THE INTERSTITIAL FLUID PRESSURE RESPONSE DURING STRESS-RELAXATION OF ARTICULAR CARTILAGE DUE TO VISCOSITY AND POROUS MEDIA EFFECTS: A COMPUTATIONAL STUDY

by

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# TABLE OF CONTENTS

1. INTRODUCTION ........................................................................................1
   - Current Modeling Approaches ...............................................................1
     - Radial Changes In Fluid Velocity .........................................................3
   - Motivations ............................................................................................3
   - Cartilage Composition ..........................................................................6
     - Collagen ............................................................................................8
     - Proteoglycans ....................................................................................8
   - Testing Apparatus ................................................................................11
     - Current Experimental Approaches .....................................................13

2. METHODOLOGY ......................................................................................14
   - Non-Newtonian Fluids ..........................................................................14
     - Carreau-Yasuda Equation ................................................................15
   - Porous Media .......................................................................................15
     - Variation Of Porosity ........................................................................19
     - Particle Diameter Changes During Compression ..................................20
     - Proteoglycan Aggregate Concentration Changes During Compression ....23

3. MODELING METHODS ............................................................................29
   - Cartilage Sample ..................................................................................29
   - Physics Models ....................................................................................30
   - Meshing ................................................................................................31
     - 3D Mesh ............................................................................................31
     - Axi-Symmetric Mesh ..........................................................................33
     - Differences Between Mesh Types ......................................................34
   - Boundary Conditions ............................................................................35
   - Sample Compression ............................................................................35

4. RESULTS ..................................................................................................38
   - UCS Results ..........................................................................................38
     - Sensitivity To Sample Diameter ..........................................................40
     - Variation Of Porosity .........................................................................42
     - Variation Of Particle Diameter ............................................................45
     - Variation Of Proteoglycan Concentration ............................................49
     - Huang et al. Comparison Of UCS Cases and Parameters .................51
   - UCF Results ..........................................................................................55
TABLE OF CONTENTS – CONTINUED

5. CONCLUSION ........................................................................................... 66
   Conclusions From The Results ..................................................................... 66
   Future Steps ............................................................................................... 67

REFERENCES CITED .................................................................................... 69
LIST OF TABLES

Table                                      Page

2.1 Carreau-Yasuda fitting parameters               17
2.2 Viscosity scaling values                        25
4.1 Parameter cases for viscosity and cartilage sample diameter, and their necessary user inputs. All values are defined to be fixed outside of fluid viscosities.                                           39
4.2 Parameter cases for porosity and particle diameter, and their necessary user inputs. For these cases, values are specified to be fixed or varied                                           39
4.3 Parameter cases for proteglycan aggregate concentration, and their necessary user inputs. For these cases, values are specified to be fixed or varied                                           40
4.4 Sample Diameter vs. mean pressure and velocity                                           45
4.5 fixed porosity change variation                                           45
4.6 varying porosity pressures                                           50
### LIST OF FIGURES

<table>
<thead>
<tr>
<th>Figure</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1</td>
<td>(top) Mechanical loading of cartilage samples during unconfined compression stress relaxation and a comparison of those results to the biphasic poroviscoelastic (BPVE) curve fit. (bottom) Comparison of mechanical loads versus time of an unconfined fast compression test case against the BPVE curve fit. Data taken from Huang et al. [8].</td>
</tr>
<tr>
<td>1.2</td>
<td>Shows fluid pressure over time during unconfined compression of cartilage samples and fluid pressure over time for the biphasic-CLE-QLV and biphasic poro-viscoelastic models during unconfined compression test cases, data taken from Huang et al. [8].</td>
</tr>
<tr>
<td>1.3</td>
<td>Zonal representation of collagen fiber size and orientation within articular cartilage [19]. The top layer is known as the superficial zone. Proceeding vertically, the next zone is the middle zone, and the final zone is the deep zone.</td>
</tr>
<tr>
<td>1.4</td>
<td>Variation of viscosity of cartilage fluid due to shear rate for a range of concentrations of proteoglycan aggregate where data was taken from Mow et al. [17].</td>
</tr>
<tr>
<td>1.5</td>
<td>Variation of viscosity of cartilage fluid due to shear rate for a range of concentrations of proteoglycan subunits where data was taken from Mow et al. [17].</td>
</tr>
<tr>
<td>1.6</td>
<td>Parametric study of variation of apparent viscosity with data taken from Mow et al. [17]. Where $\lambda_1 = 7.14 \times 10^{-2}$, $\lambda_2 = 3.27 \times 10^{-2}$, $\eta_0 = 0.005$, and $\mu_s$ varies on orders of magnitude of 110 between $10^{-1}$ and $10^{-5}$.</td>
</tr>
<tr>
<td>2.1</td>
<td>Comparison of Carreau-Yasuda fit equation to points taken from Mow et al. [17] for proteoglycan aggregates at a concentration of 50 mg/ml.</td>
</tr>
<tr>
<td>2.2</td>
<td>Comparison of Carreau-Yasuda fit equation to points taken from Mow et al. [17] for proteoglycan subunits at a concentration of 52 mg/ml.</td>
</tr>
</tbody>
</table>
Figure | Page
--- | ---
2.3 The porosity changes versus compressive strain exhibited by equation 2.9 where the value of porosity at a strain of zero is the initial porosity. Within the figure there are 3 designated curves at initial porosities of 60, 70 and 80 %. | 21
2.4 Demonstrates the change in $D_p$ over the course of compression of the sample for 4 values of $D_p$ that fall within the range of collagen fibril diameters. The initial value of $D_p$ correlates to the value of each profile at no compressive strain, where 70, 90, 100, and 120 nm values were chosen | 23
2.5 Illustrates accuracy of fit for the concentration dependent viscosity scaling equation, in Equation 2.18, against the viscosity scaling values for each concentration of proteoglycan aggregate fluid, seen in Table 2.2 | 26
2.6 Dots representing viscosities of proteoglycan aggregate at each specified concentration over a range of shear rates from the rheological study performed by Mow et al. [17] compared against the viscosity scaling equation, equation 2.17, for proteoglycan aggregates at each concentration | 27
2.7 Change of concentration of proteoglycan aggregates due to compressive strains within the system for 3 values of initial concentration. These initial values of concentration were set to be 30, 50, and 70 mg/ml. | 28
3.1 Quadrilateral mesh of the 3D cartilage sample with a base cell size of 0.015 mm. Mesh cell count: 182,080 cells | 33
3.2 View of the internal mesh of the 3D cartilage sample | 33
3.3 View of the axi-symmetric mesh for the cartilage sample, where the sample is 2.38 mm for the radius and the thickness is 1 mm. The base cell size of the mesh is 0.015 mm and increases to 120 % at the center of the mesh. Mesh cell count: 3906 cells | 34
3.4 Boundary conditions for each surface of the 3D mesh | 36
<table>
<thead>
<tr>
<th>Figure</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.5</td>
<td>36</td>
</tr>
<tr>
<td>4.1</td>
<td>41</td>
</tr>
<tr>
<td>4.2</td>
<td>42</td>
</tr>
<tr>
<td>4.3</td>
<td>43</td>
</tr>
<tr>
<td>4.4</td>
<td>44</td>
</tr>
<tr>
<td>4.5</td>
<td>46</td>
</tr>
<tr>
<td>4.6</td>
<td>47</td>
</tr>
<tr>
<td>4.7</td>
<td>48</td>
</tr>
<tr>
<td>4.8</td>
<td>49</td>
</tr>
<tr>
<td>4.9</td>
<td>51</td>
</tr>
</tbody>
</table>

3.5 Boundary conditions for the surfaces within the axi-symmetric mesh, with a reference that defines the radial direction of the sample.

4.1 Mean fluid pressure versus time during UCS compression for water, PG aggregate interstitial fluid (50 mg/ml), and PG subunit interstitial fluid (52 mg/ml) using the axi-symmetric mesh.

4.2 Mean fluid pressure profile of a vertical and bottom slice of cartilage at a solution time of 150 s for the 3D mesh with a sample diameter of 4.78 mm.

4.3 Mean fluid velocity versus time during UCS compression for a variety of sample diameters using the 3D mesh.

4.4 The figure illustrates how changes in sample diameter with a 3D mesh will affect the mean pressure over time of the fluid during a UCS test case.

4.5 Mean pressure versus time for a UCS simulation for 3 separate fixed porosity values using the 3D mesh.

4.6 UCS mean fluid pressure results using a 3D mesh of a cartilage sample at a fixed porosity of 80 % and another simulation where the porosity follows equation 2.9 with an initial porosity of 80 %.

4.7 UCS mean fluid pressure results using a 3D mesh of a cartilage sample at a fixed porosity of 70 % and another simulation where the porosity follows equation 2.9 with an initial porosity of 70 %.

4.8 UCS mean fluid pressure results using a 3D mesh of a cartilage sample at a fixed porosity of 60 % and another simulation where the porosity follows equation 2.9 with an initial porosity of 60 %.

4.9 Illustration of how changes in the collagen fibril diameters within known ranges, equated as the particle diameter $D_p$, affects mean fluid pressure within a 3D mesh simulation.
4.10 Shows the mean pressure exhibited by varying $D_p$, by the equation 2.13 with an initial value of 70 nm, and compares it to the pressure plot given by the fixed $D_p$ of 70 nm for simulations utilizing a 3D mesh. ..................................................... 52

4.11 Shows the mean pressure exhibited by varying $D_p$, by the equation 2.13 with an initial value of 90 nm, and compares it to the pressure plot given by the fixed $D_p$ of 90 nm for simulations utilizing a 3D mesh. ..................................................... 53

4.12 Shows the mean pressure exhibited by varying $D_p$, by the equation 2.13 with an initial value of 100 nm, and compares it to the pressure plot given by the fixed $D_p$ of 100 nm for simulations utilizing a 3D mesh. ..................................................... 54

4.13 Shows the mean pressure exhibited by varying $D_p$, by the equation 2.13 with an initial value of 120 nm, and compares it to the pressure plot given by the fixed $D_p$ of 120 nm for simulations utilizing a 3D mesh. ..................................................... 55

4.14 A mean pressure versus time plot of the UCS case for the 80 % varying porosity case and the 120 nm varying $D_p$ with varying porosity case both utilizing the 3D mesh. ................................. 56

4.15 UCS mean fluid pressure results that utilize the 3D mesh of cartilage samples at a fixed concentration of 30 mg/ml and a varying concentration that starts at 30 mg/ml. ................................ 57

4.16 UCS mean fluid pressure results that utilize the 3D mesh of cartilage samples at a fixed concentration of 50 mg/ml and a varying concentration that starts at 50 mg/ml. ................................ 58

4.17 UCS mean fluid pressure results that utilize the 3D mesh of cartilage samples at a fixed concentration of 70 mg/ml and a varying concentration that starts at 70 mg/ml. ................................ 59

4.18 UCS mean fluid pressure results that utilize the 3D mesh for a base case of porosity: 80%, $D_p$: 120 nm, C: 50 mg/ml and several other cases where these parameters are allowed to vary based on these initial values. ................................. 60

<table>
<thead>
<tr>
<th>Figure</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.10</td>
<td>52</td>
</tr>
<tr>
<td>4.11</td>
<td>53</td>
</tr>
<tr>
<td>4.12</td>
<td>54</td>
</tr>
<tr>
<td>4.13</td>
<td>55</td>
</tr>
<tr>
<td>4.14</td>
<td>56</td>
</tr>
<tr>
<td>4.15</td>
<td>57</td>
</tr>
<tr>
<td>4.16</td>
<td>58</td>
</tr>
<tr>
<td>4.17</td>
<td>59</td>
</tr>
<tr>
<td>4.18</td>
<td>60</td>
</tr>
</tbody>
</table>
Figure | Page
--- | ---
4.19 UCS mean fluid pressure results for a base case of porosity: 80%, $D_p$: 120 nm, $C$: 50 mg/ml and several other cases where these parameters are allowed to vary based on these initial values. These pressure profiles are compared to the UCS case of Huang et al [8]. | 61
4.20 UCF mean pressure results of the axi-symmetric simulation. | 62
4.21 UCF velocity results of the axi-symmetric simulation. | 63
4.22 UCF mean pressure results of the cartilage sample using a 3D mesh in the simulation. | 64
4.23 UCF results at a middle time step, 0.005 s, of the mean pressure profile at the center of the 3D mesh across the diameter of the cylinder. The upper surface is the moving platen and the bottom is the fixed surface of the sample. | 64
4.24 UCF results at a middle time step, 0.005 s, of the mean pressure profile of the axi-symmetric mesh across the radius of the cylinder. The upper surface of the figure is the moving platen, and the right face is the plane of symmetry about the cylinder. | 65
NOMENCLATURE

\( \eta_{app} \) apparent viscosity of the fluid
\( \lambda_1 \) relaxation time of the fluid
\( \lambda_2 \) retardation time of the fluid
\( \eta_0 \) zero shear viscosity
\( \dot{\gamma} \) shear rate of the fluid
\( \mu_\infty \) infinite shear viscosity
\( \mu_s \) nonlinear viscosity parameter
\( \mu_0 \) zero shear viscosity
\( a \) the a parameter for the Carreau-Yasuda equation
\( \lambda \) relaxation factor for the Carreau-Yasuda equation
\( n \) the power constant for the Carreau-Yasuda equation
\( p \) fluid pressure
\( k_p \) permeability factor of a porous media
\( \beta \) inertial factor of a porous media
\( v_s \) fluid velocity through the porous media
\( \rho \) fluid density
\( A \) viscous term tuning factor for a porous media
\( B \) inertial term tuning factor for a porous media
\( \chi \) volume porosity
\( D_p \) Mean diameter of particles in the porous medium
\( P_v \) porous viscous scalar pressure term
\( P_i \) porous inertial scalar pressure term
\( V_{total} \) total volume of the cartilage sample
\( V_{solid} \) volume of the solid within the sample
\( D \) diameter of cartilage sample
\( h \) thickness of cartilage sample
\( \chi_0 \) Initial volume porosity
\( h_i \) initial thickness of cartilage sample
\( \varepsilon \) strain witnessed by cartilage
\( V_{col} \) volume of collagen fibrils within the sample
\( n_s \) number of spherical particles within porous volume
\( D_{pi} \) initial particle diameter within the porous media
\( C \) concentration of proteoglycans within the interstitial fluid
\( m_{PG} \) mass of proteoglycans within the cartilage fluid
\( V_{fluid} \) volume of cartilage fluid within the sample
\( C_i \) initial concentration of proteoglycans before compression
\( F \) viscosity scaling factor
\( \dot{\varepsilon} \) rate of compression
\( t \) time
\( t_{strain} \) time at which max strain occurs
Articular cartilage is a complex material made of several fluid and solid components. A model that fully describes the responses of cartilage is required to accurately create a cartilage replacement that can be used in cases of injury or disease. Modeling of articular cartilage has proven difficult and currently no constitutive law fully describes its solid and fluid responses. Many of the current models describe the interstitial fluid as inviscid, even though it is known that proteoglycan migration within cartilage causes a viscous response within interstitial fluid. The goal of this research was to create a viscous fluid porous media model that better captures the compressive resistance of cartilage created by migration of interstitial fluid during cartilage compression. Through the creation of this model it was possible to capture the experimental magnitudes of fluid pressure within cartilage during unconfined slow compression simulations. As part of this model, a porous media approximation was used, which demonstrates that small variations in the solid matrix, comprised of collagen fibers, can cause large variations in system response. Magnitudes of mean pressure values, after 150 seconds of compression, for the viscous fluid porous media model bound the values found in experimental testing. Limitations of the fluid model are that system relaxation isn’t captured and the slope increase of pressures during compression for experiments don’t match those of the fluid model. A main conclusion drawn from the model is that viscosity of interstitial fluid plays a large role in creating compressive resistance within articular cartilage. Another takeaway is that the porous media approximation greatly impacts the magnitude of fluid pressurization, which creates a need to accurately represent the solid matrix within cartilage.
INTRODUCTION

Articular Cartilage is found in joints throughout the body. The main functions of cartilage are to support loading and lubricate the joint [21]. The constituents of cartilage are quite complex. Cartilage is composed of several solid and fluid components which together create both tensile and compressive resistance during articulation of the joint [20]. Current models solve these complexities within articular cartilage using inviscid fluids and fitting of solid mechanics properties to match system responses [3, 5, 7, 8, 20]. The present model is the first step in understanding the impact of viscous interstitial fluid in a porous system.

Current Modeling Approaches

To this point, no constitutive model has properly characterized the full range of mechanical properties of cartilage [8]. This is due to the material complexity of articular cartilage. However, several models have been created to match the experimental responses of cartilage samples. Most of these models are variations on a biphasic model, which are models that look at the solid and fluid phases within cartilage. This includes the biphasic poro-viscoelastic (BPVE), and biphasic cone-wise linear elasticity quasi-linear viscoelasticity (CLE-QLV) models [3, 5, 7, 8]. The BPVE and biphasic CLE-QLV models both match well against the experimental loads. A main difference in the two models is that the older BPVE model drastically underestimates the load exhibited by cartilage in tension, and the fluid pressure response [8]. Where max values are roughly 0.06 N and 0.12 MPa, respectively, for the BPVE case versus max values of roughly 0.275 N and 0.43 MPa, respectively, for
experiments [8]. The newer biphasic CLE-QLV model closer matches the tension load and fluid pressure response of experiments, where max values were found to be nearly 0.20 N and 0.33 MPa, respectively [8]. This illustrates how the tension-compression nonlinear response is better captured by the biphasic CLE-QLV model, but contains added complexity in fitting of parameters compared to the BPVE model [8]. The solid portion of these models is either described by an elastic or viscoelastic solid, which relies on tensile, compressive, and shear moduli that are fitted to experimental results to match loading of cartilage [3, 5, 7, 8]. In total there were eight material parameters that were obtained during testing to fit the experimental load response [3, 5, 7, 8]. The biphasic model is described by the aforementioned solid parameters and a secondary fluid portion. The fluid portion is approximated as an inviscid fluid, often times water, that is applied to Darcy’s law for an inviscid fluid [16, 20].

\[ \mathbf{w} = -k \nabla p \]  

This equation relates the flux of the fluid relative to the solid \( \mathbf{w} \), a permeability tensor \( k \), and pressure \( p \) [16, 20]. This form of Darcy’s law doesn’t account for fluid viscosity, but rather includes solely permeability to affect pressure. This creates a reliance on the solid portion of the biphasic model to create compressive resistance. The solid material parameters and fluid pressure addition, seen by equation 1.1, are then subjected to compression tests identical to those in experiments. The results for mechanical loads and fluid pressures for the BPVE and biphasic-CLE-QLV models are seen in Figures 1.1 and 1.2. Loads match well for both models, but under represent the fluid pressures of the system. This is important since fluid pressures are thought to support a portion of compressive loads. Without accurate representation of fluid pressures or the materials individually it is difficult to fully represent the response
of cartilage during loading. Although the biphasic models match loads well, it is important to note that compositional changes within cartilage create wide ranges of material properties [8,16].

**Radial Changes In Fluid Velocity**

As a way to verify fluid velocity profiles for the model, research by Armstrong *et al.*, was used to show how fluid pressure changes over the radius of a cartilage sample [2]. This study looked at analytical solutions of fluid pressure at the last time value for cartilage compression and various locations in time for relaxation. What was found is that, for all time values the fluid pressure decreases as the radial distance from the center of the sample increases [2]. The value of non-dimensional pressure decreases rather drastically from 0.8 at the center to a value 0.0 at the non-dimensional radius of the sample.

**Motivations**

Solid properties are often drastically different between cartilage specimens where material parameters can range by 25-80 % [8]. These property changes often arise from differences in composition of materials, cartilage health, and other genetic factors. It is appropriate to assume that if these drastic changes are witnessed by the solid, then there will be changes in the fluid as well. Because of the potential fluid changes, it is necessary to create a model that looks at the fluid response. The main parameters within the model that will be allowed to vary are viscosities of the fluid, and geometries of the porous solid matrix created by collagen. One of the significant parameters that has been neglected in previous models is the rheological properties of the cartilage fluid. Due to the approximation of interstitial fluid within cartilage as an inviscid fluid, viscous effects are neglected. This is illustrated in the previous biphasic models.
Figure 1.1: (top) Mechanical loading of cartilage samples during unconfined compression stress relaxation and a comparison of those results to the biphasic poroviscoelastic (BPVE) curve fit. (bottom) Comparison of mechanical loads versus time of an unconfined fast compression test case against the BPVE curve fit. Data taken from Huang et al. [8].
Figure 1.2: Shows fluid pressure over time during unconfined compression of cartilage samples and fluid pressure over time for the biphasic-CLE-QLV and biphasic poro-viscoelastic models during unconfined compression test cases, data taken from Huang et al. [8].
and specifically in work done by Huang et al. where the fluid pressure values fall short of the experimental cases [8]. Therefore, a fluid based model that looks at viscous flow with varying viscosity will produce a more complete understanding of the fluid response within the system. Incorporating viscosity is appropriate due to a study performed by Mow et al., where the proteoglycan composed interstitial fluid was found to have significant viscosity [17].

Along with the introduced viscous flow, the model will also be beneficial since parameters such as the collagen structure, and proteoglycan concentration are able to be varied to match material property ranges. A model that looks at the effects of each material individually will minimize error exhibited by minute changes in the experimental cartilage. The ability to change parameters to better look at cartilage changes may help to create a more complete cartilage model in the future and will show how variations in parameters affects the system response. Without a full characterization of the physics present in cartilage it is difficult to create a cartilage replacement that can be used within joints.

**Cartilage Composition**

Articular cartilage is a tissue found throughout the body in various joints. Water, collagen, and proteoglycans form the bulk of the extracellular matrix [21]. Within cartilage, water is the most abundant component comprising between 60-80% of the total weight [21]. Collagen and proteoglycans comprise the remainder of cartilage, where collagen fibrils consist of the majority of this remaining weight. Collagen is found as solid cylindrical fibrils, and proteoglycans are found as bottle-brush structures immersed in the cartilage fluid [19, 21]. These collagen fibrils create a porous network within the cartilage structure that is filled with water and proteoglycans [19, 21].
These three major components are distributed in various amounts to separate the cartilage into three distinct layers [19]. The three layers are defined from surface to bone as the superficial, middle and deep zones. Figure 1.3 shows this zonal structure of cartilage. The superficial zone has a thin layer of collagen fibrils that run lateral to the cartilage surface [19]. Along with collagen, the layer contains superficial cells, that are filled with superficial fluid, which lubricates the surface of the cartilage [19]. This zone contains the lowest concentration of proteoglycan aggregate. Due to this and the orientation of the collagen fibers this layer exhibits the highest tensile modulus, lateral to the surface, through any of the zones [12]. The main function of the tensile resistance of this layer is to resist degradation of cartilage during articulation [19].

The layer found beneath the superficial zone is the middle zone. This zone is a transitional zone that includes increases in proteoglycan orientation, along with an

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Figure 1.3: Zonal representation of collagen fiber size and orientation within articular cartilage [19]. The top layer is known as the superficial zone. Proceeding vertically, the next zone is the middle zone, and the final zone is the deep zone.
increase in the random orientation and fibril size of the collagen [19,21]. This change in composition is thought to increase compressive resistance and is the first region to react to any loading [21].

Progressing from the middle to deep zones, collagen organization becomes more randomized and each collagen fibril increases in size. The deep zone contains the most randomly oriented and largest collagen fibrils throughout cartilage [19]. In this layer, proteoglycans are at their highest concentration, and the collagen is at its lowest [19]. This compositional change between the collagen and proteoglycans is thought to be the cause of the compressive resistance within cartilage [19,21].

**Collagen**

Collagen composes roughly 60 % of the dry weight of the cartilage [21]. Its main mechanical function is to resist tension but also resists minimal compressive forces. Collagen fibers form a porous network that starts as relatively small orthogonally aligned fibers at the superficial layer and become larger randomly oriented fibers throughout the deep zone [6, 19]. When looking at the size change of the collagen fibers throughout the layers of cartilage, the superficial layer witnesses collagen fibril diameters of 20 nm and the deep zone has fiber diameters between 70 and 120 nm [19]. This increase in size of collagen also correlates with a decrease in concentration of collagen fibers [19]. This dichotomy within the layering of cartilage creates a highly porous network at its depth, that allows for migration of fluid during articulation [6,19].

**Proteoglycans**

Located within the porous matrix is the cartilage, or interstitial, fluid, which is primarily comprised of water. The fluid also contains a relatively small percentage of proteoglycans, where concentrations of proteoglycans within the fluid range between
50-100 mg/ml [15]. Proteoglycans (PG) are heavily glycosylated protein monomers, that comprise 10-15% of the wet weight of cartilage [21]. Proteoglycan monomers are attached to a hyaluronic acid molecule to form a proteoglycan aggregate chain [15, 17]. The aggregates are the main type of proteoglycans found within healthy cartilage. Aggregates are relatively large molecules with lengths nearing 1200 nm. The proteoglycan aggregates are found dispersed within the collagen fibril network [21]. Strong negative charges of particles within the molecule cause solubility in water [15]. This solubility leads to a cartilage fluid composed primarily of water and proteoglycans. Its migration throughout the extracellular matrix during compression is one of the main ways that cartilage is believed to resist compression [17, 21]. Compressive resistance is caused by the shear-dependent viscous nature of the proteoglycans within the interstitial fluid.

Prior to the work done by Mow et al. there had been no rheological studies published on proteoglycan solutions found within cartilage [17]. This study characterized the viscoelastic properties of proteoglycan aggregate and subunit solutions, where subunits are the monomer pieces of aggregates degraded by wear or disease, at varying concentrations. The main property used from the Mow et al. study is the shear-dependent viscosities for PG aggregates and subunits seen in figures 1.4 and 1.5. The viscosity profiles found in these figures show a shear-thinning response, where viscosity decreases with increases in shear rate. At high shear rates viscosities of aggregates were 1.5-2 times greater than that of subunits at similar concentrations [17]. These figures detail viscosity profiles of proteoglycans at concentrations between 10-52 mg/ml, which is significantly lower than concentrations found in cartilage samples, but was necessary due to limitations of rheological testing devices of that era [17]. Another notable difference between the viscosity profiles for the aggregate and subunits is that the subunits have less variation across the shear
Figure 1.4: Variation of viscosity of cartilage fluid due to shear rate for a range of concentrations of proteoglycan aggregate where data was taken from Mow et al. [17].

Figure 1.5: Variation of viscosity of cartilage fluid due to shear rate for a range of concentrations of proteoglycan subunits where data was taken from Mow et al. [17].
rates when compared to the aggregate viscosities [17].

To better understand how interstitial fluid responds to shear rates, it was necessary to look at the apparent viscosity $\eta_{app}(\dot{\gamma})$. $\eta_{app}(\dot{\gamma})$ which is the apparent viscosity, of a viscoelastic fluid, at a specific shear rate $\dot{\gamma}$ was adequately described by reduction of a four parameter Olroyd model, seen in equation 1.2, with the independent parameters $\lambda_1, \lambda_2, \eta_0$, and $\mu_s$. Where, for this model, the variables $\lambda_1, \lambda_2, \eta_0$, and $\mu_s$ represented the relaxation time, retardation time, zero shear viscosity, and nonlinear viscosity parameter, respectively.

$$\eta_{app} = \frac{\eta_0(1 + \mu_s\lambda_2\dot{\gamma}^2)}{(1 + \mu_0\lambda_1\dot{\gamma}^2)}$$

(1.2)

From the equation, it was possible for Mow et al. to create Figure 1.6, where apparent viscosity was studied parametrically based on the influence of $\mu_s$ [17]. This figure shows that increasing $\mu_s$ shifted the curve to the left, ie. the shear rate dependent phase of viscosity occurs at a lower shear rate [17]. This demonstrates that fluids of different $\mu_s$ at similar low shear rates may exhibit drastically different viscosities whereas high shear rates will have similar viscosity values. Therefore, the compression rates at which the cartilage samples are subjected to will have large effects on the interstitial fluid response. Although the viscosities have been characterized at different shears and concentrations, it is necessary to apply them to a viscous fluid model to understand their effects on cartilage.

**Testing Apparatus**

Cylindrical cartilage samples are generally tested using similar apparatuses and methods [8, 11, 16, 20]. The general setup is that a sample is placed between two flat surfaces, where the bottom one is fixed and the upper one moves, and the
Figure 1.6: Parametric study of variation of apparent viscosity with data taken from Mow et al. [17]. Where $\lambda_1 = 7.14 \times 10^{-2}$, $\lambda_2 = 3.27 \times 10^{-2}$, $\eta_0 = 0.005$, and $\mu_s$ varies on orders of magnitude of 110 between $10^{-1}$ and $10^{-5}$.

outer surface is filled with fluid [8, 11, 16, 20]. More specifically, for the Huang et al. unconfined compression tests a particular experimental setup was used [8]. This experiment used a computer-controlled micrometer stepper which compressed the upper platen against the cartilage sample, and a linear variable differential transformer was used to accurately measure the deformation of the cartilage samples [8]. The final portion of the apparatus for testing is the load cell on the platen which monitors the load expressed by the sample during deformation [8].
Current Experimental Approaches

Cartilage samples from Huang et al. were cut from articular cartilage to a median diameter of 4.78 mm and shaved to a thickness of 1.04 ± 0.15 mm so that only the deep zone of the cartilage was tested [8]. Once harvested, the samples were compressed using standard methods. For cartilage there are three standard compression testing setups, one being the confined slow compression test (CCS), another being the unconfined slow compression test (UCS), and the final being the unconfined fast compression test (UCF). For the CCS, cartilage samples are placed within a confined chamber. The upper moving platen is porous in nature, and allows for fluid migration from the system [8]. UCS and UCF are more common test types due to the ability to look at system relaxation caused by the fluid and solid components. Both test cases are defined by two impermeable flat platens, with the radial surface being open and filled with fluid [8]. Differences between the UCS and UCF are witnessed by the change in compression rates of the system. UCS cases are defined by a low strain rate, and the UCF cases are defined by a faster strain rate that is several orders of magnitude higher than the UCS case [8]. The main advantage of using multiple compression rate cases is to more accurately fit model parameters of the current biphasic models over a range of strain rates [8]. Both cases are compressed to a set strain, the strain value was chosen to be 5% to match experiments performed by Huang et al. [8]. Once samples are compressed to the appropriate strain, they are then allowed to relax until system pressure is negligible [8]. Now that the compression cases for samples were defined, and composition of the cartilage was detailed, it is possible to look at the response of the cartilage fluid and porous network under these compression cases.
METHODOLOGY

This chapter discusses various modeling techniques for the fluid found within articular cartilage. Along with this it also looks at the way that the solid matrix adds pressure to the system during compression.

Non-Newtonian Fluids

Fluids are placed into two categories; Newtonian and Non-Newtonian. Newtonian fluids are fluids that are categorized by having a viscosity that varies linearly with shear rate. Non-Newtonian fluids are those that exhibit viscosity changes due to changes in shear rate. Water is a Newtonian fluid. Due to the proteoglycans found within the interstitial fluid, this fluid exhibits non-Newtonian and viscoelastic behavior. Viscoelastic behavior describes the viscous and elastic nature of the material. The non-Newtonian behaviour can be seen in Figures 1.4 and 1.5 where viscosities vary non-linearly with shear rates. Since proteoglycan concentrations within cartilage samples range between 50-100 mg/ml, it was necessary to look at the fluid viscosity profiles from Mow et al. for concentrations within that range [15,17]. As seen in Figures 1.4 and 1.5, the highest concentrations viscosity profiles that fall within the range of cartilage sample concentrations are 50 and 52 mg/ml for the proteoglycan aggregate and subunits, respectively. To approximate the fluid viscosities from the figures, a reliable viscosity equation had to be fit to each profile. Of the possible equations, the Carreau-Yasuda equation fits this due to its shear thinning profile and adjustable upper and lower bounds [10].
Carreau-Yasuda Equation

The Carreau-Yasuda equation, in equation 2.1, relies on 5 parameters to determine viscosity, $\mu$ of the fluid [10, 22]. Shear rate dependence observed in all Non-Newtonian fluids is accounted for by $\dot{\gamma}$. The infinite-shear viscosity, $\mu_\infty$ and zero-shear viscosity, $\mu_0$ set the bounds for the fluids viscosity profile. The $a$ parameter changes the initial sloping of the viscosity profile. The relaxation factor, $\lambda$ increases or decreases the rate of convergence to $\mu_\infty$. The final variable $n$ shifts the curve vertically. Together these variables form the Carreau-Yasuda equation [22], seen in equation 2.1.

$$\mu(\dot{\gamma}) = \mu_\infty + (\mu_0 - \mu_\infty)(1 + (\lambda\dot{\gamma})^a)^{(n-1)/a}$$  \hspace{1cm} (2.1)

The variables for the equation were then fit using an iterative fitting method to the values found in Figures 1.4 and 1.5 for their highest concentration profiles for each PG type. The fitted values correlating to each Carreau-Yasuda equation can be seen in Table 2.1. Figures 2.2 and 2.1 show the comparison of the fit equations to the original points taken from Figures 1.4 and 1.5. The fit equations match well to the rheological study performed by Mow et al. [17]. Once the equations were fit it was necessary to approximate the media in which the fluid will flow through.

Porous Media

Due to the extracellular matrix of cartilage, which is primarily composed of collagen, a porous matrix exists within cartilage. This system allows for fluid to flow through the fibrils of collagen during compression which creates viscous and inertial forces within. Although it is unclear how accurate the use of Darcy’s Law is for non-Newtonian fluid flow through porous media [18], it is a reasonable place to start
Figure 2.1: Comparison of Carreau-Yasuda fit equation to points taken from Mow et al. [17] for proteoglycan aggregates at a concentration of 50 mg/ml.

Figure 2.2: Comparison of Carreau-Yasuda fit equation to points taken from Mow et al. [17] for proteoglycan subunits at a concentration of 52 mg/ml.
Table 2.1: Fitted Carreau-Yasuda equation parameters for proteoglycan aggregates and subunits of concentrations of 50 and 52 mg/ml, respectively.

<table>
<thead>
<tr>
<th></th>
<th>Aggregate</th>
<th>Subunit</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\mu_0$</td>
<td>3</td>
<td>0.5</td>
</tr>
<tr>
<td>$\mu_{\text{inf}}$</td>
<td>0.005</td>
<td>0.005</td>
</tr>
<tr>
<td>$\lambda$</td>
<td>0.35</td>
<td>0.02</td>
</tr>
<tr>
<td>$a$</td>
<td>0.5</td>
<td>0.8</td>
</tr>
<tr>
<td>$n$</td>
<td>0.55</td>
<td>0.5</td>
</tr>
</tbody>
</table>

since small shear rates due to small constant strain rates result in little variation in viscosity of the fluid. Darcy’s law is seen in equation 2.2. Where the gradient of pressure, $p$ is related to the fluid viscosity, $\mu$, permeability factor of the media, $k_p$, and fluid velocity through the media, $v_s$.

$$-\nabla p = \frac{\mu}{k_p} v_s$$  \hspace{1cm} (2.2)

Darcy’s law works well at low fluid velocities but requires an additional inertia term for higher velocities [4, 23]. This results in the Forchheimer corrected Darcy equation, where the inertial factor of the porous media, $\beta$, and fluid density, $\rho$ are added along with a fluid velocity term. This can be seen in equation 2.3.

$$-\nabla p = \frac{\mu}{k_p} v_s + \beta \rho v_s^2$$  \hspace{1cm} (2.3)

The porous media of cartilage is composed of cylindrical collagen fibrils which are difficult to apply to Darcy’s Law directly. It is appropriate to approximate the cylinders as multiple spheres of the same diameter [18]. This approximation results
in a bed of packed spheres. When the Forchheimer equation is then specialized to the Ergun equation for packed beds it results in the following equation [4,9]:

\[-\nabla p = \frac{A\mu(1 - \chi)^2}{\chi^3 D_p^2} v_s + \frac{B\rho(1 - \chi)}{\chi^3 D_p} v_s^2\]  \hfill (2.4)

In the Ergun equation the \(k_p\) and \(\beta\) terms are expanded into their relationships of volume porosity, \(\chi\), particle diameter, \(D_p\), and tuning factors \(A\) and \(B\). It is important to note that the tuning factors \(A\) and \(B\) are to tune Ergun model for specific experimental setups. For the packed bed approximation, the variables are assigned to 150 and 1.75 respectively [4,9,23]. The two portions of the equation are broken down into viscous, \(P_v\) and inertial, \(P_i\) terms shown in equations 2.5 and 2.6, respectively.

\[P_v = \frac{150\mu(1 - \chi)^2}{\chi^3 D_p^2}\]  \hfill (2.5)

\[P_i = \frac{1.75\rho(1 - \chi)}{\chi^3 D_p}\]  \hfill (2.6)

Two important variables within the viscous and inertial terms are the \(D_p\), and \(\chi\). These variables are a major contributor to the pressure drop exhibited by the Ergun equation. \(D_p\) was approximated to the diameter of the collagen fibrils found within the different layers of cartilage. This is an acceptable approximation due to the similar surface area of multiple spherical beads when compared to collagen fibrils of the same diameter [18]. The approximation create simplicity in terms of not having to model the cylinders of random orientation within the fluid. One of the potential drawbacks of this assumption is that spheres are able to pack more tightly than cylinders, resulting in smaller space between particles which further resists fluid flow. The values of the collagen fibrils within the deep zone range between 70 and 120 nm.
for their diameters [19]. This variance provides a range of values of \( D_p \) to investigate while understanding its impact upon the pressures within a cartilage sample. For this new model, \( D_p \) of 120 nm was chosen as a base value since collagen diameters are largest in the deep zone.

**Variation Of Porosity**

The other major variable within the porous media approximation is \( \chi \) which is dependent on the volume ratio of cartilage fluid versus collagen within cartilage. Due to this relationship and the relationship between the cartilage fluid leaving the system and collagen being retained, cartilage will vary based on a volume ratio of components and the strain witnessed by the sample. This relationship, seen in equation 2.7, compares the fluid volume, and the total volume of the sample, \( V_{total} \). The fluid volume is represented by the difference of the solid volume, \( V_{solid} \) from \( V_{total} \). For simplification it was assumed that the solid volume is comprised solely of collagen, this is appropriate for a model that assumes proteoglycans are found flowing within the interstitial fluid.

\[
\chi = \frac{V_{total} - V_{solid}}{V_{total}} \tag{2.7}
\]

Each component volume is then expanded into the volumetric equations of the cartilage sample and a relationship of initial porosity, \( \chi_0 \). \( V_{total} \) is dependent solely on the volume occupied by the cartilage sample whereas, \( V_{solid} \) is described by the volume of the total system multiplied by the solid volume ratio of the system. This expanded equation is seen in equation 2.8.

\[
\chi = \frac{\pi D^2 h}{4} - \frac{(1-\chi_0)\pi D^2 h}{4} \tag{2.8}
\]
Simplifying equation 2.8 and relating the sample thickness, $h$ to the initial sample thickness, $h_i$ and the sample strain, $\epsilon$ results in equation 2.9.

$$\chi = 1 - \frac{(1 - \chi_0)}{1 + \epsilon}$$

(2.9)

This equation was then applied to the range of porosities that are possible within cartilage. Since the observed range of $\chi$ within healthy cartilage is between 60 and 80 % [21], three initial $\chi$ values were chosen to be 60, 70, 80 % to capture the extents and a midpoint. These values were then plotted against the compressive strain, in Figure 2.3, of the sample to show how values will decrease. These profiles provide a range of porosities to test within the compressive simulations.

The figure shows that decreases in porosity will occur during compression for each $\chi_0$. The same volume of fluid will flow out of the system for each $\chi_0$, which results in larger porosity changes for smaller $\chi_0$ values. This is illustrated by the decreases in $\chi$ by values of 1.05, 1.58, and 2.10 for each $\chi_0$ of 60, 70, and 80 %, respectively. Along with the varying porosities, fixed porosity values of 60, 70, and 80 % will be tested within the model, where 80 % is the base case for comparisons to be made.

**Particle Diameter Changes During Compression**

Another parameter of interest is the particle diameter, and although the $D_p$ value is often assumed to hold constant during compression it is possible that orientation changes and compression of the collagen fibrils results in a varying $D_p$. The changes in $D_p$ become especially necessary due to the approximation of the collagen as a sphere rather than cylinder. A packed bed composed of spheres may lead to smaller pore space than a packed bed of spheres, so it was appropriate to look further into the changing value $D_p$. To relate $D_p$ and any parameters that would change its value, it
is necessary to start at the solid volume equation, seen by equation 2.10.

\[ V_{solid} = (1 - \chi)\pi D^2 h \]  \hspace{1cm} (2.10)

Along with this the collagen volume \( V_{col} \) equation was also looked at, in equation 2.11. Where the collagen volume is the volume of solid occupied by each sphere that is multiplied by the total number of spheres within the solid volume \( n_s \).

\[ V_{col} = (1 - \chi)\pi \frac{D^3}{6} n_s \]  \hspace{1cm} (2.11)
As before the collagen volume and solid volume are assumed to be the same and therefore it is possible to state that since solid volume is conserved that the collagen volume will be conserved. The initial volume of collagen is compared to the instantaneous volume of collagen with expanded terms and creates equation 2.12. Where $D_{pi}$ is the initial particle diameter and the other variables are consistent with previous equations.

\[
1 = \frac{(1 - \chi_0)^3}{(1 - \chi)^3} \frac{D_{pi}^3}{\pi} \frac{D_p^3}{6}
\]  

(2.12)

Through simplification equation 2.13 is arrived at where $D_p$ is the particle diameter based on the initial particle diameter, the initial porosity and the corresponding current porosity.

\[
D_p = \left(\frac{1 - \chi_0}{1 - \chi}\right)^{1/3} D_{pi}
\]

(2.13)

The equation for $D_p$ can then be used in equations 2.5 and 2.6 to allow $D_p$ to vary or be fixed based on the simulations being performed. For the fixed and varied cases, both use $D_p$ values of collagen fibril diameters. These values are between 70-120 nm within the deep zone, and are chosen to be 70, 90, 110, and 120 nm for simulations. The values were then applied to equation 2.13 so that Figure 2.4 is arrived at.

This figure shows how compressive strains across each of the possible intial $D_p$ values creates a relatively small decrease in $D_p$. Values for 70, 90, 100, and 120 nm decreased by 1.19, 1.53, 1.70, and 2.03 nm, respectively. Although small changes occur it is necessary to simulate how the changes in $D_p$ and $\chi$ affect the porous media approximation. The simulations were to be performed for the range of fixed and varied particle diameters under the UCS test.
Figure 2.4: Demonstrates the change in $D_p$ over the course of compression of the sample for 4 values of $D_p$ that fall within the range of collagen fibril diameters. The initial value of $D_p$ correlates to the value of each profile at no compressive strain, where 70, 90, 100, and 120 nm values were chosen.

Proteoglycan Aggregate Concentration Changes During Compression

A final parameter variation for analysis was how the concentration of the proteoglycan aggregate influenced interstitial fluid. The concentration of proteoglycans with literature are found to range between 50-100 mg/ml [15]. Changing volume of fluid within the system and vastly different diffusion coefficients of the proteoglycans at $2.76 \times 10^{-13} m^2 s^{-1}$ and the surrounding water at $9.94 \times 10^{-10} m^2 s^{-1}$ [13, 14], cause an increase in the concentration of proteoglycans within the cartilage fluid. Unlike
the previous volume relationship for porosity, the proteoglycan concentration relies on a mass concentration equation. Since mass concentration $C$, is simply the mass of the proteoglycans within the fluid, $m_{PG}$ divided by the volume of the fluid $V_{fluid}$, equation 2.14 was used.

$$C = \frac{m_{PG}}{V_{fluid}}$$  \hspace{1cm} (2.14)

For this equation is was assumed that the mass of proteoglycans stay constant due to the vastly different diffusion coefficients between water and proteoglycans [13,14]. Both the mass and volume portions are then expanded into their respected terms, where $C_i$ is the initial concentration and the remainder of the variables are consistent with previous definitions. This expansion results in equation 2.15.

$$C = \frac{C_i(\pi D^2/4)h_i \chi_0}{\pi D^2/4)(h_i + \epsilon h_i) \chi}$$  \hspace{1cm} (2.15)

This equation is then simplified by canceling the like terms and arrives at the final form for varying concentration seen in equation 2.16.

$$C = \frac{C_i \chi_i}{\chi(1 + \epsilon)}$$  \hspace{1cm} (2.16)

Equation 2.16 relates the $C_i$ to $\chi$, and $\epsilon$. Once the varying concentration equation was formulated it was necessary to create a viscosity profile scaling based on concentration changes seen in Figure 1.4 to be able to look at concentrations of proteoglycans larger than 50 mg/ml along with concentrations between known profiles in the figure. A scaling was necessary due to the nonlinear relationship between concentration and the viscosity profiles exhibited by the cartilage fluid. This was performed by setting the 50 mg/ml profile as the base profile, and creating a variable, $F$. $F$ is a scalar multiplier that shifts the viscosity up or down depending on whether the concentration
is higher or lower than the base concentration. Table 2.2 illustrates how decreases in concentration from 50 mg/ml correlate with a decrease in the magnitude of the viscosity profile by a value of F that is less than 1.0. The equation that F is applied

Table 2.2: The values below for C are values given by Figure 1.4 for each respective viscosity profile. The F values correlate to the required scalar multiplier of equation 2.1 with respect to the 50 mg/ml aggregate profile to create a profile that matches the respective proteoglycan concentration.

<table>
<thead>
<tr>
<th>C (mg/ml)</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>1.0</td>
</tr>
<tr>
<td>40</td>
<td>0.6485</td>
</tr>
<tr>
<td>30</td>
<td>0.4310</td>
</tr>
<tr>
<td>25</td>
<td>0.2703</td>
</tr>
<tr>
<td>20</td>
<td>0.2020</td>
</tr>
</tbody>
</table>

to has the same values as in Table 2.1 for the aggregate.

\[
\mu(\dot{\gamma}) = F \ast (\mu_\infty + (\mu_0 - \mu_\infty)(1 + (\lambda \dot{\gamma})^a)^{(n-1/a)}) 
\] (2.17)

From the known values of concentration it was necessary to fit an equation that relates the viscosity scaling to concentration for values of concentration that fall outside the given values. The best fit was achieved through the use of a concentration dependent second order quadratic function seen in equation 2.18.

\[
F = 0.0003196C^2 + 0.004173C - 0.0124 
\] (2.18)

The fit of the equation can be seen in Figure 2.5, and is shown to fit accurately over the data set from Table 2.2. This is further exemplified by Figure 2.6, where
the scale viscosity profiles overlay the viscosity values found by Mow et al. for each concentration [17]. Thus the viscosity scaling parameter will provide insight for the variance of concentration during compression and will estimate some values that fall outside of the viscosity profiles seen in Figure 1.4.

![Graph](image)

Figure 2.5: Illustrates accuracy of fit for the concentration dependent viscosity scaling equation, in Equation 2.18, against the viscosity scaling values for each concentration of proteoglycan aggregate fluid, seen in Table 2.2.

When the variation of concentration and the viscosity scaling equations are used together it is possible to model cartilage at higher proteoglycan concentrations via extrapolation. Simulations were performed for three cases of initial concentrations. The values used were 30, 50, and 70 mg/ml. These concentrations were set for a wide range of values to better characterize how changes in concentration affects the fluid
Figure 2.6: Dots representing viscosities of proteoglycan aggregate at each specified concentration over a range of shear rates from the rheological study performed by Mow et al. [17] compared against the viscosity scaling equation, equation 2.17, for proteoglycan aggregates at each concentration.

response of the system. The values of 30, and 50 mg/ml were chosen since there had been previous viscosity profiles to compare against. Whereas, the 70 mg/ml case is an extrapolation performed by equation 2.18 to give insight on how larger concentrations may affect the system. When these concentrations were evaluated with equation 2.16, Figure 2.7 was created to compare the concentrations of the proteoglycan aggregates versus the compressive strain of the cartilage sample.

Increases are seen by each concentration case during compression. The 30, 50, and 70 mg/ml case each increase by 2, 3.3, and 4.7 mg/ml at the time of 5 % compressive strain. These values are uniform throughout the sample based on equations 2.17 and 2.18, but are in actuality more likely to vary. A future rendition
Figure 2.7: Change of concentration of proteoglycan aggregates due to compressive strains within the system for 3 values of initial concentration. These initial values of concentration were set to be 30, 50, and 70 mg/ml.

of the model may need to look at spatial variation of concentration, porosity and particle diameter. After the changes in concentration were modeled the profiles for the varying initial concentrations and for the same fixed concentrations were then applied to equations 2.18 and 2.17 and simulated for the UCS setup.
MODELING METHODS

By looking at interstitial fluid as a viscous fluid an additional term of complexity is kept within the Navier-Stokes equation [1].

\[ \rho \frac{Du}{Dt} = -\nabla p + \mu \nabla^2 u + \frac{1}{3} \mu \nabla (\nabla \ast u) \] (3.1)

The porous media approximation given by the Ergun equation, in equation 2.4, is then added to the Navier-Stokes equation to further complicate the solution to a cylindrical sample of cartilage fluid under compression. Solving this system analytically becomes difficult with all of the aforementioned complexities and therefore a fluid modeling package was necessary to solve the system more effectively. To create a model of cartilage compression the fluid continuum solver known as Star-CCM+® was used. Within Star-CCM+® a cylindrical sample of cartilage was created and filled with an appropriate mesh. Once a mesh was applied, the physics of the fluid was specified to match that of cartilage fluid.

Cartilage Sample

Cartilage samples are taken as cylindrical samples during standard testing, as discussed in the Introduction chapter. To be able to compare to the results found by Huang et al. the model cylinder size was kept uniform with the experimental sample size [8]. Cartilage experimental sample diameters were tested at 4.78 mm [8] when testing against parameters and Huang et al. results. To show whether variation in cartilage diameter affects the simulation several other sample diameters were chosen. These values are 1, 2, 4, and 6 mm. For consistency within simulations, and when comparing to Huang et al. thickness of the sample was held constant. The thickness
of the experimental samples was shaved to 1.04 mm to look solely at the deep zone for the Huang et al. model [8].

Physics Models

The first physics parameters that were chosen, within Star-CCM+®, were the fluid properties. Since the composition of interstitial fluid is primarily nearly incompressible water, and the remainder of the fluid is solid proteoglycans, 10-15 % of the wet weight, it was possible to state the fluid would be incompressible. Since the fluid is assumed to be incompressible it was appropriate to apply the constant density model. Due to the viscous nature of the cartilage fluid, provided by the proteoglycans within the fluid, a viscous flow model was chosen for the physics. Within the viscous flow model a dynamic viscosity profile was created to match the profile found in equation 2.1 and table 2.1. Without the viscosity, the fluid flow would lose a major contribution to the overall system pressure and result in a model that resembles the fluid portion of the current biphasic models [3, 8, 16]. It was also necessary to determine the fluid flow characteristics of the system during compression. Since the fluid velocities were relatively low and viscosity profile values were high a laminar flow model was chosen. This was acceptable due to the dependence of flow characteristics on the Reynolds number and this value was nearly zero since viscosity values were much higher than the fluid velocity.

To solve for fluid flow and pressure changes over time, a time solver had to be selected. An implicit unsteady time solver was chosen but created a time step dependence that needed to be removed. This was accomplished by reducing time step values to 1 and $2.50 \times 10^{-4}$ s for the UCS and UCF cases, respectively, until the system no longer varied between simulations. The verification used to check time step dependence was the residuals plot, where residual values were minimized below
10^{-5} to note that time steps were reduced sufficiently. As discussed in theory, the collagen creates a porous network [8,19]. Therefore, it was necessary to designate the fluid region as a porous region that uses Darcy’s law, and more specifically the Ergun function given by equations 2.5 and 2.6, to approximate the viscous and inertial forces that are added to the fluid pressure. The equations defined previously were inserted individually as user inputs that act as an addition to fluid pressure. As an additional complexity to the porous media approximation, equations 2.9 and 2.13 were defined as user functions that affect equations 2.5 and 2.6 to further affect the values of porosity and particle diameter during sample compression.

Meshing

Based on the cylindrical sample geometries defined previously, the cylinder had to be meshed. Modeling of cartilage requires a mesh to solve the fluid motion throughout the system. For meshes there were two meshes that were chosen; a 3D mesh and an axi-symmetric mesh. The 3D mesh models a cylindrical cartilage sample fully, and the axi-symmetric mesh looks at a vertical slice of the cartilage sample in cylindrical coordinates.

3D Mesh

To create a mesh of the cylindrical cartilage sample a mesh type had to be chosen that allows for morphing of mesh cells during compression. three mesh types are available within StarCCM+: quadrilateral, polygonal, and triangular. Of the options, the quadrilateral mesh is the best choice due to its’ ability to be used in a directed mesh. The directed mesh is ideal for compression in this type of problem due to the cell faces being aligned parallel to both platens of the sample. Faces that are parallel to the cartilage better preserve their geometries during compression whereas,
other mesh types have the propensity to tangle, causing solution inaccuracies. This further allows for consistent results that are more likely to remove mesh dependence.

Once a mesh type was chosen a base cell size was adjusted until mesh dependence was no longer a concern. Since mesh dependence concerns cause invalid data it was necessary to reduce the base cell size until the results no longer varied. This resulted in a base cell size of 0.015 mm. This base size was allowed to grow as the sample progresses towards its’ center to 120 % of the original base size. Allowing cell growth to occur as the mesh progresses towards the center of the sample is useful in reducing cell count and can be seen in Figure 3.1. The directed mesh was set to have 20 layers which also helped to sustain mesh independence.

Mesh independence was achieved by looking at each parameter that produces the mesh. Compression simulations were performed with an initially coarse mesh. The mesh parameter of cell size was reduced until pressure values were no longer experiencing large pressure jumps between adjoining cells radially. The number of layers in the directed mesh were then increased until pressure jumps weren’t witnessed within the vertical direction in cylindrical coordinates. The cell growth towards the center of the cylindrical sample was increased to allow for a reduction in overall cell count, this was appropriate due to the a large portion of pressure inaccuracies being seen along the radial surface of the sample, and fewer being seen at the sample center.

A finalized quadrilateral directed 3D mesh can be seen in Figures 3.1 and 3.2. Both of the figures illustrate how, during compression, only a cell volume change will occur but won’t impact the overall shape of each cell parallel to the upper and lower cartilage surfaces.
Figure 3.1: Quadrilateral mesh of the 3D cartilage sample with a base cell size of 0.015 mm. Mesh cell count: 182,080 cells

Figure 3.2: View of the internal mesh of the 3D cartilage sample.

Axi-Symmetric Mesh

A secondary mesh scheme for the cartilage sample is the axi-symmetric mesh, which reduces the overall cell count compared to the 3D mesh. This reduction in cell count is due to the consistency in cell sizing between the two mesh types where
the axi-symmetric mesh is essentially a vertical slice of the 3D mesh. The difference between the two meshes can be seen in Figures 3.1 and 3.3 where the 3D sample has a much larger converged cell count at 182,080 cells, and the vertical 2D slice oriented about the radius of the cartilage sample has a drastically lower converged cell count of 3906.

Figure 3.3: View of the axi-symmetric mesh for the cartilage sample, where the sample is 2.38 mm for the radius and the thickness is 1 mm. The base cell size of the mesh is 0.015 mm and increases to 120 % at the center of the mesh. Mesh cell count: 3906 cells

Differences Between Mesh Types

Due to the axi-symmetric mesh being a 2D slice, versus the 3D cartilage sample mesh, there is a reduction in the overall solution time. On average the 3D mesh takes between 50 and 60 times longer to complete a full simulation compared to the axi-symmetric mesh. This change in simulation time is caused by the aforementioned reduction in the cell count between the 3D and 2D meshes. A drawback of the 2D mesh is that velocity impulses caused by a piecewise strain field often are found at initial and latter time steps during higher compression rates. Whereas, the 3D
mesh exhibits smaller impulses and results contain less noisy values at a variety of 
compression rates. The main reason for the impulse presence in the 2D mesh is the 
quadrilateral mesh, which suggests tangling of cells may occur during compression. 
For a more accurate simulation, the directed 3D mesh is used. Through further 
refinement of the axi-symmetric mesh the simulation could become more accurate, 
but doesn’t allow for use of a layered directed mesh like in the 3D mesh. After the 
meshes were chosen the next step in modeling articular cartilage was to apply the 
correct boundary conditions.

Boundary Conditions

Once the mesh and physics were chosen, the boundary conditions were defined 
and kept consistent with Huang et al. to better allow for comparisons of fluid pressure 
[8]. The upper surface was set to be an impermeable platen that was allowed to 
move to initiate sample compression. The bottom surface is a fixed plate that is 
also impermeable. The only surface that allows fluid to leave during compression 
is the outer surface. Within StarCCM+®, the surface was set as a pressure outlet 
of zero which allows for the migration of fluid. This is justifiable since the outlet 
is surrounded by a fluid filled region within experiments. The separate faces are 
highlighted for each boundary in Figures 3.4 and 3.5. From Figure 3.5, there is an 
additional boundary condition that must be set for the axi-symmetric mesh. This 
boundary is the symmetry plane that defines the center axis of the cylinder.

Sample Compression

Within standard testing a piecewise function, in equation 3.2, is used to 
characterize loading and relaxation of a sample. The function characterized by a
constant displacement rate until a predefined strain is achieved and then held until the sample is fully relaxed. Within Huang et al., there are two separate unconfined compression test cases. The differences in compression in testing are exhibited by the rate of compression where one case is strained at a much higher rate than the other. The slow compression rate, UCS, for Huang et al., is $1.8 \times 10^{-4} \text{sec}^{-1}$ [8]. Another test case is the fast compression, UCF which compresses the samples at a rate of 1
mm/s until the sample reaches its’ predefined strain. For both simulations a strain of 5 % was where the max strain was achieved. Both follow the general formulation of the piecewise equation in equation 3.2. Where the compression time $t$, and time at which the max strain occurs $t_{\text{strain}}$ are the variables for which equation the piecewise function uses. For the UCS and UCF cases, based on strain rates, $t_{\text{strain}}$ was set to be 280 and 0.05 s, respectively.

$$
\epsilon(t) = \begin{cases} 
-\dot{\epsilon} t & \text{if } 0 < t < t_{\text{strain}} \\
-\dot{\epsilon} t_{\text{strain}} & \text{if } t > t_{\text{strain}} 
\end{cases}
$$ (3.2)

Within the viscous fluid flow model it was possible to ignore the relaxation or $t > t_{\text{strain}}$ portion of the results, because without straining fluid velocities become negligible which causes pressures to go to zero.
RESULTS

UCS simulations were placed in parameter categories that look at variations of the same parameter for several simulations. These variation cases can be seen in Tables 4.1, 4.2, and 4.3. The first two parameter types are seen in Table 4.1, where the fluid type is chosen as either PG aggregate fluid, PG subunit fluid, or water, and the sample diameter cases have cartilage diameters that are set at four values between 1 and 6 mm. The set of parameters in Table 4.2 look at the ranges of experimental porosities and particle diameters, and are either fixed or allowed to vary based on aforementioned equations. The final table, Table 4.3, depicts the range of proteoglycan aggregate concentrations that are able to be modeled. The proteoglycan aggregate concentrations were tested at 3 initial values that were either fixed or allowed to vary.

**UCS Results**

Simulations were subjected to a variety of parameters that changed the fluid responses within the cartilage. The first of these parameters, and one of the most important was the viscosity parameter simulations. Water and cartilage fluid with either PG aggregates or PG subunits were simulated under the UCS test case, with fixed values of porosity, particle diameter and a standard cartilage sample size were used. The results for the pressure versus time can be seen in Figure 4.1.

This figure directly illustrates the importance of fluid viscosity on the compressive resistance. The PG aggregate and subunits both have drastically higher pressure profiles than the water case, and the only difference between the three simulations is the fluid viscosity. So the only explanation is that viscosity of the fluid is directly related to the pressures exhibited by the system during compression. The mean
Table 4.1: Parameter cases for viscosity and cartilage sample diameter, and their necessary user inputs. All values are defined to be fixed outside of fluid viscosities.

<table>
<thead>
<tr>
<th>Parameter Type</th>
<th>Fluid</th>
<th>Sample Diameter (mm)</th>
<th>Concentration (mg/ml)</th>
<th>Porosity (%)</th>
<th>Dp (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viscosity</td>
<td>PG aggregate</td>
<td></td>
<td></td>
<td>50</td>
<td>80</td>
</tr>
<tr>
<td></td>
<td>PG subunit</td>
<td></td>
<td></td>
<td>52</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Water</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sample Diameter</td>
<td>PG aggregate</td>
<td></td>
<td>1</td>
<td>50</td>
<td>80</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>6</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 4.2: Parameter cases for porosity and particle diameter, and their necessary user inputs. For these cases, values are specified to be fixed or varied.

<table>
<thead>
<tr>
<th>Parameter Type</th>
<th>Fluid</th>
<th>Concentration (mg/ml)</th>
<th>Porosity (%)</th>
<th>Dp (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Porosity</td>
<td>PG aggregate</td>
<td>Fixed</td>
<td>50</td>
<td>80 Fixed</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>70</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>60</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Varied</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Particle Diameter</td>
<td>PG aggregate</td>
<td>Fixed</td>
<td>50</td>
<td>80 Fixed</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>100</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>90</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>70</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Varied</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 4.3: Parameter cases for proteoglycan aggregate concentration, and their necessary user inputs. For these cases, values are specified to be fixed or varied.

<table>
<thead>
<tr>
<th>Parameter Type</th>
<th>Fluid</th>
<th>Concentration (mg/ml)</th>
<th>Porosity (%)</th>
<th>Dp (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PG Concentration</td>
<td>PG aggregate</td>
<td>Fixed</td>
<td>30</td>
<td>Fixed</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>50</td>
<td>Fixed</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>70</td>
<td>Fixed</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Varied</td>
<td>30</td>
<td>Varied</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>50</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>70</td>
<td></td>
</tr>
</tbody>
</table>

Viscosity of each fluid was found in the simulations to be 2.98, 0.50, and 0.000889 Pa-s for the PG aggregate fluid, PG subunits fluid, and water, respectively, which further illustrates that viscosity increases correlate to fluid pressure increases.

**Sensitivity To Sample Diameter**

Since the viscosity of the cartilage fluid was found to have substantial impact on the fluid response, it was of interest to study the relationships of other parameters with the fluid response. For the simulations, looking at how the sample size affects the system, porosity was fixed to 80 % and the proteoglycan concentration was set to a constant 50 mg/ml. The value that changed for each simulation was the sample size, and specifically the sample diameter. Before sample diameters were allowed to change a verification of the fluid only model was necessary for fluid pressure versus radius simulation results compared to those found in literature. In the simulations, pressure is highest at the center of the cylindrical sample and decreases as the radial distance from the center increase and is seen in Figure 4.2. This trend is consistent with work done by Armstrong *et al.* looking at the analytical solution [2], where they showed that pressure will be highest at the center of a sample and decrease radially.

After the simulations were found to show the same radial pressure variance as
the work performed by Armstrong et al., the thickness and compression rate of the system were held constant, and the sample diameter was allowed to vary. Intuitively, the mean velocity of the fluid leaving the system must increase as sample diameter is increased, since compression rate was held constant. This is displayed in Figure 4.3 where the plot looks at mean fluid velocity versus time during the UCS test case of samples with several cylinder diameters.

The porous media terms, equations 2.5 and 2.6, and the momentum equations all exhibit increases in the mean pressure due to the increase in these velocities as diameter increases and is seen within Figure 4.4. Table 4.4 further illustrates that the increase in diameter increases the pressure and velocity. It is interesting to note
Figure 4.2: Mean fluid pressure profile of a vertical and bottom slice of cartilage at a solution time of 150 s for the 3D mesh with a sample diameter of 4.78 mm.

that the percentage increase in volume of the sample is nearly identical in magnitude to the percentage increase in pressure.

What all of these results show is that to fully compare cartilage compression test to each other, it is important to keep uniform sample diameters or to determine accurately how this change affects the cartilage response.

Variation Of Porosity

Another parameter to test is the porosity within the solid of cartilage. There is a large variance of porosity found between samples of cartilage. These values range between 60-80 \% [21]. The wide range of possible porosities were simulated at 3 fixed porosities, which can be seen in Figure 4.5. The variation of the porosity parameter illustrates decreases in porosity, causes the fluid pressure to increase to account for a
Figure 4.3: Mean fluid velocity versus time during UCS compression for a variety of sample diameters using the 3D mesh.

larger volume of flow resistive particles when compared to the volume of fluid within the system. This is further exemplified by the relationship seen by equations 2.5 and 2.6. Table 4.5 shows how each decrease of porosity of the system by 10% results roughly in a factor of 3 increase of the mean pressure of the system.

Once the fixed porosity simulations were performed, it was essential to see how porosity changes during sample compression affects the fluid pressurization of the system. The porosity change, from equation 2.9 was determined based on the initial porosity, sample thickness, and strain. The change in porosity versus compression can be seen in Figure 2.3. This change in porosity was then applied for each of the initial
Figure 4.4: The figure illustrates how changes in sample diameter with a 3D mesh will affect the mean pressure over time of the fluid during a UCS test case.

porosities to the UCS simulation. The results for the 80 % porosity cases are found in Figure 4.6, where drastic differences can be seen between the pressure profiles of the fixed versus varying porosities, and these trends continue for the 60, and 70 % porosity cases, and can be seen in Figures 4.8 and 4.7. Looking at Table 4.6 it can be seen that this is further illustrated by the increase in pressure at the final strain for the varied versus the fixed porosity cases. Along with increases in pressures over time of the varying versus fixed porosity, there is also a continued trend that decreasing the porosity in each case continues to increase the overall pressure profile magnitude. This is illustrated in Figure 4.6 and Table 4.6, where mean pressures of the varying
Table 4.4: Change in percentage of volume, velocity, and pressure from a 1 mm diameter cartilage sample UCS compression case to the respective sample diameter.

<table>
<thead>
<tr>
<th>Diameter (mm)</th>
<th>Change in Volume (%)</th>
<th>Velocity Change (%)</th>
<th>Pressure Change (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>300</td>
<td>9.12</td>
<td>299.6</td>
</tr>
<tr>
<td>4</td>
<td>1500</td>
<td>41.95</td>
<td>1497.4</td>
</tr>
<tr>
<td>6</td>
<td>3500</td>
<td>86.12</td>
<td>3492.5</td>
</tr>
</tbody>
</table>

Table 4.5: Characterization of how changes in porosity causes changes in fluid pressure from 3D mesh simulations.

<table>
<thead>
<tr>
<th>Porosity (%)</th>
<th>( \Delta \chi ) (%)</th>
<th>Mean Pressure (MPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>80</td>
<td>0.317</td>
<td></td>
</tr>
<tr>
<td>70</td>
<td>-10</td>
<td>1.067</td>
</tr>
<tr>
<td>60</td>
<td>-20</td>
<td>3.007</td>
</tr>
</tbody>
</table>

...porosity cases are higher than those in the fixed porosity cases.

Variation Of Particle Diameter

Another parameter of the porous media approximation that was necessary to look at was the particle diameter, \( D_p \). This value is found to vary between 70-120 nm for the deep zone of articular cartilage [19], and impacts the simulation by adjusting equations 2.5 and 2.6. The two extremes of the possible \( D_p \) values and two middle points were simulated, with values being 70, 90, 100, and 120 nm. The pressure results for these simulations can be seen in Figure 4.9.

What is seen throughout the figure is that the slope of the pressure profiles for each \( D_p \) is constant but an increase in pressure magnitudes is seen as \( D_p \) is decreased.
Figure 4.5: Mean pressure versus time for a UCS simulation for 3 separate fixed porosity values using the 3D mesh.

This is consistent with equations 2.5 and 2.6 where $D_p$, a term in the denominator of both equations and thus will increase pressure for a decrease its' value. This is also consistent with the expected results of collagen fibril packing during cartilage compression. From Figure 4.9 it is shown that pressure profiles will increase more rapidly in magnitude as $D_p$ is decreased, compared to each previous $D_p$ case, due to the squared $D_p$ term in equation 2.5. The change in magnitude of pressure due to $D_p$ also illustrates well how the dominating pressure scaling term within the system is the porous viscous term for the UCS test cases due to the low velocity magnitudes, which are shown in Figure 4.3.
Figure 4.6: UCS mean fluid pressure results using a 3D mesh of a cartilage sample at a fixed porosity of 80 % and another simulation where the porosity follows equation 2.9 with an initial porosity of 80 %.

Once the fixed $D_p$ pressure profiles were looked at, it was necessary to show how equation 2.13 creates changes in $D_p$ versus cartilage sample strain. This variation of $D_p$ versus compressive strain can be seen in Figure 2.4. From the figure it is seen that the $D_p$ reduces by 1.2 and 2 nm from the start to finish of the compression for the 70 and 120 nm initial diameters, respectively. The changing $D_p$ values were then applied to the varying porosity simulation which uses an 80 % initial porosity. The results of the varying porosity and varying $D_p$ simulations were compared to the pressures found by the fixed $D_p$ cases and are seen in Figures 4.10, 4.11, 4.12, and 4.13.

Along with the increases in pressure due to the change in porosity, discussed in
the previous section, there is also an added increase of pressure over time due to the decrease in $D_p$ for each of the separate $D_p$ cases. The decrease in $D_p$ causes the observed pressure increase due to the effects of equations 2.5 and 2.6. This concept is seen in Figure 4.14 which compares the varying 80% porosity with a 120 nm fixed particle diameter case with the same case where the particle diameter is allowed to vary.
Variation Of Proteoglycan Concentration

Due to the migration of interstitial fluid and varying diffusion coefficients of water versus proteoglycans, a concentration change of proteoglycans will occur during cartilage compression. This change is exhibited by equation 2.16 for a range of concentrations that were plotted against compression in Figure 2.7. From the figure it was found that an increase in concentration of proteoglycans during compression causes an increase in the viscosity of the cartilage fluid. This is exhibited in equations 2.18 and 2.17 where increases in $C$ scales the viscosity profile higher. This increase
Table 4.6: Characterization of how changes in porosity causes changes in fluid pressure for the fixed and varied cases of porosity at 5 % strain of the sample using the 3D mesh.

<table>
<thead>
<tr>
<th>( \chi_i ) (%)</th>
<th>( \chi ) (%)</th>
<th>Varied ( \chi P ) (MPa)</th>
<th>Fixed ( \chi P ) (MPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>80</td>
<td>78.95</td>
<td>0.375</td>
<td>0.325</td>
</tr>
<tr>
<td>70</td>
<td>68.42</td>
<td>1.297</td>
<td>1.093</td>
</tr>
<tr>
<td>60</td>
<td>57.90</td>
<td>3.805</td>
<td>3.085</td>
</tr>
</tbody>
</table>

In viscosity during compression can be seen in Figure 1.4. When applied to UCS simulation cases for the 3 constant concentrations, average viscosities of 1.19, 2.96, and 5.50 \( Pa - s \) were found for the 30, 50, and 70 mg/ml concentrations, respectively. These values stay constant for the duration of compression of the cartilage sample due to the constant strain rate being applied. Figures 4.15, 4.17, and 4.17 show the pressures during compressive loading for the fixed and varied concentration cases. For the fixed concentration pressure profiles for each figure, it is seen that increases in overall concentration causes increases in the system’s fluid pressure response. This is due to the increase of the mean viscosities as proteoglycan concentration increases, which is illustrated in Figure 1.4.

For the varying concentration cases, it was seen that the initial time step pressure value was identical to the initial value of pressure for each respective fixed concentration case. It is also seen that due to the impacts of equations 2.16, 2.18, and 2.17 the pressure profile will increase more rapidly for higher concentrations of proteoglycans.
Figure 4.9: Illustration of how changes in the collagen fibril diameters within known ranges, equated as the particle diameter $D_p$, affects mean fluid pressure within a 3D mesh simulation.

Huang et al. Comparison Of UCS Cases and Parameters

From the aforementioned parameter varying models for porosity, $D_p$, and concentration it was possible to combine the pressure results to show how each parameter affects the overall system under UCS compression. These parameter variances can be seen in Figure 4.18 where all of the cases start with an 80% porosity, 120 nm particle diameter, and concentration of 50 mg/ml. As mentioned before, the varying cases all include a varying porosity parameter plus the parameter mentioned on each curve in the figure. The pressure profiles increase for each case over the
Figure 4.10: Shows the mean pressure exhibited by varying $D_p$, by the equation 2.13 with an initial value of 70 nm, and compares it to the pressure plot given by the fixed $D_p$ of 70 nm for simulations utilizing a 3D mesh.

course of the compression. Results show that the pressures increase more rapidly for the varying parameter cases when compared to the fixed case. The varying $D_p$ and concentration cases exhibit larger final pressures than the varying porosity case. This is primarily due to the contribution of each specific parameter to the porosity variation for those simulations, which are dependent on porosity to affect $D_p$ and PG concentration. The biggest conclusion drawn from Figure 4.18 is that variation in each of the parameters over the course of compression causes relatively large changes in the pressurization of the fluid. This helps to create a fluid flow model that allows for large parameter changes to match the experimental properties of cartilage which
Figure 4.11: Shows the mean pressure exhibited by varying $D_p$, by the equation 2.13 with an initial value of 90 nm, and compares it to the pressure plot given by the fixed $D_p$ of 90 nm for simulations utilizing a 3D mesh.

is an expansion on the traditional fixed parameter models.

The pressure profiles of the varying parameter, 3D mesh simulations become interesting when compared to the experimental pressure profile from the Huang et al UCS experimental case [8]. Seen in Figure 4.19, the final pressure values of the viscous fluid simulations bound the values of the experimental sample compression case. What this bounding shows is that the current fluid only 3D mesh model may over predict the pressures exhibited by the cartilage fluid during compression, if the fluid has viscoelastic properties like proposed and in conjunction with rheological work performed by Mow et al. [17]. Although the model may be overpredict the
Figure 4.12: Shows the mean pressure exhibited by varying $D_p$, by the equation 2.13 with an initial value of 100 nm, and compares it to the pressure plot given by the fixed $D_p$ of 100 nm for simulations utilizing a 3D mesh.

Pressure values, the model has proven that viscosity cannot be ignored when looking at proteoglycan dispersion and migration throughout the cartilage sample. This is due to the drastic changes in magnitudes of fluid pressures exhibited by the water and PG aggregate fluid.

Figure 4.19 also shows that there may be some compressive resistance contribution given by the collagen and any confined proteoglycans, that occurs prior to the fluid pressurization. This idea is arrived at due to the non-zero initial fluid pressure during compression within simulations, which suggests that some other material within the cartilage is initially taking the load.
Figure 4.13: Shows the mean pressure exhibited by varying $D_p$, by the equation 2.13 with an initial value of 120 nm, and compares it to the pressure plot given by the fixed $D_p$ of 120 nm for simulations utilizing a 3D mesh.

**UCF Results**

To further look at how the fluid model reacts to changes in compression rate, the axi-symmetric model was subjected to the Huang et al UCF case where a compression rate of 1 mm/s was applied until a 5 % strain was achieved. For the UCF case, the axi-symmetric mesh was used because it offers a quicker result on a simulation than the 3D mesh. This was necessary since the UCF case is characterized by more time steps than the UCS case, resulting in a longer simulation time. The mean pressure and velocity results for this case can be seen in Figures 4.20 and 4.21.
Figure 4.14: A mean pressure versus time plot of the UCS case for the 80 % varying porosity case and the 120 nm varying $D_p$ with varying porosity case both utilizing the 3D mesh.

These figures show an increasing velocity and pressure during compression during a majority of the simulation. Average values of 767 MPa and 0.0157 m/s are seen throughout the compression. This is a significant increase from the base case of the UCS model where the mean pressure was found to be 0.317 MPa. It is also important to note that the porosity, particle diameter, sample size, and concentration were kept consistent compared to that of the UCS base case. The major drawback of this case is that in the figures there is an initial pressure and velocity impulse that occurs during the first several time steps. The impulse is characterized in the figures as high starting values of velocity and pressure that dissipate after a time of 0.005 s to
anticipated values for velocity and pressure. This impulse is primarily created by the large velocity gradient across cells seen at the first time step. This change in velocity is primarily caused by the initial change in cell geometries within the axi-symmetric mesh. Another error in the axi-symmetric simulations is a significant amount of noise exhibited by the mean velocity profile that propagates into the mean pressure profile. Due to these inaccuracies caused by the axi-symmetric mesh, it was necessary to test this compression test with the 3D mesh of the cartilage sample. Figure 4.22 shows a pressure profile of the UCF test case for the 3D mesh simulation. This figure shows a reduction in noise present in the pressure profile and a reduction in the initial impulse
Figure 4.16: UCS mean fluid pressure results that utilize the 3D mesh of cartilage samples at a fixed concentration of 50 mg/ml and a varying concentration that starts at 50 mg/ml.

at the start of the compression. Outside of the differences in the noise and impulse witnessed in the pressure profiles of each mesh, there is also a difference in the mean pressures values. The 3D mesh exhibits a mean pressure of 1025 MPa compared to the mean pressure of 767 MPa for the axi-symmetric mesh where spatial profiles, seen in Figures 4.23 and 4.24, verify these values. These high values of pressure also illustrate that the increase of fluid velocity associated with faster compression rates also start the impact of the porous inertia term, equation 2.6, within the Ergun equation. The increase in the value of the inertia term is due to its dependence on a velocity squared term, whereas the viscous effects, equation 2.5, are related to a velocity scalar term.
The increase in the compression rate of the UCF case compared to the UCS case is directly responsible for the increase in the velocity. In the UCS case, the velocity values seen in Figure 4.3, regardless of sample diameter, are minimal once squared and therefore minimizes the effects of the porous inertial term for this case. Mean velocity values were exhibited as 0.0166 m/s and 32 nm/s for the UCF and UCS cases. Since the velocity values are significantly higher for the UCF case, as seen in Figure 4.21, the squared velocity value used in the porous inertial term has a larger impact on the overall system compared to the UCS case. As mentioned in the porous media section of Chapter 2. To determine whether the 3D model or axi-symmetric models
Figure 4.18: UCS mean fluid pressure results that utilize the 3D mesh for a base case of porosity: 80%, $D_p$: 120 nm, C: 50 mg/ml and several other cases where these parameters are allowed to vary based on these initial values.

are accurate it would be necessary to obtain experimental fluid pressure results to compare against for this case. Since there is currently no experimental data for fluid pressure for the Huang et al. UCF tests, this case becomes more of an example of the shortcomings of the model and differences between the 3D and axi-symmetric meshes.
Figure 4.19: UCS mean fluid pressure results for a base case of porosity: 80%, $D_p$: 120 nm, C: 50 mg/ml and several other cases where these parameters are allowed to vary based on these initial values. These pressure profiles are compared to the UCS case of Huang et al [8].
Figure 4.20: UCF mean pressure results of the axi-symmetric simulation.
Figure 4.21: UCF velocity results of the axi-symmetric simulation.
Figure 4.22: UCF mean pressure results of the cartilage sample using a 3D mesh in the simulation.

Figure 4.23: UCF results at a middle time step, 0.005 s, of the mean pressure profile at the center of the 3D mesh across the diameter of the cylinder. The upper surface is the moving platen and the bottom is the fixed surface of the sample.
Figure 4.24: UCF results at a middle time step, 0.005 s, of the mean pressure profile of the axi-symmetric mesh across the radius of the cylinder. The upper surface of the figure is the moving platen, and the right face is the plane of symmetry about the cylinder.
CONCLUSION

Conclusions From The Results

There are two main takeaways from the results of this study. The first conclusion that can be taken is that the viscosity of interstitial fluid, created by the proteoglycan aggregates and subunits, cannot be neglected when creating models that recreate articular cartilage. This is drawn out by the fact that water, an extremely low viscosity fluid, exhibits minimal fluid pressures during sample compression. The proteoglycan aggregate fluid demonstrated a several order of magnitude higher pressure profile compared to the water UCS case. The fluid pressures exhibited by the significantly higher viscosity of the proteoglycan aggregate fluid are of the same order of magnitude as the pressures from the Huang et al. study [8] for similar compression rates, which was seen in Figure 4.19. The second point was that it was shown that the porous collagen matrix is capable of drastically varying fluid pressure within the system due to the flow resistance created by the collagen fibrils. Mean pressure values range between 3.4 and 0.34 MPa over a range of fixed porosity values of 60 and 80%. The diameter of collagen fibrils varies between 70 and 120 nm and results in a pressure range between 1.05 and 0.34 MPa.

Variations in the concentration of proteoglycans within the interstitial fluid also played a major role in the fluid pressurization. Proteoglycan concentration ranges between 50-100 mg/ml for experimental samples, but only the value 50 mg/ml had an associated viscosity profile. A 30 mg/ml viscosity profile, and an extrapolated 70 mg/ml profile was also used to result in a range of pressures between 0.147 and 0.68 MPa over the range of 30 and 70 mg/ml viscosity profiles.

Along with the concentrations of proteoglycans, the health also plays an important factor in pressurization of fluid within cartilage. The proteoglycan subunit
fluid exhibits a much lower mean pressure of 0.05 MPa compared to the 0.34 MPa pressure produced by the proteoglycan aggregate fluid. This suggests that degradation of cartilage, due to disease or injury, may lead to lower magnitudes of fluid pressurization within the system.

Although simulation pressures were found to meet the magnitudes of experimental pressures at the max compression values, there was a large portion of the simulations that overpredict the pressures compared to experimental values. Overprediction occurs because the fluid simulations don’t account for any portion of compressive loading taken by the collagen fibers. Simulations suggest that a portion of the solid may initially support compressive loads, which minimize initial fluid pressure. As compression continues the fluid supports a larger portion of the loading. This must be verified using a model that includes fluid-structure interaction.

**Future Steps**

Several future research studies will be necessary to advance fluid modeling of articular cartilage. The first is that a newer rheology study must be performed to look at higher concentrations of proteoglycans within interstitial fluid that match *in situ*. This study would also help to fill the gaps present in the previous rheology study done by Mow *et al.* [17]. The previous gaps in data are primarily due to the lack of precision rheometers during the previous study, and would thus benefit from a new rheological study.

Another study to be performed is to examine the porous collagen matrix that comprises articular cartilage. The collagen within the matrix is comprised of multiple fibrils of varying diameters, and fluid flow models show that the diameter variation within the matrix will cause large fluid flow fluctuations. Therefore, a more comprehensive study of the spatial distribution of the porous matrix would be
essential to fully document its’ effects on the cartilage during compression.

The porous matrix approximation is another aspect within modeling that needs to be further inspected. For this research an Ergun equation approximation was used to impact pressures. The Ergun equations haven’t been formulated to react to changes in porous media during simulations. These changes are the packing of collagen fibrils and decrease of porosity within the porous media during compression. As a future work it is necessary to validate the Ergun equations for changing porous media due to sample compression. The current fluid model is using algebraic relationships to change the porosity and $D_p$ due to the ease of relating volumetric changes in this manner, although a proper model may find a drastically different relationship.

It was shown that a viscous fluid model with a porous media approximation cannot fully resolve the response seen by cartilage during compression let alone relaxation. To create a fully responsive model, that is capable of being varied for changes in cartilage properties, a viscoelastic fluid that is contained within a porous and elastic solid media should be looked at. This addition of the elastic solid creates a solid-fluid interaction model. This type of model would still retain the viscosity dependence that was shown to be important while also adding a solid-like elastic response to the fluid and collagen fibrils. This elastic response is likely what’s missing from the current model to create a zero pressure while still maintaining the increases in pressure as the viscous flow resistance increases that is created by the viscous flow model. The addition of the solid elastic response would also cause the solid to initially support compressive loads, and the fluid would begin to pressurize as the compression increases.


