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Section 1

This project focuses on the validation of a new computational model for bovine intervertebral disc (IVD) joint level mechanics that was recently developed in Professor O'Connell's laboratory in the Department of Mechanical Engineering. Current computational methods of modeling stress and strain mechanics in the disc, specifically in the annulus fibrosus (AF), are very inconsistent because they are unable to reliably and accurately depict in situ AF fiber mechanics. These inconsistencies result in large variability in predicted mechanical behavior of the disc joint, making it near impossible to trust conclusions drawn about predictions of mechanical stability with simulated repair or degeneration.

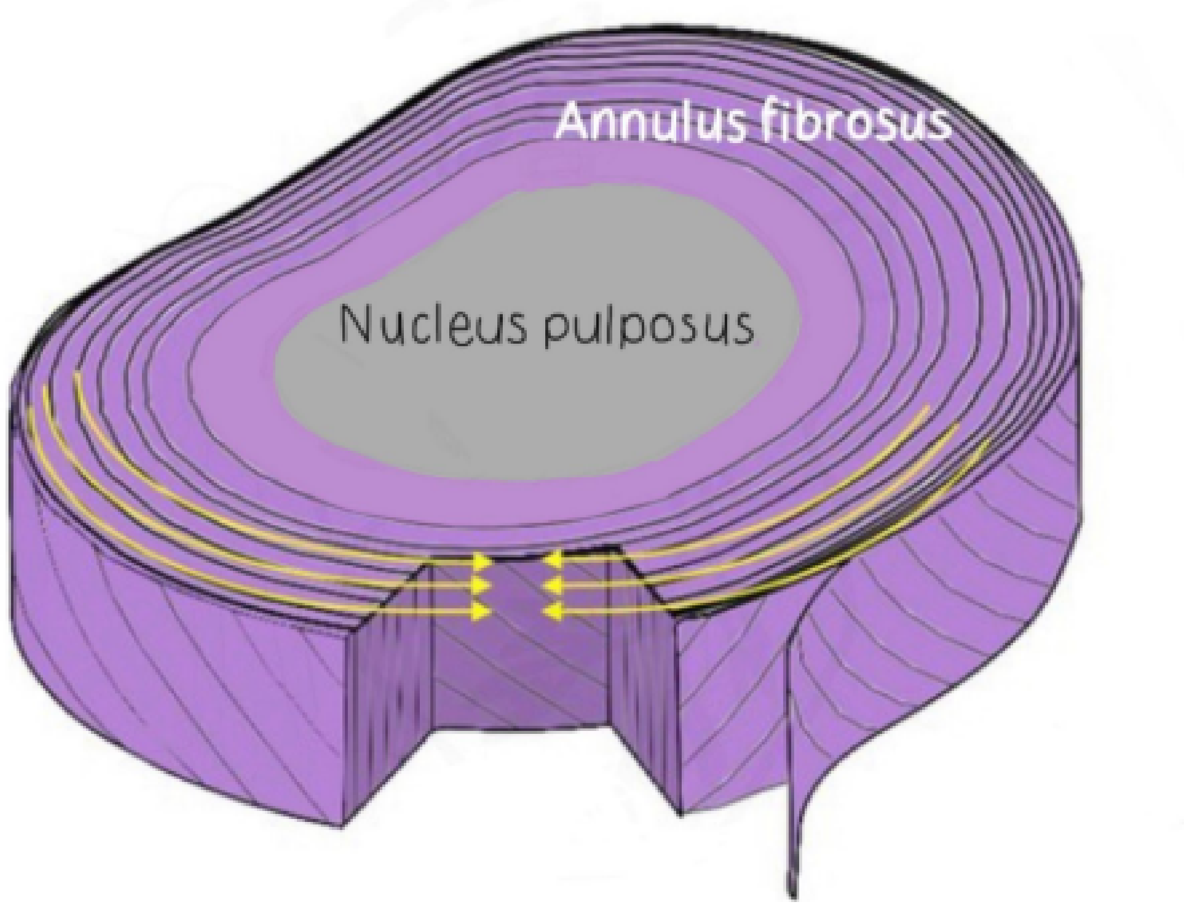
The O'Connell lab employed a new multi-scale modeling approach, where known sub-tissue properties about composition were used to calibrate tissue- and joint-level models. In this model fiber bundles in the AF were described as separate structures. Initial findings on the tissue-level model suggests that this approach greatly improves the accuracy of the model in being able to predict mechanical loading in complex conditions that are difficult to perform experimentally.

More recently, the O'Connell lab used the multi-scale structure based modeling approach to create a joint level model of the disc, which is more applicable to evaluating and predicting clinically relevant conditions. However, the model has yet to be experimentally validated. Thus, the objective of this project is to evaluate compression and torsional mechanics of the bovine intervertebral disc joint for model validation.

The potential benefit to the larger medical and scientific community this project poses is the ability to more comprehensively and accurately model joint level biomechanics of bovine discs. Bovine discs in particular are often used as a stand in for human discs in disc biomechanics studies, therefore making it important to understand and predict this tissue's behavior under different mechanical stresses accurately.

Section 2

The IVD is a soft tissue found between vertebrae that primarily gives the spine greater flexibility, and distributes mechanical loads[1]. The IVD consists of 2 main parts: the nucleus pulposus (NP) and AF[4]. The NP is a central, gelatin structure that is responsible for holding and moving water around to allow for flexibility[4]. The AF is a thick ring containing parallel collagen fiber bundles and elastin fibers that hold the NP together[4]. With back pain being the most common reason for people to seek medical attention, having a comprehensive understanding of the IVD is essential for the advancement of back pain treatment[2]. Bovine discs are often used as an animal model for intervertebral disc research because they are cheaper, more readily available, and subject to less variation than human discs. These benefits, in conjunction with the fact that bovine and human discs are very similar biochemically and mechanically, make bovine discs a good experimental stand in for human IVDs[3]. As such, bovine IVDs are a common choice for researchers. Thus, having a highly reliable and precise computational model to predict the mechanical behavior of bovine discs is important.



Finite element models (FEM) are useful computational tools that predict stress and strain distributions in complex fiber reinforced biological tissues, like the IVD[5]. However, when it comes to heterogeneous structures found in the IVD like the AF, current FEM technologies fall short by homogenizing the AF which leads to the omission of the effects of properties like osmolarity from the model[6]. Additionally, these current modeling techniques can't model subtissue level mechanics or structural changes to changes in mechanics directly[6].

This project's computational model addresses these issues by taking the heterogeneous nature of the AF into account by modeling the collagen fiber bundles as a separate material from the extra-fibrillar matrix instead of just part of a homogenous structure, which much more closely resembles the mechanical and biochemical properties of the IVD[6]. This new FEM has been experimentally validated on a tissue level, but has not been validated on a joint level yet[6]. The aim of this study is to experimentally validate this FEM using joint level mechanical testing. To do this, I will run a series of axial compressive, torsional, and simultaneous axial compressive and torsional tests on bovine motion segments and collect data, which I will then analyze against the predicted results from the model.

Section 3

This project will have 6 phases.

Phase 1: Sample preparation

The goal of this phase is to prepare bovine motion segments for mechanical testing. This includes removing excess musculature and soft tissues from the bovine tails, excising joint segments, and potting segments in polymethyl methacrylate (PMMA). Once potted, segments will be imaged using computed tomography or x-ray to measure disc height and disc area.

Phase 2: Preparing testing methods

The goal of this phase is to prepare mechanical testing methods. This includes becoming familiar with the MTS 858 MiniBionix hydraulic mechanical testing instrument, learning how to operate it, and testing spare motion segments to determine appropriate testing parameters.

Phase 3: Axial Compressive Testing

The goal of this phase is to test motion segments in axial compression. Motion segments will be subjected to a compressive stress of 0.5 MPa, with a loading rate and duration in accordance with the computational study. From these tests, load and displacement will be collected and compressive stiffness will be calculated and compared to the results of the computational model in the final phase.

Phase 4: Torsional Testing

The goal of this phase is to test motion segments in torsion. Motion segments will be subjected to a torsional stress, with a loading protocol in accordance with the computational study. From these tests, load and rotational angle will be collected and torsional stiffness will be calculated. This will be compared to the results of the computational model in the final phase.

Phase 5: Simultaneous Axial Compressive and Torsional Testing

The goal of this phase is to test motion segments in simultaneous compression and torsion. Motion segments will be subjected to a compressive and torsional stress, with a loading protocol in accordance with the computational study. From these tests, load, displacement, and rotational angle will be collected and compressive and torsional stiffness will be calculated. This will be compared to the results of the computational model in the final phase.

Phase 6: Data Analysis and Compilation

In this final phase, the experimentally collected data will be compared to the results of the computational model. To do this, the experimental and computational models data will be compared using a variety of techniques such as calculating the percent error, determining the r2 value, and creating comparative graphs among other methods.

In terms of supervision, I will be working with Shiyin Lim, who will be my day-to-day Graduate Mentor. We will have weekly meetings to discuss the project progress and any issues. I will also attend weekly lab meetings and present my research to Professor Grace O'Connell, my Faculty Mentor for this project. I will schedule meetings with Ms. Lim and Professor O'Connell to discuss data interpretation at the end of Phases 3-5 and give a formal presentation to the lab group at the end of the project. In between these meetings if I happen to need clarification or have questions, there is an open and ongoing dialogue between me and Ms. Lim, where I am encouraged to ask for help anytime I need it through text messaging and emails.

Section 4

Prior to this proposed experiment, I have worked and am currently working in UC Berkeley's O'Connell lab as a research apprentice under Shiyin Lim. I started working remotely with Shiyin in September 2020 and have been working about nine hours a week on her intervertebral disc joint level mechanics project. Last semester, I researched and presented relevant papers to help put together a research proposal, learned murine dissection techniques, collected data from over 350 images using ImageJ, and subsequently analyzed that data using Excel and Matlab. This semester I am going to be trained in bovine spine dissection which, in addition to data analysis, is essential for this project.

In regards to relevant coursework, I have taken Engineering 7 and Bioengineering 10, where I learned how to use Matlab and analyze data. I have also completed Physics 7a and Physics 7b, which provides fundamental concepts that are important for understanding the biomechanics in this project.

This study will be conducted in the O'Connell lab, of which Shiyin Lim will be supervising my work. Additionally, Dr. Grace O'Connell has given me permission to run this experiment in her lab. Finally, Minhao Zhou, the PhD student who created the model, has given me permission to run this experiment to test the accuracy of his computational model.

Section 5

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