Knee Articular Cartilage Material Properties Estimation Through FEA

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KNEE ARTICULAR CARTILAGE MATERIAL PROPERTIES ESTIMATION THROUGH FEA

A Thesis Presented

by

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of

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ABSTRACT

Osteoarthritis (OA) is a debilitating disease that leads to disability and loss of quality of life. Post-traumatic osteoarthritis (PTOA) is a version of OA that develops after acute injury to the knee. PTOA is of particular interest because the disease can manifest earlier in life compared to primary OA. Several studies have shown that changes in the mechanical properties of soft tissues in the knee (articulating cartilage and menisci) are associated with worsening OA grades. Changes to the tissue mechanical properties must be considered to generate realistic computational models of individuals who have suffered traumatic injuries to the knee. Therefore, we developed a method to non-invasively estimate subject-specific articular cartilage material properties by utilizing magnetic resonance imaging (MRI). High-resolution MR images were acquired of one subject’s knee joint before compression (uncompressed scan) and then after compression of the knee joint’s articular cartilage (compressed scan). The compression was performed by a MRI-loading device, which applied a load equal to half the subject’s body weight to the plantar aspect of the foot. Hexahedral meshes were created from the subject’s knee joint soft tissues in the uncompressed scan. The boundary conditions of the model were set to mimic the conditions in the MR-scanner: half the subject’s body weight applied to the tibia along its long axis, and the femur was fixed in all degrees of freedom. The thickness of the subject’s tibiofemoral articular cartilage tissues, as determined from the compressed MR scan, were used as a target for a Gauss-Newton optimization. FE simulations were performed iteratively with updated parameters after every iteration until the approximate tissue thickness of the compressed scan was observed, requiring 53 iterations (total of 85 hours runtime) to converge at a 0.5% tissue thickness difference between simulated results and the compressed MR-scan. The material parameter results from our simulation fall within the range of literature values, which allows us to conclude that the methodology developed during this study is reliable and produces subject-specific parameters of knee joint articular cartilage. In future work we will apply the modeling framework developed in this study to patients after traumatic injury, with the goal of improving understanding of early mechanical changes in the joint alter the probability that patient develops PTOA.
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CHAPTER 1: INTRODUCTION

1.1. Background

Osteoarthritis (OA) is a debilitating joint disease that occurs after the cartilage breaks down over time. Cartilage functions to protect the bones and acts as a lubricated surface that permits smooth sliding between adjacent bones [1]. As cartilage tissue degrades over time, bone-on-bone contact can occur, leading to significant pain and a reduction of the joint’s range of motion [3]. These symptoms make it difficult for people to engage in their day-to-day activities, such as walking or climbing stairs, which contribute to disabilities and the loss in quality of life [3]. Osteoarthritis comes at a steep cost, with the average lifetime cost of $140,300 [4].

Obesity, genetics, age and acute knee injuries have been associated with OA development [2]. The OA that develops from acute knee injuries is known as post-traumatic osteoarthritis (PTOA). PTOA is of particular interest to our lab as the causes for it are less understood, and PTOA affects younger adults than idiopathic OA. Roughly half of patients with meniscal and/or anterior cruciate ligament (ACL) injury later develop PTOA [5]. PTOA tends to manifest anywhere from 10-20 years following injury, meaning that most PTOA patients start showing symptoms of OA early in life, possibly in their 30s or 40s [5]. Studies have shown that there is a higher incidence of OA in populations with ACL/meniscal injuries when compared to the general population. [6]. To make matters worse, in the US an estimated 120,000 ACL injuries occur each year [7], indicating that a significant number of people are at risk of developing PTOA in the future, which would have a tremendous impact on society both economically and also in terms of the well-being
of the people suffering from the disease. The severity of the disease and its consequences has impelled the scientific community towards understanding the underlying mechanisms that lead to the onset of PTOA. PTOA’s mechanism would give healthcare professionals better treatment options to slow or even halt the progression of PTOA.

It has been shown by the scientific community that an association between mechanical loading and the onset of PTOA exists [8]. Several studies in animal models have shown that induced injuries to the menisci and ACL lead to the formation of OA [9-11]. Meniscal and ligamentous injuries have the effect of destabilizing the knee joint and exposing it to loads that the joint is unaccustomed to sustain. Other studies have also produced convincing evidence in support of the mechanical influence in OA onset [12]. For example, Saarakkala et al studied the composition of surface collagen in vitro [12]. The study replicated the enzymatic activity that occurs following an acute knee injury, which has been associated with the onset of PTOA. The study concluded that collagen content and dimensions were not significantly reduced by enzymatic activity, thus suggesting that the mechanism for collagen degradation in early OA is mechanical as opposed to enzymatic [12].

Altered joint loading has been identified as one of the consequences of acute knee injuries in humans [2], with injuries to the ACL and the meniscus having the greatest impact on knee loading conditions. Injuries to the meniscus and ACL impact the loading conditions of the knee joint because it disrupts their function, which leads to loading conditions that the knee joint is not designed to bear. The function of the ACL is to provide stability in anterior-posterior translations and internal-external rotation in the tibiofemoral
However, after an acute injury such as an ACL tear, the ligament does not fully heal and provide the same level of stability, even if surgery repairs or replaces the tissue. As a result of the injury, the loading conditions are altered permanently and contact stresses on the cartilage surfaces change. The meniscus, which often suffers injury along with the ACL, redistributes the compressive loads within the tibiofemoral joint, alleviating contact stresses in the cartilage [17]. Depending on the severity and location of a meniscal injury, healthcare professionals may opt to partially resect the meniscus or repair it. Resecting the meniscus, however, has the consequence of directly increasing the contact stresses in the cartilage, by hampering the meniscus’s ability to appropriately redistribute loads [18-19].

The evidence thus far presented has led some groups to attempt to use contact pressure as a means of predicting the likelihood of a patient developing PTOA. Segal et al showed that a correlation exists between OA and contact stresses in the knee by comparing control and OA cohorts [20]. Kumar et al also showed that subjects with OA exhibited larger contact forces in their knees (specifically in the medial compartment) when compared to healthy subjects [21]. The above-referenced studies characterized the joint forces using methods such as DEA (discrete element analysis) or EMG-driven musculoskeletal models. However, these simplified models do not take into consideration patient-specific tissue geometry nor complex material properties.

DEA was used only calculate the contact stresses between two articulating surfaces based on overlap [20], however finite element analysis (FEA) offers the advantage of simulating the complex interactions of solids which would otherwise be impractical (e.g.
experiments on live humans), dangerous or too costly. FE models can predict the mechanics of elements to outside forces or displacement, as well as yield additional important tensor field properties such as shear, compression, tension, contact stress, etc. For the field of biomechanics, FEA represents a powerful tool since many experiments can be simulated through FEA that would otherwise cause harm on patients or be unfeasible. FEA works by discretizing complex geometries into smaller finite elements, and then performing continuum mechanical calculations on each one of the elements. This way, problems that are too geometrically challenging can be solved numerically with a reasonable degree of accuracy. FEA can also take into consideration patient-specific data, thus minimizing the error due to difference in material parameters between patients and generic population averages in the literature (with several studies showing a large variation between subjects) [22]. To improve the confidence of FEA model simulations, patient-specific material properties must be utilized. Therefore, the aim of this study is to develop a modeling framework to quantify patient-specific material properties in articular cartilage.

1.2. Previous Work

Several studies have shown the extensive impact that material properties have on FEA model simulation results. One study found that a decrease in cartilage stiffness leads to lower contact pressures and to different areas of the cartilage experiencing higher loads than they are accustomed [23]. Articular cartilage (AC) material properties are particularly important when evaluating patients with early stages of OA, since their cartilage stiffness has been shown to be significantly lower than patients who are healthy [24]. As OA progresses the AC becomes more compliant, thus making any analysis using average
population material properties less valid. Articular cartilage material property isn’t the only parameter that impacts the results of FEA models. The stiffness of the meniscus has also been shown to influence contact stresses, with these stresses increasing significantly with an increase in the stiffness of the meniscus [19]. The increased stiffness is a result of the meniscal tissue not being able to deform properly in order to transmit compressive loads through the tibiofemoral joint.

Several methods exist for measuring mechanical properties of soft tissue, but not all of them can be used on live subjects because they may be destructive or too invasive. An example of the current in-vivo methodology for measuring the material properties of soft tissue includes techniques like indentation testing [25] and resonance sensors that come into contact with the tissue during arthroscopy [26]. However, both methods require invasive procedures that we wish to avoid. On the other hand, MR imaging techniques provide a non-invasive alternative, as the images acquired through an MR scanner could yield the geometric information needed to quantify changes in tissue thickness during external loading.

We will base our methodology on a previous study implemented in an animal model by another research group [27]. The group utilized MR scans combined with a compression device in order to deform the patella cartilage of horse specimens. The group scanned the specimens in both a compressed and uncompressed state, with the compression force being 50% of the specimen’s bodyweight. Following their data acquisition, the group segmented the data to create three dimensional (3D) models of the horse tissue, which they used to create an FE model. The group later utilized a commercial FE software (ABAQUS)
in order to iteratively deform the cartilage, using a linear elastic model to represent articular cartilage. To estimate the material properties of the cartilage, the group employed a least squares optimization algorithm, with the cartilage thickness used as a measure for how close the simulation results were to the measured cartilage thickness. We have chosen to use a variation of the least-squares method called the Gauss-Newton method, which works for non-linear least squares optimization. The Gauss-Newton method is a suitable method for the nonlinear material behaviors of the articulating cartilages.

To the best of my knowledge, no group so far has performed a similar study during in-vivo conditions on human subjects. The closest study that has used MR-imaging in combination with FEA to estimate human cartilage properties used indenters combined with MR imaging [28]; however, we wish to avoid the use of indenters since the procedure would require surgery to access the subject’s tibiofemoral cartilage. Furthermore, in the indentation study FE analysis was restricted to only 2 dimensions, which may have an impact on the final material property estimation. To address the above-mentioned shortcomings, a novel method is required, one bereft of any of the limitations inherent in invasive procedures (such as indentation tests) or FE analysis that focus only on two spatial dimensions.

The aim of this study is to develop a novel modeling framework for estimating patient-specific material parameters using FEA in combination with magnetic resonance imaging (MRI). Our method works by creating a 3D FE model of the knee’s tissues and then simulating a load equal to body weight that was applied during static compression within the MRI. The resulting tissue thickness from these simulations was compared to the
thickness measured in the MRI during static compression, the differences in the two measurements were used to drive the parameter estimation process using the Gauss-Newton algorithm.
CHAPTER 2: METHODOLOGY

To determine the subject-specific material properties of articular cartilage, finite element simulations were run in an iterative manner, with each iteration using a different material parameter and yielding the thickness of the articulating cartilage under half a body weight compression. Simulation results of cartilage thickness were compared with measurements of thickness from high-resolution MR scans of the tissues under a static compressive load. A Gauss-Newton optimization algorithm guided the parameter estimation process. Before beginning the optimization process, the model was subjected to a sensitivity analysis, which determined the effect of element size on our simulation results. To evaluate the effects that convergence-criterion may have on the optimization process (iterations and results), a separate sensitivity analysis was performed which varied the convergence criterion between optimizations.

The methodology employed in this study can be broken down into four main parts: finite element model generation, finite element simulation setup, sensitivity analysis, and parameter optimization. Each part is described below.

2.1 Finite Element Model Creation

An FE model of the knee joint was developed from the MRI scans acquired from a healthy volunteer. The geometric information necessary to create the finite element mesh was derived from the MRI scans obtained from the participant. In the first scan, the subject’s knee joint will be in an “uncompressed” state, where the tissue was allowed to remain at rest prior to scanning. The uncompressed state scan served as the source of our model’s geometry. After the first acquisition a second acquisition was performed with a
compressive force of half the subject’s body weight applied to the bottom of the foot using our MRI-loading device (see section 2.3 for a description of the device). This second scan defined the target thickness which the optimization algorithm utilized to help fine tune the input parameters into our finite element simulation, with the goal of approximating the thickness of the second acquisition.

The overall method for creating a FEA model for the knee joint begins with segmentation, where geometric data is obtained from MR scans of the knee joint and which are processed to create surface models. These models are then used to create solid hexahedral meshes which can be used to run FEA simulations. Prior to running these simulations, material properties as well as contact conditions must be specified, as well as the boundary conditions of the entire model.

2.1.1 FE Model Creation Steps

There are several steps that must take place before an FE model can be created, all of which require a great deal of work and attention to certain details that can have a significant impact on the simulation results. In the next section, a detailed explanation of each of the steps necessary to create a subject-specific model will be discussed. The main steps taken during model creation are as follows: data acquisition, segmentation, solid mesh creation, material model selection, contact surface definition, discrete spring definition.

2.1.2 Data Acquisition

The first step of the process involves the acquisition of the geometric information of the subject’s knee joint utilizing a MR scanner. The MR scanners utilizes a strong...
magnetic field (3T) to align the protons in the body to magnetic field. The MR scanner then pulsates a radiofrequency current through the subject which in turn stimulates the protons within the body to spin out of equilibrium. The radiofrequency is then turned off, allowing the protons to realign with the magnetic field. The realignment process is captured by the MRI sensors and is used to produce the MR images. For this study’s methodology, two different scans will be taken: one during the unloaded/uncompressed state and the other during a loaded/compressed state. The unloaded state will be achieved by allowing the patient to sit for 15 minutes to allow the cartilage to reach its uncompressed state (where fluid has been reabsorbed by cartilage). Images of the uncompressed state will serve as the input of the FEA simulations. After acquiring the images in the uncompressed state, the MRI loading device (a mechanical instrument that applies half of the subject’s body weight to the plantar aspect of the foot) will apply the loading to acquire the compressed state. Loading will occur for 2 minutes prior to imaging to allow the tissue to approach equilibrium. Subjects will then be loaded on to the MRI scanner where the force will be

Figure 2.1 MRI loading device
applied (Figure 2.1). The resolution of both scans will be 0.3125x0.3150 mm with a slice thickness of 0.8mm.

2.1.3 Segmentation

Segmentation is a digital image processing technique that allows the users to digitize images and create 3-D objects (referred to as surface files) by painting objects of interest in every slice of the MR scan either manually or semi-automatically. The painted pixels are then used by the program’s algorithms to create a point cloud which is then triangulated to form a surface mesh. Segmentation in our current study focuses exclusively on the knee structures, that is: distal femur, femoral cartilage, medial and lateral menisci, medial and lateral tibia cartilage, and proximal tibia (Figure 2.2). Each structure in the

![Figure 2.2 Segmentation of knee, where the structures above are a) femur, b) femoral cartilage, c) meniscus, d) tibia cartilage, e) tibia](image-url)
segmentation has its own mask, which is then utilized to create a point cloud and a surface file through the triangulation of the aforementioned point cloud. We have used the program Seg3D to segment for this project [29].

After each surface file has been created, the segmented objects need to be filtered in order to remove the noise acquired during the digitalization process. Meshes that originate from seg3D are typically rough and have step-wise contours due to the images’ thickness. To solve this issue, our lab employs MeshLab [30], which is a free mesh manipulation software that has many mesh repairing algorithms. We first remove the noise by applying a Laplace smoothing algorithm to the entire (Figure 2.3). Care must be taken to not smooth too aggressively as each smoothing iteration averages and erodes away a bit of the surface. The smoothing process may alter the thickness of our tissues if a very high number of iterations are utilized. After smoothing, the next step is reducing

Figure 2.3 Smoothing of segmented surface files: a) non-smoothed surface b.) surface after 6 iterations of Laplacian smoothing have been executed.
the number of faces of the tissue. Typically, when a segmented tissue is created, Seg3D utilizes a large amount of triangular faces to describe its geometry. The number of faces may be over 200,000, which makes reading and processing these files extremely difficult in MATLAB and to increased FE simulation computational costs.

2.1.4 Solid Mesh Generation

Solid meshes are the geometric objects that allow us to run FEA simulations. Meshes discretize complex objects, like bones and soft tissue in this case, into smaller discrete geometric elements which can be used to solve problems numerically. There are different types of solid elements available for simulations, the two most common being tetrahedral and hexahedral elements. Given the iterative nature of the project, hexahedral elements are a better choice of elements since they will help cut down on the amount of computational effort required to arrive at an accurate solution.

Figure 2.4 Implementation of the meshing algorithm: (a) sweeping in both axial and circumferential directions using cylindrical coordinates, (b) determining initial nodes, (c) generating initial low-resolution mesh, (d) correcting elements with six nodes (collapsed elements), (e) smoothing the mesh, and (f) refining and optimizing the mesh iteratively [31].
Using the structures that were created during the segmentation process, hexahedral meshes were created using custom built MATLAB code [31]. The custom code works using cylindrical coordinates to produce a sweep pattern along the circumferential and axial directions. The resulting point cloud is then used to create an initial low-resolution mesh, which is then corrected for any collapsed elements, smoothed and refined to produce the final mesh (Figure 2.4). The custom code only produces hexahedral meshes for the articulating cartilage and the menisci.

Figure 2.5 Process to generate solid meshes from the STLs of the tibia cartilage and menisci [31].
The process for meshing the tibia cartilage and the menisci is similar to the femoral cartilage, except that the tibia cartilage does a cartesian sweeping on the middle of the plateau and circumferential sweeps on the edges. The menisci are meshed using only circumferential sweeping (Figure 2.5).

Whenever meshing of any kind is created for the purpose of FEA, it is always necessary to check that the quality of these elements is acceptable. This is done by computing the Jacobian of the elements. There are two types of Jacobians that are used to measure the quality of elements, the scaled Jacobian and the isoparametric Jacobian produced when one maps the coordinates of an element to the element’s local coordinate system. FEBio [32] (the FEA simulation software that we will use) uses the determinant of the isoparametric Jacobian to measure the quality of each element, this Jacobian is defined with the following equation:

$$\frac{\partial}{\partial \xi} \frac{\partial}{\partial \xi}$$
geometries that are encountered in knees. Therefore, it was deemed necessary to expand the tolerance of the Jacobians down to 0.01, as the custom-built MATLAB code was having difficulties maintaining some elements above the minimum acceptable tolerance whilst still trying to conform to the soft tissue’s geometry.

2.1.5 Material Model Selection

Every structure in a FEA simulation must be assigned a material model. The material model determines how much a material will strain when it is exposed to a certain amount of stress. Or, on the other hand, if the material is subjected to a strain, the material model will predict the amount of stress induced by the strain. The models for each of the soft tissues were chosen to best represent both the tissue behavior and the behavior under the loading conditions of the data acquisition. A more detailed explanation will be given in the discussion sections. Appendix A.1 contains all of the parameter choices for each tissue in the model (including the bones). The initial guesses for the material parameters were obtained from Open Knee [34]. Before delving into the material models of each tissue, we will briefly discuss the continuum mechanics theory that FEBio uses to compute the deformation of our models.

2.1.5.1 Continuum Mechanics Overview

It is beneficial for the reader to know how FEBio computes the deformation tensor and subsequently the deviatoric right Cauchy-Green deformation tensor, as such, the formulations used by FEBio are included here. FEBio defines the deformation gradient as:

\[
F = \frac{\partial \varphi}{\partial X}
\]  

(2.4)
Where $\varphi$ is the mapping between the material coordinates and the space coordinates, $F$ is the deformation gradient and $x$ denotes the location of material particles relative to the material coordinates. As mentioned previously, $J$ is the determinant of the deformation tensor $\mathbf{F}$. From the deformation tensor FEBio computes the right Cauchy-Green deformation tensor:

$$\mathbf{C} = \mathbf{F} \cdot \mathbf{F}^T \quad (2.5)$$

On the above equation, $T$ is the transpose. Finally, the deviatoric right Cauchy-Green deformation tensor can be computed using the following expression:

$$\mathbf{C} = J^{-2/3} \mathbf{C} \quad (2.6)$$

2.1.5.2 Articulating Cartilage

For the articulating cartilage, the chosen model was the Neo-Hookean model. The Neo-Hookean model is a nonlinear hyper-elastic material model that is often used to predict the stress-strain behavior of materials undergoing large deformations such as rubbers. The strain energy equation for the Neo-Hookean material is as follows:

$$W = C_1(I_1 - 3) + \frac{1}{2} K(\ln J)^2 \quad (2.2)$$

Where $C_1$ and $K$ are material constants, $J$ is the determinant of the deformation gradient tensor and $I_1$ is the first invariant of the deviatoric right Cauchy-Green deformation tensor. $C_1$ is the material parameter that we will be optimizing during this project, hence its value has not been predefined here. The Neo-Hookean model behaves close to the linear model during small deformations, which allows us to make a conversion from the linear model material parameters to the Neo-Hookean material model parameters. This can be done with the following equation:
Again, it must be emphasized that this formula is not where we will derive the values of our material parameters, they merely serve as a means to check that our optimized material values fall within the range of reported material stiffness in the literature. It is worth noting that in FEBio, the Neo-Hookean model can be utilized by using the broader Moony-Rivlin model and setting the second constant to zero. This causes the Moony-Rivlin Material model to behave exactly like the Neo-Hookean material model.

\[ C_1 = \frac{\mu}{2}; \quad K = \frac{\lambda}{2} \]  

(2.3)

2.1.5.3 Meniscus

The menisci on the other hand were defined as a Fung Orthotropic materials, owing to the tissue’s anisotropic behavior which depends strongly on the fiber’s direction (this behavior is present to a certain extent in articulating cartilage, but its anisotropic behavior is minimal and therefore an isotropic model can still yield relatively accurate predictions). The strain energy equation for the Fung Orthotropic model is defined as:

\[ W = \frac{1}{2} c (e^Q - 1) + U(f) \]  

(2.7)

Where

\[ \tilde{Q} = c^{-1} \sum_{a=1}^{3} [2\mu_a M_a : \tilde{E} + \sum_{b=1}^{3} \lambda_{ab} (M_a : \tilde{F} (M_b : \tilde{F})] \]  

(2.8)

For the equations above \( \tilde{E} = (C - I)/2 \), \( M_a = V_a \otimes V_a \). defines the directions of material axis. Vector was determined by computing the longest axis of each element, thus setting the proper anisotropic behavior of the menisci. The Lame constants \( \lambda_{ab} \) and
\( \mu a \) are related to the Young’s moduli, Shear moduli and Poisson ratio by the following expression:

\[
\begin{bmatrix}
\lambda_{11} + 2\mu_1 & \frac{\lambda_{12}}{\lambda_{21}} & \frac{\lambda_{13}}{\lambda_{23}} & 0 & 0 & 0 \\
\frac{\lambda_{21}}{\lambda_{22}} & \lambda_{22} + 2\mu_2 & 0 & 0 & 0 & 0 \\
\frac{\lambda_{31}}{\lambda_{32}} & 0 & \lambda_{33} + 2\mu_3 & 0 & 0 & 0 \\
0 & 0 & 0 & 1 & \frac{1}{2} (\mu_1 + \mu_2) & 0 \\
0 & 0 & 0 & 0 & \frac{1}{2} (\mu_2 + \mu_3) & 0 \\
0 & 0 & 0 & 0 & 0 & \frac{1}{2} (\mu_3 + \mu_3)
\end{bmatrix}
\]

\[
\begin{bmatrix}
\frac{1}{E_1} & \frac{v_{12}}{E_1} & \frac{v_{13}}{E_1} & 0 & 0 & 0 \\
-v_{21} & \frac{1}{E_2} & -\frac{v_{23}}{E_2} & 0 & 0 & 0 \\
\frac{E_2}{v_{31}} & -\frac{E_3}{v_{32}} & \frac{E_3}{1} & 0 & 0 & 0 \\
-E_3 & -E_3 & E_3 & 0 & 0 & 0 \\
0 & 0 & 0 & 1 & 0 & 0 \\
0 & 0 & 0 & 0 & \frac{1}{G_{12}} & 0 \\
0 & 0 & 0 & 0 & 0 & \frac{1}{G_{31}}
\end{bmatrix}
\]

The menisci in our model also incorporated their meniscal horn attachments, however unlike the rest of the tissue which was segmented and then given a specific material property, the meniscal horns were instead represented as a set of linear springs. The equation to determine the stiffness of each spring was the following:

\[
k_i = \frac{E}{NL_i}A
\]
where $k_i$ represents the $i^{\text{th}}$ spring stiffness, $L_i$ represents the $i^{\text{th}}$ spring length (measured from the meniscal horn to the point of attachment on the tibia), $E$ is the young’s modulus, whose value was set to 600 MPa, $N$ is the number of quads on the horn face, and $A$ is the total area of the horn face. The length of each spring was defined as the distance between the center of a quad in the meniscal horn face to the point on the tibia chosen to be the attachment of the meniscal horn.

### 2.1.5.4 Bones

The bones were defined as rigid bodies. The bones were selected as rigid bodies because their rigidness are several orders of magnitudes larger than the soft tissue, meaning that they deform considerably less and thus do not significantly impact the deformation of the soft tissue during simulations. This is an advantage during simulations because it drastically reduces the amount of computation cost, while still yielding a very close answer to a simulation that incorporates a deformable bone.

### 2.2: FEA Simulation Setup

The finite element simulation setup is very important because this is the part of the process where we try to replicate the conditions of the experimental setup. As such it is necessary to address what steps were taken to ensure that the setup conditions most closely resemble that which would be encountered in the experiment. The main setup parameters that must be considered during this phase are the force application, contact definition, contact parameters selection, time steps and boundary conditions. Simulations were run in FEBio [34], by writing a FEBio input file using the GIBBON add on [35].
2.2.1 Force Application and Boundary Conditions

The appropriate force application in FE analyses is critical to obtain valid results. In our model, we worked under the assumption that all the force is transmitted from the bottom of the foot through the distal shaft of the tibia. This modeling decision has a huge impact on simulations because the direction of the tibia shaft is not necessarily aligned to the z-axis of the model (which is aligned to the z-axis of the MR-scanner). This places a restriction on how to apply the force boundary condition in our model, with the force needing to be applied on the same direction as the tibia shaft. Hence, the need to define a local coordinate system whose z-axis is aligned to with the direction of the tibia shaft becomes important. We define this coordinate system by applying an algorithm employed in DSX software [36]. The rotation matrix yielded by Miranda’s algorithm is then used to rotate the force from a z-axis force in the global coordinate system to a z-axis force in the local tibial coordinate system [36]. To simulate the force being applied during the compressed MRI scan, we take half the weight of our subject and convert it into a force equivalent, in this case the subject weighed approximately 170 lbs., which results in a force application of 380 N.

FEA simulations require boundary conditions to give the system some physical meaning. Boundary conditions can be numerically imposed on a model by either applying a reaction force (a force opposite to the applied load on some other portion of the body), by fixing nodes in certain degrees of freedom or by fixing the center of mass of rigid bodies. In this study, the boundary conditions that we are interested in setting up are the peripheral nodes on the meniscus to simulate the effects of the knee capsule and the center of mass of
the distal femur was fixed to simulate the relative static condition of the femur during the compression.

### 2.2.3 Contact Definition

Setting up contact definitions in FE models is critical in order to simulate the interactions between tissues. In FEBio, we can simulate these tissue interactions by placing contact definitions which set up non-penetrating boundary conditions along the tissue interfaces. FEBio enforces these boundaries by utilizing a penalty factor, which produces a force proportional to the amount of penetration between the two surfaces that have been identified as being in contact. Care must be taken to not choose penalty factors that are too large, because the stiffness induced by these penalty factors can cause the global stiffness matrix to become ill-conditioned. On the other hand, if the penalty factor is too small, an inadequate amount of force will be produced, allowing tissues to completely penetrate into one another, giving inaccurate results. Determining the right penalty factor can be a challenge, which is why FEBio gives the user the option to turn on the auto-penalty option, which calculates the appropriate penalty factor using the following equation:

$$\varepsilon_i = \frac{E A}{V}$$  \hspace{1cm} (2.11)

Where $\varepsilon_i$ is the penalty factor, $E$ is the instantaneous elastic modulus of the tissue (this one is updated after every time step), $A$ is the area of the element the integration point belongs to and $V$ is the volume of the element. The penalty parameter (a user defined parameter not to be confused with $\varepsilon_i$) takes a different role depending on whether the autopenalty option is enabled or not. In the case where the autopenalty is enabled, the user defined penalty parameter serves as a scale for the result from equation 2.11. If the auto-penalty is turned
off, the penalty parameter becomes the penalty factor. For the purposes of this study we have selected a penalty parameter of 0.1.

We opted to use the auto penalty factor in this study because the penalty factor would scale proportionally to the stiffness of our model, thus the contact stiffness would not be too large in the early stages of the simulation (which leads to numerical instabilities) and would not be inadequate during the latter portions of the simulations, where a small penalty factor might not stop tissues from penetrating into one another once larger forces are prescribed.

Another important consideration during contact definition is the type of contact relationship between the two interacting tissues. In our study we have chosen two different contact relationships: sticky interfaces and sliding-elastic interfaces. Sticky interfaces are used when defining contact between bone and soft tissue. Sticky relationships allow two non-conforming surfaces to be connected to one another, and to provide a non-penetrative boundary. This is ideal for structures like the bone which have complicated geometries. It also allows the tissue to stay attached to the bone during the entire simulation, and this is important because an underlying assumption of articulating cartilage is that it is attached to the bone and is not free to slide relative to the bone. The rest of the tissues were defined as sliding elastic. Sliding-elastic interfaces provide a non-penetrating frictionless boundary between soft tissues, which is what we would expect of contacts between two articulating cartilage surfaces and between articulating cartilage and the menisci.

To define contact between the different tissues, FEBio requires that the user gives it the two surfaces involved in a contact relationship. Each surface has its own id, and a
surface pair is formed by telling FEBio that two surface id’s form part of that surface pair. Each surface pair also has its own identification number (id), which gets called on by the surface relationship. The surface pair requires that we define a master and a slave pair. Which surface is defined as either master or slave may impact the stiffness matrix computations depending on the type of contact relationship defined. In the case of “sliding-elastic” surfaces, which surface is defined as master or slave does not bear an impact, because of the “two_pass” option, which ensures that both surfaces have the contact equations integrated over them. This is not the case with “sticky” relationships or other forms of tied relationships, because the presence of a rigid set of nodes (like the bone for example) as the slave surface make it possible that the reaction forces may not propagate correctly through the master surface. Hence, for rigid body to soft tissue interactions, we always choose the rigid body as the master surface.

2.2.4 Simulation Parameters

Time steps are critical for FEA simulations, as they allow us to discretize the application of force over the length of the simulation. This is especially important for problems involving non-linear material models, as their stiffness ultimately depends on the instantaneous strain of the material. During this study, we prioritized reducing the amount of time steps necessary to complete a simulation because of the iterative nature of an
optimization. We found that using 10 time-steps allowed our models to converge without any problems.

Another option that FEBio gives its user are load-curves. This allows the user to define the loading conditions at time steps by multiplying the applied force by a scaling factor. We decided to create a load curve that applies most the force in the first two thirds of the simulation and tapering off close to the end (Figure 2.6). This was done to ensure that the final time step would not be susceptible to any ill conditioning resulting from large

![Loading curve of the force application](image)

*Figure 2.6 Loading curve for simulation force application*
deformations in elements, since this is the step where the measurement of the cartilage thickness takes place.

### 2.2.5 FEBio Input File Creation

The final step necessary to run a simulation in FEBio is the creation of an input file. This step was done by using the GIBBON [34] add on in MATLAB, which allows users to parse through the model data and write it as a text file which FEBio may read. Using this add-on is critical to this project because it allows us to automatically update the parameters in the input file after every iteration, thus allowing the process to run uninterrupted. There are a few steps that have to be taken before writing the input file. The first step requires the user to join the nodes of the entire model. The node joining process is done by concatenating the lists of the locations of the nodes of every tissue and the bones into a single variable (Figure 2.7). The order in which the structures are added does not

![Figure 2.7 Portion of the MATLAB script which allows the user to join the nodes of the entire model, as well as update the tissue’s hexahedral table](image)

26
matter, so long as the nodes in the hexahedral or quadrilateral tables point to the correct node location.

To point to the correct nodes from the tissue hexahedral tables we update the number of each node in the hexahedral/quadrilateral tables to correspond to the newly joined nodes. Updating the nodal tables requires the addition of the size of the nodes table of the previous tissue. To illustrate what we mean by this we use provide a snippet of our code (Figure 2.7) to show that we have defined the femoral cartilage to be the first structure in our joined node variable (Line 401). The structure that follows the femoral cartilage was the medial meniscus. Line 416 shows that we are adding the length of the rows in the femoral nodal array to each value in the matrix containing the hexahedral nodes for the medial meniscus. Thus, when FEBio reads the values in the medial meniscus’ table, FEBio will automatically know to look for the nodes added after the femoral cartilage nodes in the node table. The same process has to be repeated for each tissue and for both the hexahedral and quadrilateral table (bones are also joined, although in their case only their surface elements are updated). To make sure that the joining process worked correctly, we create patches for each tissue using the joined nodes table. This visual inspection can also be performed using FEBio pre-view, although it is less time consuming to use MATLAB’s patch function.

GIBBON allows the user to create a structure for each tissue in accordance to FEBio’s rules. FEBio requires each structure to have a defined material model (rigid in the case of bones), a specific material ID that links the tissue to the material model, a tissue
density and in the case of Fung Orthotropic materials, the local axis that defines the preferential direction.

Similar to contact surfaces, nodes belonging to a particular boundary condition must be declared before establishing said nodes as fixed on a particular degree of freedom. These nodes can be obtained by using MATLAB’s “unique” function on the surfaces which the user wants to fix, which will return an array containing the nodes (without repetition).

Figure 2.8 A graphical representation of the entire model, a frontal view has been presented, the lines coming out of the menisci are the discrete spring elements that make up that surface. Each boundary condition must also contain its own id and specify which node set is been fixed and which degree of freedom is been fixed. The code that
allows use to define all of these conditions can be found in appendix A.3. The final result of this process can be opened in FEBio’s Postview for visualization (Figure 2.8). Our first simulation was run using the parameters of the tissues defined in appendix A.1.

2.3: Sensitivity Analysis

Sensitivity analyses serve as a tool to help researchers quantify the impact that certain modelling decisions may have on their simulation results. There are many aspects of this model that could potentially impact our solution, however very few of them also impact solution time as well, and given the iterative nature of this project it is important to know both the impact on computational cost and on the solution itself. For these sensitivity analyses, we will be focusing on number of elements in the model and the convergence criteria for the optimization. It should be noted that the sensitivity analysis on the number of elements will be done prior to starting the optimization.

2.3.1 Mesh Element Size

FEA simulations are known to be sensitive to the density of mesh elements, with solutions changing in response to the number of elements used to discretize an object [37]. Mesh density also has a significant impact on the amount of time necessary to run a simulation. For example, we ran simulations with models that had a couple thousand (5,800) elements which required 6 minutes to converge while more refined models with 185,600 elements required over 4 hours to converge. To quantify the effects of mesh
density changes on both the simulation results and the time required to finish them, we ran a sensitivity analysis, varying the mesh density in each iteration and comparing the results.

2.3.2 Convergence Criteria

Perhaps one of the most influential factors in both the accuracy and total run time of our project is the convergence criterion. The convergence criterion tells our optimization algorithm when an acceptable answer has been reached. A convergence criterion that is too loose will allow the algorithm to find an acceptable set of parameters more quickly, however this results in an increase in the range of parameters that could be considered the “right answer” per our convergence criteria. On the other hand, we can narrow down the range of parameters that would qualify as the right answer, as long as we are willing to increase how strict our convergence criterion is. There is a limit however to how practical a strict convergence criterion may be, as the amount of iterations necessary may be too excessive. For this study we used a convergence criterion of 0.5% difference in thicknesses for the first optimization trial. We then varied our convergence criterion from 1% to 0.25% tissue thickness difference with a decrease of 0.25% in convergence criterion per optimization.

2.4: Optimization

Optimization in general is a process by which the result of a function is approximated by iteratively changing the value of the input parameters to find the set that yields the smallest difference or an acceptable target value. A myriad of fields of study employ optimization, including engineering, because of its ability to numerically determine the required value of parameters in situations where analytical approaches are impossible.
Our study is no different, and an optimization must be performed to determine the value of the parameters of the knee’s soft tissue because the complex interactions between a multitude of different tissues and their unconventional geometries makes it impractical to attempt an analytic approach. Out of the many optimization algorithms available, we decided to use the Gauss-Newton algorithm. The Gauss-Newton algorithm gives the advantage of minimizing the cost function after each iteration, we will review the mechanics of it to clarify why it was a desirable choice.

2.4.1 Gauss-Newton Formulation

The gauss-newton method works towards minimizing the residual function after every subsequent iteration [38]. The residual function is defined as the difference between the set of target values and the set of iterated values, which can be expressed as:

\[ r_i(\beta) = y_i - f(x_i, \beta) \]  

(2.12)

Where \( r_i \) is the cost function, \( y_i \) is the target value and \( f(x_i, \beta) \) is the value produced by our model. To minimize the residual function, the Gauss-Newton method offers a way to estimate the parameters \( \beta \) needed for the next iteration. The parameters are updated via the following expression:

\[ \beta^{(s+1)} = \beta^{(s)} - (J^T J)^{-1} J^T r(\beta^{(s)}) \]  

(2.13)

In this expression, \( (s+1) \) denotes the set of parameters for the next iteration, while \( s \) denotes the parameters of the current iteration. It is important to note that both \( \beta \) and are column vectors. \( J_r \) is defined as the Jacobian matrix, which can be formulated as:

\[ (J_r)_{ij} = \frac{\partial r_i(\beta^{(s)})}{\partial \beta_j} \]  

(2.14)
The above equation forms a matrix that is $i$ rows in length and $j$ columns in width. It must be noted that the expression above requires the derivative of the residual function with respect to the parameters. We cannot apply this derivative to our model directly because the function setup for FEA simulations is very complex and involves other parameters that we are not optimizing for. As a way to work around this limitation, we define the derivative of equation 2.14 numerically. This is achieved by going back to the definition of a derivative, a derivative is defined as the secant line connecting two points within a curve:

$$\frac{\partial r_i(\beta^{(s)})}{\partial \beta_j} = \frac{r_i(\beta^s) - r_i(\beta^{s-1})}{\beta_j^s - \beta_j^{s-1}}$$

(2.15)

Notice that in equation 2.15 we are utilizing $\beta^{s-1}$, which are the parameters of a previous simulation (and their residuals). This extra set of parameters means that two initial guesses are required in order to begin the optimization procedure. Given that to find the next set of parameters the inverse of the Jacobian matrix is required, ill-conditioning of the matrix can occur, which leads to numerical instabilities that cause bad solutions to be yielded by the algorithm. As such a safety feature has been added to our implementation of the Gauss-Newton algorithm.

### 2.4.2 Safety Feature

Ill-conditioning is a constant issue when dealing with numerical methods that involve matrix inverses. This problem begins to manifest itself when the product of a function gets close to the accepted value [39]. A variety of strategies have been implemented by mathematicians to address this issue but some of them may far exceed the
complexity necessary to approximate the relatively small number of parameters that we are optimizing for. So instead we’ve opted for employing linear interpolations to estimate the new material parameters once the Jacobian for the residuals becomes ill-conditioned. To do so, we employ the following expression:

$$\beta_{i}^{s+1} = \beta_{i} + \beta \left( \frac{y_{i} - J_{i}(P)}{y_{i}} \right)$$  \hspace{1cm} (2.16)

One detail that we can notice about the expression above is that this interpolation will independently update each of the parameters in our model. The only downside to this method is that the number of iterations necessary to reach the solution increases as the change in parameter magnitude decreases when compared to the regular Gauss-Newton method. However, this issue is mitigated by the fact that the Gauss-Newton method has placed our parameters close to the solution space, so even if the interpolation is slower, we won’t need to interpolate a lot further to reach the desired answer.

### 2.4.3 Target Value

As mentioned earlier, the Gauss-Newton algorithm requires a target value to compute the residual function. In this study, we have chosen that target value to be articulating cartilage thickness after compression. To define a target value, we first considered finding the average thickness of the whole tissue after every simulation and compare that to the average thickness of the compressed MR scan. We determined however that this comparison was not optimal for several reasons, which we will elaborate upon in the discussion section (section 4.1.2).

We instead determined that a better comparison would be to measure the thickness of elements that are above a certain compression threshold. The chosen threshold was set
to 0.3 MPa in the third principal stress (which reports the maximum compression of an element). The elements that met this criterion had their thicknesses measured by first finding the center of the quadrilateral belonging to the contact surface of that element. The center of all the quadrilaterals on the opposite surface (the surface attached to the bone) were computed and the distance between the surface quadrilateral and the bottom quadrilaterals were computed to find the pair with the minimum Euclidean distance. This distance however is not the thickness as the centers of both quadrilaterals may not be aligned. To find the actual thickness, the distance vector was projected onto the normal vector belonging to the bottom quadrilateral using the expression for a vector projection:

\[ a_1 = \frac{a \cdot b}{b \cdot b} b \]  

(2.17)

where \( a_1 \) is the projection of the distance vector onto the normal face vector. The norm of vector \( a_1 \) is then computed to measure the thickness of the tissue. It is important to realize that the thickness computed above corresponds to the elements present in the uncompressed model. To make a comparison across the different scans, we need to identify which elements in the compressed model correspond to the ones that were chosen above. The average thicknesses for the cartilages were computed and the values are 2.596, 2.847, and 2.6833 mm for the femoral, lateral and medial tibia cartilage respectively.

2.4.4 Compressed Model Element Identification

The first issue that we encounter when trying to compare elements across two different MR scans is that their origins may not necessarily align with one another. This makes any comparison virtually impossible because the two models do not share the same frame of reference. Fortunately, multiplying the compressed model with rotation and
translation matrices (which we get from MeshLab) which can place the compressed tissue in a reference frame close to the reference frame of the uncompressed model. The first step then is to find the appropriate rotation and translation matrix. MeshLab provides a convenient tool which allows users to align meshes together by selecting points on the surface of interest which the user considers as being the same point on the other surface that must be aligned. MeshLab only requires four points to be chosen, but more can be selected which generally yield a better approximation. We selected the most distal points on the femoral condyles, as well the furthest lateral and medial points of the femoral cartilage for both surfaces. For the tibia cartilage, we picked the most anterior and posterior point on the surfaces and the furthest lateral and medial points. After the points have been selected, MeshLab overlays the two meshes close to one another, and the user can then process them, which tells MeshLab to run algorithms that will fine tune the alignment between the surfaces. From this process, MeshLab creates a transformation matrix which includes both the rotation and translation of the surface of interest. This transformation matrix can be exported as a text file which can be read in MATLAB, after which the nodes of the tissue of interest are rotated and translated to the desired destination using the transformation matrix.

The next step in the process is to identify the surface quadrilateral on the compressed model that correspond to those on the uncompressed model. We achieve this by calculating a distance vector from the center of the quadrilateral of the top surface of the tissue in the uncompressed model to the all the quadrilateral centers on the compressed model’s surface. A search radius is required to identify the centers of compressed surface
quadrilaterals that may correspond to the uncompressed model. An adequate search radius is tricky to get because the two tissue surfaces may not be perfectly aligned in space, with gaps between the tissues appearing which may require a larger search radius. However, increasing said search radius to close said gap has the negative effect of identifying more elements on the compressed surface that do not really correspond to the uncompressed surface. To tackle this issue, we excise the portion of the distance vector that corresponds to the gap between the two surfaces and instead focus only on the portion of the distance that runs along the uncompressed surface. To get the proper distance, the rejection vector is computed from the distance vector using the expression:

\[
a_2 = a - \frac{a \cdot b}{b \cdot b} b
\]

Where \(a_2\) is the rejection vector, \(a\) is the distance vector and \(b\) is the quadrilateral’s normal vector (the quadrilateral from the uncompressed surface). We decompose the distance vector into rejection vector.

\[\text{Figure 2.9 Decomposition of distance vector into rejection vector}\]
vector calculated between the centers of the compressed and uncompressed facets into the rejection and projection (Figure 2.9). The projection is computed with respect to the normal vector from the uncompressed facet, and the resulting vector constitutes the relative vertical distance between the two surfaces. The rejection vector does the opposite, computing instead the in-plane distance between the two facets. The rejection vector allows us to set a search radius that will not be affected by any vertical gaps produced by small misalignments or user input noise.

Once the vector rejection is obtained, the norm of it is computed. If the norm falls below a certain threshold (defined by the user), the quadrilateral on the compressed surface is considered to correspond to the quadrilateral on the uncompressed surface, and we proceed to include said quadrilateral in our thickness measurements.
CHAPTER 3: RESULTS

3.1. Initial Simulation Results

The results of the first simulation vary between different regions of the tibia and femoral cartilage (Figure 3.1). In the lateral tibia, for example, the maximum contact stress was 1.1 MPa; the average stress on the areas of compression was about 0.6 MPa. The medial tibia cartilage experienced an average stress of 0.5 MPa in the areas of compression. The femoral cartilage also exhibited contact stresses similar to the tibia cartilage, with regions that oscillate between 0.5 – 0.7 MPa and average peak contact stresses of 1.1 MPa.

![Figure 3.1 Contact stresses on the tibia (a.) and femoral cartilages (b.)](image)

3.2. Optimization Results

The optimization process required a total of 53 iterations to successfully converge to the subject-specific parameters. The second guess for the values for were chosen based on the initial results, and they were 1.1, 1.04 and 0.7 MPa for the femoral cartilage, the medial tibia and the lateral tibia, respectively. These values were picked from an analysis of the initial results, which suggested that the stiffness of the lateral tibia was too high, given that it exhibits larger contact stresses than the other two tissues. After the conclusion of the optimization, the parameters were 1.657 MPa, 0.688 MPa and 0.8377 MPa for the
femoral cartilage, medial tibia cartilage and lateral tibia cartilage, respectively. (See appendix B for the evolution of the optimization.)

3.3. Mesh Refinement Sensitivity Analysis

We found that the change in simulations results with increasing number of elements was negligible except for the second-to-last refinement step (this is a total of 51,200 elements for the femoral cartilage, and 20,800 elements for both tibia cartilages) where the value of mean compression remained around -0.472 MPa with very little change for the femoral cartilage, -0.454 MPa to -0.400 MPa for the medial tibia cartilage, and -0.457 MPa with infinitesimal change in the lateral tibia cartilage (Figure 3.2-3.4).

![Figure 3.2 Plot of the average displacement and compression of the femoral cartilage](image)

*Figure 3.2 Plot of the average displacement and compression of the femoral cartilage*
Figure 3.3 Plot of the average displacement and compression of the medial tibia cartilage

Figure 3.4 Plot of the average displacement and compression of the lateral tibia cartilage
The mean displacements did not vary substantially, with the femoral cartilage averaging a nodal displacement from 0.14 mm to 0.16 mm in all of the refinement steps (Figure 3.2). The time required to finish each simulation increases proportionally to the number of elements in the model (Table 3.1). The relative low amount of change between the last two refinement steps and the high computational costs of the last refinement step (approximately 5 hours) which would be magnified by the number of iterations led us to choose refinement step 4 as our model for the rest of the optimizations.

### Table 3.1 Simulation time per number of elements in the model

<table>
<thead>
<tr>
<th>Refinement Step</th>
<th>Total Number of Model Elements</th>
<th>Time per iteration (sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>5800</td>
<td>367</td>
</tr>
<tr>
<td>1</td>
<td>11600</td>
<td>671</td>
</tr>
<tr>
<td>2</td>
<td>23200</td>
<td>1044</td>
</tr>
<tr>
<td>3</td>
<td>46400</td>
<td>2471</td>
</tr>
<tr>
<td>4</td>
<td>92800</td>
<td>5823</td>
</tr>
<tr>
<td>5</td>
<td>185600</td>
<td>17245</td>
</tr>
</tbody>
</table>

### 3.4. Optimization Criterion Sensitivity Analysis

We ran four different optimizations using a different convergence criterion in each successive optimization (Table 3.2). We start with a relative loose convergence criterion of 1% difference between the simulated thickness and the compressed scan thickness. The number of iterations that were necessary to reach the convergence criteria were 18, resulting in a total of 29 hours needed to optimize the parameters with the given criteria. The number of iterations required to complete an optimization increase significantly with a stricter convergence criterion (Table 3.2). The differences in tissue thickness between the simulation and the compressed MR model also showed a significant decrease with
respect to the convergence criterion (Table 3.3), with differences in the last optimization being below a micrometer.

Table 3.2 Number of iterations per convergence criteria and results

<table>
<thead>
<tr>
<th>Convergence Criteria</th>
<th>Number of Iterations</th>
<th>Parameters Femoral Cartilage [MPa]</th>
<th>Parameters Medial Tibia Cartilage [MPa]</th>
<th>Parameters Lateral Tibia Cartilage [MPa]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1%</td>
<td>18</td>
<td>1.2969</td>
<td>0.8505</td>
<td>0.775</td>
</tr>
<tr>
<td>0.75%</td>
<td>31</td>
<td>1.4295</td>
<td>0.7635</td>
<td>0.8234</td>
</tr>
<tr>
<td>0.50%</td>
<td>53</td>
<td>1.6576</td>
<td>0.688</td>
<td>0.8377</td>
</tr>
<tr>
<td>0.25%</td>
<td>105</td>
<td>1.9013</td>
<td>0.5513</td>
<td>0.9928</td>
</tr>
</tbody>
</table>

Table 3.3 Tissue thickness differences per convergence criteria

<table>
<thead>
<tr>
<th>Convergence Criteria</th>
<th>Number of Iterations</th>
<th>Thickness Differences Femoral Cartilage (mm)</th>
<th>Thickness Differences Medial Tibia Cartilage (mm)</th>
<th>Thickness Differences Lateral Tibia Cartilage (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1%</td>
<td>18</td>
<td>0.0086</td>
<td>0.0101</td>
<td>0.0052</td>
</tr>
<tr>
<td>0.75%</td>
<td>31</td>
<td>0.0071</td>
<td>0.0075</td>
<td>0.0042</td>
</tr>
<tr>
<td>0.50%</td>
<td>53</td>
<td>0.005</td>
<td>0.005</td>
<td>0.0039</td>
</tr>
<tr>
<td>0.25%</td>
<td>105</td>
<td>0.000969</td>
<td>0.002</td>
<td>0.0016</td>
</tr>
</tbody>
</table>

The rate of increase of the required iterations was higher than the increase of convergence criteria strictness (i.e. dividing the convergence criteria by 2 does not result in a doubling of the number of iterations, but almost tripling them). The change with stricter convergence criteria is considerable, with the femoral condyle yielding a parameter that is 46% larger in the last optimization. We can see a similar difference between the first and final optimizations of the tibia cartilage with the medial tibia cartilage’s parameter decreasing 35% from the first optimization and the lateral tibia cartilage parameter increasing by 28% from the first iteration. The changes in optimized parameters do not seem to plateau at any point, with the parameters changing significantly across all convergence criterion change at an average 13% change in parameters with every 0.25% reduction in convergence criteria (Figure 3.5).
Figure 3.5 Optimized parameters per convergence criteria

The rate at which the parameters change is consistent across the different converge criterion, with the parameters changing in a mostly linear manner (Figure 3.6-3.8). One oddity that may stand out is the 0.5% convergence criterion trial in the lateral tibia cartilage. The behavior can be as a result of our method switching over to the linear interpolation and having reached the convergence criterion before the other tissues. As a result, the parameters that have already converged are not updated for the next iteration.
Figure 3.6 Optimization progress per criterion for femoral cartilage

Figure 3.7 Optimization progress per criterion for lateral tibia cartilage
Figure 3.8 Optimization progress per criterion for medial tibia cartilage
CHAPTER 4: DISCUSSION AND CONCLUSIONS

4.1 Discussion

The purpose of the present study was to create a methodology to estimate the in-vivo subject-specific material parameters of articulating cartilage. We accomplished this objective by using a combination of MRI-based models of the knee joint before and after compression, along with iterative FEA methods and a Gauss-Newton optimization algorithm.

Our model’s stress results, which were concordant to literature values [40], provide confidence that our model was a reasonable approximation. Another study using FEA simulated a joint loading of 700N produced results similar to our own [41], with the reported max contact stress being 2.4MPa. The max contact stress reported in our model was 1.1 MPa, which is almost half the reported stress of the aforementioned study, a value which can be expected given that their loading was twice as high as our own.

We were able to successfully iterate FE simulations until a set of parameters were found that satisfied our convergence criterion. The values of the material parameters that our method estimated were between 1.9 MPa and 0.5 MPa (see Table 3.2). These values are within the ranges of values reported previously in the literature [42], with the widest range reported in the literature is between 3.1 MPa to 0.25MPa. It should be noted that the results presented in the literature vary significantly between studies, which suggests that the literature does not have an agreed upon value. Finally, we found that our methodology
was particularly sensitive to the choice of convergence criterion, with results differing significantly between convergence strictness.

### 4.1.1 Discrete Element Choice

We chose hexahedral elements to serve as the discrete element that described the geometry of soft tissues. FEA simulations of solids typically involve the choice between tetrahedral and hexahedral elements, each having their own advantages and disadvantages. Tetrahedral elements offer the advantage of more easily fitting complex geometries, however they have the disadvantage of being overall less accurate and requiring more computational effort [43]. On the other hand, hexahedral elements have the advantage of being more computationally efficient and producing relatively more accurate results than tetrahedral elements, however this is offset by the difficulty of creating elements that better fit complex geometries.

### 4.1.2 Target Value

As mentioned earlier, we did not take the average thickness over the entire tissue as our target value because of the problems inherent to comparing the tissue as a whole. The first of these problems is that several regions of the cartilage will not come into contact with other tissues or exhibit any significant amount of deformation during the simulation. This is especially true for the femur, where a large portion of the condyles (specifically as you move proximally towards the shaft) sees no contact or force application of any kind. Taking inactive regions into account during the averaging of the element thicknesses may
result in an underestimation of the magnitude of deformation seen in elements that do come under compression.

User induced noise was introduced during the segmentation process which can add (or sometimes reduce) the number of data points being averaged for thickness. Unfortunately, manually segmentation never perfectly replicates tissue geometry, and while there is reliable consistency in the segmentation process, the user can have an impact on the overall volume and shape of the tissue. User added noise is most common close to the bone/cartilage boundary, where many gray pixels makes it difficult to distinguish which structure the pixels may belong to. Noise can also be added when a person who’s segmenting a structure gets close to the tibia’s spine, as the presence of other soft-tissues (like the ACL and PCL) may introduce uncertainty. Other places where segmentation errors can occur include the anterior and posterior edges of the tibia, where cartilage may not have a well-defined boundary, especially close to the fibula (our group does not segment the fibula nor the cartilage that meets it).

4.1.3 Optimization Criterion

The convergence criterion for the optimizations plays a critical role in the parameters yielded by the algorithm. For our first optimization a strict criterion was necessary because the initial guess included material parameters close to the population average. Choosing parameters close to the population average always carries the disadvantage of yielding results that are close to the target values. We can observe that this is the case, as the results of the first simulation using population averages yielded differences of less than 2.5% (Appendix B) for each of the tissues. Therefore, choosing a
convergence criterion close to 1% tissue difference would’ve resulted in a quick optimization yielding results that would be distant from the subject-specific parameters for stricter convergence criterion. Therefore, we chose an initial convergence criterion of 0.5% (before running the sensitivity analysis). Our rational for this choice was confirmed after running the optimization sensitivity analysis, where significant differences between the solutions yielded by different convergence criterion were observed.

4.1.4 Geometric Influences on Results

The observed compression differs significantly between the different tissues, producing optimization results that are seemingly disparate between each other (1.901 MPa, 0.5513 MPa and 0.9928 MPa for the femoral, medial tibia and lateral tibia cartilage respectively). We infer that these observed differences could be as a result of differences in geometry between the tissues of the different compartment of the knee, specifically the meniscus. First, we must consider that there is a large amount of variability in the measurements of mechanical properties of human cartilage, so we expect some variability in our measurements. Several studies on cadaver models have shown that the range of material elastic modulus can vary from 2.6 MPa to 18.6 MPa (in the linear elastic model) [44], which if we convert this into Neo-Hookean parameters yields a range of 0.25 MPa to 3.1 MPa for $c_1$. It should be noted that these studies were performed using indentation

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Initial Thickness (mm)</th>
<th>Target Thickness (mm)</th>
<th>First Iteration Thickness (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Femoral Cartilage</td>
<td>2.6525</td>
<td>2.5963</td>
<td>2.5559</td>
</tr>
<tr>
<td>Lateral Tibia Cartilage</td>
<td>3.0579</td>
<td>2.8476</td>
<td>2.7152</td>
</tr>
<tr>
<td>Medial Tibia Cartilage</td>
<td>2.8598</td>
<td>2.6833</td>
<td>2.839</td>
</tr>
</tbody>
</table>
testing and that the methodology of the testing might have an impact on the results (including the quality of the cadaver and the application of force).

![Figure 4.1 A top view of the knee joint with the medial meniscus (left) and lateral meniscus (right)](image)

The results from the first iteration (Table 4.1) suggest that the differences yielded by the GN were necessary to match the target values, given that the femoral and lateral tibia cartilage deform more than what the target value allows, while the medial tibia cartilage does not deform much. Thus, to match the observed deformations, the medial tibia cartilage was made more compliant while the femoral and lateral tibia cartilage were made stiffer by the Gauss-Newton algorithm. A factor that may affect the observed deformations is the state of the meniscus. The meniscus plays an important role in distributing and dissipating the loads applied to the knee joint. It has been shown using FEA that meniscal
resections have a substantial effect on the contact stresses and stress distribution in articular cartilage [44]. The change in stresses can have an impact on how the cartilage deforms, which would ultimately impact the observed deformations in the compressed MR scan (which we use for comparison with our simulation results). One should also consider that geometric differences between the two menisci exist, and the difference in geometry can change the way in which articular cartilage undergoes loading and deforms. These differences are particularly evident when examining the geometry of the medial meniscus relative to the lateral meniscus. In our model the medial meniscus appears to be longer but narrower than the lateral meniscus (Figure 4.1). The geometric difference of the narrower medial meniscus leads to less dissipation (Figure 4.2) of the loading on the medial compartment of the knee, thus causing larger observed deformations as a result of the increased loading.

*Figure 4.2 Strain energy density of menisci*
To match the target deformation, the optimization algorithm would have to increase the energy dissipation in the medial tibia cartilage. There are two ways of achieving this result. The first would be to increase the stiffness of the lateral tibia and femoral cartilage to decrease the two tissue’s energy dissipation (thus transmitting more of the load onto the medial tibia cartilage). The other option is to decrease the stiffness of the medial tibia cartilage, to increase the deformation and the energy dissipation. The optimization did both, as our original guess was that the lateral tibia cartilage would be more compliant than the medial tibia cartilage, and by the end of the optimization the medial tibia cartilage was more compliant than the lateral tibia cartilage.

Another explanation for the differences in the observed deformations is that the area of the medial compartment is relatively larger compared to the area of the lateral compartment. This difference in area can lead to greater compressive stresses as there is a smaller area for the force to be distributed, while the strain in both compartments remains similar. The results on our first simulation indicate that using the same material parameters produces the same compression on both tissues, but that the tissue strain is not the same (Figure 4.3). The equality in compression produces a force imbalance that leads to larger

![Figure 4.3 Third principal Lagrange strain (left) and third principal stress (right)](image)

\[ \text{Figure 4.3 Third principal Lagrange strain (left) and third principal stress (right)} \]
deformations in the medial compartment, thus the optimization algorithm increased the
tissue stiffness in the medial compartment and increased the stiffness on the lateral
compartment to reduce the discrepancies in tissue strains.

Another issue that could potentially explain the differences between tissue
stiffness is the small amount of deformation experienced during the compressed MR scan.
For example, the average change in thickness from the uncompressed to compressed scan
is of 0.2 mm. The resulting deformation produces a strain of approximately 6.6% for both
the medial and lateral tibia cartilage. This very small deformation means that it is hard for
the differences between two Neo-Hookean parameters to become evident, making a wider
range of parameters capable of producing the same target values as specified by our
convergence criteria during optimization. The wide range of acceptable values can only be
reduced by increasing the strictness of the convergence criterion, which leads to a
substantial change in answers between optimizations. The behavior of parameter
optimization with respect to the convergence criterion (Table 3.2) indicates that our
inferences are correct, and that the small deformations are making it more difficult for the
optimization algorithm to arrive to an acceptable answer.

Another item for discussion is the results of the mesh sensitivity analysis. Unlike
the previously referenced literature [38] our model did not show substantial changes in
either the average compressive stress or the average displacement of the model relative to
our mesh density. The change is small between refinement steps (Figure 3.2), with a
minimal amount of noise. We infer that the negligible changes produced during this
sensitivity analysis reflects the small deformations experienced by the model as a whole.
The noise seen in in the sensitivity analysis results could be a result of the ill conditioning of the stiffness matrix that occurs during simulations that involve contact (Figures 3.2-3.4). This is because the stiffness of the contacts can be larger than the stiffness of the elements, resulting in numerical instabilities during matrix inversions. Ill conditioning also limits the range of parameters that produce a converged simulation as well, as we found out during our simulations, with low stiffness (less than 0.4 MPa for $c_i$) tending to produce too many negative Jacobians and ultimately provoke simulation failures.

### 4.1.5 Material Models

There are several considerations when choosing the appropriate material model for soft tissues in the knee joint. Soft tissues in the knee are complex structures that have multiple layers, each layer having different material stiffness [44]. Moreover, the presence of water gives articulating cartilage a viscoelastic component to its behavior, making modeling such a tissue challenging. Biphasic models model the viscoelastic response, but it is important to remember time dependence since it places a constraint in the type of experimental setups that can yield the information necessary to classify a subject-specific response. The experiments which can usually capture these behaviors are conducted using indentation tests, which can yield the time varying behavior of the tissue being studied. However, our MR scans happen in a quasi-static environment, and because the compressed scan is taken after the water has been allowed to exit the tissue, it is not possible to quantify the viscoelastic effects.

Therefore, we chose simpler models that can approximate the behavior of the soft tissues. Studies that use linear elastic models to describe the behavior of cartilage are not
uncommon in the literature, and these models do indeed produce acceptable answers over small deformations. However, we chose the hyper elastic Neo-Hookean model for this study because we want to develop a method that can yield patient-specific material models that can be used to describe activities that involve large deformations. The elastic model would start to yield more erroneous answers at larger deformations, making it more inadequate.

We decided to model the menisci with the more complex Fung-Orthotropic model because the menisci exhibit deformations that are strongly dependent of the directions of the fibers. The Fung-Orthotropic model manages to reasonably capture the directional behavior and allow us to create a realistic representation of the meniscus’ behavior [45]. Unlike other models in the literature (e.g. Open Knee [34]), our model does not include ligamentous tissue like the ACL or the posterior cruciate ligament (PCL). These tissues were not included because of the limited rotations during compression of the knee joint in the MR scanner. The ACL and PCL serve mostly to stabilize the knee joint during translations, therefore their presence during this study would have minimally impacted the simulation results while adding more computational costs to the model. Considering that the simulation performed in this study will be an extensively iterative process, any increase in computational costs would be magnified by the number of iterations.

4.1.6 Contact Stress Gridding

The contact stress yielded by our model appears similar (in peak and average stress) to the stresses experienced during other studies [40], but a peculiar gridding pattern emerges during the visualization of the results (Figure 3.1). We infer that the pattern could
be as a result of our refinement process, because the process relies on interpolating the points of the original mesh in order to produce new elements for our sensitivity analysis. During loading, these new points might not be coming into full contact with the opposite surfaces, and thus produce the pattern mentioned above. There could be two solutions to this problem, the first one being loading the knee joint to produce higher deformations, which would engage more of the elements on the refined mesh and produce a more consistent contact stress map. The second solution could be to implement a Laplacian smoothing along the surface elements, which would even out the surfaces by taking the new points into consideration, thus engaging more of the new elements during compression.

4.1.7 Joint Tissue Limitations

Not all of the tissues present in the joint were utilized during our simulations. For example, the ACL, the PCL and the patella (along with its soft tissues) were all excluded. These exclusions were driven because of the limitations present in our current methodology. The engagement of the aforementioned tissues would not be observed during the quasi-static compression of the MRI-loading device because there wouldn’t be much loading on the excluded tissues. Therefore, their presence in the model would only add more computational cost without adding any relevant information. We are aware that there is a strong interest in the patellofemoral joint from a clinical perspective, given that a plethora of diseases can result from anomalies in its function. However, at this time we do not possess a method to quantify the deformation of the patella cartilage in vivo, thus
making our current methodology inapplicable to estimating the cartilage material properties of the patella.

4.1.8 Measuring Impact of Treatments

Our current methodology has the potential to measure the impact that treatments that are meant to alter the cartilage have on the tissue. The types of treatments that could be quantified with our methodology include all of those treatments that directly affect the solid phase of the cartilage’s extra cellular matrix (ECM). These could be treatments such as stem cell therapies, or even scaffold implants. Our methodology would be indeed a potent tool for understanding the changes following these treatments as ECM reconstruction could be measured based on the impact on cartilage stiffness. Treatments that rely on viscoelastic materials such as hydrogels can be measured, since they might change the manner in which the soft tissue deforms, thus it is possible to quantify the changes in deformation and stresses that would result from the addition of hydrogels into the cartilage.

4.1.9 Transient State Response

The transient response is often of interest whenever a model that has viscoelastic properties is implemented. However, it is also interesting to observe the transient response in solid elastic models, since they show the evolution of the loading. One of the peculiarities that stands out for our transient response is how the area of loading changes slightly between one step to the next. From time 0.79 to the last time step, the area of loading on the cartilage that interacts with the meniscus seems to diminish slightly (Figure 4.4). This is counter intuitive since one would expect that the total area of loading would
only increase with higher loading. One explanation for the observed behavior could be that as the cartilage is being loaded, less of the loading is transmitted through the menisci, thus the total area decreases. Another explanation could be that the observed behavior is a result of the noise inherent in the loading condition. The developer of FEBio has written about the inherent difficulties of running simulations that use forces as their loading condition, stating that matrix ill-conditioning is prevalent and on top of that the models have a more difficult time balancing the force equations during dynamic analysis. Our model could be experiencing the latter (the former manifesting itself during simulations that used less stiff constants). Unfortunately, other than changing material constants or changing the material model altogether, there aren’t many options available to address the ill-conditioning and force balancing issues present for our particular loading conditions.

Figure 4.4 Transient response of the tissue during different time steps
4.2. Conclusions

In this study we successfully utilized FEA to determine the subject-specific material parameters of articular cartilage in the knee joint of one subject. Based on the model results, which are concordant with previous studies [40], we are confident that our methodology yielded tissue material parameters that are relevant to the study of subject-specific cartilage material parameters.

The modeling framework developed for this thesis represents a significant contribution to the field because we developed a tool that can be used to determine subject-specific material properties in a non-invasive manner, which is suitable for in vivo applications. This tool will allow researchers in the field of biomechanics to develop better FE models that can more realistically model a subject’s joint during complex motions.

4.3. Future Work

While the methodology presented in this study has proven to be effective, several improvements could be implemented to make the overall method more robust. The first improvement to the methodology would be increasing the loading during the compressed MR scan acquisition. This would provide the cartilage with greater deformations. As explained above, small deformations have an impact on both sensitivity analyses by limiting our ability to capture the behavior of the tissue deformation at higher stresses and strains, thus making it more difficult to arrive to local minima in the parameter space (larger differences in parameters and their results would help ease matrix ill-conditioning and produce a more robust residual Jacobian). In particular, a larger strain would allow the
algorithm to narrow down the regions of acceptable Neo-Hookean parameters, since the behaviors of the parameters become more distinguishable at larger strains.

The second improvement to the methodology could be in the form of spatially varying material properties. It is known from the literature [44] that the cartilage ECM varies throughout the thickness of the tissue. This change of course would add greater computational costs, but including this variation could allow us to more accurately simulate the deformation of the articulating cartilage, which could lead to a further narrowing of the range of parameters that are considered appropriate.

The number of iterations that are required to optimize the material parameters can also be reduced by implementing additions to the Gauss-Newton algorithm that would speed up its descent towards the local parameters’ minima. This can be achieved through the gradient descent, which accelerates the rate of change of parameters by taking the gradient of the function in the parameter space. The Levenberg-Marquardt algorithm would thus be great fit for this problem, as it combines both the gradient descent method when the parameters are far from any local minima and switches back to the Gauss-Newton when the parameters are close to the local minima [46]. Thus, the algorithm avoids the lethargic nature of the Gauss-Newton algorithm when the initial guess is far from the actual parameters, and it also avoids moving past the solution as the gradient descent method typically does. The algorithm would in fact be necessary if a spatially varying model were to be implemented or if more tissues like the meniscus were optimized for as well. Optimizing the menisci is even more challenging because of the extra number of parameters (11 parameters per meniscus).
Future changes to the MR acquisition methodology could also be implemented in the future, allowing us to consider the viscoelastic response of the tissue. This would allow us to change the simplistic Neo-Hookean model into a more realistic biphasic model. The ability to determine the subject-specific biphasic response would lead to better FEA simulations during dynamic activities, where the biphasic response may be present and thus must be considered.

The methodology presented here can help improve FE models by giving researchers the ability to use patient-specific material models that produce realistic results. Better FE models can help assess the complex mechanisms that lead to the development of early OA in patients with post traumatic injuries. With this information, digital biomarkers can be developed which would ultimately give researchers the ability to predict the risk of early OA. Such a predictive tool would lead to better treatments that reduce the risk of OA and which may prevent the disease altogether.


Eriksson, Jerry, and Mårten E. Gulliksson. “Local Results for the Gauss-Newton Method on Constrained Rank-Deficient Nonlinear Least Squares.” Mathematics of


APPENDIX A: MATERIAL PROPERTIES OF FIRST SIMULATION

A.1. Material Properties For The First Simulation

A full list of the material parameters for each of the soft tissues and the bones will be offered in this section. The material Properties are not limited only to the parameters of the material model itself. The correct density and bulk modulus must be used, they were not presented in the main body of this thesis because they were not parameters of interest (as far as the optimization goes). Materials with anisotropic behavior such as the menisci also had too many parameters to present in the main body of the thesis and so they are presented here. It should be noted that all of these values were obtained from Open Knee’s user manual [33]. We will start by examining the articulating cartilage, followed by the menisci and culminating with the bones.

A.1.1 Femoral and Tibia Cartilage

Note: While the material model is set to “Mooney-Rivlin”, setting parameter c2 to 0 reduces it to the Neo-Hookean model.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>Material Model</td>
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</tr>
<tr>
<td>Density</td>
<td>$1.5 \times 10^6$</td>
<td>kg/mm$^3$</td>
</tr>
<tr>
<td>c1</td>
<td>0.856</td>
<td>MPa</td>
</tr>
<tr>
<td>c2</td>
<td>0</td>
<td>MPa</td>
</tr>
<tr>
<td>K</td>
<td>8</td>
<td>MPa</td>
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A.1.2 Menisci

_Table A.2 Model and parameters of the menisci_

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<thead>
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<tbody>
<tr>
<td>Material Model</td>
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<td>Density</td>
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<td>E1</td>
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<tr>
<td>E2</td>
<td>27.5</td>
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A.1.2 Bones

_Table A.3 Model and parameters of the Femur and Tibia_

<table>
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</tr>
</thead>
<tbody>
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<tr>
<td>Density</td>
<td>1.13E-03</td>
<td>Kg/mm³</td>
</tr>
</tbody>
</table>

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APPENDIX B: OPTIMIZATION RECORDS

This section of the appendix will show the evolution of the first optimization. Other optimizations are not included in this document and only their final results are reported.

### Table B.1 Optimization Records of a 0.5% criteria Optimization

<table>
<thead>
<tr>
<th>Iteration</th>
<th>F(x) parameter</th>
<th>M(b) parameter</th>
<th>L(x) parameter</th>
<th>F(x) difference</th>
<th>M(b) difference</th>
<th>L(x) difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.92</td>
<td>0.883</td>
<td>0.885</td>
<td>0.00308654</td>
<td>0.00627795</td>
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APPENDIX C: MATLAB CODE FOR FEBIO

C.1 Main File: Inverse FEA

The following code comes from the main file which creates the FEA model and then writes out the FEBio input file for simulation. We have commented the custom-built functions that we developed to make the code work. The preprocessing section will be introduced later.
C.2 Pre-Processing: Hexahedral Meshing
C.3 Gauss Newton Class