the uncinate fasciculus contributes [101]. It is also connected to the encoding and consolidation of common episodic memories such as autobiographical memory [101]. The uncinate fasciculus has a variety of roles in language and language retrieval, including retrieving proper names for people, some semantic memory components and general linguistic abilities like speech production, speech comprehension, syntax and most semantic memory components [101]. It has also been connected specifically to face encoding and the naming of famous faces and objects [103], [104]. Finally, in terms of socio-emotional processing, the uncinate fasciculus oversees valuing stimuli, processing social rewards and the higher-level emotional meaning of concepts [101].

2.2.23 Lobes of the Human Brain

The frontal area of the human brain is called the cerebrum [105]. The cerebrum is broken into four major lobes, or divisions of tissue [105]. The cerebrum is shown in colour in Figure 49. The other areas of the brain, called the cerebellum and the brain stem, are also shown in black and white in Figure 49.
The cerebrum consists of two cerebral hemispheres. The outer of these two layers is called the cortex, and it is comprised of grey matter [105]. The second layer is called the inner layer, and it is comprised of white matter [105]. There are four lobes in the cortex, denoted the frontal lobes, the parietal lobes, the temporal lobes and the occipital lobes [105]. Each of these lobes contains axon fiber tracts which are represented in the Brain Axon Fiber Tract GHBMC Model. The following subsections will discuss each of these four lobes in detail.

### 2.2.23.1 Frontal Lobes

The frontal lobes are the largest of the four lobes and are located in front of the cerebral hemispheres, limited posteriorly by the central sulcus [105]. The frontal lobes are organized into five parallel biological circuits, each responsible for a different purpose [107]. These circuits include a motor circuit involving the SMA, an oculomotor circuit involving the frontal eye fields, and three cognitive and affective circuits, namely the dorsolateral prefrontal, lateral orbital and cingulate or medio-dorsal circuits [107]. Each of these circuits is made up of many parts, such as a section of the circuit that covers a particular frontal region, projections to the striatum, connections with the globus pallidum and substantia nigra, and a return link to the original frontal region via the
thalamus [107]. Strain-induced or other damaging lesions anywhere along the axis of any of the circuits produce distinct behavioural disorders associated with that circuit [107].

There are three main regions of the frontal lobes, denoted the motor, premotor and prefrontal regions [107]. The precentral gyrus, part of the primary motor cortex, is situated on the lateral portions of the frontal lobes between the central sulcus and the inferior and frontal sulci [108]. Medially, this cortex is contiguous with the paracentral lobule [108]. The precentral and postcentral gyri continue in the anterior part of the paracentral lobule [108]. This contains the SMA [108]. The precentral gyrus directs, regulates and coordinates motions on the contralateral side of the body [108]. The gyrus has a somatotopic organization, a sort of “cortical motor homunculus”, which succinctly portrays the functional representation of the parts of the body on the primary motor cortex [108].

The premotor cortex lies between the primary motor cortex and prefrontal cortex [108]. It extends onto the medial surface and is made up of the posterior portion of the superior, middle and inferior frontal gyri and the anterior portion of the precentral gyrus [108]. The premotor cortex collaborates with other areas to choose appropriate movements and is important in planning and carrying out limb movements [108]. The premotor cortex is crucial for social cognition, including empathy, as well as learning, particularly imitation-based learning [108].

The prefrontal cortex is a sizable, multimodal association area that controls higher cognitive skills like attention, working memory, prospective and temporal memory, behaviour planning, including the ability to make decisions and solve problems, movement programming, language and self-control [108]. The prefrontal cortex, also known as the lateral prefrontal and the orbitomedial prefrontal cortex, can be further divided into lateral and medial sections because of its size [108].

The lateral prefrontal cortex is divided into regions known as the dorsolateral prefrontal cortex (DLPFC) and the ventrolateral prefrontal cortex (VLPFC) [108]. The DLPFC
encompasses Brodmann areas 9 and 46, while the VLPFC encompasses Brodmann areas 44, 45 and 47 [108].

The DLPFC is the more dorsal component of the lateral prefrontal cortex, located in the anterior portion of the superior and middle frontal gyrus [108]. It is linked to the brain regions in charge of somatosensory and spatial information [108]. Working memory upkeep, attention, set-shifting, reward assessment and motor planning are among its core responsibilities [108]. While the DLPFC in the right hemisphere is crucial for verbal and spatial thinking as well as arithmetic reasoning, the DLPFC in the left hemisphere is crucial for developing verbal and spatial information in working memory [108].

The ventral lateral prefrontal cortex, or VLPFC, is the more ventral part of the lateral prefrontal cortex. It is situated above the medial orbitofrontal cortex and in the rostral part of the inferior frontal gyrus, laterally to the gyrus rectus [108]. The inferior frontal sulcus and the lateral sulcus separate the VLPFC superiorly and inferiorly, respectively [108]. It is active during motor inhibition and during orienting of attention [108]. While the right hemisphere's VLPFC is crucial for regulating motor responses and reflexive reorienting to rapid perceptual onsets, the left hemisphere's VLPFC is engaged in cognitive control to retrieve information from semantic memory [108].

The frontal operculum is a portion of the VLPFC located inferiorly to the DLPFC and the ventral portion of the premotor cortex [108]. The precentral operculum, the opercular part of the inferior frontal gyrus (also known as the pars opercularis), the triangular part of the inferior frontal gyrus (also known as the pars triangularis), and the orbital part of the inferior frontal gyrus are additional divisions of the frontal operculum [108]. The pars opercularis and pars triangularis contain Broca's area, or the union of Brodmann areas 44 and 45 [108]. Broca’s area is responsible for speech production, facial neuron control, and language processing [108]. Broca's area typically resides in the left hemisphere and regulates the motor motions necessary for speech production in right-handed people [108]. When people attempt to interpret ambiguous emotional expression in facial images, the corresponding area in the right hemisphere is active, and it oversees regulating the emotional overtone of the uttered words [108]. Both right and left
Brodmann areas 44 and 45 are active in the detection of errors in musical syntax [108]. Finally, Broca’s area may contain mirror neurons and have an important role in imitation [108].

The orbitomedial prefrontal cortex is divided into medial prefrontal cortex (MPFC) and the orbital prefrontal cortex (OPFC) [108]. The MPFC encompasses Brodmann areas 25 and 32, while the OPFC encompasses Brodmann areas 11, 12, 13 and 14 [108].

The medial prefrontal cortex is in the anterior cingulate gyrus and in the subcallosal area on the medial surface of the frontal lobes [108]. It plays a major role in emotional behaviour and the control of basic drives [108].

The anterior cingulate gyrus and the subcallosal region on the medial surface of the frontal lobes are where the medial prefrontal cortex is found [108]. The medial prefrontal cortex has direct connections with the cerebral structures of the limbic lobes [108]. The medial prefrontal cortex is crucial for the integration of sensory information, control of autonomic responses, learning, emotional and reward-related behaviour, as well as the pleasure of food [108].

The SMA is located primarily on the medial aspect of the superior frontal gyrus, anterior to the premotor cortex of the lower extremity, and above the cingulate sulcus [108]. On the lateral aspect of the superior frontal gyrus, it is located superior to the premotor area [108]. It is connected with the contralateral SMA through the corpus callosum [108]. The SMA is involved in the planning of complex movements as well as coordinating two-handed movements [108]. The portion of the SMA located on the medial surface of the superior frontal gyrus in the upper part of the paracentral sulcus is called the supplementary eye field [108]. The supplementary eye field is involved in the generation and control of eye movement together with the frontal eye field and the superior colliculus [108].

The frontal lobes are a complex network with many distinct areas and functions. This means that a wide variety of conditions and changes can occur if this area is damaged. A
non-exhaustive but detailed list of conditions that can result from strain-based damage or other types of damage to the frontal lobes is presented in Table 3 below.

**Table 3: Conditions or Changes Attributed to Damage in the Frontal Lobes [105], [107]–[112]**

<table>
<thead>
<tr>
<th>Abulia or decreased motor activity</th>
<th>Issues with remembering plans made (prospective memory)</th>
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</thead>
<tbody>
<tr>
<td>Akinetic mutism</td>
<td>Jocularity</td>
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<tr>
<td>Amotivation</td>
<td>Lack of ambition (apathy)</td>
</tr>
<tr>
<td>Amyotrophic lateral sclerosis (ALS)</td>
<td>Lack of foresight or insight</td>
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<tr>
<td>Anterior cingulate cortex syndrome</td>
<td>Lack of self-monitoring</td>
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<tr>
<td>Anterior opercular syndrome (Foix-Chavany-Marie syndrome)</td>
<td>Lack of sense of responsibility</td>
</tr>
<tr>
<td>Apathy</td>
<td>Medial frontal apathetic syndrome</td>
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<tr>
<td>Aspontaneity</td>
<td>Movement control issues</td>
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<tr>
<td>Attention deficit hyperactivity disorder (ADHD)</td>
<td>Obsessive-compulsive disorder</td>
</tr>
<tr>
<td>Broca’s aphasia</td>
<td>Orbitofrontal disinhibition syndrome</td>
</tr>
<tr>
<td>Concreteness</td>
<td>Parkinson's disease</td>
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<tr>
<td>CTE</td>
<td>Personality changes</td>
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<tr>
<td>Decision making deficiencies</td>
<td>Poor decision making/choices</td>
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<tr>
<td>Depression</td>
<td>Poor humor appreciation (caused by damage to the right hemisphere)</td>
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<tr>
<td>Design dysfluency (caused by damage to the right hemisphere)</td>
<td>Poor motor programming</td>
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<tr>
<td>Disinhibition</td>
<td>Poor planning skills</td>
</tr>
<tr>
<td>Distractibility</td>
<td>Poor problem-solving abilities</td>
</tr>
<tr>
<td>Distress</td>
<td>Poor task maintenance</td>
</tr>
<tr>
<td>Disturbed social behaviour</td>
<td>Reduced affect and mood swings</td>
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<tr>
<td>Dysexecutive syndrome</td>
<td>Rigidity</td>
</tr>
<tr>
<td>Emotional dysregulation</td>
<td>Sensitivity to interference</td>
</tr>
<tr>
<td>Euphoria/mania</td>
<td>Sexual disinhibition</td>
</tr>
<tr>
<td>Executive dysfunction and disturbances</td>
<td>Slowness</td>
</tr>
</tbody>
</table>
Hypo-emotionality/de-energization
Impaired generative cognition
Impaired set shifting (stuck-in set perseveration)
Impaired social judgement
Impersistance
Impulsiveness
Inability to switch from one task to another (perseveration)
Inappropriateness
Increased gambling or risk-taking behaviour
Irresponsibility

Social and moral reasoning impairment
Speech and language
Spontaneous recall poorer than recognition
Tactlessness
Theory of mind deficits
Transcortical motor aphasia (caused by damage to the left hemisphere)
Verbal dysfluency (caused by damage to the left hemisphere)
Verbal-action dissociation
Working memory deficits

2.2.23.2 Occipital Lobes

The occipital lobes are the posterior or rear-most of the four lobes in the human brain [110]. They are mostly engaged in the representation of visual information and higher-order processing of it, such as the abstraction of direction, motion, colour and depth information from visual inputs [108].

The primary visual cortex and the parastriate and peristriate sections, which together make up the visual association cortex, make up the majority of the occipital lobes [110]. The visual association cortex encompasses Brodmann area 17 [110]. In the cuneus and lingual gyrus, the main visual cortex is located on the banks of the calcarine sulcus. The lateral geniculate body of the thalamus provides inputs to the main visual cortex. Due to the "stria-like" myelin staining of the cortical layers, also known as the "Stria of Gennari," the primary visual cortex is also referred to as the striate cortex.

The superior cuneus, the inferior lingual gyrus, the lateral occipital gyrus and the superior occipital gyrus of the occipital lobes make up the visual association cortex [108]. The visual association cortex encompasses Brodmann areas 18 and 19 [113]. The cuneus lies above calcarine fissure on the medial surface of the occipital lobes [108]. The parieto-
occipital sulcus borders it anteriorly, and it frequently extends onto the posterior pole [108]. On the medial surface of the occipital lobes, between the calcarine sulcus and the posterior half of the collateral sulcus, the lingual gyrus is located beneath the calcarine fissure [108]. It continues on the occipital pole posteriorly, and anteriorly it joins the parahippocampal gyrus [108].

In the visual association cortex, visual information from the primary visual cortex divides into two separate visual pathways [108]. These pathways are denoted as the ventral stream and the dorsal stream [108].

The ventral stream is known as the “what” pathway, meaning this stream carries information about perceptual features [108]. This enables the development of long-term representations, which are essential for classifying and identifying forms and objects [108]. Through the ILF, this pathway connects the occipital lobes to the temporal lobes [108].

The dorsal stream is referred to as the "where" pathway because it facilitates the visual control of skilled activities and continuously processing information about objects and their locations [108]. This pathway provides for the recognition of objects in the environment because it links the primary visual cortex to the temporal lobes via the ILF [108].

The visual association cortex performs a variety of tasks, such as detecting light intensity, colour perception, identifying visual patterns (such as distance, depth, size and number), recognizing objects (such as shape or orientation), encoding words and faces and encoding visual-spatial information [108]. This cortex helps to assign meaning to what a person is seeing [108]. The visual association cortex may also play a role in generating or recalling dreams [108].

General symptoms of poor vision, trouble finding items in space or a propensity to bump into things are examples of signs of injury to the occipital lobes [113]. There are also specific symptoms and conditions that result from strain-induced or other damage that occurs in the occipital lobes. These are discussed below.
Cortical blindness is a term usually used to refer to the complete loss of vision due to bilateral occipital lobe lesions [113]. They may occur either consecutively or simultaneously [113]. The primary cause of this is hypoxia to the visual cortex [113].

Crossed quadrant hemianopsia occurs when there is a homonymous quadrantanopsia in diametrically opposed quadrants of the visual field [113]. It results from lesions of the superior and inferior banks of the calcarine sulcus, with each lesion occurring on a different side of the visual cortex [113]. It is sometimes referred to as a “checkerboard defect” [113].

Visual agnosia describes the inability to identify familiar objects by sight despite having normal visual acuity [113]. This phenomenon results from damage to the visual association cortex, as well as to the parietal and temporal lobes [113].

Prosopagnosia refers to the inability to recognize familiar faces [113]. It usually results from bilateral occipital lobe lesions [113]. It involves damage to the connections between the visual association and the temporal cortex [113]. The temporal cortex serves memory, so these lesions prevent visual perceptions from being stored in memory [113].

Colour agnosia is the ability to perceive colour, but the inability to give it a name [113]. It often occurs in association with alexia [113]. There is a disruption in the connection between the visual association cortex and the language center [113].

Alexia is a term which describes the inability to read despite having normal vision [113]. The left occipital lobe receives information from the right hemifield first before passing it on to the left (or dominant) angular gyrus in the parietal lobe, which is the route involved in reading [113]. The angular gyrus is concerned with the formation and interpretation of written words [113]. The left angular gyrus receives information from the left hemifield via the splenium of the corpus callosum, which is located in the right occipital lobe [113]. Damage to the left angular gyrus results in alexia with agraphia, a condition in which the patient can neither read nor write [113].
In the case of alexia without agraphia, the ability to write is preserved [113]. Therefore, the person can write but not read their own writing [113]. The primary left visual cortex and the connection fibers from the right occipital lobe that have crossed the corpus callosum are both disrupted because of a lesion in the left occipital lobe [113]. Due to the lesion in the left visual cortex, a right hemianopsia results [113]. The lesion in the region of the crossing fibers prevents visual information from reaching the angular gyrus even though there is vision in the left hemifield [113]. However, because the angular gyrus remains intact, the patient can still write [113].

Cerebral dyschromatopsia manifests as the ability to name colours, but the inability to perform colour vision tests such as pseudoisochromatic plates [113]. A contemporaneous bilateral superior homonymous hemianopsia is common, which points to injury to both occipital lobes' inferior regions [113]. Cerebral dyschromatopsia may also be found in patients with prosopagnosia since the relevant area of the occipital-temporal junction has been damaged [113].

Optic ataxia is characterized by an inability to locate objects in visual space [113]. These patients have difficulty when they attempt to reach for or point to a particular object. It may be limited to one side of the body or one hemifield. The area of damage lies between the occipital and parietal lobes [113].

Palinopsia refers to a condition in which images remain perceived that are no longer in view [113]. These images commonly occur only in the blind visual field [113]. They are typically paroxysmal and tend to occur in association with other neuro-ophthalmologic symptoms [113]. Parietal and occipital lobe lesions have been implicated [113].

2.2.23.3 Parietal Lobes

The parietal lobes are positioned above the temporal lobes, behind the frontal lobes and in front of the occipital lobes in the human brain [108]. The parietal lobe has three key functional areas [108]. These are the anterior area, the superior parietal cortex and the inferior parietal cortex [108]. The anterior area includes the primary somatosensory cortex and the parietal operculum, which are two regions primarily involved in...
perception and sensation [108]. The superior parietal cortex is responsible for integrating visual and sensory information to generate the perception of self [108]. The inferior parietal cortex is mostly involved in speech comprehension [108].

The first area that comprises the anterior area is the primary somatosensory cortex [108]. The postcentral gyrus, which is dorsal to the central sulcus and is bordered caudally by the Sylvian fissure, serves as the definition of the main somatosensory cortex [108]. The primary somatosensory cortex is bounded posteriorly by the inferior and superior postcentral sulcus [108]. This area's functions include processing and receiving bodily sensations derived from touch and proprioceptive stimuli [108]. In contrast to proprioceptive inputs, which include perceptions of joint positioning movement, discriminative touch encompasses the sensations of touch, pressure and vibration [108]. The primary somatosensory cortex also has a role in monitoring body temperature and processing information about pain, itching and tickling stimuli [108].

The position of the receptive area in the skin and the location of the neurons in the postcentral gyrus are strictly correlated in the primary somatosensory cortex, which is organized somatotopically [108]. The representation of the body on the primary somatosensory cortex is not balanced, with the most sensitive body parts, such as the fingers and lips, taking up more space than the least sensitive body parts, such as the neck or lower back [108]. This means that damage to specific areas of the primary somatosensory cortex can have vastly different effects on the ability to feel and touch [108].

The second area that comprises the anterior area is the parietal operculum [108]. The frontoparietal operculum, which also includes the front inferior section of the inferior parietal lobes, is made up of the inferior regions of the precentral and postcentral gyri [108]. The parietal operculum is often referred to as the secondary somatosensory cortex [108]. The parietal operculum is involved in the perception of touch, pain and temperature [108]. The parietal operculum contains Brodmann area 43, which is located inferiorly to the precentral gyrus which contains Brodmann areas 1, 2 and 3.
The second of the key areas that make up each of the parietal lobes is the superior parietal lobule [108]. The superior parietal lobule covers Brodmann areas 5 and 7 [108]. The top portion of the postcentral sulcus ventrally, the intraparietal sulcus laterally and caudally, and the parieto-occipital sulcus dorsally define the superior parietal lobule [108]. The superior parietal lobule contains the somatosensory association cortex that lies directly dorsal to the primary somatosensory cortex [108]. This region carries out the sensory integration required to produce spatial awareness, including processing of sensory or tactile input, visuospatial and attentional information, perception of position, working memory and long-term memory [108].

Positioned closely to and encompassing the superior parietal lobule is the posterior parietal cortex [114]. The posterior parietal cortex is not only involved in higher-order sensory analysis, but also plays an important role in motor control, as shown by Mountcastle et al. (1975) and by Hyvärinen (1981) [115], [116]. The posterior parietal cortex is crucial for visuomotor transformations [114]. It creates a biological "vision for action" system, which translates visual information into motor commands automatically [114]. Additionally, the posterior parietal cortex is essential for performing motor cognitive tasks like coding motor intention, comprehending action and intention and creating peripersonal visuomotor spatial representations [114]. In order to complete the sensorimotor transformations required for motor planning and sensory guiding of movements, it is also in charge of integrating sensory and motor inputs [114].

The third of the key areas that make up each of the parietal lobe is the inferior parietal lobule [108]. The inferior parietal lobule lies between the lateral fissure inferiorly and the horizontal segment of the intraparietal sulcus superiorly [108]. The intraparietal sulcus, which divides the inferior parietal lobule from the superior parietal lobule, forms the anterior boundary of the inferior parietal lobule [108]. The inferior parietal lobule is separated from the supramarginal gyrus by the primary intermediate sulcus [108]. Caudally, the angular gyrus is separated from the occipital lobe by the parieto-occipital sulcus in each hemisphere [108].
The supramarginal gyrus is involved in language perception and processing, processing of the phonological aspects of words and speech motor planning [108]. The angular gyrus plays a role in attention, mathematical and spatial cognition, semantic processes, visual symbol recognition and visual guiding of hand and limb motions [108]. The angular gyrus translates written words into a form accessible by Wernicke’s area [108]. The angular gyrus is also thought to be involved with the theory of the mind, such as the ability to infer and reason about another person’s state of mind [108].

Strain-induced or other lesions in the postcentral gyrus are associated with changes in the somatosensory thresholds, impairment of the position sense, and deficits in stereognosis, or tactile perception [108]. Strain-induced or other lesions in the parietal lobes can cause sensory deficits such as sensory loss in half of the body, or various sensations of numbness, tingling and prickling [108]. Lesions of the left superior parietal lobe can cause ideomotor apraxia, which is defined as the inability to manipulate and use common objects and to translate an idea into motion [108]. Astereognosia, the inability to identify objects by touch, can also be caused by parietal lobe damage [108]. Non-dominant hemisphere superior parietal lobe lesions can cause the impairment of the sense of one’s position or the inability to determine the body position in space [108]. Damage to the supramarginal gyrus in the left hemisphere can cause alexia, agraphia and anomia [108]. Lesions in the dominant hemisphere of the brain can cause Gerstmann syndrome [108]. These disorders are characterized by dyscalculia or acalculia, right-left confusion, dysgraphia and finger agnosia [108].

The paracentral lobule lies between the parietal and frontal lobes [108]. This lobule plays a role in motor and sensory innervations of the contralateral lower extremity, and regulation of physiological function such as defecation and micturition [108]. Damage to the paracentral lobule is associated with contralateral lower limb weakness and urinary incontinence [108].

Decreased white brain matter in the parietal lobes has also been linked to ADHD in children and adolescents [117].
2.2.23.4 Temporal Lobes

The temporal lobes lie below the parietal lobes and behind the frontal lobes, above the cerebellum. These lobes are primarily involved in auditory processing, including roles like language comprehension, higher-level cross-modal associative functions, learning and memory [108]. Auditory and speech functions are localized in the upper portion of the temporal lobes [108]. Associative functions are localized in the lowest part of the temporal lobes [108]. Learning and memory are localized in the middle sections of the temporal lobes [108]. The following paragraphs will discuss the areas that make up the temporal lobes, and their respective Brodmann areas to help describe their locations and purposes.

The superior temporal gyrus covers Brodmann areas 22, 39, 40, 41 and 42 [108]. Dorsally and posteriorly inside the superior temporal gyrus is the transverse gyrus, also known as the Herschel’s gyrus [108]. These areas contain the primary auditory cortex, which processes auditory stimuli [108]. These areas also process speech, sound and music using a topographical map of the cochlea and a tonotopic map [108].

Wernicke’s area is located dorsally in the superior temporal gyrus, and it surrounds the auditory cortex [108]. Wernicke’s area is responsible for the comprehension of speech [108]. Wernicke's area is often found in the hemisphere of the brain opposite from a person's dominant hand, though there is significant individual variation [108]. As previously discussed, Wernicke’s area is connected to Broca’s area through the arcuate fasciculus, and is involved in language comprehension, semantic processing, language recognition, and language interpretation [108].

The middle temporal gyrus encompasses Brodmann area 21 and is located between the superior and the inferior temporal gyrus [108]. It is dorsally bounded by the angular gyrus and the occipital lobes, putting it at the rear of the temporal lobes [108]. The middle temporal gyrus has a role in higher-order cognitive and linguistic functions like determining distance, recognizing familiar faces and understanding what words mean when reading [108].
The inferior temporal gyrus encompasses Brodmann areas 20 and 37, lying under the middle temporal gyrus and posteriorly is bounded by the inferior occipital lobes [108]. The inferior temporal gyrus is involved in higher-level associative cognitive functions such as semantic memory, language, visual perception and sensory integration [108].

The fusiform gyrus encompasses Brodmann area 37 and is located between the lingual gyrus and the parahippocampal gyrus [108]. The posterior end of the fusiform gyrus is in the occipital lobes [108]. The fusiform gyrus is involved in the higher visuo-auditory processing functions such as facial recognition, colour processing, word and number recognition and category processing [108].

The temporal pole covers Brodmann area 38 and occupies the most rostral part of the temporal lobes [108]. It is the point where the superior, middle and inferior temporal gyri meet [108]. Ventromedially, it blends with the perirhinal area [108]. It has a dorsal, lateral and mesial surface [108]. The temporal pole is involved in social and sexual behaviour as well as cognitive visual functions [108]. It contributes to autobiographical memory, the processing of emotional language, facial and visual pattern identification, mnemonic matching and learning tasks, and linguistic integration [108]. It is a place for the representation of unique entities such as proper names of peoples and places [108].

The left anterior temporal pole is the area responsible for mapping meaning onto sound, determined from tasks such as object naming [108].

The medial surface of the temporal lobes comprises most of the limbic lobe, which is part of the limbic or emotional system [108]. Along with the limbic lobe, this network of cortical and subcortical structures also includes the cingulate gyrus, amygdala, anterior thalamic nuclei and olfactory cortex [108]. The limbic lobe consists of two layers of brain tissue called the limbic gyrus and the intralimbic gyrus [108].

The limbic gyrus includes the parahippocampal gyrus including the etorhinal cortex, and covers Brodmann areas 27, 28, 35, 36 and 38 [108]. The cingulate gyrus covers Brodmann areas 23, 24, 25, 26 and 29 to 33 [108]. The subcallosal area covers Brodmann areas 24, 25 and 32 [108]. The intralimbic gyrus covers the hippocampus, the dentate
gyrus and the supracallosal gyrus or indusium griseum [108]. This gyrus also serves as the basis of emotion [108].

Through its subcomponents, the limbic lobe is involved in long-term memory, the development of new long-term memories and the voluntary recall of prior knowledge and experiences. It oversees processing emotional aspects of memory and recall [108]. Additionally, these subcomponents regulate stress, depression, spatial behaviour, spatial memory processes, processing of olfactory sense and olfactory memory, as well as learning and memory, particularly conscious memory [108]. The coordination of behavioural reactions to environmental cues and responses containing emotional content is also influenced by these subcomponents [108]. The limbic lobe is connected to emotional memory, visual recognition of emotionally significant events, motivation, autonomic responses and hormones related to emotions. It is also connected to fear, the ability to recognize faces that express fear, processing of scenes and objects and autobiographical memory [108].

There are several specific conditions that are attributed to strain-induced or other types of damage in the temporal lobes [108]. Pure word deafness is one such condition that involves the loss of auditory comprehension and preservation of visual comprehension [108]. The main sign of pure word deafness is that while speaking is easy and reading is normal, understanding spoken language is exceedingly challenging [108]. Another condition, auditory agnosia, is the inability to recognize nonverbal sounds [108]. A special type of auditory agnosia is called amusia, which is the impossibility to process music [108]. Wernicke’s aphasia is a condition, also referred to as fluent aphasia or receptive aphasia [108]. People with this disorder can produce many words with grammatically correct sentences and normal prosody, but what they say does not make sense [108]. Prosopagnosia, also known as face blindness, is a deficit in recognizing familiar faces [108]. In addition to head trauma, it can also be acquired through stroke [108]. Synesthesia is a condition in which a stimulus is perceived simultaneously by more senses [108]. There are different types of this condition, but the most frequent is the grapheme-colour synesthesia [108]. This specific type of synesthesia consists in the
perception of a particular colour when seeing letters or numbers [108]. Prosopagnosia is the inability to recognize familiar faces and occurs if a lesion occurs in the fusiform gyrus [108]. Visual agnosia and alexia can also occur because of damage to the temporal lobes [108]. Associative agnosia is the inability to name objects that can be perceived and drawn and is linked to lesions in the anterior left temporal lobes [108]. Bilateral lesions in the occipitotemporal associative regions have been associated to the inability to recognize by sight recognized items that can be described, which is known as perceptual agnosia [108]. Another condition is alexia, which is the inability to understand written language [108]. It can be pure, meaning without agraphia, if a lesion occurs in the occipital lobes and splenium of the corpus callosum [108]. A lesion in the medial occipitotemporal region and in the fusiform gyrus causes achromatopsia, which is a lack of colour perception [108]. Apraxia is another condition. It is the inability to perform skilled movements [108]. If the conceptual system is damaged and this results in a loss in gesture perception and output, it may be ideational [108]. It can also be of the type called ideomotor, meaning there is impairment to hand gestures and in the use of tools [108]. Insular and left inferior frontal lesions can cause the orobuccal apraxia, while left parietal or prefrontal lesions might cause dyspraxia [108]. A paraneoplastic autoimmune condition called limbic encephalitis can affect the insula, orbitofrontal cortex, cingulated gyrus, hippocampus and amygdala [108]. Symptoms include headache, irritability, mental confusion, memory impairment, personality changes and sleep disturbances [108]. Klüver-Bucy syndrome is an extremely rare condition that can occur with head trauma [108]. It occurs with bilateral lesions of the amygdala and is characterized by visual agnosia, placidity, bulimia, hypersexuality, hyperorality and memory impairment [108]. CTE can also occur with repeated head impacts and damage occurring in the temporal lobes [118]. ADHD and depression have also been linked to damage in the temporal lobes [117], [119].

2.2.24  Axon Fiber Tracts and Pathways found in the Lobes of the Human Brain

In the human brain, there are several axon fiber tracts that are isolated within one set of left and right lobes. There are also several axon fiber tracts that serve as connecting axon
fiber tracts that link different lobes of the brain together. These connecting tracts share characteristics, roles and functions from each of the lobes to which they are connected. Section 2.2.23 has discussed the four key lobes of the brain in detail, and Section 2.2.24 will briefly discuss the locations of the axon fiber tracts that exist within and connect each of the four key lobes of the brain.

2.2.24.1 Striato-occipital Tract

The striato-occipital tract links the striatum and the occipital lobes. Its location in the Brain Axon Fiber Tract GHBMC Model is shown in Figure 50.

![Figure 50: Location of the Striato-occipital Tract in the Brain Axon Fiber Tract GHBMC Model](image)

2.2.24.2 Striato-parietal Tract

The striato-parietal tract links the striatum and the parietal lobes. Its location in the Brain Axon Fiber Tract GHBMC Model is shown in Figure 51.
2.2.24.3 Superficial-Frontal Tract

The superficial-frontal tract is located entirely in the frontal lobes. This is the axon fiber tract in the Brain Axon Fiber Tract GHBMC Model that represents the axon fibers present within the frontal lobes. The location of this tract is shown in the Brain Axon Fiber Tract GHBMC Model in Figure 52.
2.2.24.4 Superficial-Frontal-Parietal Tract

The superficial-frontal-parietal tract links the frontal lobes and the parietal lobes. The location of this tract is shown in the Brain Axon Fiber Tract GHBMC Model in Figure 53.
2.2.24.5 Superficial-occipital Tract

The superficial-occipital tract is located entirely in the occipital lobes. This is the representative tract in the Brain Axon Fiber Tract GHBMC Model for the axon fibers present in the occipital lobes. The location of this tract is shown in the Brain Axon Fiber Tract GHBMC Model in Figure 54.

Figure 54: Location of the Superficial-occipital Tract in the Brain Axon Fiber Tract GHBMC Model

2.2.24.6 Superficial-Ocipital-Temporal Tract

The superficial-occipital-temporal tract links the occipital lobes and the temporal lobes. The location of this tract is shown in the Brain Axon Fiber Tract GHBMC Model in Figure 55.
2.24.7 Superficial-Parietal Tract

The superficial-parietal tract is located entirely in the parietal lobes. This is the representative tract in the Brain Axon Fiber Tract GHBMC Model for the axon fibers present in the parietal lobes. The location of this tract is shown in the Brain Axon Fiber Tract GHBMC Model in Figure 56.
2.2.24.8 Superficial-Parietal-Occipital Tract

The superficial-parietal-occipital tract links the parietal lobes and the occipital lobes. The location of this tract is shown in the Brain Axon Fiber Tract GHBMC Model in Figure 57.
2.2.24.9 Superficial-Parietal-Temporal Tract

The superficial-parietal-temporal tract links the parietal lobes and the temporal lobes. The location of this tract is shown in the Brain Axon Fiber Tract GHBMC Model in Figure 58.

![Image of the Superficial-Parietal-Temporal Tract](image)

**Figure 58: Location of the Superficial-parietal-temporal Tract in the Brain Axon Fiber Tract GHBMC Model**

2.2.24.10 Superficial-Temporal Tract

The superficial-temporal tract is located entirely in the temporal lobes. This is the representative tract in the Brain Axon Fiber Tract GHBMC Model for the axon fibers present in the temporal lobes. The location of this tract is shown in the Brain Axon Fiber Tract GHBMC Model in Figure 59.
Figure 59: Location of the Superficial-temporal Tract in the Brain Axon Fiber Tract

GHBMC Model

2.2.25 Human Brain Axon Fiber Tract Quick Reference Summary

Table 4 provides a breakdown of nine general categories of brain injuries and disorders that can occur resulting from blunt impact-induced axon fiber strain damage or related DAI s. These groups are generalized and broadly defined because each axon fiber tract in the brain is responsible for many functions, and the brain has at least a partial ability to re-allocate how tasks and functions are distributed in the event of injury. Summarizing the research completed in Chapter 2, the following nine groups of disorders outlined in Table 4 were created.
### Table 4: Disorder Categories and their Associated Group Numbers

<table>
<thead>
<tr>
<th>Disorder Group Number</th>
<th>Grouping</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Speech and language disorders</td>
</tr>
<tr>
<td>2</td>
<td>Reading and writing disorders</td>
</tr>
<tr>
<td>3</td>
<td>General brain function: executive control (attentional control, cognitive inhibition, inhibitory control, working memory, and cognitive flexibility), problem solving ability, overall intelligence, processing speed, vision</td>
</tr>
<tr>
<td>4</td>
<td>Emotional disorders</td>
</tr>
<tr>
<td>5</td>
<td>Pain</td>
</tr>
<tr>
<td>6</td>
<td>Memory disorders (short and long term)</td>
</tr>
<tr>
<td>7</td>
<td>Somatosensory disorders (touch, pressure, temperature, position, movement, and vibration)</td>
</tr>
<tr>
<td>8</td>
<td>Motor control and movement</td>
</tr>
<tr>
<td>9</td>
<td>Longer term injuries (Parkinson's disease, CTE, etc.)</td>
</tr>
</tbody>
</table>

The functions and purpose of each of the parcellated brain axon fiber tracts were then cross-referenced with Table 4, and the results of this are in Table 5. Table 5 also provides an identifier code and quick reference column for each of the parcellated brain axon fiber tracts discussed in Chapter 2.
<table>
<thead>
<tr>
<th>Axon Fiber Tract Full Name</th>
<th>Tract Short Reference Code</th>
<th>Tract Short Reference Code</th>
<th>Chapter Section</th>
<th>Disorder Groupings</th>
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<tr>
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<td>CB</td>
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<td>EmC</td>
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</table>
2.3 Conclusions

The background research and content presented in Chapter 2 is a summary and overview of work completed by scientists, researchers and engineers from more than the past one hundred years. The human brain is a complicated organ in the body, with many different roles, responsibilities and functions. The high importance and involvement of the brain with many systems in the body means that any sort of blunt impact-induced tissue or brain axon fiber strain injury could have detrimental and potentially long lasting and life altering effects. Utilizing modern tools such as advanced finite element head models, MRI and related imaging technology and tractography analysis help confirm theorized connections between areas of the brain and their functionality. These tools will ultimately help in strengthening known links between sports and other physical recreation activities, head impacts and brain injuries such as concussions.
Chapter 3

3 Evaluating Three Types of Simple Artificial Intelligence Algorithms to Instantaneously Predict Brain Strain-based Injury Metrics Based on Head Impact Kinematics

This chapter was co-authored by Dr. Haojie Mao, Kalish Gunasekaran, and Oliver Ma, with data collected and methodology developed by Yanir Levy, and edits provided by Dr. George Knopf and Dr. Katarina Grolinger.

3.1 Chapter Abstract

This chapter establishes a relationship between various blunt impact variables measured during an impact and two metrics which correlate to predicting occurrences of brain tissue strain and mTBIs in finite element brain models: MPS and CSDM. These metrics are firstly calculated from the outputs of brain finite element models to which the kinematics data was applied, and secondly through an artificial intelligence algorithm directly from the kinematics data. A ranking of kinematic input variable combinations is provided based on how strongly correlated the different combinations are to the chosen metrics. In a secondary study, increasingly smaller divisions of data are used to evaluate the performance of three artificial intelligence algorithms with a fixed set of kinematic input variables. The work in this chapter confirms that the relationship between blunt impact variables and brain strain metrics can be predicted using artificial intelligence to a high degree of accuracy.

3.2 Introduction to Finite Element Head and Brain Models and Brain Tissue Injury Metrics

Helmets are an essential piece of equipment for protection against mTBIs, DAI and other head injuries in sports and other physical recreation activities. As outlined previously, dynamic forces that induce shearing forces to brain tissue are thought to be a major driver in mTBIs. Research into brain tissue strain developed during brain trauma
has frequently been studied using finite element head models, as it allows researchers a cost-effective and ethical way to study this complex biomechanical challenge.

Impacts studied on finite element models of the brain are often evaluated and compared using brain injury metrics. Common injury metrics for evaluating include MPS and CSDM. Within the context of a finite element model of the head with defined materials, MPS can also be called the first principal strain and it indicates the maximum value of tensile strain in an element. CSDM provides a volume-based correlation of the extent of damage that could be attributed to mTBIs and DAI. This metric predicts DAI by calculating the MPS level as a volume fraction of the finite element head model [120]. CSDM is associated with the tensile strains of the cumulative volume of brain tissue over a predefined critical level. CSDM is frequently expressed with an accompanying number, such as CSDM\textsubscript{25}. For example, if the CSDM\textsubscript{25} value of the entire brain model is equal to 0.5, this means that for that brain model 50\% of its volume experiences strains over 0.25, or 25\%. This chapter focuses on ice hockey-related helmeted impacts and uses MPS and CSDM\textsubscript{25} values as correlates for mTBIs. MPS can be used as a correlate because it is theorized that brain injuries, including mTBIs, are caused by the straining of brain tissue during impact as explained in Chapter 1, while CSDM\textsubscript{25} can be used as a correlate because of its numerical representation of the volume fraction of brain tissues that experience strain over the critical damage threshold in the finite element [7], [120], [121].

Given the focus in the field of brain injury research on brain tissue strain, plus recently developed capabilities to quickly predict these tissues strains such as in Wu et al. (2019), it became possible to immediately evaluate brain-strain-based injury metrics [122]. The challenge lies in selecting which algorithms can be best used to accurately predict the strain-based metrics for a given impact scenario, with the selected approach applied to real-world helmet designs once validated.

This first portion of this chapter aims to develop and implement an AI to predict which kinematic metric or combination of kinematic metrics were best able to produce accurate output MPS and CSDM\textsubscript{25} values, and therefore potentially to predict the risks of mTBIs through correlate metrics. The second portion of the chapter aims to compare a variety of
candidate AI algorithms to see which method is best suited to predicting correlate MPS and CSDM metrics from the collected kinematic inputs.

3.3 Data Collection and Methods

3.3.1 Collection of Brain Tissue Strain Data and Metrics through Experimental and Computational Approaches

Data for Chapters 3 to 5 was collected using a re-creation of an industry standard method for physical helmet evaluation, which was originally based on the helmet testing procedure for Hockey STAR [7], [15]. These tests were performed by Bauer Hockey Ltd.. A National Operating Committee on Standards for Athletic Equipment dummy head form was used to replicate ice hockey-related head impacts in lab. The impactor used to replicate a real-life expected impact to the head varied slightly from the original Hockey STAR methodology, as a pneumatic impactor was used in place of a pendulum impactor [7], [123]. The location of the front, rear and top points of impact on the test assembly are shown in Figure 60a. These points of impact were confirmed using slow motion video and pointed tip impactor heads [7]. The test apparatus was instrumented with three Endevco 7264C-2KTZ-2-240 accelerometers measuring linear acceleration and three channels of a DTS6DX Pro mounted in the center of mass of the head form to measure rotational velocity [7]. Two Endevco Model 136 amplifiers provided excitation voltage and signal conditioning [7]. Three impact speeds were used for evaluating the different helmets. Low energy impacts were conducted at 2.6 meters per second, medium or middle energy impacts were conducted at 4.6 meters per second, and high energy impacts were conducted at 6.0 meters per second [7]. The front and rear energy impacts were directed at the center of gravity of the head form test apparatus as shown in Figure 60a, but the side impacts were not [7]. This added an element of tangential loading to the test [7]. Each helmet model was evaluated by being hit twice with the 19.94-kilogram impactor per direction and per speed, with four to five helmet samples of each type used in the testing [7]. In total, six helmet models labelled A to F were evaluated, yielding 672 impacts with corresponding kinematics measured [7]. Six different helmets were evaluated on the head-form over the course of testing [7]. Four impact directions and
three impact magnitudes were tested [7]. The kinematic data of each helmet impact, such as linear acceleration, rotational acceleration and rotational velocity, were collected at a frequency of 20 kHz [7]. A filter chain was applied to the data streams, with a hardware CFC 1000 filter amplifier used on all data collection channels, a software CFC 1000 filter on the linear acceleration stream, and a software CFC 155 filter on the rotational velocity stream [7]. Kinematics data, after being recorded in each test, was input into a customized MATLAB script, which orientated the data to fit the base GHBMC head and brain finite element model [7]. The simulation performed only contained the base GHBMC head and brain finite element model, and did not feature a helmet or impactor, as the recorded kinematics were prescribed directly to the head model. For each impact case, the base GHBMC head and brain finite element model was solved using LS-DYNA, and MPS and CSDM$_{25}$ were calculated from each simulation case [7]. The total run time for the 672 cases, using 2 CPUS on a Lenovo workstation with 2 Intel Xeon Gold 5118 Processors (12 cores each at 2.3 gigahertz) and 128 gigabytes of DDR4 memory was 1,344 hours, or about 2 hours per case [7]. The MPS and CSDM$_{25}$ values were then appended onto a master Excel file, containing all the kinematic data and testing information [7]. This master file served as the source for all AI algorithms used in this study. The data collection and processing pipeline developed in Levy et al. (2021) is shown in Figure 60 [7].
3.3.2 Application of Statistical and Artificial Intelligence Algorithms to Brain Strain Metrics Data

3.3.2.1 Applying Artificial Intelligence to Identify Critical Combinations of Parameters

In the first part of the study, the recorded kinematic data from each helmet impact test and the calculated MPS and CSDM\textsubscript{25} values were input into IBM’s SPSS Statistics (SPSS). The multilayer perceptron was chosen from SPSS to begin with as it provides the user with visuals and has a short network generation time, which was useful for troubleshooting and testing various combinations of data. Multilayer perceptrons are also one of the most popular neural networks [124]. Multilayer perceptrons are a supervised form of feedforward artificial neural network used to create a predictive algorithm for one or more dependent or target variables based on the values of the predictor variables [125], [126]. This procedure utilized a single hidden layer network structure with twelve
inputs to predict two outputs simultaneously (MPS and CSDM₂₅). A reduced example of this type of network is shown in Figure 61.

![Multilayer Perceptron Network](image)

**Figure 61:** Example Structure of a Multilayer Perceptron, generated in SPSS, Used in the First Part of the Study. MPS Values are Represented by the Node Labelled Average Strain. CSDM₂₅ Values are Represented by the Node Labelled CSDM₂₅. LinX, Y, Z: Linear Accelerations in X, Y and Z Directions. RotvX, Y, Z: Rotational Velocities Around X, Y and Z Axes. The bias node allows the Multilayer Perceptron to adjust itself to the data flexibly, resulting in stronger fit.

The multilayer perceptron in SPSS is a feedforward architecture, meaning that data only moves from input nodes through the hidden layer of nodes to the output nodes. A model was created for determining which kinematic data variables were most accurate in predicting real MPS and CSDM₂₅ values from the accelerometer head-form tests using a multilayer perceptron. Different combinations of kinematic inputs were used as covariates within the multilayer perceptron to predict MPS and CSDM₂₅ values, and then
these values were compared to the real calculated MPS and CSDM$_{25}$ values from the finite element head models. Data was normalized to an end value between zero and one by subtracting the minimum value and then dividing by the range of the data. Combinations of inputs were tested with a random subset of data used for training, and the remainder for testing. A random set of 70% of the 672 test cases were used for training the multilayer perceptron, while the remaining 30% were used for testing the validity of the learning method. An R-squared value was calculated for each combination tested, and these R-squared values were used as the main comparator to determine which combinations of kinematic inputs to the regression model were most accurate. The combinations were then ranked in order based on their respective R-squared values. Any kinematic input combination that had an R-squared value below 0.95 was removed, as it was deemed to not be strongly correlated enough relative to the other kinematic input combinations for further consideration.

3.3.2.2 Collinearity Evaluation

In the second part of the study, various AI algorithms were applied to the master dataset with a set of fixed input parameters, training datasets and testing datasets, all of which were developed using work conducted in part one of the study. These fixed input parameters were linear acceleration and rotational velocity in the x, y and z planes. The three AI algorithms, detailed in Section 3.3.2.3 below, were used to predict MPS and CSDM$_{25}$ values for a singular helmet model or group of helmet models out of the six total helmet models being tested. This selected helmet model or group of helmet models was excluded from the creation of the randomized training and test sets used to develop the algorithm. This meant the algorithm was tasked with predicting data it had not seen before. The fixed input parameters were slightly modified from the results of part one of this study to ensure that there were no collinearity issues in the training of the AI algorithm. Collinearity was evaluated by using a Pearson correlation coefficient table and by calculating the variance inflation factor (VIF) for each independent variable [127]. Each of the twelve exogenous independent kinematic variables was regressed against the other independent input variables [128]. For example, if $X_1$, $X_2$, $X_3$ and $X_4$ are all exogenous variables, the regression model for $X_3$ is defined approximately as the sum of
X_1, X_2 and X_4. The R-squared value for this regression model was then extracted and the VIF was calculated using Equation 1.

\[ VIF = \frac{1}{1 - R^2} \]  \hspace{1cm} (1)

The tolerance was calculated using Equation 2.

\[ Tolerance = 1 - R^2 \]  \hspace{1cm} (2)

The cutoff point used to declare multicollinearity was chosen to be a VIF of less than 10, or a tolerance greater than 0.1 [128]. Multicollinearity calculations were done in Python with the statsmodels module [128].

3.3.2.3 Evaluating Three Candidate Artificial Intelligence Algorithms with a Helmet Data Exclusion Study

3.3.2.3.1 Multilayer Perceptron

The first candidate algorithm evaluated in part two of this study was the same multilayer perceptron as detailed in part one. The multilayer perceptron utilizes a feedforward structure with a single hidden layer of nodes, and the six inputs identified through the Pearson correlation coefficient table and VIF calculations. An example of the structure of a multilayer perceptron was shown in Figure 61.

3.3.2.3.2 Bayesian Regularization Algorithm

The second candidate algorithm evaluated was created using the nftool neural network fitting tool in MATLAB. Within nftool, there were three options for algorithms to develop and train neural networks: the Levenberg-Marquardt algorithm, the Bayesian regularization algorithm, and the Scaled Conjugate Gradient algorithm. The Bayesian regularization algorithm was chosen to be implemented as it consistently produced a higher R-squared value and lower root mean square error than the other two algorithms when evaluated in a preliminary study with multiple hidden layers. This algorithm also had good generalization for difficult, small or noisy datasets, and minimized overfitting issues where the network became too specialized with the data on which it was trained.
Bayesian regularization involves minimizing a combination of squared errors and weights, followed by determining the correct combination so that the network created generalizes well [129], [130]. An example of a Bayesian regularization structure is shown in Figure 62.

![Figure 62: Example Bayesian Regularization Structure Used in Part Two of the Study [131]](image)

The dataset in question is a small dataset, making Bayesian regularization a good candidate algorithm for prediction. The final structure of the chosen Bayesian regularization algorithm was created with ten hidden layers, as this number of hidden layers performed the best in the preliminary study of this option.

### 3.3.2.3.3 Random Forest Regression Model

The third model used was a random forest regression model, executed in Python using the scikit-learn machine learning library [128]. The random forest regression model used averaging to improve its predictive accuracy and to control overfitting [132]–[134]. An example of the structure is shown in Figure 63.
Figure 63: Example Random Forest Regression Structure Used in Part Two of the Study [135]

In this structure, each tree in the ensemble is constructed from a sample taken with replacement from the training set [132]–[134]. Additionally, when each node was split in construction of the tree, the best split was found either from all input features or a random subset of a user-inputted size variable [132]–[134]. Both of these randomness sources helped decrease the variance of the estimation, as the individual decision trees tended to overfit and have a high variance [132]–[134]. The variance reduction was significant enough that this traditionally yielded a better overall structure than an individual decision tree, which helped improve prediction quality [132]–[134].

3.3.2.4 Statistical Metrics and Procedure to Evaluate the Three Artificial Intelligence Algorithms

Once the kinematic input set was finalized from the multicollinearity calculations, each combination of one, two and three helmets’ MPS and CSDM values were predicted with each prediction model. After each model predicted all forty-one combinations of one, two and three helmets’ tissue strain metrics, prediction quality metrics were used to evaluate the models. Examples of these prediction quality metrics included the R-squared value, the mean squared error, the root mean squared error and the mean absolute error. The equation for the R-squared coefficient is shown in Equation 3.
\[ R^2 = 1 - \frac{RSS}{TSS} \]  \hspace{2cm} (3)

RSS represents the sum of squares of residuals and TSS represents the total sum of squares. The equation for mean squared error is shown in Equation 4.

\[ \text{Mean Squared Error (MSE)} = \frac{1}{n} \sum_{i=1}^{n} (Y_i - \hat{Y}_i)^2 \]  \hspace{2cm} (4)

In this equation, \( n \) is the number of data points, \( Y_i \) are the observed values, \( \hat{Y}_i \) are the predicted values, and \( i \) is a counter variable for each of the values in the MSE calculation. The root mean squared error is found by Equation 5.

\[ \text{Root Mean Squared Error (RMSE)} = \sqrt{\frac{\sum_{i=1}^{N} (Y_i - \hat{Y}_i)^2}{N}} \]  \hspace{2cm} (5)

In Equation 5, \( i \) is a counter variable for each of the values in the RMSE calculation, \( N \) is the number of non-missing data points, \( Y_i \) are the observed values and \( \hat{Y}_i \) are the predicted values. The mean absolute error is found by Equation 6.

\[ \text{Mean Absolute Error (MAE)} = \frac{\sum_{i=1}^{n} |\hat{Y}_i - Y_i|}{n} \]  \hspace{2cm} (6)

In Equation 6, \( \hat{Y}_i \) are the predicted values, \( Y_i \) are the observed values, and \( n \) is the total number of data points.

In the case for all of MSE, RMSE and MAE values, the closer the result is to zero, the better the algorithm is at predicting results. In the case of the R-squared value, a value closer to one indicates a strong correlation.

Each algorithm’s predicted results for each selection of data it was provided was plotted against the actual results using a series of box plots. The goal of this portion of the study was to determine which of the three prediction models was the most accurate and
efficient at predicting each test case’s MPS and CSDM_{25} values, given a variety of test cases.

### 3.4 Results

Table 6 shows variable definitions for each of the kinematic inputs used in the analysis. The R-squared values for each of the chosen kinematic variable combinations for MPS and CSDM_{25} are shown in Table 7.

**Table 6: Kinematic Input Variable Definitions**

<table>
<thead>
<tr>
<th>Short Form</th>
<th>Kinematic Input Variable (Maximum Values)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LinA_{X}</td>
<td>Linear Acceleration, X direction</td>
</tr>
<tr>
<td>LinA_{Y}</td>
<td>Linear Acceleration, Y direction</td>
</tr>
<tr>
<td>LinA_{Z}</td>
<td>Linear Acceleration, Z direction</td>
</tr>
<tr>
<td>RotV_{X}</td>
<td>Rotational Velocity, X axis</td>
</tr>
<tr>
<td>RotV_{Y}</td>
<td>Rotational Velocity, Y axis</td>
</tr>
<tr>
<td>RotV_{Z}</td>
<td>Rotational Velocity, Z axis</td>
</tr>
<tr>
<td>RotA_{X}</td>
<td>Rotational Acceleration, X axis</td>
</tr>
<tr>
<td>RotA_{Y}</td>
<td>Rotational Acceleration, Y axis</td>
</tr>
<tr>
<td>RotA_{Z}</td>
<td>Rotational Acceleration, Z axis</td>
</tr>
<tr>
<td>RPLA</td>
<td>Resultant Peak Linear Acceleration, across all directions</td>
</tr>
<tr>
<td>RPRV</td>
<td>Resultant Peak Rotational Velocity, across all directions</td>
</tr>
<tr>
<td>RPRA</td>
<td>Resultant Peak Rotational Acceleration, across all directions</td>
</tr>
</tbody>
</table>
The five strongest correlated kinetic input variable combinations are shown in Table 8, as generated by the multilayer perceptron algorithm. This information is taken from Table 7, and the combinations are ranked based on CSDM$_{25}$ value. However, it should be noted that the order of the top five kinematic input variable combinations in Table 8 does not change if MPS R-squared values are used.
Table 8: Strongest Correlated Kinematic Input Variable Combinations for Predicting both MPS and CSDM$_{25}$ Values, Ranked by R-Squared Value

<table>
<thead>
<tr>
<th>Variable Combination Number</th>
<th>Associated Kinematic Input Variable Combination</th>
<th>R-Squared Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>$LA_{x,y,z} + RotV_{x,y,z} + RotA_{x,y,z} + RPLA + RPRV + RPRA$</td>
<td>0.988</td>
</tr>
<tr>
<td>7</td>
<td>$LA_{x,y,z} + RotV_{x,y,z} + RotA_{x,y,z}$</td>
<td>0.985</td>
</tr>
<tr>
<td>4</td>
<td>$LA_{x,y,z} + RotV_{x,y,z}$</td>
<td>0.978</td>
</tr>
<tr>
<td>5</td>
<td>$RotV_{x,y,z} + RotA_{x,y,z}$</td>
<td>0.955</td>
</tr>
<tr>
<td>14</td>
<td>$RPLA + RPRV + RPRA$</td>
<td>0.955</td>
</tr>
</tbody>
</table>

All other variable combinations had an R-squared value that was less than 0.95 for both MPS and CSDM$_{25}$. Therefore, these other variable combinations were deemed to not be strongly correlated enough relative to the kinematic input combinations shown in Table 8. These lower scored combinations were not examined further.

Figure 64 shows a comparison of the R-squared values, comparing the difference in correlation results of each kinematic input variable combination for the calculation of MPS and CSDM$_{25}$ values.
After the ranking of the kinematic input variable combinations was established and the Pearson correlation coefficient calculations were done to eliminate any collinearity issues, comparison metrics were calculated for each of the three candidate algorithms. In terms of selecting inputs for the comparison of the candidate algorithms, Combination 4 was chosen from Table 8 as it was the highest ranked combination to have no collinearity issues between its variables. Collinearity is to be avoided as it is desirable to have each of the inputs to any artificial intelligence algorithm be uniquely determined. Without this, the statistical significance of each of the independent kinematic input variables is undermined.

For part two of the study, comparison metrics were calculated for each of the three candidate algorithms. The R-squared values, mean squared error values, root mean squared error values and mean absolute errors values were calculated for each of the completed predictions the candidate algorithms were asked to perform, and the results of these metrics are shown in Figures 65, 66, 67 and 68 respectively. Overall, R-squared values were strongly correlated, reaching 0.95 and above (Figure 65), mean squared
errors were low, on the order of 0.001 (Figure 66), root mean squared errors were less than 0.05 (Figure 67), and mean absolute errors were mostly less than 0.03, except for the prediction of MPS using a multilayer perceptron (Figure 68). The prediction results were taken from the first run of each candidate algorithm. This is important to highlight as the resulting prediction data, and subsequently the comparison metrics, would likely change if the AI models were run again. Box plots were used to display the ranges of data for each comparison metric, separated by number of helmets excluded, MPS versus CSDM$_{25}$, and by type of prediction algorithm used. Working with the six helmets, six single-helmet-exclusion cases, 15 two-helmet-exclusion cases and 20 three-helmet-exclusion cases were evaluated. This totaled 41 exclusion combinations. The scales for each of Figures 65 to 68 are uniform, meaning direct comparisons can be made between plots within each figure. The middle line in each boxplot represents the median value, which splits the second and third quartiles of the data. The first and fourth quartiles are indicated with the whiskers of each plot, and the extremity values are at the top and bottom of the boxplots. The Y-axis was standardized for each figure to allow for accurate comparisons. A total of three points exceeded the standardized Y-axis range of the plots and are not shown in their respective subplots in Figures 66, 67 and 68. However, these points are not omitted from the dataset.
Figure 65: Number of Helmets Excluded from Training vs. R-Squared Value, Multilayer Perceptron vs. Bayesian Regularization vs. Random Forest Regression
Figure 66: Number of Helmets Excluded from Training vs. Mean Squared Error, Multilayer Perceptron vs. Bayesian Regularization vs. Random Forest Regression
Figure 67: Number of Helmets Excluded from Training vs. Root Mean Squared Error, Multilayer Perceptron vs. Bayesian Regularization vs. Random Forest Regression
3.5 Discussion

The work completed in this chapter demonstrated the feasibility to accurately predict strain-based tissue injury metrics such as average MPS and CSDM\textsubscript{25} with R-squared values above 0.95 using three AI algorithms for ice hockey-related head impacts. This novel finding will help ice hockey helmet designers and manufacturers to immediately examine the potential effects of impacts on the brain after collecting linear and rotational...
kinematics data of the head. The combination of kinematic input variables with the highest R-squared correlation value was Combination 15, which was expected as it contains all 12 potential input variables. The next three highest ranked combinations all contained rotational velocity, which indicates that rotational velocity is more highly weighted than linear or rotational acceleration and is a better predictor of mTBIs than other kinematic inputs [136]. The R-squared values in Table 7 show that when rotational velocity is not included in the set of kinematic inputs to the multilayer perceptron, the algorithm’s prediction ability decreases significantly.

The multilayer perceptron was able to predict both MPS and CSDM25 values to a high degree of accuracy for the training and testing splits that were examined. Table 7 shows that the multilayer perceptron was able to predict MPS values more accurately than CSDM25 values. There were only large differences in the R-squared values in Combinations 8 and 10. Combinations 8 and 10 were difficult to utilize because they only had one input each, and neither peak linear acceleration nor peak rotational acceleration are known to be good predictors of MPS or CSDM25 values in isolation [137], [138]. The difference in prediction ability can largely be ignored, as neither value that was predicted by the multilayer perceptron was strongly correlated and can be disregarded. As such, the multilayer perceptron was able to predict both MPS and CSDM25 to a high degree of accuracy and precision. As expected, Combination 15, which had the greatest number of kinematic inputs, was the variable combination with the highest R-squared value, and subsequently was the best predictor of both MPS and CSDM25 values for this data set [139].

The results based on the kinematic inputs of Combination 14 were of interest. It was found that when using only resultant peak linear acceleration, rotational velocity and rotational acceleration as the input kinematic variable combination, this combination was quite effective in the prediction of MPS and CSDM25 values. When exclusively utilizing the resultant peak values in the multilayer perceptron, there was a 75% reduction in the amount of data that had to be processed, while a high quality of prediction was maintained. This data reduction occurs because the non-peak kinematics do not have to
be entered as an input to the AI algorithm. Results that support this claim were also found in work done by Knowles and Dennison (2017) using the Simulated Injury Monitor (SIMon) Model which found peak rotational velocity and rotational acceleration to be good predictors of CSDM\textsubscript{15} and MPS in nearly all cases [140]. Using either of the peak combinations discussed may help to streamline prediction calculations and pipelines in future studies. Peak kinematics being a good predictor of tissue strain also aligns with the biomechanical understanding of how mTBIs occur, as the time at which the highest magnitude of rotational kinematics closely correlates with the time at which the highest tissue strain occurs during an impact. This maximum strain correlates to the tissue damage that occurs in the brain. When inertia eventually causes the head and brain to cease rotating, the strain levels will return to zero, but the damage caused at the time of peak strain will still exist. The results found in Combination 14 confirm the close relationship between peak kinematics, peak tissue strain and tissue damage.

In part two of the study, each of the three candidate algorithms was evaluated against all forty-one exclusion cases for both MPS and CSDM\textsubscript{25} data predictions. Since the objective of part two of the study was to study the performance of each type of algorithm as it predicted outcomes using continuous variables, metrics such as the mean squared error and the R-squared value were studied, and general trends were observed across all the chosen metrics [141]. The random forest regression model was best able to adapt to the dataset, with the multilayer perceptron performing well but slightly worse overall. The multilayer perceptron performed slightly better on single helmet exclusion cases than the random forest regression, but the random forest regression performed better in the two and three helmet exclusion cases. The Bayesian regularization performed the worst of the three candidate algorithms examined. The R-squared value for all models decreased as more helmets were excluded, to varying degrees. This was expected as, by moving more data from the training sets to the testing sets, the candidate algorithms had less data to develop relationships with and more data to predict. This corresponded with the mean squared error, root mean squared error and mean absolute error values all trending upwards as more helmets were excluded. For the results of each of the two brain tissue strain metrics being studied by the candidate algorithms, the R-squared values were
comparable, the mean absolute error values were higher for the MPS than the CSDM\textsubscript{25} predictions, and the mean squared error and root mean squared error values were higher for the CSDM\textsubscript{25} predictions than the MPS predictions.

In terms of training time, the Bayesian regularization was by far the slowest, with an average training time of five minutes per prediction. The random forest regression completed one prediction in three seconds on average, and the multilayer perceptron finished a prediction in 51 milliseconds on average. The time it took all three of the candidate algorithms to generate results was significantly lower than the original finite element modelling process. This accomplished the desired order of magnitude reduction in time, from several days and hours to minutes or seconds. The practical applications of maintaining a high results prediction accuracy with this level of computational resource minimization are similar to the potential shown with the development of a convolution neural network for the prediction of MPS and brain area tissue strain by Wu et al. (2019) [122]. Wu et al. (2019) used a more complicated approach involving conceptualizing head rotational velocity profiles as two-dimensional images for input to their convolution neural network, but they aspired to generate regional results within the brain [122]. The study conducted in this chapter was focused on the entirety of the brain, as opposed to individual specific parts, so the simpler approach of applying the random forest regression model was tailored to this problem more appropriately. A more detailed approach to predicting a higher resolution of strain in the brain is discussed in Chapter 5.

The Universal Brain Injury Criterion (UBrIC) is a head injury metric developed by Gabler et al. (2018) that is applicable over a broad range of kinematics encountered in automotive crashes and sports [142]. UBrIC would be a valuable additional metric to examine AI predictability of head injury metrics in future work. An AI algorithm that can accurately predict UBrIC would be valuable as UBrIC is a head injury metric which has been shown to be closely aligned with head and brain impact finite element modelling results [7].

Multilayer perceptron optimization should also be further explored. Further tuning and optimization of this multilayer perceptron may yield higher quality results and eliminate
outlier values. Moving the multilayer perceptron from SPSS to a Python or MATLAB-based setup would allow for a greater number of options for tuning, such as using the multi-verse optimizer, which has been shown to be effective in training multilayer perceptrons [143], [144]. Exploring other types of algorithms and other types of languages may also be worth consideration. It may also be worth exploring the adaptation of this procedure for American football or other contact sports.

The main limitation of this study was that there were only 672 available tests completed between the six helmets from the data source [7]. Larger databases, particularly ones that focus on ice hockey helmet evaluation, on the order of hundreds of cases, are not widely available [139]. Having more data available would reduce the error in the prediction process and would allow more exclusion and prediction options [145]. Additionally, it was noted that when comparing predicted versus actual MPS and CSDM_{25} values, there were gaps between clusters of data because there were no MPS and CSDM_{25} values available for those ranges within the tested 672 cases. The location of these gaps varied for each helmet. Eliminating these gaps and having a more equal spread of data would reduce the overall error and increase prediction consistency.

3.6 Chapter Conclusions

In this chapter, a multilayer perceptron was implemented to rank the best kinematic input variable combinations for predicting MPS and CSDM_{25} values for different helmeted head impacts. Rotational kinematics, specifically rotational velocity, was confirmed to be an accurate kinematic for the prediction of brain strain loadings. In part two of this chapter, three candidate AI algorithms were evaluated in a helmet exclusion and prediction study. The random forest regression model performed the best, followed closely by the multilayer perceptron, and lastly the Bayesian regularization. Each candidate algorithm examined took significantly less time than the original finite element modelling process used to generate the original results, while still maintaining a high level of prediction accuracy. It was also confirmed that using a smaller data set to predict a larger number MPS and CSDM_{25} values resulted in a decreased but still acceptable level of prediction accuracy and error. For example, it was discovered that utilizing the
peak rotational velocity, peak linear and peak rotational acceleration as a kinematic input combination provided a simple and streamlined option for prediction inputs for future tests. The results of this chapter demonstrate that AI algorithms can be used to successfully predict MPS and CSDM_{25} values at least during ice hockey-relevant head impacts. In turn, this will help researchers and engineers to process physical head impact data with greater efficiency and at significantly lower computational costs than previously possible. The positive results discussed in this chapter led to further development of this concept, leading to the work discussed in Chapter 5.
Chapter 4

4 Quantifying the Effect of a Helmet in the Reduction of Blunt Impact-induced Brain Axon Fiber Tract Strain using an Advanced Finite Element Model of the Head

4.1 Chapter Abstract

This chapter focuses on the development and evaluation of a brain and head finite element model that incorporates detailed axon fiber tracts, and how this advanced model can be used to demonstrate the benefits of wearing helmets in activities where impacts to the head are common. A comparison of brain finite element models is presented, and critical axon fiber strain damage thresholds are defined. Helmeted impact data and bare head impact data are compared on a tract-by-tract basis. The results from the completed analyses show that the results generated from simulating impacts using the Brain Axon Fiber Tract GHBMC Model are helpful in quantifying axon fiber tract axial strain, an excellent correlate for mTBIs. These results are also useful in evaluating new helmets designed to prevent brain injuries in sports where impacts occur, such as ice hockey.

4.2 Introduction and the State of the Art in Finite Element Head and Brain Modelling

As outlined in Chapter 1, finite element modelling of the head and brain is one of the best tools that researchers have available to them to understand, study and analyze how and why mTBIs occur as a result of impacts to the head and upper body. The human head is comprised of many parts, including circulatory and nervous tissues, bones, muscles and other smaller organs such as those present in the ear and the eye. Each of these components of the head react differently to dynamic forces, and they also have vastly different material properties. A comprehensive, and detailed finite element model can account for all of these parts and their respective properties. Furthermore, the running of finite element models to predict how the head and brain react to impacts has no ethical concerns and is highly repeatable, as opposed to animal testing, which is costly, not as repeatable and carries ethical concerns involved with the treatment and sacrifice of the
animals after testing. This makes finite element modelling of the head and brain an excellent choice for researchers interested in studying mTBIs and DAI.

There are several existing validated head and brain models currently used in research and industry work. These include the SIMon Model, the Total Human Model for Safety (THUMS) Model, the Kungliga Tekniska Högskolan (KTH) Model, the Worcester (formerly Dartmouth) Head Injury Model (WHIM) and the base GHBMC Model.

The SIMon Model was developed in 2003 by Takhounts et al. (2003) [146]. It was designed to have simple geometry for short run times and was based on work originally done by Bandak and Eppinger (1994), DiMasi et al. (1995) and Bandak et al. (2001) [147]–[149]. The model includes elements that represent a rigid skull, cerebrospinal fluid, cerebrum, cerebellum, brain stem, ventricles, bridging veins, the falx and the tentorium [150]. A Kelvin-Maxwell viscoelastic material is used as the material for the brain tissue [150]. This model does not contain a high level of detail beyond the named components, opposed to more modern models [150].

The THUMS Model was developed by Toyota Central Research and Development Lab in Nagakute, Japan and first distributed in 2000 [150]. This model was originally developed by Toyota for evaluating occupant safety in its vehicles. This model is a full human body finite element model. There are several versions of the THUMS Model for different genders and ages of people, which is valuable for studying the effects of impacts on different ages of people [151]. The THUMS model contains finite element representations of the facial bones and skull, the cerebrum with distinct white and grey matter areas, the cerebellum, the cerebrospinal fluid, the brainstem, the meningeal membranes such as the dura mater and pia mater, the falx cerebri, the tentorium cerebelli and the sagittal sinus [150], [151]. Grey and white matter in the brain was modelled using a linear viscoelastic material [150], [151].

The KTH Model was proposed Kleiven and Hardy (2002) [152]. This model includes finite element representations of the scalp, skull cerebrum, cerebellum, meninges, cerebrospinal fluid, bridging veins and a simplified model of the neck. This model was
experimentally validated in 2006 [153]. Two validated versions of the model exist, and they are slightly different. The first validated version has the brain modelled using a hyperelastic Mooney-Rivlin constitutive material, combined with a linear viscoelastic model to account for rate effects [150]. The Mooney-Rivlin material and associated shear constants are from Mendis et al. (1995), updated in scale to correspond to a long-term effective modulus of 520 Pa [154]. The second validated version of the model has a brain modelled using an Ogden material, which is described in Kleiven (2007) as the more commonly used of the two [155].

The WHIM used to be known as the Dartmouth Head Injury Model. The WHIM was created from high resolution T1 weighted MRIs of an athlete who was clinically diagnosed with a mTBI [156]. The model contains finite element representations of the skull, facial bones, cerebrum with combined white and grey matter, cerebellum, brainstem, corpus callosum, meningeal layers, cerebrospinal fluid, falx cerebri and tentorium cerebelli [150], [156]. The material used in the brain is the same as the one used in the Ogden version of the KTH Model in Kleiven (2007) [150].

The base GHBMC Model uses MRI and computerized tomography (CT) scans of an average adult male as a base for meshing a computer aided design (CAD) finite element model of the head and brain [150]. This model includes finite element representations of the skin, skull, facial bones, sinuses, cerebrum, cerebellum, lateral ventricles, corpus callosum, thalamus, brainstem, falx, tentorium, bridging veins and meningeal layers [150]. A Kelvin-Maxwell viscoelastic material was used to model the gray and white matter in the finite element representations of the brain [150]. The base GHBMC Model was validated through experimental data published in Hardy et al. (2001) and in Hardy et al. (2007), and brain pressure measures from Nahum et al. (1997) [157]–[159].

A comparison of the features and statistics of each of the above models is shown in Table 9.
Table 9: Comparison of Existing Widely Available Validated Finite Element Head and Brain Models [150]

<table>
<thead>
<tr>
<th>Model Name</th>
<th>Number of Elements</th>
<th>Number of Nodes</th>
<th>Head Mass (kg)</th>
<th>Finite Element Brain Material</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIMon</td>
<td>46,000</td>
<td>42,500</td>
<td>1.10 (brain only)</td>
<td>Viscoelastic</td>
</tr>
<tr>
<td>THUMS</td>
<td>62,000</td>
<td>38,000</td>
<td>1.08 (brain only)</td>
<td>Viscoelastic</td>
</tr>
<tr>
<td></td>
<td>18,000</td>
<td>20,000</td>
<td>4.44</td>
<td>Mooney-Rivlin (Hyperelastic)</td>
</tr>
<tr>
<td>KTH</td>
<td>21,000</td>
<td>17,000</td>
<td>4.52</td>
<td>Ogden (Hyperelastic)</td>
</tr>
<tr>
<td>WHIM</td>
<td>115,000</td>
<td>101,000</td>
<td>4.56</td>
<td>Ogden (Hyperelastic)</td>
</tr>
<tr>
<td>GHBMC (base)</td>
<td>230,000</td>
<td>190,000</td>
<td>1.19 (brain only)</td>
<td>Viscoelastic</td>
</tr>
</tbody>
</table>

While these models feature detailed models of the skin and bones, none of them feature definitive axon fiber tract modelling accurate to real human brains. There exists a gap in the library of finite element models widely available to researchers, as studying impact-induced strain in brain axon fiber tracts is necessary for further understanding where and how mTBIs occur due to blunt impacts. Work completed by Gerber et al. (2018) and Wu et al. (2019) served as the inspiration for the creation of a finite element head and brain model featuring defined axon fiber tracts based on an existing validated head and brain finite element model [160], [161]. While the previous development of this model by the members of Dr. Mao’s research group is not central to the content of this chapter, this chapter does aim to compare and contrast the results output from the validated base GHBMC and the Brain Axon Fiber Tract GHBMC Models with existing data and also to quantify the effect a helmet has in decreasing brain axon fiber strain with new data, which is a better correlate for mTBIs and DAIs than MPS and CSDM$_{25}$ [162].
4.3 Evolving the Base GHBMC Model into an Atlas-based, Parcellated Axon Fiber Embedded Head Model

As noted previously, the Brain Axon Fiber Tract GHBMC Model was developed from the base GHBMC Model, which has been used extensively in the automotive safety industry for mTBI research [160], [163]. Axon tractography was completed using the three-dimensional tractography method known as diffuse tensor imaging. Brain masking, atlas registration and fiber parcellation was done using 3Dslicer and DSI Studio, which yielded three dimensional tractography generation of the whole brain. A custom MATLAB script was used to convert from points to lines for use in the finite element meshing process, which was completed in HyperMesh. Material properties were also added at this time. Lastly, using anatomical references, the whole brain tractography was embedded into the base GHBMC Model. It was decided to use a one percent axon representation, meaning that only one percent of the axons were modelled in the brain. This was done to maximize computational cost savings while still maintaining a high quality of results. Optimization to lower the computational cost of running this model while still maintaining a high quality of results was done in previous work completed by Dr. Mao’s research group. This model, with added axon fiber tract details, was named the Brain Axon Fiber Tract GHBMC Model.

The Brain Axon Fiber Tract GHBMC Model features detailed tractography of 33 key brain axon fiber tracts. The finite element modelling statistics for these tracts are shown in Table 10.

<table>
<thead>
<tr>
<th>Name of Parcellated Axon Fiber Tract</th>
<th>Number of Axon Fibers Per Tract (1% Model)</th>
<th>Number of Finite Elements Per Tract</th>
<th>Average Number of Finite Elements Per Tract</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arcuate Fasciculus</td>
<td>112</td>
<td>6,851</td>
<td>61.17</td>
</tr>
<tr>
<td>Cingulum Bundle</td>
<td>159</td>
<td>6,530</td>
<td>41.07</td>
</tr>
<tr>
<td>Pathway</td>
<td>Length (mm)</td>
<td>Width (mm)</td>
<td>Density (%)</td>
</tr>
<tr>
<td>-------------------------------------------------------</td>
<td>-------------</td>
<td>------------</td>
<td>-------------</td>
</tr>
<tr>
<td>Cortico-Ponto-Cerebellar Pathway</td>
<td>9</td>
<td>521</td>
<td>57.89</td>
</tr>
<tr>
<td>Corona-Radiata-Frontal Tract</td>
<td>77</td>
<td>5,026</td>
<td>65.27</td>
</tr>
<tr>
<td>Corona-Radiata-Parietal Tract</td>
<td>15</td>
<td>969</td>
<td>64.60</td>
</tr>
<tr>
<td>Corpus Callosum</td>
<td>550</td>
<td>31,060*</td>
<td>56.47</td>
</tr>
<tr>
<td>Corticospinal Tract</td>
<td>81</td>
<td>5,455</td>
<td>67.35</td>
</tr>
<tr>
<td>External Capsule</td>
<td>20</td>
<td>1,626</td>
<td>81.30</td>
</tr>
<tr>
<td>Extreme Capsule</td>
<td>22</td>
<td>1,653</td>
<td>75.14</td>
</tr>
<tr>
<td>Internal Capsule</td>
<td>23</td>
<td>555</td>
<td>24.13</td>
</tr>
<tr>
<td>Inferior Longitudinal Fasciculus</td>
<td>176</td>
<td>9,426</td>
<td>53.56</td>
</tr>
<tr>
<td>Intracerebellar Input and Purkinje Tract</td>
<td>165</td>
<td>3,191</td>
<td>19.34</td>
</tr>
<tr>
<td>Intracerebellar Parallel Tract and the Cerebellum</td>
<td>260</td>
<td>3,517</td>
<td>13.53</td>
</tr>
<tr>
<td>Inferior Frontal-Occipito Fasciculus</td>
<td>77</td>
<td>6,232</td>
<td>80.94</td>
</tr>
<tr>
<td>Middle Cerebellar Peduncle</td>
<td>54</td>
<td>3,113</td>
<td>57.65</td>
</tr>
<tr>
<td>Middle Longitudinal Fasciculus</td>
<td>177</td>
<td>8,750</td>
<td>49.44</td>
</tr>
<tr>
<td>Tract</td>
<td>Length</td>
<td>Width</td>
<td>Angle</td>
</tr>
<tr>
<td>--------------------------------------</td>
<td>--------</td>
<td>-------</td>
<td>-------</td>
</tr>
<tr>
<td>Posterior Limb of Internal Capsule</td>
<td>22</td>
<td>1,116</td>
<td>50.73</td>
</tr>
<tr>
<td>Frontostriatal Tract</td>
<td>169</td>
<td>5,498</td>
<td>32.53</td>
</tr>
<tr>
<td>Superior Longitudinal Fasciculus</td>
<td>327</td>
<td>17,859*</td>
<td>54.61</td>
</tr>
<tr>
<td>Striato-Occipital Tract</td>
<td>14</td>
<td>748</td>
<td>53.43</td>
</tr>
<tr>
<td>Striato-Parietal Tract</td>
<td>17</td>
<td>747</td>
<td>43.94</td>
</tr>
<tr>
<td>Superficial-Frontal Tract</td>
<td>855</td>
<td>27,177</td>
<td>31.79</td>
</tr>
<tr>
<td>Superficial-Frontal-Parietal Tract</td>
<td>113</td>
<td>3,375</td>
<td>29.87</td>
</tr>
<tr>
<td>Superficial-Occipital Tract</td>
<td>63</td>
<td>1,460</td>
<td>23.17</td>
</tr>
<tr>
<td>Superficial-Occipital-Temporal Tract</td>
<td>88</td>
<td>3,019</td>
<td>34.31</td>
</tr>
<tr>
<td>Superficial-Parietal Tract</td>
<td>424</td>
<td>13,574</td>
<td>32.01</td>
</tr>
<tr>
<td>Superficial-Parietal-Occipital Tract</td>
<td>117</td>
<td>3,316</td>
<td>28.34</td>
</tr>
<tr>
<td>Superficial-Parietal-Temporal Tract</td>
<td>293</td>
<td>10,436</td>
<td>35.62</td>
</tr>
<tr>
<td>Superficial-Temporal Tract</td>
<td>200</td>
<td>5,861</td>
<td>29.31</td>
</tr>
<tr>
<td>Thalamo-Frontal Tract</td>
<td>228</td>
<td>10,218</td>
<td>44.82</td>
</tr>
<tr>
<td>Thalamo-Occipital Tract</td>
<td>38</td>
<td>1,753</td>
<td>46.13</td>
</tr>
</tbody>
</table>
A total of 5,058 individual brain axon fibers and 206,397 beam elements were modelled in the one percent finite element model. The corpus callosum and superior longitudinal fasciculus are marked with stars in Table 10 because they are represented by multiple parts in the Brain Axon Fiber Tract GHBMC Model. The corpus callosum is represented by seven different parts (CC1 to CC7) and the superior longitudinal fasciculus is modelled as three different parts (SLF-I to SLF-III).

Table 11: Brain Axon Fiber Tract GHBMC Model Statistics

<table>
<thead>
<tr>
<th>Model Name</th>
<th>Number of Elements</th>
<th>Number of Nodes</th>
<th>Head Mass (kg)</th>
<th>Finite Element Brain Material</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain Axon Fiber Tract GHBMC Model</td>
<td>476,950</td>
<td>601,605</td>
<td>4.37</td>
<td>Solid brain elements: Kelvin-Maxwell viscoelastic material. Brain axon fibers: Elastic material (MAT type 1 in LS-DYNA), viscoelastic material (MAT type 6 in LS-DYNA), Hyperelastic Mooney-Rivlin material (MAT 27 in LS-DYNA)</td>
</tr>
</tbody>
</table>

The newly added axon fibers are shown in Figure 69, surrounded by the dura mater meninge that represents the shape of the brain.
The development of this type of advanced model allows researchers to focus on specific tract injuries, as opposed to the whole brain, which was a limitation of previous models.

4.4 Comparison of the Base GHBMC Model and the Brain Axon Fiber Tract GHBMC Model

A median plane slice wireframe comparison of the difference between the base and Brain Axon Fiber Tract GHBMC Models is shown in Figure 70.
By increasing the density of elements in the finite element model, more detailed impact-induced strain results can be analyzed, which gives researchers more information. In particular, the cerebellum and deep brain areas are more detailed in the Brain Axon Fiber Tract GHBMC Model than in the base GHBMC model.

This added finite element density increases the run time and resultant output of the Brain Axon Fiber Tract GHBMC Model. A comparison of the size and the run times of the models is shown in Table 12.

<table>
<thead>
<tr>
<th>Statistic</th>
<th>Base GHBMC Model</th>
<th>Brain Axon Fiber Tract GHBMC Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Input File Size</td>
<td>34.3 MB</td>
<td>81.5 MB</td>
</tr>
<tr>
<td>Computational Cost</td>
<td>2 Hours</td>
<td>34 to 40 Hours</td>
</tr>
<tr>
<td>Output File Size</td>
<td>7 GB</td>
<td>48 GB</td>
</tr>
</tbody>
</table>

For an accurate comparison between the Brain Axon Fiber Tract GHBMC Model and the base GHBMC Model, results from simulations with the same input kinematics must be consistent. Due to the interactions between the newly added finite elements representing
the axon fiber tracts and the existing solid and shell finite elements that make up the brain tissue components, the strain magnitudes and patterns of the elements present in both models will not be identical. The Brain Axon Fiber Tract GHBMC Model and the base GHBMC Model have been compared analytically in previous work conducted by members of Dr. Mao’s research group. A visual comparison was also conducted to confirm these analytical results using a median plane slice of each of the finite element models at the same time step. Results of this median plane slice comparison are shown in Figure 71.
Figure 71: Comparison of Strain Patterns and Magnitudes, Base GHBM Model (Left Column) Versus Brain Axon Fiber Tract GHBM Model (Right Column). Low Energy Impact Case. The Cerebrospinal Fluid Elements Are Hidden in Both Models. 71A and 71B Show the Base State of the Models (t=0 Milliseconds); 71C and 71D Show the Peak Strain Condition of the Models (t=15 Milliseconds); 71E and 71F Show the End State of the Models (t=80 Milliseconds).
Figures 71C and D show the peak strain condition of the simulation, and the same areas of the brain tissue finite elements are strained. The strain patterns are equivalent between the base GHBMC Model and the Brain Axon Fiber Tract GHBMC Model and this aligns with the previous comparative analytical work done by members of Dr. Mao’s research group. Therefore, while the addition of the parcellated axon fiber tract elements does slightly change the output of the model, the results remain accurate and can be compared between models fairly.

4.5 Comparing the Cumulative Reduction of Blunt Impact-induced Axon Fiber Strain Bare Head Cases of Various Helmets

The Brain Axon Fiber Tract GHBMC Model uses two-point beam elements with a constant thickness to represent axon fibers in the brain. The elongation of these beam elements under load is quantified by axial strain measurements. The Brain Axon Fiber Tract GHBMC Model uses true strain behaviour as opposed to engineering strain. The difference in equations and behaviour is shown in Figure 72, along with the axial strain measurement process that is involved with calculating the damage-causing strain.

\[
\varepsilon_e = \frac{\Delta L}{L_0} = \frac{L - L_0}{L_0} \quad \varepsilon_t = \int_{L_0}^{L} \frac{\delta L}{L} = \ln(1 + \varepsilon_e)
\]

**Figure 72: Blunt Impact-induced Strain in Brain Axon Fiber Tracts**
The threshold at which axon fiber tracts are damaged has been studied in Bain and Meaney (2000) [164]. This study found several different critical strain thresholds in \textit{in vivo} testing. The breakdown of the various thresholds described is in Table 13.

**Table 13: Strain Thresholds from Bain and Meaney (2000) [164]**

<table>
<thead>
<tr>
<th>Bain and Meaney (2000) Strain Threshold</th>
<th>Converted True Strain Threshold</th>
<th>Threshold Identifier</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.13</td>
<td>0.116</td>
<td>Conservative</td>
<td>Lowest strain threshold used to evaluate electrophysiological impairment and damage in the study</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Lowest Lagrangian strain damage</td>
</tr>
<tr>
<td>0.14</td>
<td>0.123</td>
<td>Conservative</td>
<td>threshold from the morphological damage study</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Optimal Lagrangian strain damage</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Optimal</td>
<td>threshold from the study</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Optimal strain threshold used to study</td>
</tr>
<tr>
<td>0.18</td>
<td>0.154</td>
<td>Optimal</td>
<td>electrophysiological impairment and damage</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Highest strain threshold used to study</td>
</tr>
<tr>
<td>0.21</td>
<td>0.175</td>
<td>Optimal</td>
<td>electrophysiological impairment and damage</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Highest Lagrangian strain damage</td>
</tr>
<tr>
<td>0.28</td>
<td>0.222</td>
<td>Liberal</td>
<td>threshold intended to minimize the detection of false positives</td>
</tr>
<tr>
<td>0.34</td>
<td>0.259</td>
<td>Liberal</td>
<td></td>
</tr>
</tbody>
</table>

The threshold of 0.21 was chosen as the critical brain axon fiber strain threshold as Bain and Meaney (2000) reported this value balanced specificity and sensitivity measures used in their study better than the other suggested values [164]. After completing the running of all 672 helmeted impact cases and nine bare head impact cases, these cases were post-processed, and axial strain values were output to Excel datasheets for each tract. Two groupings of data were performed at this time. For the first grouping, helmeted impact cases were grouped only by direction and impact energy. For the second grouping,
helmeted impact cases were grouped together by helmet type, impact energy and direction. An average case for each division was created by averaging the output Excel datasheets within each grouping. This averaging process was repeated for the bare head cases. For the helmeted data, only low energy data was compared to the bare head data for each direction. Bare head data was only collected at low impact energy, so only the low energy helmeted data was used to ensure a fair comparison. Maximum axial strain values, in both the various average helmeted cases and the bare head cases, were extracted for each element. The difference between these values measures the change in brain axon fiber tract axial strain. The comparison performed in Figure 73 aims to quantify the overall performance of helmets in a population of ice hockey players, since it is unreasonable to assume all ice hockey players wear the same model of helmet. The result of the comparison performed in Figures 74 to 79 was the change in impact-induced axial strain that each of the different specific helmet models was able to be quantified.

4.6 Methods of Head Impact Kinematics Data Collection

The same helmeted impact kinematics data was used from the collection work detailed in Section 3.3. Each of the 672 helmeted impact cases from Chapter 3 was re-run using the Brain Axon Fiber Tract GHBMC Model. Kinematics were scaled to the correct units with a bespoke MATLAB script prior to addition to the model, as opposed to performing the adjustment with scaling factors in the model. The Brain Axon Fiber Tract GHBMC Model uses kilograms, millimeters and milliseconds as units.

Bare head impact kinematics data was collected by Bauer Hockey Ltd. using the same test methodology and same dummy head and neck setup described in Chapter 3. However, due to concerns about the surface integrity of the dummy head in testing at higher impact speeds, only low energy impacts at 2.6 meters per second were conducted. Two front tests, four rear tests and three side tests were conducted per the testing procedure outlined in Chapter 3.
4.6.1 Results and Discussion

The average axial strain experienced in the brain axon fiber tracts for a low energy impact for each case is shown in Table 14. The percentage reduction in axon fiber strain between an average bare and average helmeted impact is also calculated and shown.

Table 14: Average Maximum Axial Strain in Brain Axon Fiber Tracts Experienced by Various Groups of Helmeted and Bare Head Impact Cases

<table>
<thead>
<tr>
<th>Helmet</th>
<th>Average Maximum Axial Strain in Brain Axon Fiber Tracts from Frontal Impacts</th>
<th>Average Maximum Axial Strain in Brain Axon Fiber Tracts from Rear Impacts</th>
<th>Average Maximum Axial Strain in Brain Axon Fiber Tracts from Side Impacts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Helmet A only</td>
<td>0.0264</td>
<td>0.0344</td>
<td>0.0253</td>
</tr>
<tr>
<td>Helmet B only</td>
<td>0.0279</td>
<td>0.0308</td>
<td>0.0260</td>
</tr>
<tr>
<td>Helmet C only</td>
<td>0.0262</td>
<td>0.0325</td>
<td>0.0207</td>
</tr>
<tr>
<td>Helmet D only</td>
<td>0.0276</td>
<td>0.0316</td>
<td>0.0244</td>
</tr>
<tr>
<td>Helmet E only</td>
<td>0.0292</td>
<td>0.0308</td>
<td>0.0304</td>
</tr>
<tr>
<td>Helmet F only</td>
<td>0.0278</td>
<td>0.0304</td>
<td>0.0248</td>
</tr>
<tr>
<td>All Helmets</td>
<td>0.0269</td>
<td>0.0305</td>
<td>0.0250</td>
</tr>
<tr>
<td>Together</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bare Head</td>
<td>0.0352</td>
<td>0.0406</td>
<td>0.0496</td>
</tr>
<tr>
<td>Percentage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reduction of Axon Fiber Strain, Bare vs. Helmeted</td>
<td>23.6%</td>
<td>24.9%</td>
<td>49.6%</td>
</tr>
</tbody>
</table>

Examining these results, helmets offer the greatest reduction in average axial strain in side impacts. The reduction in average axial strain that helmets provide in frontal and rear
impacts is approximately half as much as the reduction in average axial strain in side impacts. All groupings of helmets were lower than bare head average axial strain in all of the frontal, rear and side directions. While it is useful to examine the data in this simplified format because one number can represent the entire axial strain of all tracts examined in the brain, it should be noted that the results are skewed due to the large amount of averaging that takes place, firstly within tracts themselves, and secondly by the number of helmet impact cases that are averaged together within each grouping. Therefore, a better approach is to examine data on a tract-by-tract basis, as done in Sections 4.6.1.1 and 4.6.1.2.

4.6.1.1 Tract-Specific Results for Average Helmet Case

Impact cases were grouped by direction for this analysis case, with only the low energy helmeted impacts used to compare evenly to the bare head impact cases. The change in the average maximum axial strain experienced by each tract from wearing a helmet compared to a bare head impact is shown in Figure 73. Standard error bars to communicate the standard deviation of the sampling distribution of each tract are also provided.
Figure 73: Change in Average Maximum Axial Strain, Bare Head Impacts vs. Helmeted Impacts
The results presented in the graph in Figure 73 are in line the results displayed in Table 14. Side impacts had a larger overall decrease in axon fiber axial strain than the front or rear impacts. Although examining impacts on a per-tract basis removes the ability to simplify to one number the entire strain experienced in an impact by the Brain Axon Fiber Tract GHBMC Model, examining data in this manner is a more accurate and representative method of analysis.

For the front impact case, the theoretical highest amount of dynamic force experienced by the brain will be in the frontal lobes of the brain due to its proximity to the impact. In the frontal direction, the tracts that experienced the highest decreases in axial strain were the intracerebellar input and Purkinje tract, the corona-radiata-frontal tract and the internal capsule.

For the rear impact case, the theoretical highest amount of dynamic force experienced by the brain will be in the occipital lobes, parietal lobes and the cerebellum. The tracts that experienced the largest decrease in axon fiber axial strain in the case of rear impacts were the inferior longitudinal fasciculus, the superficial-occipital-temporal tract and the middle cerebellar peduncle. These tracts are all located near the rear of the cranium and close to the impact area. Additionally, most tracts that experienced large strain decreases in the case of a rear impact are in plane with the impactor.

Comparing the reduction in average axial strain in the front and the rear impact directions, the results are similar in terms of magnitude. This was expected as, when impacted, the head is rotating in the same plane in both a front and rear impact, albeit in a different direction. The impact energy for all of these comparative tests is the same, so the reduction in average axial strain for both front and rear impacts should be similar. Similarity in the front and rear directions were found, which reaffirms the finite element modelling and the impact setup process are working as intended, and that the outputs of the model can be trusted.

For the side impact case, the theoretical highest amount of dynamic force experienced by the brain will be in the temporal and occipital lobes, due to the location of the impact
point. The tracts that experienced the largest decrease in axon fiber axial strain in the case of side impacts were the superficial-occipital tract, superficial-parietal-occipital tract, the superficial parietal-temporal tract and the superficial superficial-occipital-temporal tract. These tracts are all in the vicinity of the impact side and in-plane with the impactor, so a large strain decrease was expected in this comparison.

The results from this finite element study are aligned with the results of Kraus et al. (1970), as a large reduction in axon fiber tract axial strain will correspond with a decrease in the incidence rate of mTBIs [16]. These results show that wearing a helmet while participating in an activity where head impacts are expected, such as ice hockey, can decrease the magnitude of brain axon fiber tract strain. As brain axon fiber tract strain is a correlate for mTBIs and DAI, wearing a helmet while participating in these activities will lower the incidence rate and severity of brain injuries.

The above analysis compared an average bare head impact case to an average ice hockey helmeted impact case. Six different ice hockey helmet models were included in the average helmeted case above. To continue this analysis, it is useful to compare the change in average maximum axial strain from the bare head impacts to each individual helmet model. This is done in Section 4.6.1.2.

4.6.1.2 Tract-Specific Results for Individual Helmet Cases

The same directional tract-by-tract analysis was conducted for each individual ice hockey helmet, highlighting the individual effectiveness of each of the six models of helmets that were evaluated in the study. The results of this further analysis are shown in Figures 74 to 79.
Figure 74: Change in Average Maximum Axial Strain, Bare Head Impacts vs. Helmet A Impacts
Figure 75: Change in Average Maximum Axial Strain, Bare Head Impacts vs. Helmet B Impacts
Figure 76: Change in Average Maximum Axial Strain, Bare Head Impacts vs. Helmet C Impacts
Figure 77: Change in Average Maximum Axial Strain, Bare Head Impacts vs. Helmet D Impacts
Figure 78: Change in Average Maximum Axial Strain, Bare Head Impacts vs. Helmet E Impacts
Figure 79: Change in Average Maximum Axial Strain, Bare Head Impacts vs. Helmet F Impacts
The results in Figures 74 to 79 demonstrate results in line with the previously completed analyses, showing that, overall, wearing a helmet of any type decreases the axon fiber axial strain experienced in the brain during an impact. As seen in the previous two analyses, the decrease in axial strain in the side impacts was higher than the decrease in strain in the frontal or the rear impacts. The results in Figures 74 to 79 are consistent with literature such as Kraus et al. (1970), in that they demonstrate that wearing a helmet while participating in activities where head impacts are expected, such as ice hockey, decreases brain axon fiber tract strain and protects users from injuries such as mTBIs and DAI.

Figures 80 to 82 show the same data as in Figures 74 to 79, although it has been re-ordered so that the frontal, rear and side tract-by-tract results of each helmet are grouped together. Utilizing this ordering of data allows for easier study of the performance of each helmet in reducing the axon fiber tract axial strain. Standard error bars to communicate the standard deviations of the sampling distributions are also provided.
Figure 80: Change in Average Maximum Axial Strain, Frontal Bare Head Impact versus Six Helmet Models’ Frontal Impacts
Figure 81: Change in Average Maximum Axial Strain, Rear Bare Head Impact versus Six Helmet Models’ Rear Impacts
Figure 82: Change in Average Maximum Axial Strain, Side Bare Head Impact versus Six Helmet Models’ Side Impacts
In the frontal impact direction, all six helmets performed at approximately the same level. Helmets A and C consistently showed the largest decreases in each tract when comparing helmeted impact and bare impact cases, meaning they performed better than the rest in this assessment. Helmet E consistently showed a smaller decrease when the bare and helmeted impact cases were compared, meaning it performed poorly in this assessment. Helmets B, D and F showed similar decreases in each tract when compared. As noted previously, the intracerebellar input and Purkinje tract, the corona-radiata-frontal tract, and the internal capsule tracts experienced the largest decrease in axon fiber axial strain under frontal loading conditions. The tracts that had the largest variation in calculated error were the cortico-ponto-cerebellar pathway, the internal capsule and the intracerebellar input and Purkinje tract.

In the rear impact direction, similar results to the frontal impact direction were observed. Again, all six helmets performed at approximately the same level. Helmets B and F consistently showed the largest decreases in each tract when comparing helmeted impact and bare impact cases, meaning these helmets performed better than in the rest of this assessment. Helmet A consistently showed a smaller decrease when the bare and helmeted impact cases were compared, meaning it performed poorly in this assessment. Helmets C, D and E showed similar decreases in each tract when compared. As noted previously, the inferior longitudinal fasciculus, the superficial-occipital-temporal tract and the middle cerebellar peduncle experienced the largest decrease in axon fiber axial strain under rear loading conditions. The tracts that had the largest variation in calculated error were the internal capsule, the cortico-ponto-cerebellar pathway and the intracerebellar input and Purkinje tract. The same set of axon fiber tracts produced a large variation in calculated error in the frontal and rear impact directions.

In the side impact direction, the largest decreases in strain were observed. The largest differences in helmet performance were also observed. The superficial-occipital tract, the superficial-parietal-occipital tract, superficial-occipital-temporal tract and superficial-parietal-temporal tract experienced the largest strain decreases across all helmets. Helmets B, C and F performed the best in terms of reducing axon fiber axial strain during
side impacts. Helmet E was consistently the worst performer of the six helmet models evaluated. Out of any tract in any direction, the superficial-occipital tract in the side direction experienced the largest decrease in strain. The side impact error values were lower compared to the magnitudes of the decrease in strain. The tract that experienced the highest error of the side impacts was the cortico-ponto-cerebellar pathway.

The results shown in Figures 80 to 82 are consistent with the literature, such as Kraus et al. (1970) [16]. The results from the finite element study comparing the axon fiber axial strain levels of bare head impact cases to helmeted impact cases definitively show that wearing a helmet while participating in activities where impacts are expected, such as ice hockey, will decrease the incidence rate and severity of brain injuries such as mTBIs and DAI.

4.7 Chapter Conclusions

This chapter focused on the development and evaluation of a detailed brain and head finite element model and using this model to demonstrate the benefits of wearing helmets in activities where impacts to the head are common, such as ice hockey. A comparison of widely available and validated head and brain models was presented, and statistics were given for each model, such as number of elements per model and model mass. The Brain Axon Fiber Tract GHBMC Model was presented, and it was compared to the base GHBMC Model from which it is derived. Critical axon fiber strain damage thresholds were defined. A detailed analysis was conducted using the Brain Axon Fiber Tract GHBMC Model which quantified the benefits of wearing a helmet during head impacts in helmeted and bare impact cases. Both an average helmeted analysis case and a helmet-specific analysis case were examined, and these cases were compared to equivalent bare head testing on a tract-by-tract basis. A comparison of helmet models on a tract-by-tract basis was also conducted. Under front, rear and side impact conditions, helmets reduced axon fiber strains on average by 23.6%, 24.9% and 49.6% respectively. These analyses show that the results from the Brain Axon Fiber Tract GHBMC Model align with the current literature and research in that helmets are an effective tool for preventing brain injuries in activities where impacts to the head are common. Furthermore, it has been
shown that finite element modelling is an effective tool for quantifying axon fiber axial strain, which is a correlate for mTBIs and DAIs.
Chapter 5

5 Selection, Development and Implementation of an Artificial Intelligence Pipeline for the Prediction of Blunt Impact-induced Brain Axon Fiber Tract Strain

5.1 Chapter Abstract

This chapter focuses on the research, development and implementation of an artificial intelligence model to predict brain axon fiber tract axial strain, a strong correlate for DAI. After completing a qualitative and quantitative evaluation of five different prediction algorithms, CatBoost was selected as the best candidate algorithm. A total of 369 datasets and corresponding hyperparameter sets were created using data from previous simulation work to train the CatBoost algorithm. A literature review yielded six axon fiber tracts for evaluation based on their relation to concussive mTBIs. These six axon fiber tracts were used to evaluate the performance of the algorithm. Overall, the novel prediction pipeline comprised of the fully developed and open source CatBoost algorithm was able to successfully predict axon fiber tract axial strain in these six tracts with low error and high correlation.

5.2 Introduction to the Relationship between Artificial Intelligence and Head and Brain Impacts

AI is the intelligence of machines and the branch of computer science and engineering that aims to create it [165]. The field of AI encompasses the science and engineering of making intelligent machines, especially intelligent computer programs [165]. AI is often used to describe machines or computers that mimic cognitive functions that humans associate with the human mind, such as learning and problem solving. Machine learning (ML) is a branch of AI concerned with the design and development of algorithms to build mathematical models based on provided sample data to make predictions without being explicitly programmed to perform the task [166]. This sample data is also known as training data.
AI and ML are powerful concepts that can be applied to advance the field of prevention of brain injuries through the prediction of strain in the brain caused by an impact. The work done in Chapter 2 showed that a multilayer perceptron can be accurately used to predict mTBI metrics such as MPS and CSDM. Previously completed studies utilizing AI and ML concepts to predict tissue strain caused by impacts and subsequent injuries such as concussions in the brain include Wu et al. (2019), Zhan et al. (2021), and in Ghazi et al. (2021) [122], [167], [168]. These studies primarily focused on regional brain strains with less detailed models than the Brain Axon Fiber Tract GHBMC Model. An effective and validated AI model trained using output data from the Brain Axon Fiber Tract GHBMC Model presents potentially broad implications for the field of brain injury research. An AI model also may be able to outperform an equivalent finite element model in terms of calculation time, computing resources and cost, meaning that these cheaper and effective models can be deployed on a wider scale outside the laboratory. Additionally, AI may also be able to detect new connections between impact kinematics and brain axon fiber tract strain, allowing researchers to explore these new relationships and acquire a deeper understanding of the mechanisms of mTBIs.

5.3 Types of Artificial Intelligence Models and an Overview of Specific Models

The problems that can be solved using AI models can be organized by several key distinctions. By understanding these points of distinction, the correct model can be selected for the task at hand.

The first important classifier is whether the problem requires the use of a supervised, semi-supervised, unsupervised or reinforcement learning. Supervised learning maps an input to an output based on example input-output combinations [169]. These combinations come from a set of training examples, with an input object and a desired output value [169]. An algorithm using supervised learning will analyze the training data and create an inferred function, which can then be applied to map new examples. This training data is entirely labelled, meaning that the model should not have to label or infer the label from the dataset [170]. Common types of algorithms that utilize supervised
learning include linear regression models, decision trees and multilayer perceptrons. Semi-supervised learning is similar to supervised learning, with the major difference being that only a small amount of training data is labelled, with the remaining majority not labelled. This structure can produce a considerable improvement in learning accuracy for training data with a lesser amount of labeling [171]. This type of learning exists because it is costly to label data using skilled human experts. Semi-supervised learning methods utilize the notion that even though the relations between the unlabeled data or datasets are unknown, they carry important information about the dataset or group parameters. Unsupervised learning is a type of algorithm that learns patterns from sets of unlabeled data [172]. These methods exhibit self-organization that captures patterns as probability densities or as a combination of neural feature preferences [172]. Unsupervised learning is frequently applied to problems such as creating pictures, generating videos or synthesizing speech [172]. Unsupervised learning can be used to recognize patterns, rules, trends and meaningful insight in data that a human would not be able to recognize [172]. Reinforcement learning is another level within the supervision spectrum, where the chosen algorithm is given only a numerical performance score as guidance along with unlabeled data. The goal of reinforcement learning is to find a balance between the exploration of uncharted territory in the data and the exploitation of the current knowledge extracted from analysis completed in the data [173]. Partially supervised reinforcement algorithms can combine the advantages of supervised algorithms and reinforcement algorithms [174]. Reinforcement learning algorithm applications include computerized games of chess and go, robotic limbs and self-driving cars.

The post-processed output of the Brain Axon Fiber Tract GHBMC Model is fully labelled data, meaning a model that uses supervised learning to predict blunt impact-induced brain axon fiber strain is optimal for this problem. Within the realm of supervised learning, there are two classic types of problems. These types of problems are classifier problems and regression problems. Classifier problems involve predicting the class of given data points based on a mapping function from input variables to output variables [175]. In classification, target outputs are provided with input data as part of a
training dataset. Examples of classification algorithms include naïve Bayes models and k-nearest neighbour models. Regression problems study the relationship between a certain number of features and a continuous target variable, and usually involve a quantitative or numerical answer, as opposed to a classification which tends to involve coming up with qualitative answers [175], [176]. A regression problem can be as simple as a simple linear regression, plotting a straight line through a set of data. Some other examples of regression algorithms include gradient boosting regressors, support vector regressors and random forest regressors. The three most common metrics used for evaluating a trained regression model are error, bias and variance [176]. The nature of the problem is that of regression because the desired output is quantitative and qualitative.

After a literature review was conducted on the available types of supervised learning regression algorithms, three main structures were chosen for further research. These structures are deep neural networks (Section 5.3.1), random forest regression algorithms (Section 5.3.2) and gradient boosting machines (GBMs) (Section 5.3.3).

5.3.1 Deep Neural Networks

Deep neural networks are the result of decades of research that started with a single layer perceptron, originally proposed in 1958 by American psychologist Frank Rosenblatt [177]. This original idea was criticized because it failed to solve linearly inseparable problems [178]. However, a single layer perceptron with a signal activation function was able to solve the logical “exclusive or” problem, meaning that the logical operation is true if and only if its arguments differ, which was of value to researchers [179]. Subsequent research in this field yielded multilayer perceptrons, used for the training of multilayer neural networks [180]. When employing a monotonically growing, continuous and bounded function as the activation function of the neuron elements of the hidden layer, a perceptron with one hidden layer is the universal approximator, which means that it can approximate any continuous function with any level of precision [181]. The greater number of neurons in each hidden layer, the better the accuracy of approximation of the function [179]. However, if the dimension of the hidden layer became too large, a phenomenon known as the overfitting of the network can take place [179]. Up until 2006,
the prevailing scientific paradigm was that no perceptron required more than one or two hidden layers to be sufficient for solving different problems [179].

Work by Geoffrey Hinton changed this prevailing scientific paradigm in 2006, and researchers switched to using neural networks with a much higher number of layers [182]–[185]. Networks of this type were called deep neural networks [179]. Deep neural networks are neural networks with multiple layers of neuron elements [183]–[193]. The first types of deep learning networks to come into existence were deep belief neural networks and deep perceptrons [179]. The main difference between the deep perceptron and deep belief neural networks is that, in general, deep belief neural networks are not feedforward neural networks [179]. Other network structures that have merged since the shift to deep neural networks include the deep convolutional neural network, the deep recurrent neural network, the deep autoencoder and the deep recurrent convolution neural network [179]. Hinton’s proposed greedy layer-wise algorithm was the largest contributor to the paradigm shift [179]. This algorithm became an effective method for the training of deep neural networks [182]. It was shown that compared to the traditional one- or two-layer neural network, a deep neural network performed nonlinear transformations and presentation of data more effectively [179]. This type of network performs a deep hierarchical transformation of the input space of patterns in its operation [179]. As a result, the first hidden layer extracts a low-level space of features of input data, and the second hidden layer detects a space of features of higher level of abstraction, and so on [179]. This theory and subsequent related developments in the field completed the shift from single- and double-layer multilayer neural networks to deep neural networks [179].

Further work in the field of deep learning networks led to the introduction of concepts such as the restricted Boltzmann machine, the autoassociative approach and the stochastic gradient method utilizing a rectified linear unit activation function [179]. These concepts are explained in more detail in Golovko (2017) [179].

Deep neural networks have several advantages, making them attractive to researchers to solve problems such as predicting impact induced brain axon fiber strain. These
advantages are that there is no need to use or have a fully labelled dataset for training, models are cost-effective once trained, models are scalable and that they are effective at producing high quality prediction results [194]. Deep neural networks have several drawbacks as well, such as requiring a massive amount of data to be effective combined with a high processing power and large memory requirements to solve the network [194]. Additionally, they suffer from what is called “black box syndrome”, meaning the inner workings of the network are not easily accessible and therefore hard to debug and understand [195]. The correlations that deep neural networks find and utilize are often unnoticed by human experts. Even considering these disadvantages, the significant advantages that deep neural network structures provide to researchers mean this model type is still an excellent choice for approaching and solving prediction problems.

5.3.1.1 TabNet

TabNet is a deep neural network originally proposed by Arik and Pfister (2019) [196]. It is a novel high-performance and interpretable canonical deep tabular data learning architecture specifically designed for tabular data [196]. Arik and Pfister (2019) designed TabNet to outperform ensemble decision tree-based approaches that dominate most applications with regards to tabular data [196]. TabNet enables gradient descent based end-to-end learning for tabular data, which has several benefits [196]. An example of a relevant benefit to the prediction of blunt impact-induced brain axon fiber strain includes alleviating the need for feature engineering, a crucial component of tree-based tabular data learning techniques that permits the development of end-to-end models and representation learning [197]–[199]. Another relevant example is that TabNet enables useful application scenarios such as data-efficient domain adaption, generative modeling and semi-supervised learning [197]–[199]. The first main contribution that the TabNet architecture provides to the field is allowing for the input of raw tabular data without any preprocessing and training using gradient descent-based optimization [196]. The second major contribution of the architecture of TabNet is sequential attention, which allows for enhanced interpretability and learning because the learning capacity is employed for the most important elements at each decision-making stage [196]. Salient features are the
defining elements that distinguish one target from another, or key pieces of distinct information that facilitate recognition of an image, object, environment or person [200].

TabNet is based on the functionality of using conventional deep neural network building blocks to implement a decision tree-like output manifold [196]. Representing decision trees with deep neural network building blocks allows for a redundancy in representation [201]. The key to this design's hyperplane decision boundaries, which may be modified to a linear combination where coefficients dictate the proportion of each feature, is individual feature selection [196]. TabNet, while using this architecture, outperformed decision trees while also reaping their benefits [196]. When building a sequential multi-step architecture, TabNet first learns sparse instance-wise feature selection from the data it is given [196]. Based on the picked features, each step contributes to a portion of the decision [196]. It then improves its learning capacity via nonlinear processing of the selected features, and finally it mimics ensembling via higher dimensions and more steps [196]. The full backend logic and mathematical theory for TabNet are available in Arık and Pfister (2019) [196].

TabNet was evaluated against several tabular datasets, such as the Forest Cover Type dataset, the Rossmann Store Sales dataset and the Adult Census Income dataset [196]. These datasets were chosen because they have published benchmarks for comparison purposes [196]. The Adam optimization algorithm and the Glorot uniform initialization were used for the training of all models, and hyperparameters were optimized on a validation set of data [196], [202]. TabNet outperforms other variants on a wide range of non-performance-saturated tabular datasets and yields both interpretable feature attributions and insights into its global behaviour [196]. For example, on the Rossmann Store Sales dataset, TabNet outperforms a multilayer perceptron, XGBoost, LightGBM and CatBoost with mean square error as the performance metric [196]. The performance results of TabNet on these test datasets is a strong indicator that it may also be a useful architecture for predicting impact-induced brain axon fiber strain.
5.3.2 Random Forest Regression

The original random forest regression algorithm was developed by Leo Breiman and Adele Cutler in 2001, as outlined in Li (2013) [203]. Breiman and Cutler used this approach to show in a number of studies how using ensembles of trees, where each tree is developed in line with the realization of a random vector, can result in improvements in classification or prediction accuracy [204].

Random forests are a collection of tree predictors configured so that each tree relies on the values of a random vector sampled independently and with the same distribution for all trees in the forest [132]. The generalization error for random forests converges to a limit as the number of trees in the forest becomes large [132]. The strength of each individual tree in the forest and the correlation between the trees affect the generalization error of a forest of tree classifiers [132]. Using a random selection of features to split each node yields error rates that compare favourably to similar methods from the time it was released, such as Adaboost [132], [205]. Furthermore, random forests are more robust with respect to noise, which makes them more desirable [132].

The primary driving force behind random forests is that they take advantage of well-understood simple mechanisms that reduce prediction error for unstable predictors, such as trees using techniques like bagging [204]. These variance gains can be enhanced by reducing the correlation between the quantities being averaged [204]. Random forests seek to affect such correlation reduction by a further injection of randomness [204]. As opposed to single tree approaches like bagging, which evaluate all allowable splits on all variables to get the best split for a given node of a constituent tree, this method uses a subset of the covariates that is randomly chosen [204]. This gives random forests exceptional prediction accuracy, which is attained for a wide range of settings of the single tuning parameter employed [204].

Random forests have an improved performance over single decision trees and are quite efficient compared to artificial neural networks, particularly when large datasets are used, as random forests can handle up to thousands of explanatory variables [203]. Random
forests are robust for outliers [203]. Random forest models also can provide useful internal estimates of error, strength, correlation and variable importance, which may be valuable to researchers [204]. They are quite simple models overall and easily parallelized [132]. Random forests support hyperparameters for increased prediction accuracy but are usually good enough that the default hyperparameters often produce a good prediction result [132]. With enough trees, overfitting is not a problem usually faced by random forest models [132]. The full backend and logic used in the random forest algorithm is explained in Breiman (2001) [132].

Random forest models do have some disadvantages compared to other models and approaches. The largest limitation for random forests is that if the number of trees is too high, the algorithm can be too slow and ineffective for rapid predictions [132]. Even though they train quickly, random forests tend to be slower in creating predictions after the training process is completed [132]. To keep the model size appropriate for time-sensitive problems, a compromise must be struck between increasing the number of trees and employing fewer trees to reduce overfitting. Depending on the dataset being used, this may not be viable [132]. Random forests present an interesting and potentially useful approach to predicting brain impact-induced axonal strain and were investigated further through the implementation of the scikit-learn random forest regression model.

5.3.2.1 scikit-learn Random Forest

scikit-learn is a popular free machine learning library for Python that has an implementation of random forests available. scikit-learn classifies random forests as an ensemble method, the goal of which is to combine the predictions of several base estimators built with a given learning algorithm to improve generalizability or robustness over a single estimator [128]. Random forests are an averaging method, with the driving principle to build several estimators independently and then to average their predictions [128]. On average, the combined estimator is usually better than any of the single base estimators because its variance is reduced [128]. The random forest algorithm in scikit-learn is called RandomForest [128]. RandomForest is fitted with an array denoted $X$ of
shape n_samples by n_features which holds the training samples, and an array denoted $Y$
of shape n_samples which holds the target values for the training samples [128].

In RandomForest, each tree in the ensemble is built from a sample drawn with
replacement from the training set $X$ [128]. When each node is split during construction of
a tree, the optimal split is found either from all input features or a random subset of size
max_features [128]. These two sources of randomness decrease the variance of the forest
estimator [128]. Individual decision trees typically exhibit high variance and tend to
overfit as previously described [128]. The injected randomness in forests yield decision
trees with somewhat decoupled prediction errors [128]. By taking an average of those
predictions, some errors can cancel out, which is useful [128]. RandomForest achieves a
reduced variance by combining diverse trees, sometimes at the cost of a slight increase in
bias [128]. In practice, the variance reduction is often significant, which yields an overall
better model [128]. It should be noted that in contrast to the original work done by
Breiman, the scikit-learn implementation of RandomForest combines classifiers by
averaging their probabilistic prediction, instead of letting each classifier vote for a single
class [128].

The main parameters in RandomForest are n_estimators and max_features [128]. The
variable n_estimators is the number of trees in the forest [128]. If this number is larger,
this is better as the chances of overfitting are lower, but the overall model will take longer
to compute [128]. Furthermore, there are diminishing returns if there are too many trees
[128]. The variable max_features is the size of the random subsets of features to consider
when splitting a node [128]. In the highly successful simple implementation of
RandomForest that was completed to evaluate its usefulness in predicting blunt impact-
duced brain axon fiber strain in Chapter 2, these parameters and others were swept over
in the hyperparameter training process to create an optimal model.

5.3.3 Gradient Boosting Machines

GBMs are powerful ML tools that have a wide range of practical applications [206].
They benefit from being highly customizable to the specific problem to which they are
applied [206]. The most common approach to building a model from labelled data in a supervised environment is to build only a single strong predictive model [206]. Another approach is to build multiple or an ensemble of models for the particular learning task [206]. In practice, however, this second approach usually relies on combining many relatively weak and simple models to obtain a stronger ensemble or group prediction [206]. A common implementation of this second approach is the random forest and neural network ensembles [132], [207]. This implementation relies on simple averaging of all the models in the ensemble [206]. Gradient boosting, however, is based on a different constructive strategy of ensemble or group formation [206]. The primary notion of gradient boosting is to add new models to the ensemble sequentially [206]. At each specific iteration, a new, albeit weak, base-learner model is trained with respect to the error of the entire learnt ensemble up until this point [206].

In GBMs, the learning procedure consecutively fits new models to provide a more accurate estimate of the response variable [206]. The primary goal of this algorithmic framework is to build new base-learners that are maximally correlated with the loss function's associated negative gradient for the entire ensemble or group [206]. The loss functions applied can be varied and even arbitrary, but to give users the best idea of whether the model is improving in subsequent iterations, the most used error function is a classic squared-error loss error function [206].

This degree of flexibility makes the concept of GBMs highly customizable to any particular data-driven task [206]. GBMs have substantial freedom in model design, making the choice of the most appropriate loss function a matter of trial and error [206]. GBMs are also relatively simple to implement, meaning experimentation with different model designs is easily available [206]. Furthermore, GBMs have shown to be useful and successful in several practical applications, and in various machine-learning and data-mining challenges as outlined in Bissacco et al. (2007), Hutchinson et al. (2011), Pittman and Brown (2011) and Johnson and Zhang (2012) [208]–[211].

The original structure for GBMs was defined in Friedman (2001) [212]. This structure is shown in Equation 7, where \((x, y)\) are the labelled training pairs, \(N\) is the number of data
points, $\Psi(y, f)$ is the specified loss function, $h(x, \theta)$ is the parameterized base-learner functions and $\hat{f}_0$ is the initial guess.

**Friedman's Gradient Boost Algorithm [212]**

**Inputs:**

- input data $(x, y)_{i=1}^N$
- number of iterations $M$
- choice of the loss-function $\Psi(y, f)$
- choice of the base-learner model $h(x, \theta)$

**Algorithm:**

1: initialize $\hat{f}_0$ with a constant
2: for $t = 1$ to $M$ do
3: compute the negative gradient $g_t(x)$
4: fit a new base-learner function $h(x, \theta_t)$
5: find the best gradient descent step-size $\rho_t$:
   \[ \rho_t = \arg\min_{\rho} \sum_{i=1}^N \Psi[y_i, \hat{f}_{t-1}(x_i) + \rho h(x_i, \theta_t)] \]
6: update the function estimate:
   \[ \hat{f}_t \leftarrow \hat{f}_{t-1} + \rho_t h(x, \theta_t) \]
7: end for

This structure provides flexibility and variability, and as such has been developed into several distinct algorithms. Some of the leading GBMs are outlined in Sections 5.3.3.1 to 5.3.3.3.

However, there are several drawbacks with GBMs [206]. The most notable issue with GBMs in practice is their memory consumption [206]. The cost of storing a predictive model is a function of the number of boosting iterations used for the learning [206]. The models are considerably massive if this number of boosting iterations is high [206]. Additionally, the large demand for memory in the learning process results in a slower evaluation speed [206].

To use a fitted GBM model to obtain predictions, all base-learners in the ensemble must be evaluated [206]. Even though the base-learners are simple, if they are many in
number, obtaining predictions at a fast pace can become time-consuming [206]. Other than to decrease the complexity of the model, another way to bypass this problem is to use parallelization to obtain predictions when the GBM ensemble is already learnt, or to use mini-batch learning [213].

Overall, GBMs are highly applicable and customizable. They allow for relatively easy result interpretation and provide researchers with insights into the fitted model once that process has been completed. GBMs can be designed to be very specific or novel for particular tasks, such as impact-induced brain axon fiber strain prediction. This high flexibility has led to development of a wide range of GBM algorithms, some of which are discussed immediately below.

5.3.3.1 XGBoost

XGBoost is an open source, scalable ML system for tree boosting [214]. The gradient tree boosting algorithm that is used as the basis for XGBoost is derived from the same algorithm structure proposed by Friedman et al. (2000) [215]. XGBoost features both a classifier and a regressor. Only the regressor was explored in this research due to the nature of the results for which the model is being developed to predict [214].

XGBoost takes given datasets of size \( n \) by \( m \), where \( n \) is the number of examples in the dataset and \( m \) is the number of features for each example within the dataset [214]. A tree ensemble model uses \( K \) additive functions generated by the algorithm to predict an output [214]. This is shown in Equation 8 below [214].

\[
\hat{y}_i = \phi(x_i) = \sum_{k=1}^{K} f_k(x_i), f_k \in F,
\]

where \( F = \{ f(x) = w_{q(x)} \} (q : R^m \rightarrow T, w \in R^T) \) is the space of regression trees [214].

In Equation 8, \( q \) represents the structure of each tree that maps an example to the corresponding leaf index and \( T \) is the number of leaves in the tree [214]. Each \( f_k \) corresponds to an independent tree structure \( q \) and leaf weights \( w \) [214]. Unlike standard decision trees, each regression tree contains a continuous score on each leaf, therefore, \( w_l \)
is used to represent the score on $i$-th leaf [214]. For a given example, XGBoost uses the
decision rules in the trees (given by $q$) to classify it into the leaves and calculate the final
prediction by summing up the score in the corresponding leaves (given by $w$) [214]. The
full mathematical theory of the backend of XGBoost is available in Chen and Guestrin
(2016) [214].

XGBoost incorporates a regularized model to prevent overfitting [214]. Two additional
techniques are used in XGBoost to prevent overfitting in the prediction process [214].
The first technique is shrinkage, introduced by Friedman [11]. Shrinkage scales newly
added weights by a factor $\eta$ after each step of the tree boosting process [214]. Shrinkage
reduces the influence of each individual tree and leaves space for future trees to improve
the model [214]. The second technique to prevent overfitting is column subsampling, also
known as feature subsampling [214]. Using column subsampling prevents overfitting
even more so than the traditional row subsampling, which is also supported in XGBoost
[214]. Subsampling by rows or columns increases variance between trees in a model and
allows the model to converge quicker [214].

In conclusion, XGBoost is used widely by data scientists to achieve state-of-the-art
results on many ML challenges and problems. Due to its wide use and popularity, a
simple implementation of XGBoost was trialed in this research for evaluating impact-
induced brain axon fiber strain.

5.3.3.2 LightGBM

LightGBM was developed to overcome the unsatisfactory efficiency and scalability of
other GBMs when dealing with high feature dimensions and large data sizes [216]. The
reason many gradient decision tree algorithms struggle with these issues is that they need
to scan all the data instances to estimate the information gain of all the possible split
points, which is quite time consuming [216]. LightGBM introduces and uses two novel
techniques, called Gradient-based One-Side Sampling (GOSS) and Exclusive Feature
Bundling (EFB) [216]. These techniques aim to improve the performance of LightGBM
over other similar GBM algorithms.
The costliest part of using a GBM is learning the decision trees, and the most time-consuming part in learning a decision tree is trying to find the best split points [212], [216]. LightGBM was developed out of the popular histogram-based algorithm that is shown in Equation 9.

**Histogram-based Algorithm used in LightGBM [216]**

```
Input: I: training data, d: max depth
Input: m: feature dimension
nodeSet ← {0} ▷ tree nodes in current level
rowSet ← {{0, 1, 2, ...}} ▷ data indices in tree nodes
for i = 1 to d do
    for node in nodeSet do
        usedRows ← rowSet[node]
        for k = 1 to m do
            H ← new Histogram() ▷ Build histogram
            for j in usedRows do
                bin ← I.f[k][j].bin
                H[bin].y ← H[bin].y + Iy[j]
                H[bin].n ← H[bin].n + 1
            Find the best split on histogram H.
        ... Update rowSet and nodeSet according to the best split points.
```

The histogram-based algorithm works by finding the optimal split points based on feature histograms [216]. Its big O notation cost is defined as $O(#data \times #feature)$ for histogram building and $O(#bin \times #feature)$ for finding the split point [216]. #bin is usually much smaller than #data, so #data drives the main computational complexity in histogram building [216]. The goal with LightGBM is to reduce the training data by reducing #data or #feature to speed up the training of the GBM [216]. Common approaches for this are to down sample the data instances or reduce the number of features by filtering weak features [216]–[220]. However, these methods are not possible here. The former is based on AdaBoost, and therefore cannot be directly applied to the GBM because AdaBoost requires native weights for data instances, and there are no native sample weights in the GBM [216], [221]. The latter relies on the assumption that features contain significant redundancy, which might not always be true in practice. LightGBM uses GOSS and EFB to overcome these issues [216].
GOSS works by keeping all the instances with large gradients and performing random sampling on the small gradient instances [216]. To compensate for the change in data distribution in computing the information gain, GOSS creates a constant multiplier for the small gradient data instances [216]. The procedure for GOSS is shown in Equation 10 below.

**GOSS Algorithm [216]**

```python
Input: I: training data, d: iterations
Input: a: sampling ratio of large gradient data
Input: b: sampling ratio of small gradient data
Input: loss: loss function, L: weak learner
models ← [], fact ← \( \frac{1-a}{b} \)
topN ← a \times \text{len}(I), randN ← b \times \text{len}(I)
for i = 1 to d do
    preds ← models.predict(I)
g ← loss(I, preds), w ← {1,1,...}
    sorted ← GetSortedIndices(abs(g))
topSet ← sorted[1:topN]
    randSet ← RandomPick(sorted[topN:len(I)], randN)
    usedSet ← topSet + randSet
    w[randSet] \times = \text{fact} \triangleright Assign weight \text{fact} to the small gradient data.
    newModel ← L(I[usedSet], −g[usedSet], w[usedSet])
models.append(newModel)
```

The first step in GOSS is to sort the data instances according to the absolute value of their gradients and selects the top \( a \times 100\% \) instances [216]. GOSS then randomly samples \( b \times 100\% \) instances from the rest of the data [216]. \( a \) is defined as the sampling ratio of the large gradient data, and \( b \) is the sampling ratio of the small gradient data [216]. Both variables are defined by the user. Subsequently, GOSS amplifies the sampled data with small gradients by a constant defined by \( \frac{1-a}{b} \) when calculating the information gain [216]. The information gain is usually measured by the variance after splitting each node at the most informative feature [216]. Accordingly, more focus is put on the under-trained instances without much change in the original data distribution [216]. The theoretical analysis and backend mathematics for GOSS are presented in Ke et al. (2017) [216].
The second technique introduced in LightGBM is EFB. The goal of EFB is to effectively reduce the number of features [216]. High-dimensional data are usually very sparse [216]. The sparsity of the feature space allows for the possibility of designing a nearly lossless approach to reduce the number of features [216]. In a sparse feature space, many features are mutually exclusive, meaning they never take non-zero values simultaneously [216]. Those exclusive features can be bundled into a single feature, which is known as an exclusive feature bundle [216]. A carefully designed feature scanning algorithm can build histograms from these the same way histograms are built from individual features [216]. Using exclusive feature bundles allows the complexity of building the desired histograms from big O notation $O(#data \times #feature)$ to $O(#data \times #bundle)$, while the size of #bundle is much less than of #feature [216]. The implementation of EFB allows for significantly faster training speed without a decrease in accuracy [216].

Ke et al. (2017) compared the full implementation of LightGBM to XGBoost and a baseline version of LightGBM without GOSS and EFB [216]. Experiments were conducted on multiple public databases to gauge accuracy and speeds of the full implementation [216]. The full implementation of Light GBM was the fastest of the three algorithms and it maintained a similar accuracy compared to the baseline models [216]. The promising results from Ke et al. (2017) meant LightGBM was trialed in this research for evaluating impact-induced brain axon fiber strain.

### 5.3.3.3 CatBoost

CatBoost is a newer GBM than XGBoost or LightGBM, with new critical algorithmic advances [222]. Ordered boosting, one of CatBoost’s techniques, was introduced to combat an issue in previous GBMs called a prediction shift [222]. Prediction shift was caused by a special kind of target leakage [222].

CatBoost uses binary decision trees as base predictors [222]. A decision tree model is built by recursive partition of the feature space $R^m$ into many disjoint regions, or tree nodes, per the values of some splitting attributes $a$ [215], [223], [224]. These attributes are usually binary variables that identify that some feature $x^k$ is greater than a defined
Each leaf of the tree or final region is mapped to a value, such value being an estimate of the response $y$ in the region for the regression task [222]. $R_j$ is a variable that is used to represent the disjoint regions corresponding to the leaves of the tree [222]. The decision tree $h$ can be written as shown in Equation 11 below [222].

$$h(x) = \sum_{j=1}^{J} b_j \mathbb{1}_{\{x \in R_j\}}$$

Prediction shift, the main issue that CatBoost was created to solve, is caused by a special kind of target leakage [222]. The gradient conditional distribution and base predictors for the function $F^t$ are shifted as each new trained model is created in the gradient boosting process, leading to loss in prediction quality [222]. Base predictors are oblivious decision trees, meaning that the same splitting criterion is used across an entire level of the tree. This means that the trees are balanced, less prone to overfitting and they allow the execution at testing time to be significantly sped up [225]–[227]. Prokhorenkova et al. (2017) introduced the concept of ordered boosting to fix this problem [222]. Assuming a model is taught with $I$ trees, to make an unshifted residual $r^{I-1}(x_k, y_k)$, model $F^{I-1}$ needs to be trained without the example $x_k$ [223]. Unbiased residuals are needed for all training examples, therefore no examples may be used for training $F^{I-1}$ [222]. It is possible to maintain a set of models differing by examples used for their training [222]. A model trained without it can then be used to calculate the residual on the example [222]. If one random permutation $\sigma$ of the training examples is taken, Prokhorenkova et al. (2017) proposed that $n$ different supporting models $M_1, \ldots, M_n$ are maintained such that the model $M_i$ is learned using only the first $i$ examples in the permutation [222]. At each step, to obtain the residual for the $j$-th sample, the model $M_{j-1}$ is used, which is shown in the Figure 83 [222].
The ordered boosting algorithm is shown in Equation 12.

\begin{equation}
\text{Algorithm for Ordered Boosting [222]}
\begin{align*}
\text{input} &: \{(x_k, y_k)\}_{k=1}^n, I; \\
\sigma &\leftarrow \text{random permutation of } [1, n]; \\
M_i &\leftarrow 0 \text{ for } i = 1..n; \\
\text{for } t \leftarrow 1 \text{ to } I \text{ do} \\
\quad &\text{for } i \leftarrow 1 \text{ to } n \text{ do} \\
\quad &\quad r_i \leftarrow y_i - M_{\sigma(i)-1}(x_i); \\
\quad &\text{for } i \leftarrow 1 \text{ to } n \text{ do} \\
\quad &\quad \Delta M \leftarrow \text{LearnModel}((x_j, r_j): \\
\quad &\quad \sigma(j) \leq i); \\
\quad &\quad M_i \leftarrow M_i + \Delta M; \\
\text{return } M_n
\end{align*}
\end{equation}

The full backend and mathematical theory are available in Prokhorenkova et al. (2017) [222].

CatBoost was compared against XGBoost and LightGBM [222]. The ordered boosting module was used in CatBoost to maximize its performance, as opposed to using CatBoost in plain mode without the ordered boosting module [222]. CatBoost outperformed the other algorithms on all the considered publicly available datasets [222]. The empirical results from this comparative study are available in Prokhorenkova et al. (2017) and

Figure 83: Ordered Boosting Principle, Examples are Ordered according to $\sigma$ [222]
demonstrate that CatBoost outperforms leading GBMs such as XGBoost and LightGBM [222]. This warranted evaluating CatBoost for studying impact-induced brain axon fiber strain in this research.

5.4 Rationale for Algorithm Selection

After initial research was completed and a list of potential algorithms was created for assessing impact-induced brain axon fiber strain, qualitative and quantitative evaluations were completed for the list of potential algorithms. These assessments allowed a single algorithm to be chosen for full development, as the development cost for this size of data available was quite high.

5.4.1 Algorithm Qualitative Comparison

A qualitative comparison was conducted for each potential algorithm. The points of evaluation for each algorithm were whether the algorithm was good for large datasets, if the algorithm supported hyperparameter training through Optuna (See Section 5.5), whether the algorithm had a faster training and prediction speed than Adaboost when used as a baseline, if the algorithm can be simply implemented in Python 3.6 and whether the algorithm supported multi-in single-out predictions and multi-in multi-out predictions using the Graphics Processing Unit (GPU) and PyTorch. A simple implementation in Python 3.6 was defined as being able to be written in a single Jupyter notebook file with minimal difficulty. Multi-in single-out prediction algorithms are standard AI algorithms that take in multiple data points as input and predict a single value as an output. Multi-in multi-out prediction algorithms are more advanced prediction regression algorithms that allow for the prediction of multiple outputs at once. The qualitative comparison is shown in Table 15.
### Table 15: Qualitative Comparison of AI Methods

<table>
<thead>
<tr>
<th>Algorithm Name (Type)</th>
<th>Good for large datasets</th>
<th>Supports hyper-parameter training in Optuna</th>
<th>Faster training time than Adaboost</th>
<th>Faster prediction time than Adaboost</th>
<th>Supports simple Python 3.6 implementation</th>
<th>Supports multi-in single-out predictions on GPU and through PyTorch</th>
<th>Supports multi-in multi-out predictions on GPU and through PyTorch</th>
</tr>
</thead>
<tbody>
<tr>
<td>TabNet (deep neural network)</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>XGBoost (GBM)</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>LightGBM (GBM)</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>CatBoost (GBM)</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>scikit-learn Random Forest (random forest regression)</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

After analyzing the results from the qualitative analysis, two conclusions were drawn. Firstly, XGBoost and LightGBM are both GBMs, and have the same strengths and weaknesses. LightGBM is a newer algorithm with some minor improvements, but overall, it is less popular than XGBoost, which was found to be well supported in
literature for test cases and examples. Therefore, it was decided to continue with XGBoost and cease further examination of LightGBM to save implementation time. Secondly, even though the scikit-learn RandomForest algorithm is not particularly good for datasets as large as the brain, the implementation cost of this algorithm was comparatively small to the other algorithms, so it was evaluated anyway.

5.4.2 Algorithm Setup and Data Structure

All candidate algorithms were set up in Python 3.6, distributed through Anaconda and executed through Jupyter Notebooks [228]. The necessary support packages such as Pandas and NumPy were installed using Anaconda in a new environment [229], [230]. Nvidia CUDA, a program that allowed software to use the GPU for processing, was also installed for testing purposes. Training datasets were created from results calculated from the outputs of the Brain Axon Fiber Tract GHBMC Model. These Brain Axon Fiber Tract GHBMC Model results were originally calculated for analysis work performed in Chapter 4. The results from each impact case in Chapter 4 contain a time history measuring strain for each of the elements in the Brain Axon Fiber Tract GHBMC Model from 0 to 80 milliseconds. The Brain Axon Fiber Tract GHBMC Model was calculated every 0.5 milliseconds in time, but for the AI work only every millisecond was taken to reduce data quantity, as opposed to half millisecond. The outputs of each impact case, regardless of direction or impact energy, were parcellated to each of the 41 tracts. The corresponding nine sets of kinematics for each impact were appended to the top of each parcellated tract output file so that the kinematics time histories aligned with the time histories of the tract-specific strain output from the Brain Axon Fiber Tract GHBMC Model. Impact cases of similar direction and impact magnitude were then grouped together and combined into a single dataset for training and prediction. Initially, this process was done without parcellating the Brain Axon Fiber Tract GHBMC Model outputs and combining like cases together into one dataset, but the resultant training files proved to be too large for the memory present in the available workstation computers to utilize effectively. Candidate algorithms were provided a training file, a specified direction and energy impact and tract. The rotational acceleration kinematics were dropped as their correlation to strain-induced brain injuries is similar to rotational
velocity and using linear acceleration and rotational velocity as the combination of inputs to the algorithm has approximately the same correlation as using linear acceleration, rotational velocity and rotational acceleration as explained in Chapter 3 [7]. Dropping rotational acceleration resulted in a smaller amount of input data to the candidate algorithms. The kinematics data was then scaled to match the same range as the strain data, ensuring the entire dataset was scaled to the same range. Once completed, X and Y datasets were created from each training set. X datasets represent training inputs, which were the kinematics in this case. Y datasets represent training outputs, which were the strain values in this case. These data pre-processing steps were completed for each of the candidate algorithms. Candidate algorithms were tested on a workstation with two Intel Xeon Silver 4216 central processing units running at 2.10 gigahertz, 96 gigabytes of random-access memory, a Nvidia RTX A4000 GPU and Windows 10 Enterprise.

Testing datasets were set up in the same manner as the training datasets. The outputs of the simulation cases and the corresponding kinematics that were used for the testing datasets were fully independent of the outputs of the training simulation cases and their corresponding kinematics. However, data was only used from matching tracts, directions and impacts to predict like data (e.g., corpus callosum training data from low frontal impacts was only used to predict corpus callosum test data for low frontal impacts). This ensured that any evaluated algorithm was only tested on unfamiliar data, allowing for fair comparison between algorithms’ performance.

5.4.2.1 TabNet Algorithm Set Up

The simple implementation of the TabNet algorithm was set up using the PyTorch version of TabNet, and Optuna to find exact hyperparameter values. Optuna and the hyperparameter search process is outlined in Section 5.5. Several parameters were chosen for values to be swept for. TabNet-specific hyperparameters, optimizer parameters and other variables are outlined in Table 16.
### Table 16: TabNet Hyperparameters, Optimizer Parameters and Other Variables

<table>
<thead>
<tr>
<th>Literature Variable Name</th>
<th>Python Variable Representation</th>
<th>Range and Step, Options or Specified Values</th>
<th>Description of Variable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Masking Type</td>
<td>mask_type</td>
<td>entmax, sparsemax</td>
<td>Masking function to use for selecting features [196], [231].</td>
</tr>
<tr>
<td>Decision Prediction Layer and Attention Embedding Width</td>
<td>n_da</td>
<td>0 to 64, step: 4</td>
<td>Variable represents width of the decision prediction layer and the width of the attention embedding for each mask [196], [231].</td>
</tr>
<tr>
<td>Number of Steps</td>
<td>n_steps</td>
<td>3 to 10, step: 1</td>
<td>Number of steps in the architecture [196], [231].</td>
</tr>
<tr>
<td>Gamma</td>
<td>gamma</td>
<td>1.0 to 2.0, step: 0.1</td>
<td>Coefficient for feature reusage in the masks. A value close to 1 will make mask selection the least correlated between layers [196], [231].</td>
</tr>
<tr>
<td>Gated Linear Units Count</td>
<td>n_shared</td>
<td>1 or 5</td>
<td>Number of shared gated linear units at each step [196], [231].</td>
</tr>
<tr>
<td>Momentum</td>
<td>momentum</td>
<td>0.01 to 0.4, step: 0.01</td>
<td>Momentum for batch normalization [196], [231].</td>
</tr>
<tr>
<td>Lambda Sparse</td>
<td>lambda_sparse</td>
<td>0.000001 to 0.001, logarithmic: True</td>
<td>Extra sparsity loss coefficient. The larger this coefficient is, the sparser the model will be in terms of feature selection [196], [231].</td>
</tr>
<tr>
<td>Optimizer Function</td>
<td>optimizer_fn</td>
<td>Adam</td>
<td>Pytorch optimizer function [232].</td>
</tr>
<tr>
<td>Parameter</td>
<td>Value</td>
<td>Description</td>
<td></td>
</tr>
<tr>
<td>----------------------------</td>
<td>----------------</td>
<td>-----------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Learning Rate</td>
<td>lr 2e-2</td>
<td>Step size at each iteration while moving toward a minimum of a loss function [196], [231], [232].</td>
<td></td>
</tr>
<tr>
<td>Weight Decay</td>
<td>weight_decay 1e-5</td>
<td>A regularization technique applied, usually the L2 norm of the weights of the neural network [196], [231], [232].</td>
<td></td>
</tr>
<tr>
<td>Patience</td>
<td>patience</td>
<td>Number of consecutive epochs without improvement before performing early stopping [232].</td>
<td></td>
</tr>
<tr>
<td>Minimum Learning Rate</td>
<td>min_lr 1e-5</td>
<td>Minimum learning rate [196], [231], [232].</td>
<td></td>
</tr>
<tr>
<td>Scheduler Function</td>
<td>scheduler_fn</td>
<td>Pytorch scheduler to change learning rates during training [232].</td>
<td></td>
</tr>
<tr>
<td>Verbosity</td>
<td>verbose 1</td>
<td>Verbosity for notebooks plots [228], [231].</td>
<td></td>
</tr>
<tr>
<td>k-fold Cross Validation Splits</td>
<td>N_splits 20</td>
<td>k-fold cross validation is a procedure used to estimate the skill of the model on new data [128].</td>
<td></td>
</tr>
<tr>
<td>Batch Size</td>
<td>batch_size 2,048</td>
<td>How many samples per batch to load [196], [231], [233].</td>
<td></td>
</tr>
<tr>
<td>Virtual Batch Size</td>
<td>virtual_batch_size 128</td>
<td>Size of the mini batches used for &quot;ghost batch normalization&quot; [196], [231], [233].</td>
<td></td>
</tr>
<tr>
<td>Number of Workers</td>
<td>num_workers 0</td>
<td>How many subprocesses to use for data loading. 0 means that the data will be loaded in the main process</td>
<td></td>
</tr>
</tbody>
</table>
Drop Last | drop_last | False

True: drops the last incomplete batch, if the dataset size is not divisible by the batch size. False: if false and the size of dataset is not divisible by the batch size, then the last batch will be smaller [196], [231], [233].

After the optimal parameters were found using Optuna, they were stored in a Python dictionary and saved to the workstation hard drive. These parameters were then loaded into the prediction portion of the code and the model was fit to the supplied training dataset along with these parameters. The prediction model was also supplied with like test data as explained previously, and the fit model was used to predict the test data. Mean squared error was used as a scoring method as root means squared error is not currently offered as a metric within TabNet.

Next, the predicted data was put through a Butterworth filter provided through the SciPy library [234]. This filter was used to smooth the output time history plot. This signal processing technique was implemented as it was noted the raw output time history tended to contain significant noise and contained outliers that tended to skew overall predictions. Optimization for the Butterworth filter was done manually through trial and error on the raw predicted data output from the TabNet model. Increments of one with a range of 1 to 10 were used for optimizing the filter order and increments of .01 with a range of 0.01 to .99 were used for optimizing the cutoff frequency. Final values for the Butterworth filter were a filter order $N$ of 6 and a cutoff frequency $W_n$ of 0.1.

The filtered time history values were much closer than the raw prediction time history values, so this system was applied to all algorithms being evaluated, including TabNet. An example of the improvement provided by the Butterworth filter is shown in Figure 84.
Similar performance gains in accuracy were seen across all evaluated algorithms when the Butterworth filter was implemented.

![Graph showing strain over time with True Values, Predicted Values, and Filtered Values]

**Figure 84: Example Predicted Axon Strain Time History Plot comparing Raw Prediction Values (Purple), Filtered Prediction Values (Red) and True Values (Green)**

From the simple implementation of TabNet and subsequent test prediction, several evaluation metrics were recorded. These metrics were prediction time, Pearson correlation coefficient, mean squared error, mean absolute error and R-squared value. These metrics were saved for comparison to other algorithms.

### 5.4.2.2 XGBoost Algorithm Set Up

The simple implementation of the XGBoost algorithm was set up using the PyTorch version of XGBoost. Hyperparameter values were originally expected to be found using Optuna, but there were issues in the implementation of Optuna with XGBoost that resulted in a necessary switch from Optuna to a Sklearn’s GridSearchCV. GridSearchCV serves the same purpose as Optuna in finding the optimal algorithm parameters for an AI model to predict test data from training data. GridSearchCV exhaustively generates candidates from a grid of parameter values specified within a supplied parameter grid.
Several XGBoost-specific parameters were chosen for values to be swept for using GridSearchCV. These parameters and other variables relevant to the model are outlined in Table 17.

### Table 17: XGBoost Hyperparameters, Optimizer Parameters and Other Variables

<table>
<thead>
<tr>
<th>Literature Variable Name</th>
<th>Python Variable Representation</th>
<th>Range and Step, Options or Specified Values</th>
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<tbody>
<tr>
<td>Eta or Learning Rate</td>
<td>learning_rate</td>
<td>0.05, 0.10, 0.15, 0.20</td>
<td>Step size shrinkage used in update to prevent overfitting. After each boosting step, the weights of features can be directly acquired, and Eta shrinks the feature weights to make the boosting process more conservative [214].</td>
</tr>
<tr>
<td>Number of Estimators</td>
<td>n_estimators</td>
<td>100, 500, 1,000</td>
<td>Maximum number of boosting trees (or rounds) to be used in building the model [214]</td>
</tr>
<tr>
<td>Maximum Depth</td>
<td>max_depth</td>
<td>4, 6, 8, 10</td>
<td>Maximum depth of a tree. Increasing this value makes the model more complex and more likely to overfit. 0 indicates no limit on depth [214].</td>
</tr>
<tr>
<td>Gamma or Minimum Split Loss</td>
<td>min_split_loss</td>
<td>0.0, 0.1, 0.2, 0.3, 0.4</td>
<td>Minimum loss reduction required to make a further partition on a leaf node of the tree. The larger the Gamma is, the more conservative the algorithm will be [214].</td>
</tr>
<tr>
<td>Lambda</td>
<td>reg_lambda</td>
<td>0.0001, 0.001</td>
<td>L2 regularization term on weights. Increasing this value makes the model more conservative [214].</td>
</tr>
</tbody>
</table>
Minimum sum of instance weight (or hessian) needed in a child. If the tree partition step results in a leaf node with the sum of instance weight less than min_child_weight, then the building process gives up further partitioning. In a linear regression task, this corresponds to the minimum number of instances needed to be in each node. The larger min_child_weight is, the more conservative the algorithm will be [214].

Subsample ratio of the columns when constructing each tree. Subsampling occurs once for every tree constructed [214].

Number of cross validation splits [128].

After the optimal parameters were found via GridSearchCV, they were utilized when the model was fit to the supplied training data. Predictions were then made from the supplied kinematics and compared to the supplied testing data outputs. The same Butterworth filter ($N$ equal to 6, $W_n$ equal to 0.1) was applied to the data to remove outliers and increase prediction accuracy. Lastly, the same metrics were recorded to evaluate the simple implementation of XGBoost. These metrics, the same as used in the simple implementation of TabNet, were prediction time, Pearson correlation coefficient, mean squared error, mean absolute error and R-squared value. These metrics were saved for comparison to other algorithms.

### 5.4.2.3 CatBoost Algorithm Set Up

The simple implementation of CatBoost, like the previous two simple implementations, was set up using the PyTorch version of the algorithm. Hyperparameter values were
optimized using Optuna. Several parameters were chosen to have their values be swept for. CatBoost-specific hyperparameters, optimizer parameters and other variables are outlined in Table 18.

**Table 18: CatBoost Hyperparameters, Optimizer Parameters and Other Variables**

<table>
<thead>
<tr>
<th>Literature Variable Name</th>
<th>Python Variable Representation</th>
<th>Options or Specified Values</th>
<th>Description of variable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss Function</td>
<td>loss_function</td>
<td>RMSE</td>
<td>Method of evaluating how well specific algorithm models the given data [222], [231].</td>
</tr>
<tr>
<td>Task Type</td>
<td>task_type</td>
<td>GPU</td>
<td>The processing unit type to use for training [222], [231].</td>
</tr>
<tr>
<td>Boosting Type</td>
<td>boosting_type</td>
<td>Plain</td>
<td>Boosting scheme [222], [231].</td>
</tr>
<tr>
<td>Overfitting Detector Type</td>
<td>od_type</td>
<td>Iter</td>
<td>The type of the overfitting detector to use [222], [231].</td>
</tr>
<tr>
<td>L2 Regularization Term</td>
<td>l2_leaf_reg</td>
<td>Uniform logarithmic distribution between 1e-3 and 3</td>
<td>Coefficient at the L2 regularization term of the cost function [222], [231].</td>
</tr>
<tr>
<td>Border Count</td>
<td>max_bin</td>
<td>100 to 600, step: 10</td>
<td>The number of splits for numerical features [222], [231].</td>
</tr>
<tr>
<td>Eta or Learning Rate</td>
<td>learning_rate</td>
<td>Uniform linear distribution between 0.01 and 0.04</td>
<td>The learning rate, used for reducing the gradient step [222], [231].</td>
</tr>
<tr>
<td>Parameter</td>
<td>Value</td>
<td>Description</td>
<td></td>
</tr>
<tr>
<td>-----------------------------------</td>
<td>------------------------------------</td>
<td>------------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Number of Iterations</td>
<td>n_estimators</td>
<td>10 to 2,000, step=10</td>
<td></td>
</tr>
<tr>
<td>Maximum Tree Depth</td>
<td>max_depth</td>
<td>Integer values between 3 and 10, step: 1</td>
<td></td>
</tr>
<tr>
<td>Random Seed</td>
<td>random_state</td>
<td>42</td>
<td></td>
</tr>
<tr>
<td>Minimum Number of Training Samples in a Leaf</td>
<td>min_data_in_leaf</td>
<td>Integer values between 1 and 300</td>
<td></td>
</tr>
<tr>
<td>Number of Folds</td>
<td>n_splits</td>
<td>10</td>
<td></td>
</tr>
</tbody>
</table>

The maximum number of trees that can be built when solving machine learning problems [222], [231].

Depth of the tree [222], [231].

The random seed used for training [222], [231].

The minimum number of training samples in a leaf. It should be noted that CatBoost does not search for new splits in leaves with samples count less than this specified value [222], [231].

Number of k-fold validation folds [128].

After the optimal parameters were found for the simple implementation of CatBoost based on the training set provided, these values were saved. They were then utilized along with the training data to fit the model in preparation for predicting the supplied test data strain outputs from its kinematics. The same Butterworth filter \(N\) equal to 6, \(W_n\) equal to 0.1 was applied to the raw predicted strain data to remove outliers and increase prediction accuracy. Lastly, the same metrics were recorded to evaluate the simple implementation of CatBoost. These metrics, the same as used in the simple implementation of TabNet and XGBoost, were prediction time, Pearson correlation coefficient, mean squared error, mean absolute error and r-squared value. These metrics were saved for comparison to other algorithms.
5.4.2.4 RandomForest Algorithm Setup

The setup for the RandomForest algorithm utilizes GridSearchCV, as Optuna does not support the Sklearn package for hyperparameter optimization. Hyperparameter optimization for forests of random trees is substantially less important than for GBMs or deep neural networks, and often the default hyperparameters are suitable for the problem at hand. Several RandomForest-specific parameters were chosen for values to be swept for using GridSearchCV. These parameters and other relevant variables are outlined in Table 19.

<table>
<thead>
<tr>
<th>Literature Variable Name</th>
<th>Python Variable Representation</th>
<th>Range and Step, Options or Specified Values</th>
<th>Description of variable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bootstrap</td>
<td>bootstrap</td>
<td>True, False</td>
<td>Whether bootstrap samples are used when building trees. If false, the whole dataset is used to build each tree [128].</td>
</tr>
<tr>
<td>Maximum Tree Depth</td>
<td>max_depth</td>
<td>800, 900, 1,000</td>
<td>The maximum depth of the tree. If none, then nodes are expanded until all leaves are pure or until all leaves contain less than min_samples_split samples [128].</td>
</tr>
<tr>
<td>Maximum Number of Features</td>
<td>max_features</td>
<td>auto, sqrt</td>
<td>The number of features to consider when looking for the best split [128].</td>
</tr>
<tr>
<td>Minimum Number of Samples at a Leaf Node</td>
<td>min_samples_leaf</td>
<td>1, 2</td>
<td>The minimum number of samples required to be at a leaf node. A split point at any depth will only be considered if it leaves at least min_samples_leaf training samples in each of the left and right branches. This</td>
</tr>
</tbody>
</table>
may have the effect of smoothing the model, especially in regression [128].

<table>
<thead>
<tr>
<th>Minimum Samples for Split</th>
<th>min_samples_split</th>
<th>5, 10</th>
<th>The minimum number of samples required to split an internal node [128].</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Trees</td>
<td>n_estimators</td>
<td>1,000, 1,200</td>
<td>The number of trees in the forest [128].</td>
</tr>
<tr>
<td>Number of Cross Validation Splits</td>
<td>cv</td>
<td>3</td>
<td>Number of cross validation splits [128].</td>
</tr>
</tbody>
</table>

After the parameters were optimized for the simple implementation of RandomForest based on the training set provided, the values were saved. The optimal values were subsequently utilized, along with the training data, to fit to the implementation of the algorithm. The algorithm was then used to predict the supplied test data strain outputs from its corresponding test kinematics. Again, the Butterworth filter ($N$ equal to 6, $W_n$ equal to 0.1) was applied to the raw predicted strain data to remove outliers and increase prediction accuracy. Lastly, the same metrics were recorded to evaluate the simple implementation of RandomForest. These metrics, the same as used previously, were prediction time, Pearson correlation coefficient, mean squared error, mean absolute error and r-squared value. These metrics were saved for comparison to other algorithms.

5.4.3 Algorithm Quantitative Comparison

Each of the simple implementations outlined above were run on several test axon fiber elements in several test directions and impact energies to thoroughly evaluate their prediction capabilities. Prediction capabilities were averaged over each recorded metric. The axon fiber finite elements that were evaluated, and their directions and impact energies, are outlined in Table 20 below.
Table 20: Axon Fiber Elements used in Algorithm Quantitative Comparison

<table>
<thead>
<tr>
<th>Axon Fiber Element Number</th>
<th>Tract</th>
<th>Evaluated Directions</th>
<th>Evaluated Impact Energy Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>1710923</td>
<td>AF</td>
<td>Front</td>
<td>High</td>
</tr>
<tr>
<td>1777899</td>
<td>IFOF</td>
<td>Front, rear, side</td>
<td>Low, mid, high</td>
</tr>
<tr>
<td>1780923</td>
<td>IFOF</td>
<td>Front, rear, side</td>
<td>Low, mid, high</td>
</tr>
<tr>
<td>1716848</td>
<td>Sup_F</td>
<td>Front</td>
<td>Mid, high</td>
</tr>
<tr>
<td>1821962</td>
<td>Sup_F</td>
<td>Front</td>
<td>Mid, high</td>
</tr>
</tbody>
</table>

Preliminary tests were completed on the arcuate fasciculus finite element number 1710923 with a frontal impact direction and high energy. This was because the high energy produced the highest strain values, and therefore had the most variation in prediction values. Additionally, the dataset for the arcuate fasciculus was the first one ready for training and evaluation, and rear and side impacts were still being simulated. The superficial-frontal tract was selected as a tract for analysis because of its large coverage of the frontal portion of the brain, and this tract was used for a more in-depth confirmation of the candidate algorithms’ ability to evaluate frontal impacts. The inferior fronto-occipital fasciculus was used as a final confirmation of all directions and impact energies to show that the algorithm being evaluated was sufficient for rear and side impacts, as this tract spans the length of the center of the brain anatomically.

The resulting average metrics recorded for each algorithm are shown in Table 21.

Table 21: Results of Algorithm Quantitative Comparison

<table>
<thead>
<tr>
<th>Algorithm</th>
<th>Average Prediction time (Seconds, RTX A4000 GPU)</th>
<th>Average Pearson Correlation Coefficient (Filtered)</th>
<th>Average Mean Squared Error (Filtered)</th>
<th>Average Mean Absolute Error (Filtered)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TabNet</td>
<td>1,368.1</td>
<td>0.558</td>
<td>0.0026</td>
<td>0.01139</td>
</tr>
<tr>
<td>XGBoost</td>
<td>613.11</td>
<td>0.984</td>
<td>0.0001</td>
<td>0.0317</td>
</tr>
<tr>
<td>CatBoost</td>
<td>189.844</td>
<td>0.995</td>
<td>0</td>
<td>0.00142</td>
</tr>
<tr>
<td>RandomForest</td>
<td>2,782.69</td>
<td>0.994</td>
<td>0</td>
<td>0.00139</td>
</tr>
</tbody>
</table>
The results of the algorithm qualitative comparison showed that the GBMs (XGBoost, CatBoost) and the random forest models outperformed the deep neural network for predicting impact-induced brain axon fiber strain. The RandomForest algorithm produced good results, but the amount of time the algorithm took to produce a prediction was far too long for this algorithm to be further considered for optimization. This was expected as the RandomForest algorithm was not built for use on large databases, and this was known before the simple implementation began [128]. Of the two GBMs, both performed quite well in all major metrics that were evaluated, but CatBoost was able to make predictions over three times faster on the supplied datasets than XGBoost, which is key due to the high number of predictions that need to be made to predict the entire Brain Axon Fiber Tract GHBMC Model. Furthermore, CatBoost had a marginally higher average Pearson correlation coefficient, a lower average mean squared error value and a lower average mean absolute error value. Therefore, based on the results of this analysis, CatBoost was selected as the algorithm that would be fully developed for the prediction of impact-induced brain axon fiber strain.

5.5 Optuna

5.5.1 Introduction to Optuna

Optuna is an algorithm created by Preferred Networks, Inc. and originally released in 2019 [231]. Optuna handles one of the most cumbersome tasks required in the problem of the prediction of impact-induced brain axon fiber strain, which is hyperparameter optimization [231]. Several other implementations of hyperparameter optimization exist but they have their own shortcomings and problems which Optuna aims to overcome [231]. For large-scale experiments with numerous candidate models of various types, large parameter spaces and numerous conditional variables, some existing hyperparameter optimization frameworks call for the user to statically construct the parameter search space for each model. This search space can be challenging to describe in these frameworks [231]. When the parameter space is not correctly described by the user, the application of the advanced optimization method can be in vain [231]. Secondly, many existing hyperparameter search optimization frameworks do not feature an efficient
pruning strategy [231]. For high-performance optimization with constrained resource availability, parameter searching strategies and performance estimation strategies are both crucial [235]–[237]. Another shortcoming of previous architectures is a difficult installation process, often requiring multiple install lines and convoluted instructions [231].

To accommodate a variety of prediction models in different situations, Optuna improves on previous hyperparameter search optimization algorithms by being able to handle both small- and large-scale experiments with minimum setup requirements [231]. By utilizing define-by-run programming, which enables the user to dynamically construct the search space, as well as an easily customizable efficient sampling algorithm and pruning algorithm, Optuna enhances previous hyperparameter search algorithms [231]. Optuna is simple to install and features a flexible architecture that may be used for a wide range of applications, from light-weight experiments carried out via interactive interfaces to heavy-weight distributed computations [231].

The define-by-run principle is a trending philosophy in deep learning frameworks that allows the user to dynamically program deep networks [231]. It is useful because the user does not have to support the full burden of specifically defining everything in advance about the optimization strategy [231]. Optuna formulates the hyperparameter optimization as a minimization or maximization process calculated using an objective function [231]. This objective function takes a set of hyperparameters as an input and returns its validation score, which it uses to choose optimal hyperparameters [231]. The overall optimization process is called a “study” and each evaluation of the objective function within a study is called a “trial” [231]. Optuna builds the objective function over time through the interaction with trials [231]. The parameter search spaces are constructed dynamically by the methods of the trial object during the runtime of the objective function [231]. With this functionality, Optuna users can easily represent a wide variety of parameter spaces, and even express heterogeneous parameter spaces with intuitive, modular and simple Python code [231]. A comparison of equivalent code in HyperOpt and Optuna is presented in Akiba et al. (2019), and the Optuna code is simpler
to understand and implement [231]. The full backend and mathematical logic used in Optuna is available in Akiba et al. (2019) [231].

The parameters used in the finalized CatBoost model are the same as the ones used in the simple implementation in Section 5.3.3.3 and were created through trial-and-error search space definitions from the quantitative evaluation completed in Section 5.4.3.

5.6 Dataset Structures

Training datasets were set up in the same manner as explained in Section 5.4.2, with kinematic data aligned to the axon fiber strain time histories for each axon fiber element in the Brain Axon Fiber GHBMC Model.

Testing datasets, used to evaluate the performance of the algorithms, also followed this same structure. These testing datasets were fully independent of the training datasets. Utilizing a standardized data structure allowed for an easy comparison between datasets of different types. This also allowed plotting templates and analysis techniques to be standardized across all types of data input or output.

Prediction datasets, or those that contain unfamiliar kinematics data for which the selected algorithm was asked to predict strain data, share the same structure as in Section 5.4.2. However, before predictions are made by the selected algorithm, the strain data portion of the dataset is blank.

5.7 Prediction Results

5.7.1 Chosen Tracts and Algorithm Evaluation Metrics

Although CatBoost can predict any of the parcellated tracts outlined in Chapter 2, selected tracts were used to evaluate the performance of the algorithm. These tracts were selected based on existing studies that linked damage to those tracts to mTBIs. The tracts that were selected based on this literature review were the cingulum bundle, corpus callosum, corona-radiata-frontal and corona-radiata-parietal tracts, corticospinal tract and
superior longitudinal fasciculus. These tracts, shown in the Brain Axon Fiber Tract Model, are presented in Figure 85.

![Image of brain with fiber tracts](image)

**Figure 85: Tracts in the Brain Axon Fiber Tract GHBMC Model with Links to mTBI, Surrounded by the Dura**

Using high-definition tracking, Shin et al. (2012) found the cingulum bundle and corpus callosum to have decreased extension and volume of their white matter pathways after mTBI [238]. Additionally, specific fiber tracts were discontinuous in the corona radiata and cingulum bundle after mTBI, indicating axonal shearing occurred after impact [238]. June et al. (2020) used MRI and DTI to compare 51 participants with a mean age of 65.1 ± 11.23 who had had a mTBI in their medical history to 150 participants with a mean age of 66.6 ± 10.97 with no history of mTBI [239]. Participants with prior mTBI showed damage to their anterior corona radiata and superior longitudinal fasciculus in this study [239]. Wu et al. (2020) found a decreased level of mean diffusivity in the corticospinal tract of concussed athletes, and widespread white-matter areas of high school football players six months after impact-induced injury [240]. After synthesizing the results of this literature review, the data for the selected axon fiber tracts were set up for prediction with CatBoost.
The predictions were evaluated on several bases, however, all bases focused on predicting maximum axial strain values as the maximum axial strain point will be representative of the damage caused to each axon fiber tract finite element, and therefore representative of overall injury. The complete time history across the evaluation period of 0 to 80 milliseconds was completed, but for simplicity of analysis purposes, data was reduced to maximum strain values only. The first evaluation method was the correlation between the actual and predicted data. This was done by plotting the predicted maximum axial strain data against the real maximum axial strain data and calculating the R-squared value of this relation. The second method of evaluation was calculating the residual values, found by subtracting the predicted maximum axial strain values from the real maximum axial strain values. This second method of evaluation also involved plotting the real and the predicted maximum axial strain values against each other on the same scatter plot to visualize the raw difference. The third evaluation method involved calculating MSE, RMSE and MAE, as defined in Chapter 3. These performance evaluation metrics enable the comparison of the results of the predictions of each of the selected tracts in each impact direction. All three of these metrics are also standard AI algorithm performance metrics used in accepted literature.

In addition to these three methods of evaluation, individual element prediction time and total tract prediction time were tracked. Prediction speed will vary based on processor speed and available memory. All predictions in this chapter were made using a workstation running Windows 10 Enterprise with two Intel Xeon Silver 4216 CPUs, each with a base speed of 2.10 GHz, and 96 GB of RAM.

5.7.2 Results

A selection of various types of helmets, impact energies and impact directions were predicted. Performance metrics including R-squared value, MSE, RMSE, MAE, average residuals and prediction time are shown in Tables 22 to 26. Plots for each of the predictions made for each impact case and tract are presented in Appendices A to E.
Table 22: Evaluation Metrics for a Frontal, High Energy Impact to Helmet A

<table>
<thead>
<tr>
<th>Axon Fiber Tract</th>
<th>R-Squared Value</th>
<th>MSE</th>
<th>RMSE</th>
<th>MAE</th>
<th>Avg. Residual</th>
<th>Average Per Element Prediction Time (s)</th>
<th>Total Per Tract Prediction Time (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CB</td>
<td>0.9007</td>
<td>1.6E-04</td>
<td>1.2E-02</td>
<td>4.0E-03</td>
<td>3.2E-03</td>
<td>5.67</td>
<td>37,031.79</td>
</tr>
<tr>
<td>CC</td>
<td>0.9523</td>
<td>8.6E-05</td>
<td>9.2E-03</td>
<td>4.7E-03</td>
<td>4.7E-04</td>
<td>4.46*</td>
<td>138,527.66**</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>33,044.61</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5,888.60</td>
</tr>
<tr>
<td>CRF</td>
<td>0.8154</td>
<td>2.8E-03</td>
<td>5.3E-02</td>
<td>1.6E-02</td>
<td>1.2E-02</td>
<td>6.57</td>
<td>2,562.11</td>
</tr>
<tr>
<td>CRP</td>
<td>0.9751</td>
<td>5.1E-05</td>
<td>7.2E-03</td>
<td>5.5E-03</td>
<td>1.9E-03</td>
<td>6.08</td>
<td>37,712.01**</td>
</tr>
<tr>
<td>CST</td>
<td>0.7654</td>
<td>3.2E-03</td>
<td>5.6E-02</td>
<td>1.5E-02</td>
<td>1.4E-02</td>
<td>0.47</td>
<td>(12,570.67)</td>
</tr>
<tr>
<td>SLF</td>
<td>0.9839</td>
<td>4.0E-05</td>
<td>6.3E-03</td>
<td>4.5E-03</td>
<td>7.5E-04</td>
<td>2.11*</td>
<td></td>
</tr>
</tbody>
</table>

Table 23: Evaluation Metrics for a Frontal, High Energy Impact to Helmet F

<table>
<thead>
<tr>
<th>Axon Fiber Tract</th>
<th>R-Squared Value</th>
<th>MSE</th>
<th>RMSE</th>
<th>MAE</th>
<th>Avg. Residual</th>
<th>Average Per Element Prediction Time (s)</th>
<th>Total Per Tract Prediction Time (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CB</td>
<td>0.9256</td>
<td>1.4E-04</td>
<td>1.2E-02</td>
<td>5.6E-03</td>
<td>4.8E-03</td>
<td>5.75</td>
<td>37,551.03</td>
</tr>
<tr>
<td>CC</td>
<td>0.8984</td>
<td>2.1E-04</td>
<td>1.5E-02</td>
<td>7.6E-03</td>
<td>4.3E-03</td>
<td>4.60*</td>
<td>142,869.55**</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(20,409.94)</td>
</tr>
<tr>
<td>CRF</td>
<td>0.7544</td>
<td>4.2E-03</td>
<td>6.5E-02</td>
<td>2.0E-02</td>
<td>1.6E-02</td>
<td>6.69</td>
<td>33,607.01</td>
</tr>
<tr>
<td>CRP</td>
<td>0.8308</td>
<td>4.6E-04</td>
<td>2.1E-02</td>
<td>1.2E-02</td>
<td>8.5E-03</td>
<td>6.69</td>
<td>6,486.05</td>
</tr>
<tr>
<td>CST</td>
<td>0.7745</td>
<td>3.7E-03</td>
<td>6.1E-02</td>
<td>2.0E-02</td>
<td>1.9E-02</td>
<td>0.95</td>
<td>5,185.88</td>
</tr>
<tr>
<td>SLF</td>
<td>0.8905</td>
<td>2.9E-04</td>
<td>1.7E-02</td>
<td>9.6E-03</td>
<td>5.8E-03</td>
<td>2.22*</td>
<td>39,633.47**</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(13,211.16)</td>
</tr>
</tbody>
</table>
### Table 24: Evaluation Metrics for a Rear, Low Energy Impact to Helmet C

<table>
<thead>
<tr>
<th>Axon Fiber Tract</th>
<th>R-Squared Value</th>
<th>MSE</th>
<th>RMSE</th>
<th>MAE</th>
<th>Avg. Residual</th>
<th>Average Per Element Prediction Time (s)</th>
<th>Total Per Tract Prediction Time (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CB</td>
<td>0.9080</td>
<td>3.4E-05</td>
<td>5.8E-03</td>
<td>1.6E-03</td>
<td>2.7E-04</td>
<td>4.31</td>
<td>28,166.09</td>
</tr>
<tr>
<td>CC</td>
<td>0.8883</td>
<td>5.5E-05</td>
<td>7.4E-03</td>
<td>2.3E-03</td>
<td>4.6E-04</td>
<td>3.31*</td>
<td>102,946.58**</td>
</tr>
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<td></td>
<td>(14,706.65)</td>
</tr>
<tr>
<td>CRF</td>
<td>0.9038</td>
<td>2.9E-04</td>
<td>1.7E-02</td>
<td>4.3E-03</td>
<td>1.6E-03</td>
<td>3.56</td>
<td>17,878.85</td>
</tr>
<tr>
<td>CRP</td>
<td>0.9711</td>
<td>1.7E-05</td>
<td>4.1E-03</td>
<td>2.9E-03</td>
<td>1.4E-03</td>
<td>7.32</td>
<td>7,089.44</td>
</tr>
<tr>
<td>CST</td>
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<td>2.0E-04</td>
<td>1.4E-02</td>
<td>4.0E-03</td>
<td>2.4E-03</td>
<td>6.72</td>
<td>36,653.87</td>
</tr>
<tr>
<td>SLF</td>
<td>0.9880</td>
<td>1.0E-05</td>
<td>3.2E-03</td>
<td>2.2E-03</td>
<td>1.3E-03</td>
<td>3.74*</td>
<td>66,803.81**</td>
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<td>(22,267.94)</td>
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### Table 25: Evaluation Metrics for a Rear, Mid Energy Impact to Helmet D

<table>
<thead>
<tr>
<th>Axon Fiber Tract</th>
<th>R-Squared Value</th>
<th>MSE</th>
<th>RMSE</th>
<th>MAE</th>
<th>Avg. Residual</th>
<th>Average Per Element Prediction Time (s)</th>
<th>Total Per Tract Prediction Time (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CB</td>
<td>0.8089</td>
<td>1.4E-04</td>
<td>1.2E-02</td>
<td>5.2E-03</td>
<td>3.7E-03</td>
<td>6.91</td>
<td>45,095.18</td>
</tr>
<tr>
<td>CC</td>
<td>0.8504</td>
<td>1.4E-04</td>
<td>1.2E-02</td>
<td>4.3E-03</td>
<td>1.9E-03</td>
<td>3.77*</td>
<td>117,106.78**</td>
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<tr>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td>(16,729.54)</td>
</tr>
<tr>
<td>CRF</td>
<td>0.7835</td>
<td>1.8E-03</td>
<td>4.3E-02</td>
<td>1.2E-02</td>
<td>1.0E-02</td>
<td>0.72</td>
<td>3,598.90</td>
</tr>
<tr>
<td>CRP</td>
<td>0.9500</td>
<td>5.0E-05</td>
<td>7.1E-03</td>
<td>5.2E-03</td>
<td>2.0E-03</td>
<td>2.97</td>
<td>2,874.62</td>
</tr>
<tr>
<td>CST</td>
<td>0.0001</td>
<td>5.3E-01</td>
<td>7.3E-01</td>
<td>7.0E-01</td>
<td>6.9E-01</td>
<td>6.67</td>
<td>3,629.78</td>
</tr>
<tr>
<td>SLF</td>
<td>0.8770</td>
<td>2.3E-04</td>
<td>1.5E-02</td>
<td>9.9E-03</td>
<td>8.6E-03</td>
<td>2.53*</td>
<td>45,167.81**</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td>(15,055.94)</td>
</tr>
</tbody>
</table>
Table 26: Evaluation Metrics for a Side, High Energy Impact to Helmet A

<table>
<thead>
<tr>
<th>Axon Fiber Tract</th>
<th>R-Squared Value</th>
<th>MSE</th>
<th>RMSE</th>
<th>MAE</th>
<th>Avg. Residual</th>
<th>Average Per Element Prediction Time (s)</th>
<th>Total Per Tract Prediction Time (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CB</td>
<td>0.8160</td>
<td>2.0E-04</td>
<td>1.4E-02</td>
<td>8.4E-03</td>
<td>-1.2E-03</td>
<td>1.52</td>
<td>9,944.28</td>
</tr>
<tr>
<td>CC</td>
<td>0.7800</td>
<td>5.5E-04</td>
<td>2.4E-02</td>
<td>1.5E-02</td>
<td>8.0E-03</td>
<td>2.92*</td>
<td>90,619.29**</td>
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<tr>
<td>CRF</td>
<td>0.7619</td>
<td>2.8E-03</td>
<td>5.3E-02</td>
<td>1.8E-02</td>
<td>7.2E-05</td>
<td>5.25</td>
<td>26,406.33</td>
</tr>
<tr>
<td>CRP</td>
<td>0.8253</td>
<td>2.2E-04</td>
<td>1.5E-02</td>
<td>9.9E-03</td>
<td>6.0E-03</td>
<td>11.62</td>
<td>11,260.47</td>
</tr>
<tr>
<td>CST</td>
<td>0.8138</td>
<td>1.4E-03</td>
<td>3.7E-02</td>
<td>1.3E-02</td>
<td>4.0E-03</td>
<td>3.45</td>
<td>18,837.85</td>
</tr>
<tr>
<td>SLF</td>
<td>0.8355</td>
<td>2.1E-04</td>
<td>1.4E-02</td>
<td>8.2E-03</td>
<td>-8.4E-04</td>
<td>3.25*</td>
<td>58,113.50**</td>
</tr>
</tbody>
</table>

The corpus callosum and the superior longitudinal fasciculus were modelled using seven and three finite element parts, respectively. Some table entries are marked with a single or double star. Entries marked with a single star indicate the average time it took to predict the axial strain of an element across all seven and three parts, respectively, that made up those tracts. Entries marked with a double star indicate the sum of the total times it took to predict each of the parts in the tract, with the average total time for each of the seven and three parts, respectively, shown in parentheses.

5.7.3 Discussion

After the predictions were completed and the data analyzed through Tables 22 to 26, several observations were noted.

The first and most significant overall observation noted across all impact cases predicted for was that the average residual value in all but two tracts across all cases was positive. The only negative average residual values were in the cingulum bundle and in the superior longitudinal fasciculus in the high energy side impact prediction for Helmet A. Overwhelmingly positive residuals mean that CatBoost was consistently underpredicting
axial strain levels. Underprediction of the axial strain is concerning because, if deployed outside the laboratory, this algorithm would be underreporting axial strain levels, and therefore understating the effect of brain axon fiber strain related injuries. However, the margin of the average residual was usually on the order of hundredths or thousandths of a decimal place, meaning most values were quite close to their actual maximum axial strains. Furthermore, the overwhelming majority of the residuals in the graphs shown in Appendices A to F demonstrate that the difference between the predicted and real maximum axial strain values is within the range of -0.05 to 0.05. The number of residual outlier points, or points outside this range, is smaller than the number of points within the range, indicating consistently accurate and precise made predictions by CatBoost.

The second overall observation from the data was that the correlation between the actual and predicted maximum axial strain values is quite high, as evidenced by the R-squared correlation values between the two being greater than 0.7. Although the data did not reach the strength of correlation as seen in Chapter 3, there were many more points per impact cases here than in the data in Chapter 3, which led to a lower R-squared value. Only in one tract in one case, the corticospinal tract in the mid energy rear impact to Helmet D, was the R-squared value below 0.7 or was no correlation of any type found. For this particular instance, CatBoost predicted the strain levels to be an order of magnitude higher than the actual data. It should be noted that this particular instance was an outlier in terms of all evaluation metrics.

The third overall observation from the data was that the MSE, RMSE and MAE values were no larger than 0.1, except in the case of the corticospinal tract prediction in the mid energy rear impact to Helmet D. For MSE, RMSE and MAE, values closer to zero are desired, so these predictions have low error. Low error values are another indicator of a high quality of prediction achieved by CatBoost.

The fourth overall observation is that there was a variation in both the average and total prediction time per tract in each of the five cases examined. The cingulum bundle prediction, for example, took as little as 1.52 seconds per prediction and as high as 6.91 seconds per element prediction, depending on the impact case. In terms of total time for
prediction, the cingulum bundle took as low as 9,994.28 seconds and as high as 45,095.18 seconds. Predictions for one impact case were run all at once, and as some tracts are larger than others, the predictions for these tracts took longer. The smaller tracts were predicted faster, and once completed the computation resources of the processor would be committed to the remaining unfinished tracts. The deviation in average prediction time and total prediction time would be reduced if the prediction for each tract was run on separate computers with equal computational power, or sequentially on the same workstation.

In the predictions for the high energy impacts in the frontal direction to Helmet A (Table 22) and to Helmet F (Table 23), the corona-radiata-frontal tract and the corticospinal tract were the tracts that had the worst overall prediction metrics. In the case of Helmet A, the corpus callosum and the superior longitudinal fasciculus had the best overall prediction metrics, while in the case of Helmet F, the cingulum bundle and the superior longitudinal fasciculus had the best overall prediction metrics.

In the prediction for the low and mid energy rear impacts to Helmets C (Table 24) and D (Table 25), respectively, the corona-radiata-parietal tract had the best overall prediction metrics. In the case of Helmet C, the corpus callosum had the worst overall metrics, although all metrics in this case were quite good. In the case of Helmet D, the corona-radiata-frontal tract and the corticospinal tract had the worst metrics. There was no correlation found for the corticospinal tract in this impact case.

In the prediction for the side impact case to Helmet A (Table 26), all evaluation metrics were lower than for the frontal or rear impact cases. The corona-radiata-parietal tract and superior longitudinal fasciculus had the best overall prediction metrics, while the corona-radiata-frontal tract had the worst overall prediction metrics.

The accuracy of the prediction results and strength of correlation achieved by the implementation of CatBoost presented in this chapter are comparative to the results of Wu et al. (2019), Zhan et al. (2021) and Ghazi et al. (2021) [122], [167], [168]. Error levels for the implementation of CatBoost are comparable to the nine percent error for
peak strain magnitude described in Shim et al. (2020) [241]. The speed of prediction that
was achieved in Shim et al. (2020) and in Zhan et al. (2021) was not matched by
CatBoost, but the finite element models used in this work are more detailed in their
geometry and have more elements overall that need to be predicted, which takes more
time [167], [241]. Increases in overall prediction speed may be achieved by reducing the
number of elements predicted per tract, such as by predicting every second or third
element in the tract. This concept was not explored here but may be an area of future
research for the rapid estimation of brain axon fiber tract strain.

5.8 Chapter Conclusions

This chapter focused on the research, development and implementation of an AI model to
predict brain axon fiber tract axial strain. A quantitative and qualitative evaluation of five
different AI algorithms for predicting brain axon fiber tract axial strain was conducted.
CatBoost, a GBM, was selected as the best candidate algorithm from preliminary testing.
Nine data libraries containing sets for each of the 33 parcellated axon fiber tracts from the
Brain Axon Fiber Tract GHBMC Model were created, dividing data by front, rear and
side impact directions and low, mid and high energy levels. The nine libraries contain a
total of 369 training databases, due to some axon fiber tracts having multiple finite
element parts. In turn, 369 sets of corresponding hyperparameters were generated from
these training databases. Six tracts were selected based on their relation to mTBI through
a literature review. CatBoost was used to predict the time history and maximum axial
strain values for every finite element in these tracts, and performance evaluation metrics
were calculated from these prediction values. Overall, CatBoost was quite successful in
producing accurate and precise prediction values with low error. The results were
comparable to similar existing studies conducted from the literature. Some areas of future
research and work were identified, but overall, the novel prediction algorithm and
pipeline developed was successful in predicting brain axon fiber axial strain.
Chapter 6

6 Thesis Conclusions

This thesis examined the structure, function and anatomy of the brain, and how dynamic force-inducing impacts to the head and body can cause deficiencies in brain function and tissue damage. It also analyzed the benefits offered by new tools that researchers have available to them to study this relation. This thesis has shown novel research progress made in the field of impact-related brain injury prevention in sports, particularly ice hockey. mTBIs are still frequently occurring and poorly understood injuries that are epidemic in sports and other physical recreation activities generally where head and body impacts are expected to occur. Using research tools, such as anatomically accurate computational head finite element models of the brain derived from medical imaging and AI algorithms to augment current mTBI prevention and care techniques, the purpose of this thesis is to reduce and mitigate the risk posed to participants in such activities. Each of the chapters in this thesis covered a different topic related to either mTBI research or tools used for studying mTBIs.

6.1 Summary of Research

Chapter 1 introduced the concepts of impact-induced head and brain injuries. A review of the incidence rate of mTBIs in different ice hockey leagues was presented using results from the literature, showing that mTBIs are prevalent in ice hockey. Different types of sports-related impact injuries, such as focal and diffuse brain injuries, were introduced. Protective tools for brain injuries including helmets were reviewed, and a survey of the existing studies completed showed their benefits in reducing mTBIs. The research rationale was established, and the research scope was defined. Lastly, an outline of the various sections of this thesis was presented.

Chapter 2 introduced the parcellation of axon fiber tracts and regions of the brain. A detailed literature review of the research into the structure, function and responsibilities of each of the parcellated axon fiber tracts was completed. Areas of the brain including
the frontal, parietal, temporal and occipital lobes, the brain stem and the cerebellum were discussed, and their respective axon fiber tracts were introduced. The concept of using Brodmann areas as a map for the anatomy of the brain was used. Medical images of each of the 33 parcellated axon fiber tracts were provided, along with the equivalent tract shown in the Brain Axon Fiber Tract GHBMC Model, allowing readers to compare the two approaches to visualizing axon fiber tracts. A table summarizing the links of each tract to nine disorder and dysfunction groups was created to provide researchers with a resource for quick reference. The brain was shown to be a key organ in the body that handles several important functions of the body. Injuries to the brain can affect different areas, and as these areas are responsible for different functions, the results of the injury can be varied. Using tools such as advanced finite element models and medical imaging technology to confirm theorized connections between areas of the brain and their functionality was identified as an area of high research importance, as this will help strengthen the known links between sporting activities, head impacts and brain injuries.

Chapter 3 established the relationship between the different components of a blunt impact, defining them as kinematic input variables, and various metrics which serve as correlates for brain tissue strain and mTBI in an existing finite element brain model. The chosen correlates for mTBI were MPS and CSDM25. Experimental helmeted impact data collection methods for six helmet models were detailed, with three impact energy levels and three impact locations defined. A multilayer perceptron was used to rank combinations of kinematic input variables in terms of their ability to predict MPS and CSDM25. Confirming existing results from the literature, rotational velocity was found to be the best predictor of MPS and CSDM25. Peak linear acceleration, rotational velocity and rotational acceleration were found to be an unexpectedly good combination of kinematic combination. After a collinearity check was completed and using the kinematic input variable combination found earlier, three types of AI algorithms were evaluated in their ability to predict an increasing amount of unfamiliar MPS and CSDM25 data with a decreasing amount of training data. The random forest regression algorithm and the multilayer perceptron outperformed the Bayesian regularization algorithm in this second test. The results from work completed in this chapter show that AI algorithms can be used
to successfully predict MPS and CSDM\textsubscript{25} values for head impacts in sports such as ice hockey, which will help researchers and engineers process physical head impact data with greater efficiency and at significantly lower computational costs than previously possible.

Chapter 4 utilized the helmeted impact data collected in the previous chapter, and divided the data by impact direction, energy level and helmet model. Bare head data was also collected, albeit at only the low impact energy, as the dummy head model was at risk of damage at higher energy levels. Several existing brain finite element models were compared, and the Brain Axon Fiber Tract GHBMC Model was detailed. The Brain Axon Fiber Tract GHBMC Model was both visually compared to the base GHBMC Model using strain patterns taken from the same kinematics applied to each, and analytically compared in previous work done the members of Dr. Mao’s research group. In both the visual and analytical comparisons, it was confirmed that the two models produced comparable results. The low energy helmeted cases and bare head cases were simulated using the Brain Axon Fiber Tract GHBMC Model and compared in terms of change in beam element axial strain. Results on an axon fiber tract-by-tract level for a helmet-by-helmet case and for a general, averaged helmet case were reported. The axon fiber tracts with the largest decreases were listed, as well as the axon fiber tracts with the largest variation in calculated error. Detailed finite element models of the brain and head like the Brain Axon Fiber Tract GHBMC Model can help researchers and engineers strengthen their understanding of, and the link between, impacts and mTBIs.

Chapter 5 combined the baseline AI work completed in Chapter 3 with the outputs of the Brain Axon Fiber Tract GHBMC Model simulations completed in Chapter 4. The result of this combination was an AI pipeline that can predict axon fiber tract strain from helmeted impact data. A literature review of various types of AI methods that were considered as candidate algorithms was completed. Simple implementations of each type of algorithm were compared using a qualitative and quantitative comparison of ease of implementation, prediction accuracy and precision. The final algorithm chosen was CatBoost, a GBM. Helmeted impact data collected from Chapter 4 was divided by axon
fiber tract, by impact type and by energy level to create impact databases. By implementing Optuna, a hyperparameter training library, a corresponding set of hyperparameters was created to go with each of these impact databases to improve model accuracy. Five test predictions were completed on separate data not used in the training or validation. The cingulum bundle, corpus callosum, corona-radiata-frontal and corona-radiata-parietal tracts, corticospinal tract and superior longitudinal fasciculus were selected for further analysis in each of these test cases after the completion of a literature review, as they are the axon fiber tracts most related to mTBI. Evaluation metrics for each of these tracts were calculated, such as MSE and MAE. CatBoost performed well but tended to underpredict the axon fiber tract axial strain. Error values were found to be comparable to other algorithms used in papers in the accepted literature. The result of the work completed in Chapter 5 was a novel pipeline for the prediction of axon fiber axial strain based on the inputs of linear acceleration and rotational velocity. Such inputs were collected from laboratory experiments and directly prescribed to the finite element model, which is an excellent correlate for mTBIs occurring in sports and other physical recreation activities where head impacts occur.

6.2 Novelty, Significance and Impact of Research Work

The work conducted in this thesis demonstrates the first, large-scale application of experimental laboratory blunt impact data to a finite element model of the brain that contains accurate axon fiber tract modelling. Different ice hockey helmet models were also able to be compared on an axon fiber tract level to bare head impacts for the first time. Using the outputs from these models, the first implementation of AI to predict tract-specific axon fiber tract strain in the brain due to impact was achieved. Although the focus of this thesis is on sports and specifically ice hockey-related impacts to the head, the work covered in Chapters 4 and 5 is significant to the multidisciplinary field of mTBI research. With appropriate starting kinematics data and knowledge of impact criteria, the novel AI pipeline developed could be applied to other areas of impact research in other sports, such as American football, boxing or soccer, or to transportation occupant safety research, such as in the automotive or aerospace industries. Removing the helmet and the
impactor from the simulation and prescribing the kinematic impact data directly to the head and brain model as part of the novel AI pipeline makes it generalizable to different active research areas. Finite element models and AI are two of the best tools available to researchers and engineers conducting mTBI prevention research, and the state of the art of both tools has been advanced with the work completed for this thesis.

6.3 Areas of Future Work

Several areas of future work were identified in the writing of this thesis. The first area is to increase the amount of impact data available for AI training, validation and testing. For example, only nine low energy bare head cases across three directions were completed and used in Chapter 3. Increasing the number of bare head impact cases will eliminate uncertainty that utilizing a small amount of data in comparisons may cause. Bare head cases in this thesis were only evaluated at the low energy impact level. While there may be challenges with evaluating the dummy head model at higher energy levels as permanent damage may occur from testing, the data would still be valuable for bare to helmeted comparisons. The number of helmet models evaluated in this thesis was six, which could also be increased. If new helmeted data was collected, the process of transferring the kinematic data into the Brain Axon Fiber Tract GHBMC Model, running the simulation and then post-processing the data for analysis would be relatively straightforward. Studying more helmet models will help manufacturers develop better products to reduce the rate of occurrence and severity of mTBIs, DAI and other head and brain injuries in ice hockey and other sports and physical recreation activities where head and body impacts are expected to occur.

The second area of future work identified was the validation and continued improvement of the Brain Axon Fiber Tract GHBMC Model. The base GHBMC Model that was used in Chapter 3 has been validated against existing accepted literature, but the addition of the axon fiber tract finite element parts means the model will need to be re-validated. The interaction between the beam elements used to represent axon fiber tracts and the shell and solid elements used to represent other tissues and bones in the brain and head need to be further explored, as this interaction is fundamental to the understanding of mTBIs and
DAIs. In certain impact cases, particularly those conducted with high energy, there were instances of the ends of axon fiber tracts exiting the meninges of the brain, such as the dura. This is not anatomically possible unless a massive injury occurs, which is not realistic to be expected from the kinematics used as inputs in this thesis. During the process of visualizing the results of the head impact simulations, it was noted that strain concentrations occurred frequently at the end of the axon fiber within each tract. This should be investigated further to confirm that this behaviour is accurate to what occurs in real blunt head impacts. The overall behaviour and response of the model to blunt impacts, particularly how the axon fibers behave under dynamic loads, should be validated beyond what was used in this research.

Building on the previous area of future work, a fundamental component of mTBIs that is not included in significant detail in any model discussed in this thesis is the behaviour of the cerebrospinal fluid surrounding the brain. The cerebrospinal fluid is included as a solid element in both the base GHBMC Model and the Brain Axon Fiber Tract GHBMC Model. Augmenting the Brain Axon Fiber Tract GHBMC Model to include a computational fluid dynamics representation of cerebrospinal fluid would allow researchers to study coup contrecoup injuries and how changes in the pressure of the cerebrospinal fluid around the brain may lead to axon fiber tract damage.

A third area of future work would be to optimize the flow of data within the CatBoost algorithm selected for use in Chapter 5. Currently, all data is stored in comma separated value files and read in when needed, but if more data was added to increase the size of the training databases, this process would become increasingly time consuming. Using a better file type to store data will remedy this issue.

The AI algorithm selected in Chapter 5, CatBoost, was released in its current version in 2019. AI is a constantly evolving field, so ensuring the best available algorithm is used for brain axon fiber tract strain prediction is crucial. Therefore, ensuring that the current state-of-the-art algorithms are used for brain axon fiber tract strain prediction is necessary, and if new models offer improvements to the work completed in Chapter 5, the new model should be implemented.
Furthermore, the current CatBoost AI algorithm selected for use in Chapter 5 uses a multi-in single-out Pytorch implementation. Updating the algorithm to run with Tensorflow would allow the storage of data in tensors as opposed to a large table within a comma separated values file and should also allow for multiple predictions to be made at once. This could greatly increase the speed at which prediction results are available for analysis, opening new avenues for research and for the implementation of concussive mTBI detection systems in sports and other physical recreation activities, transportation occupant safety and even the military sector.

6.4 Closing

In closing, mTBIs are a constant threat to people participating in sports and other physical recreation activities where head and body impacts are to be expected, such as ice hockey. Researchers and engineers have made significant progress since the risks of brain injuries to participants in ice hockey were fully realized in the 20th century. The work completed in this thesis continues to advance the fields of brain injury prevention and sports and physical recreation activity safety. With continued progress in these fields, the end goal of improving safety, and in particular making the game of ice hockey safer for everyone involved, can and will be achieved.
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Appendices


Figure 86: Correlation of Actual vs. Predicted Element Maximum Axial Strain Values, Front High Impact, Helmet A, CB Tract

$R^2 = 0.9007$
Figure 87: Maximum Axial Strain Values, Actual vs. Predicted, Front High Impact, Helmet A, CB Tract
Figure 88: Residuals for Front High Impact Prediction, Helmet A, CB Tract
Figure 89: Correlation of Actual vs. Predicted Element Maximum Axial Strain Values, Front High Impact, Helmet A, CC Tract

Figure 90: Maximum Axial Strain Values, Actual vs. Predicted, Front High Impact, Helmet A, CC Tract
Figure 91: Residuals for Front High Impact Prediction, Helmet A, CC Tract
Figure 92: Correlation of Actual vs. Predicted Element Maximum Axial Strain Values, Front High Impact, Helmet A, CRF Tract

Figure 93: Maximum Axial Strain Values, Actual vs. Predicted, Front High Impact, Helmet A, CRF Tract
Figure 94: Residuals for Front High Impact Prediction, Helmet A, CRF Tract
Figure 95: Correlation of Actual vs. Predicted Element Maximum Axial Strain Values, Front High Impact, Helmet A, CRP Tract

Figure 96: Maximum Axial Strain Values, Actual vs. Predicted, Front High Impact, Helmet A, CRP Tract
Figure 97: Residuals for Front High Impact Prediction, Helmet A, CRP Tract
**Figure 98**: Correlation of Actual vs. Predicted Element Maximum Axial Strain Values, Front High Impact, Helmet A, CST Tract

**Figure 99**: Maximum Axial Strain Values, Actual vs. Predicted, Front High Impact, Helmet A, CST Tract
Figure 100: Residuals for Front High Impact Prediction, Helmet A, CST Tract
Figure 101: Correlation of Actual vs. Predicted Element Maximum Axial Strain Values, Front High Impact, Helmet A, SLF Tract

Figure 102: Maximum Axial Strain Values, Actual vs. Predicted, Front High Impact, Helmet A, SLF Tract
Figure 103: Residuals for Front High Impact Prediction, Helmet A, SLF Tract
Appendix B: Axial Strain Prediction Figures for Frontal High Energy Impact, Helmet F, Selected Axon Fiber Tracts

Figure 104: Correlation of Actual vs. Predicted Element Maximum Axial Strain Values, Front High Impact, Helmet F, CB Tract
Figure 105: Maximum Axial Strain Values, Actual vs. Predicted, Front High Impact, Helmet F, CB Tract
Figure 106: Residuals for Front High Impact Prediction, Helmet F, CB Tract
Figure 107: Correlation of Actual vs. Predicted Element Maximum Axial Strain Values, Front High Impact, Helmet F, CC Tract

Figure 108: Maximum Axial Strain Values, Actual vs. Predicted, Front High Impact, Helmet F, CC Tract
Figure 109: Residuals for Front High Impact Prediction, Helmet F, CC Tract
Figure 110: Correlation of Actual vs. Predicted Element Maximum Axial Strain Values, Front High Impact, Helmet F, CRF Tract

Figure 111: Maximum Axial Strain Values, Actual vs. Predicted, Front High Impact, Helmet F, CRF Tract
Figure 112: Residuals for Front High Impact Prediction, Helmet F, CRF Tract
Figure 113: Correlation of Actual vs. Predicted Element Maximum Axial Strain Values, Front High Impact, Helmet F, CRP Tract

Figure 114: Maximum Axial Strain Values, Actual vs. Predicted, Front High Impact, Helmet F, CRP Tract
Figure 115: Residuals for Front High Impact Prediction, Helmet F, CRP Tract
**Figure 116:** Correlation of Actual vs. Predicted Element Maximum Axial Strain Values, Front High Impact, Helmet F, CST Tract

![Graph showing correlation between actual and predicted maximum axial strain values.](image)

**Figure 117:** Maximum Axial Strain Values, Actual vs. Predicted, Front High Impact, Helmet F, CST Tract

![Graph showing comparison of actual and predicted maximum axial strain values for axon elements.](image)
Figure 118: Residuals for Front High Impact Prediction, Helmet F, CST Tract
Figure 119: Correlation of Actual vs. Predicted Element Maximum Axial Strain Values, Front High Impact, Helmet F, SLF Tract

Figure 120: Maximum Axial Strain Values, Actual vs. Predicted, Front High Impact, Helmet F, SLF Tract
Figure 121: Residuals for Front High Impact Prediction, Helmet F, SLF Tract
Appendix C: Axial Strain Prediction Figures for Rear Low Energy Impact, Helmet C, Selected Axon Fiber Tracts

Figure 122: Correlation of Actual vs. Predicted Element Maximum Axial Strain Values, Rear Low Impact, Helmet C, CB Tract
Figure 123: Maximum Axial Strain Values, Actual vs. Predicted, Rear Low Impact, Helmet C, CB Tract
Figure 124: Residuals for Rear Low Impact Prediction, Helmet C, CB Tract
Figure 125: Correlation of Actual vs. Predicted Element Maximum Axial Strain Values, Rear Low Impact, Helmet C, CC Tract

Figure 126: Maximum Axial Strain Values, Actual vs. Predicted, Rear Low Impact, Helmet C, CC Tract
Figure 127: Residuals for Rear Low Impact Prediction, Helmet C, CC Tract
Figure 128: Correlation of Actual vs. Predicted Element Maximum Axial Strain Values, Rear Low Impact, Helmet C, CRF Tract

Figure 129: Maximum Axial Strain Values, Actual vs. Predicted, Rear Low Impact, Helmet C, CRF Tract
Figure 130: Residuals for Rear Low Impact Prediction, Helmet C, CRF Tract
Figure 131: Correlation of Actual vs. Predicted Element Maximum Axial Strain Values, Rear Low Impact, Helmet C, CRP Tract

Figure 132: Maximum Axial Strain Values, Actual vs. Predicted, Rear Low Impact, Helmet C, CRP Tract
Figure 133: Residuals for Rear Low Impact Prediction, Helmet C, CRP Tract
Figure 134: Correlation of Actual vs. Predicted Element Maximum Axial Strain Values, Rear Low Impact, Helmet C, CST Tract

Figure 135: Maximum Axial Strain Values, Actual vs. Predicted, Rear Low Impact, Helmet C, CST Tract
Figure 136: Residuals for Rear Low Impact Prediction, Helmet C, CST Tract
Figure 137: Correlation of Actual vs. Predicted Element Maximum Axial Strain Values, Rear Low Impact, Helmet C, SLF Tract

R² = 0.988

Figure 138: Maximum Axial Strain Values, Actual vs. Predicted, Rear Low Impact, Helmet C, SLF Tract
Figure 139: Residuals for Rear Low Impact Prediction, Helmet C, SLF Tract
Appendix D: Axial Strain Prediction Figures for Frontal Medium Energy Impact, Helmet D, Selected Axon Fiber Tracts

Figure 140: Correlation of Actual vs. Predicted Element Maximum Axial Strain Values, Rear Mid Impact, Helmet D, CB Tract
Figure 141: Maximum Axial Strain Values, Actual vs. Predicted, Rear Mid Impact, Helmet D, CB Tract
Figure 142: Residuals for Rear Mid Impact Prediction, Helmet D, CB Tract
**Figure 143:** Correlation of Actual vs. Predicted Element Maximum Axial Strain Values, Rear Mid Impact, Helmet D, CC Tract

**Figure 144:** Maximum Axial Strain Values, Actual vs. Predicted, Rear Mid Impact, Helmet D, CC Tract
Figure 145: Residuals for Rear Mid Impact Prediction, Helmet D, CC Tract
Figure 146: Correlation of Actual vs. Predicted Element Maximum Axial Strain Values, Rear Mid Impact, Helmet D, CRF Tract

Figure 147: Maximum Axial Strain Values, Actual vs. Predicted, Rear Mid Impact, Helmet D, CRF Tract
Figure 148: Residuals for Rear Mid Impact Prediction, Helmet D, CRF Tract
Figure 149: Correlation of Actual vs. Predicted Element Maximum Axial Strain Values, Rear Mid Impact, Helmet D, CRP Tract

Figure 150: Maximum Axial Strain Values, Actual vs. Predicted, Rear Mid Impact, Helmet D, CRP Tract
Figure 151: Residuals for Rear Mid Impact Prediction, Helmet D, CRP Tract
Figure 152: Correlation of Actual vs. Predicted Element Maximum Axial Strain Values, Rear Mid Impact, Helmet D, CST Tract

Figure 153: Maximum Axial Strain Values, Actual vs. Predicted, Rear Mid Impact, Helmet D, CST Tract
Figure 154: Residuals for Rear Mid Impact Prediction, Helmet D, CST Tract
Figure 155: Correlation of Actual vs. Predicted Element Maximum Axial Strain Values, Rear Mid Impact, Helmet D, SLF Tract

Figure 156: Maximum Axial Strain Values, Actual vs. Predicted, Rear Mid Impact, Helmet D, SLF Tract
Figure 157: Residuals for Rear Mid Impact Prediction, Helmet D, SLF Tract

Figure 158: Correlation of Actual vs. Predicted Element Maximum Axial Strain Values, Side High Impact, Helmet A, CB Tract
Figure 159: Maximum Axial Strain Values, Actual vs. Predicted, Side High Impact, Helmet A, CB Tract
Figure 160: Residuals for Side High Impact Prediction, Helmet A, CB Tract
Figure 161: Correlation of Actual vs. Predicted Element Maximum Axial Strain Values, Side High Impact, Helmet A, CC Tract

Figure 162: Maximum Axial Strain Values, Actual vs. Predicted, Side High Impact, Helmet A, CC Tract
Figure 163: Residuals for Side High Impact Prediction, Helmet A, CC Tract
Figure 164: Correlation of Actual vs. Predicted Element Maximum Axial Strain Values, Side High Impact, Helmet A, CRF Tract

Figure 165: Maximum Axial Strain Values, Actual vs. Predicted, Side High Impact, Helmet A, CRF Tract
Figure 166: Residuals for Side High Impact Prediction, Helmet A, CRF Tract
Figure 167: Correlation of Actual vs. Predicted Element Maximum Axial Strain Values, Side High Impact, Helmet A, CRP Tract

Figure 168: Maximum Axial Strain Values, Actual vs. Predicted, Side High Impact, Helmet A, CRP Tract
Figure 169: Residuals for Side High Impact Prediction, Helmet A, CRP Tract
Figure 170: Correlation of Actual vs. Predicted Element Maximum Axial Strain Values, Side High Impact, Helmet A, CST Tract

Figure 171: Maximum Axial Strain Values, Actual vs. Predicted, Side High Impact, Helmet A, CST Tract
Figure 172: Residuals for Side High Impact Prediction, Helmet A, CST Tract
Figure 173: Correlation of Actual vs. Predicted Element Maximum Axial Strain Values, Side High Impact, Helmet A, SLF Tract

Figure 174: Maximum Axial Strain Values, Actual vs. Predicted, Side High Impact, Helmet A, SLF Tract
Figure 175: Residuals for Side High Impact Prediction, Helmet A, SLF Tract
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