Design of a Force-Controlled Cartilage Bioreactor

Midyear Report

FC Bioreactor
Jeffery Guo[1], Chanul Kim[2], Emilio Lim[2], Griffin Radtke[1], Sydney Therien[2]
Departments of Mechanical Engineering[1] and Biomedical Engineering[2]
Client: *Dr. Corinne Henak*
Advised by: *Dr. Corinne Henak* and *Dr. Paul Campagnola*
Teaching Assistant: *Patrick Dills*
University of Wisconsin – Madison
11 December 2023

Executive Summary

In this report, we summarize the midyear status of the design of a force-controlled cartilage bioreactor intended for our client, Dr. Corinne Henak. Osteoarthritis (OA), typically simplified as a disease characterized by the deterioration of articular cartilage, can be better understood as a biochemical alteration or imbalance in joint tissue. The Henak Lab and recent scientific literature have discovered a link between cartilage redox imbalance and osteoarthritis-like damage. The Henak Lab has also found time-dependency in the connection between cyclic mechanical loading and cartilage redox imbalance, but only over timescales on the order of seconds and minutes. Dr. Henak requires a force-controlled cartilage bioreactor capable of applying cyclic compressive loading to cartilage samples to better understand the relationship between cyclic loading over several days to weeks, cartilage metabolism (i.e., cartilage redox imbalance), and cartilage disease state (e.g., OA). To this end, the team has translated communicated client needs to engineering design specifications and designed a prototype force-controlled bioreactor that they will build, fabricate, and validate over the upcoming spring semester.

The design specification requires incubator compatibility, biocompatible force application and control, and meeting budget constraints. The bioreactor must fit in the Henak Lab's incubator and all its components must be able to withstand typical *in vivo* temperature and humidity that the incubator will replicate. The bioreactor must be able to withstand autoclave sanitation procedures. The bioreactor should be force-controlled, applying approximately 6 N of uniaxial compressive force to each cartilage sample, and the loading profile should be sinusoidal or triangular. The interface material between each cartilage sample and compressive pillar should be biocompatible and low friction. The total cost of the bioreactor must be less than $5000.

The overall prototype bioreactor design comprises a bioreactor casing which houses six compressive pillars with low-friction, biocompatible interfaces, six voice coil actuators (VCAs), a printed circuit board (PCB) for each VCA, a six-well sample dish tray, six plungers to interface the VCAs with the sample dishes, and a separate housing for the VCAs and other electronics. The bioreactor casing has been designed in SolidWorks, and it will be 3D-printed with Formlabs BioMed Clear V1, a biocompatible resin. The compressive interface material will be polytetrafluoroethylene (PTFE or Teflon). The bioreactor will use the Thorlabs VC125C/M VCA for force application. The current input for each VCA will be from a triangle wave generator PCB, provided by Professor Mark Allie from the UW-Madison Department of Electrical and Computer Engineering, that receives wall power from a medical grade CUI Inc wall adapter. Preliminary oscilloscope tests with the PCB have verified its ability to generate a roughly triangular 8.275 V output at a frequency of 2.63 Hz. The bioreactor will be fully fabricated and validated in accordance with the design specifications over the upcoming spring semester.

Table of Contents

Introduction

An estimated half billion individuals worldwide live with OA, causing significant detriment to quality of life and over $100 billion in annual direct & indirect costs [1]. While its expression varies, OA is often simplified as a general degradation of articular cartilage, although it is more properly understood as a biochemical alteration in synovial joint tissue. While symptom-based treatment for the disease is commonplace, treatment for the condition itself, due to its inherent complexity, is far beyond the current scientific horizon. That mentioned complexity arises from the variety of signaling pathways involved in OA progression—here, we will focus on cartilage metabolism, or redox balance, as a specific agent in OA [2].

Literature has identified cartilage redox balance, synonymous in the context/scope of this work with metabolism, as a potential cause for OA. Metabolic dysregulation—or imbalance in the reliance on energy-producing cellular pathways (i.e., glycolysis & oxidative phosphorylation)—is common in many disease types. Nonetheless, the causative agent of this imbalance in redox state within the context of OA remains unknown.

Dr. Henak – our client, an Assistant Professor in the Department of Mechanical Engineering – and her lab, in part, investigate the relationship between cartilage metabolism – used interchangeably within this context with redox balance – and disease state. Recent work both within her lab and the literature has postulated mechanical loading as this causative agent, with loading inducing metabolic dysfunction and OA-esque damage, as outlined within **Figure 1** [3], [4]. Further, via metabolic imaging techniques involving mechanical loading, this dysfunction has been demonstrated as a time-dependent phenomena. These imaging techniques, however, are limited to small timescales (i.e., less than one hour), thereby clearly necessitating a method by which to apply these mechanical insults over greater periods of time (i.e., several days to several weeks) [3]. Herein lies the primary focus of this project—to capture the full picture of cartilage metabolic dysfunction and its relation to OA, Dr. Henak seeks to investigate this balance over greater timescales.

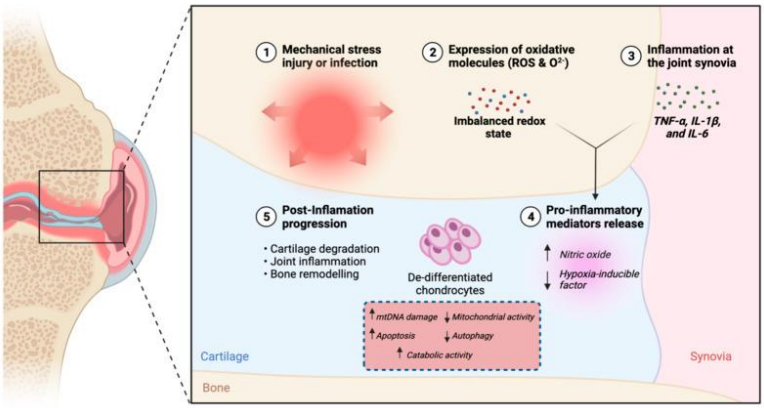


Figure 1. OA is mechanically mediated; with an applied mechanical load, metabolic (redox) state becomes imbalanced, resulting in pro-inflammatory cytokine release, cascading disease progression, and eventual cartilage degradation.

From that research focus arose the problem statement and overall client need for this project. That is, to characterize the long-term relation between mechanical loading, cartilage metabolism, and cartilage disease state, the Henak Lab requires a bioreactor to apply a controlled, cyclic, uniaxial compressive force to articular cartilage samples over long (i.e., hours, days, or weeks) timescales, as depicted within **Figure 2**. With that general client need comes several design specifications, briefly described below and more comprehensively discussed in a design specification table in **Appendix A**:

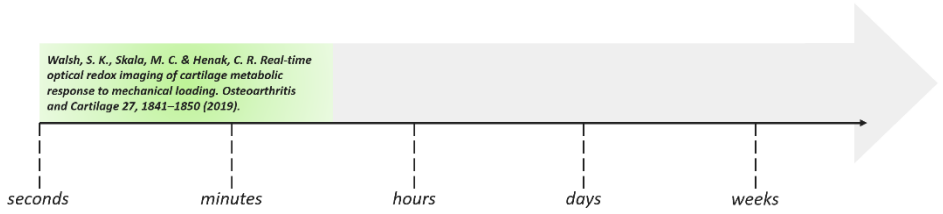


Figure 2. The Henak Lab has characterized the relationship between cartilage metabolic balance and loading on short timescales; the cartilage bioreactor is intended to fill this remaining timescale gap.

> Broadly, the bioreactor must meet three characteristic requirements: that is, it must apply the desired forces, must be incubator-compatible, and must remain within the allotted budget of $5000. Regarding the first, the client requires that the force output be both force-controlled (i.e., to avoid creep-related sample liftoff arising from the poroelastic nature of cartilage) and capable of outputting sufficient force to induce approximately 20% uniaxial compressive engineering strain, that the force profile – as previously mentioned – is cyclic with a triangular or sinusoidal profile (i.e., with a frequency of 0.1 – 10 Hz) to approximate in vivo loading, and that the material in contact with the cartilage (i.e., when in compression) is both low-friction and biocompatible. The second requirement is more straightforward: simply, the bioreactor must fit within the Henak Lab's incubator (20 x 21 x 25 in^3), operate within the incubator (i.e., humid and at 37° C), and capable of biosafety-relevant sanitation procedures (e.g., autoclave, UV, general ethanol cleansing, etc.) to avoid culture contamination.

With those design criteria determined, work was then able to begin on overall conceptualization and design.

Our design approach took inspiration from the literature. Prior work has been done in the field of tissue engineering to design a cartilage bioreactor comparable to the needs of our client, providing useful insight into potential conceptual designs, as depicted within **Figure 3** [5]. With an overall conceptualization of the components of a previously implemented bioreactor meeting client needs, the team opted to subdivide into three primary teams to best progress towards project completion: a housing and actuation team (Griffin and Sydney), an electronics team (Emilio and Jeffery), and a compressive interface team (Chanul). With those subdivisions made in the early weeks of the

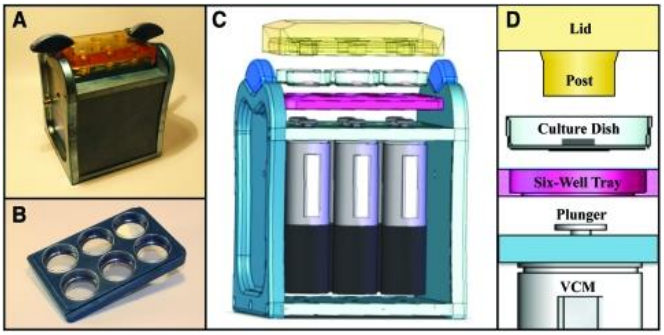


Figure 3. Prior work provides inspiration for the overall schematic build of a force-controlled cartilage bioreactor.

semester, work progressed over the course of the ME 351 period in every sub-team, yielding useful, tangible results with which to build off in the second term of senior design. That is, with careful research and review, components meeting every design requirement were selected, tested if possible, and included within the team's analytical prototype – as depicted in summary within **Figure 4** – with implementation of component selection to begin at the start of the ME 352 period. It should be noted that since this is a project for research, there are no applicable industry standards that are sufficiently relevant to include in this report. Instead, prior bioreactor designs such as that of Lujan et. al. and the Flexcell 5000C will be examined as relevant prior art.

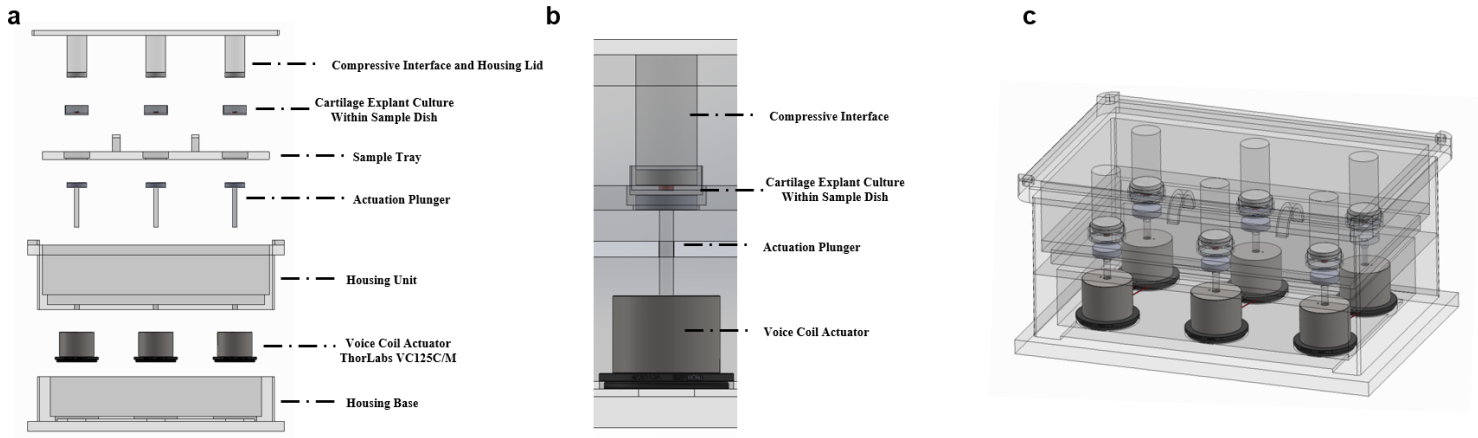


Figure 4. An overall depiction of our end-of-year analytical prototype. Exploded **[a]**, unit **[b]**, and trimetric **[c]** views are provided. Perspective **[b]** depicts active compression of the cartilage sample, with housing components left unlabeled to direct focus to active components within the bioreactor.

Actuation

Determining Necessary Force

To fabricate a bioreactor that could induce the strain requested by the client, some calculations were performed to approximate the magnitude of the force required. This magnitude approximation will also inform what type of actuator is best suited for this purpose. This was done by relating two equations for stress: the 1st Piola-Kirchoff stress, or engineering stress, and the Young's Modulus equation. The 1st Piola-Kirchoff stress (π) equation relates force sustained after deformation to its reference area:

$$\pi = \frac{F_{applied}}{A_{reference}} \quad (1)$$

Where:
$F_{applied}$ = Force experienced by material after it has been fully deformed [N]
$A_{reference}$ = Cross-sectional area of sample before sustaining deformation [m^2]

Since the cartilage samples can be approximated as linear and elastic for the purpose of magnitude estimation, a rearrangement of the Young's Modulus equation can be used that solves for the stress experienced by the sample (σ):

$$\sigma = E\varepsilon \quad (2)$$

Where (with respect to the axis of loading):
E = Cartilage's approximate Young's Modulus [MPa]
ε = Engineering strain experienced by sample [$\frac{mm}{mm}$]

By setting the two stress terms π and σ equal, this creates an equation that can be used to solve for $F_{applied}$:

$$F_{applied} = E\varepsilon A \quad (3)$$

All variables in Equation 3 have been given as specifications. For cylindrical samples with a Young's Modulus of 1MPa, a 6mm diameter, and experiencing 20% strain:

$$F_{applied} = 5.7 \text{ N}$$

Therefore, the team will use 5.7N as an approximation of a reference range of forces desired by the Henak Lab to apply to the cartilage samples while in the bioreactor. It is sufficient to produce a ballpark number with some approximations because error in this value can be corrected for during the calibration of the actuator with the circuit.

Actuation Mechanism Selection

Several different mechanisms of actuation were considered to produce this force output. Based on the Lujan et. al. design, [5], the first mechanism considered was a voice coil actuator (VCA) system. To perform a thorough analysis of the available options, hydrostatic, pneumatic, and closed-loop displacement control systems were also evaluated. Each of these mechanisms was researched and will be detailed in this section.

Voice Coil Actuators. VCAs are an electric and force-controlled mechanism of force application. When current is fed through the wire coil in the base, the wire coil interacts with the magnet assembly it is coupled to and produces a Lorenz force that thrusts the magnet assembly away from the base. In this way, force output is directly proportional to current input:

$$F = B \, x \, I \quad (4)$$

Where: [6]
F = Force [N]
B = Magnetic Flux Density [T]
I = Current [A]

VCAs are very precise since there are fewer places to experience frictional losses, such as those that might come from gear trains or surface-on-surface rubbing [7]. Oscillating systems—such as this bioreactor—are a common use for VCAs [6]. They are sold in a variety of shapes, sizes, and weights, so there would be little trouble finding one that could fit in the incubator. Two important parameters to consider in selecting a VCA are the force constant (how much force output is generated from 1A of current) and stroke (how far the magnet assembly can move). As with dimensions, VCAs come in a diversity of these properties. A VCA schematic can be seen in **Figure 5** below.

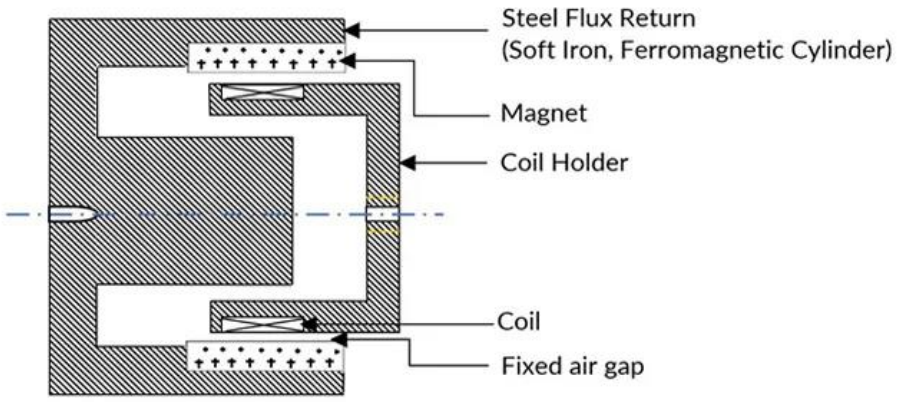


Figure 5. Diagram of a VCA with components labeled [8].

One clear downside of VCAs is their high cost. A single actuator for this application, depending on the dimensions, could cost between $500 and $1000+. Since one actuator per sample is required to ensure force control with cartilage's poroelastic creep behavior, this would become the largest area to dedicate the $5000 budget. Though theoretically, VCAs would fit all specifications, further investigation was made to mitigate the issue of cost.

Pneumatic Actuators. The motion of pneumatic actuators comes from compressed air being fed through a port in an airtight chamber, which thrusts a piston in the chamber forward. A rod attached to the piston transfers the force outside the chamber. To return the piston to its original position, either a spring or a second port that is fed compressed air causes the piston to move in the opposite direction. An example pneumatic actuator can be seen in **Figure 6**. Instead of being electrically powered, pneumatic actuators are powered by an external compressed air tank.

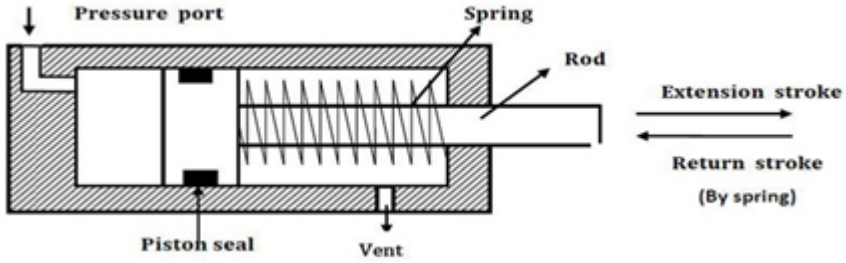


Figure 6. A general schematic illustrating how a spring-return actuator operates [9].

Pneumatic actuators are a good choice for situations where multiple actuators are required, as a single air tank can power multiple at once [9]. They also are cheaper than VCAs, in part because there are no electric components [10]. Whether they are more precise than VCAs differs from source to source [9] [10]. However, friction is generated between the piston seal and the pressure chamber. This creates losses that need to be accounted for during calibration. Even after mitigating this, long periods of operation would cause the piston seal to wear and the friction coefficient to change. Without a closed-loop control system that would give force readouts to a PID controller and modulate the pressure created in the chamber, this actuator would be subject to creep (especially at the high temperatures of the incubator) and lose the ability to output the correct force.

An additional consideration is whether the pneumatic actuator can resolve travel distances as small as is required by the bioreactor. In cartilage samples of 2mm height experiencing 20% strain, the total displacement of the sample's upper face will be 0.4mm. This means that a small amount of air that corresponds with moving the actuator 0.4mm forward would need to be supplied each cycle. There are few pneumatic actuators on the market that have 0.4mm within their stroke range, with the bottom of these ranges typically being much larger. Between frictional losses and stroke range limitations, moving forward with pneumatic actuation was decided against.

Hydrostatic Actuation. A hydrostatic actuator is like a pneumatic actuator in the sense that they both generate force from controlling air pressure in a vacuum chamber. Instead of deflecting a rigid piston, though, a hydrostatic actuator deflects a flexible membrane that pushes the sample into a compressive interface. This mechanism can be seen in **Figure 7** below:

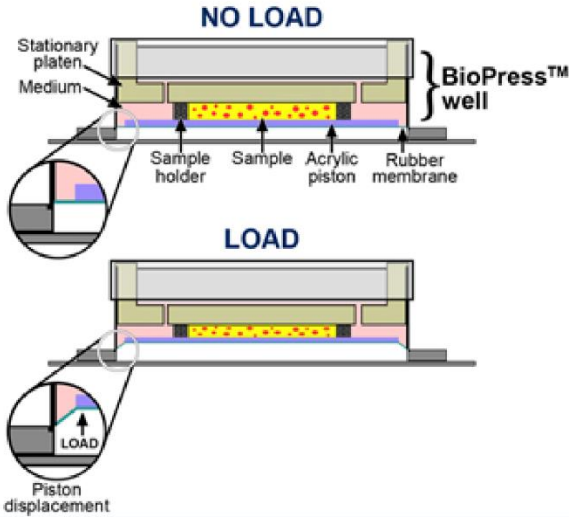


Figure 7. Flexcell's FX5000C compression system hydrostatic actuator in loaded and unloaded conditions [11]. Notice the membrane deflection in the circle on the left.

Force control is easily achieved here by control of membrane deflection. However, this system also has the issue of maintaining correct force output with sample creep. A closed-loop PID control system would be required to mitigate this, and this becomes expensive. Additionally, it cannot be guaranteed that membrane deflection would produce a uniform strain profile due to

its elasticity. Sample holders and membrane edges as well as the air inlet would be specific locations of inhomogeneity in the strain profile. According to client specifications, the compression should be uniform. This rules hydrostatic actuation out of consideration.

After investigating these two mechanisms as well as others that did not end up showing as much promise, it became clear that the best way to achieve force control for the purposes of this project was with a VCA. A design matrix for this decision can be found in **Appendix B**. Pneumatic or hydrostatic actuation would need a PID creep compensation system. This is not an issue with a VCA because a VCA will continue forward until it encounters a sufficient reaction force. In other words, the VCA will create 5.7N of force regardless of what is sandwiched between the magnet assembly and the compressive interface. This means that as the sample exhibits poroelastic behavior and creeps, it will consistently experience the same 5.7N it did on day one of the experiment.

Actuator Product Selection

After selecting voice coil actuation as the mechanism to produce the force, the search for a product that fit the specifications could begin. There are a few key parameters that were highly relevant in selecting the proper VCA, as well as several design considerations that conversations with industry experts were able to provide over the phone. First, the parameters will be discussed, then the design considerations. This will lead to the VCA selection.

Parameters

Force constant [N/A]. The force constant is a measure of how much force the VCA will output when supplied with one amp of current. A high force constant is desired because that means less power is required to operate the VCA and associated circuit. It is safer for the bioreactor operators to have minimized exposure to high voltage sources. Running the circuit at a lower power also means that it is less likely to fry.

Stroke [mm]. In any actuator, the stroke is the length at which the actuating arm extends during a cycle. In VCAs specifically, the stroke is how much the magnet assembly will displace from the coil when activated. If the stroke is too small, the desired deflection will not be fully created (though this is unlikely as it has been established that the deflection experienced by the samples will be around 0.4mm). If the stroke is too large, the small 0.4mm deflection may be too small to sufficiently resolve. The VCA could also be too large for the bioreactor if the stroke is too large.

Duty cycle [%]. In any circuit, the duty cycle measures for what percentage of the time the circuit is on versus off. While not expressly a property of VCAs, it was important to track potential actuator's performances at different duty cycles. The triangle wave circuit will have a duty cycle of 50%. If the circuit is later updated to something with a microcontroller, the duty cycle will be 100%. It is important that the VCA purchased operates successfully at both duty cycles at the temperature and humidity conditions in the incubator.

Maximum operating temperature [°C]. Due to the high temperature that the actuators will operate at, it is important to validate that the VCA can withstand this heat. According to the product design specifications, it must comfortably operate at 37°C.

Design Considerations

Horizontal translation. For a VCA to work, the coil and magnet assemblies cannot be attached. Products with a linear bearing down the center of the coil and magnet assemblies allow force to be generated along the axis without the coil bumping into the magnet. In VCAs without a linear bearing, additional reinforcements will be required to ensure that the movement is linear.

Tolerance. The typical tolerance in a VCA is about 10-15% of its force constant, according to the gentleman spoken to from Moticont Motion (a motion control company). This means that the force output may be different from actuator to actuator but should not change over the course of a single actuator's life in service. It is therefore possible to calibrate each actuator once they are ordered so that they produce the exact force output required. However, this means supplying each of the six VCAs with a slightly different current. This is doable but could make circuit design more challenging.

Magnet damage. Magnets used in VCAs create extremely precise force outputs as long as they aren't damaged. Damage could result from mishandling the voice coil or running it at too hot of a temperature. Damage should not result if the magnet experiences temperatures of less than 80°C. However, if a VCA is run at 100% duty cycle at near-maximum power in a 25°C environment, the coil would be ~120°C and the magnet would be ~80°C. Operating this VCA at incubator temperature (37°C) would damage the magnet. Therefore, sizing the VCA up so it doesn't run at maximum power will increase both the longevity and efficacy of the device.

Using these parameters and design considerations, four actuators from Moticont and one from ThorLabs were critically evaluated. A design matrix that details the deliberation can be found in **Appendix C**. In the end, the VCA from ThorLabs—VC125C/M—was selected. Specifications for VC125C/M can be found in **Table 1** below:

Table 1. Relevant design specifications for ThorLabs VC125C/M [12].

ThorLabs VC125C/M Specifications	
Force Constant	12.4 N/A
Stroke	12.7 mm
Coil Diameter	44.5 mm
Maximum Operating Temperature	230°F/110°C
Cost	$530.40
Linear Bearing?	No

The force constant is in an appropriate range and will be more efficiently powered than the other actuators. The stroke is 12.7mm, which should be small enough to resolve the force but large enough to be able to move the full extent of where the plunger needs to go between being on and off. This actuator is comfortably larger than the bare-bones specifications required, almost twice

as large. This will help protect the magnet from heat damage. Confidence that it can withstand the heat is further inspired by the maximum operating temperature of 110C.

One downside with the selected VCA is cost. It costs $530 for one and ThorLabs does not offer any sort of unit discount on higher volume orders. Another downside is the possibility for horizontal translation. It will be very important to fix this, as the plunger goes through a narrow hole in the tray. Brushing up against the sides of the tray wall could create friction, which would decrease the precision of the force applied. Adding a flexure could resolve this and will be investigated next semester.

Overall, the ThorLabs VC125C/M satisfies all design specifications in theory. One VCA has been ordered, and as soon as it arrives, testing can begin to validate the specifications in practice. This will be a focus of early next semester.

Interface Materials

Polytetrafluoroethylene (PTFE)

The bioreactor design utilizes VCAs to generate force. The force pushes the plunger and the sample containing a culture dish upward. A compressive pillar is used because it is necessary to counteract this force by applying compressive strain to the tissue. The material used for this pillar must be an appropriate interface material as it directly contacts cartilage tissue and media.

To find the interface material used in the bioreactor, several factors must be considered:

1. The material should withstand the warm and humid environment of the incubator. The bioreactor enters a culture incubator. It is typically maintained at 37°C and is a humid environment for cell cultivation, so the material must withstand this environment, and should not expand or deform due to temperature or humidity changes.
2. It must not be cytotoxic and should be chemically inert. As it directly contacts cartilage tissue and media, the interface material should not release or react with chemicals that could interfere with cell growth and proliferation during cultivation.
3. The material should be frictionless and not adversely affect the tissue sample due to the uniaxial compressive strain generated by the bioreactor. Mechanical compression-induced friction is a significant concern, and a material with a low friction coefficient is preferable to minimize the impact on the tissue.
4. The material must be sterilizable as it is used in tissue culture. Contamination of media and tissue in biological research is a severe issue, so the material should be able to withstand sterilization methods such as autoclaving at high temperatures and pressure.

Three materials were considered as candidates for the interface material: BioMed Clear Resin from FormLabs, Borosilicate glass (Pyrex), and Polytetrafluoroethylene (PTFE). BioMed Clear Resin, known for its biocompatibility and chemical inertness, is commonly used in cell and tissue culture research [13]. It also has a high melting temperature, allowing for sterilization through autoclaving, Ethylene Oxide, and gamma radiation [13]. However, BioMed Clear Resin is not frictionless and, crucially, is too expensive compared to other materials. Given the team's

budget of $5000, and considering that much of it must be allocated to the VCAs, BioMed is not the ideal material.

Borosilicate glass, commonly known as Pyrex, is a material frequently seen not only in laboratories but also in kitchens. It is sturdy, has a high melting temperature, and can be easily sterilized using autoclave. Being chemically inert, it is commonly used in laboratories to store reagents [14]. However, for our specific use, the material has a significant drawback: it is challenging to fabricate. The fabrication of such hard glass requires specialized equipment, which is rarely available in companies or schools, and outsourcing the fabrication does not align with the goals of this design class. Therefore, Borosilicate glass was excluded from our material selection.

Although there were several material candidates, the material that met the design criteria was PTFE. PTFE is chemically inert, nontoxic, and nonflammable. It also has a low coefficient of friction, resulting in less shear stress on the tissue [15]. The material has high-temperature resistance with a melting temperature of 635°F (335°C), making it suitable for autoclaving without any issues [15]. Previous research supports its suitability for biological research, especially in tissue culture applications.

In summary, PTFE emerges as the clear choice for our design, offering a blend of essential characteristics that not only meet but exceed our criteria, ensuring a reliable and effective solution for our intended applications.

Fabrication Plan

PTFE will be purchased from McMaster-Carr. The company sells PTFE in the form of a rod, making it the best choice for our pillar design and eliminating the need to machine PTFE into a cylindrical shape for a pillar. The PTFE rod purchased from McMaster will be cut into six pieces using a band saw, and then the ends will be machined flat and smooth using a lathe. Additionally, a path for the screw will be created using a lathe and drill. The top plate will be precisely crafted using a mill to create six holes for attaching the PTFE pillars. The top plate and PTFE pillars will be fastened together using button head socket cap screws along with flat washers.

Electronics

General Concept

To drive a VCA, a circuit must be designed that can change current according to the specifications of the VCA. The general idea of the circuit will consist of an input source from a microcontroller or signal generator to produce the desired wave profile that feeds into a series of amplifier circuitry and then outputs into VCA. The general schematic of the circuit can be seen below in **Figure 8**. V1 represents the input source, U1 represents a power operational amplifier with R1 and C1 being interchangeable and variable according to the circuit needed, and V_{out} represents the output connection to the VCA. U1 needs to be a power operational amplifier as it needs to be able to output a high voltage and high current to drive the voice coil actuator at the desired force.

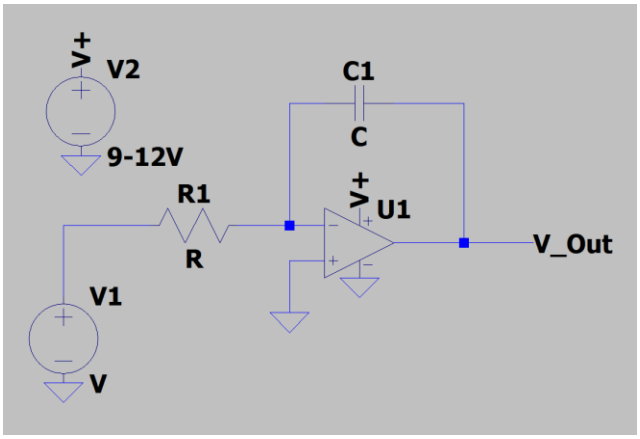


Figure 8. General circuit schematic to drive the voice coil.

The ideal wave profile would be similar to a modulus sine wave. This is shown in **Figure 9**. With that said, Dr. Henak would be open to accepting a triangular-like wave with a frequency output of 1Hz. This can be achieved in two ways. The first being directly using a signal generator or microcontroller to obtain a triangle or sine wave profile. The second would be using a DC supply from a wall adapter to power a series of amplifier circuitries. The wave profile and amplification can be effectively changed by changing the resistor and capacitor combinations on the amplifier circuitry.

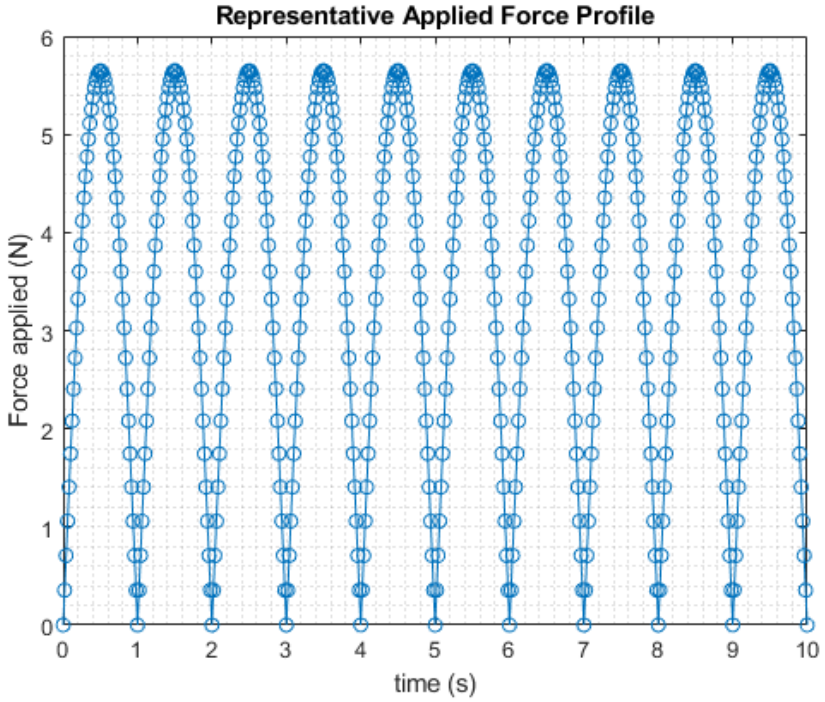


Figure 9. Ideal wave profile of a modulus sine wave.

Circuit Board

The initial idea on making a circuit that has a variable current or voltage depended on changing the resistor value through a programmable rheostat. This would effectively create a

change in current which would drive the VCA. However, this method would be very tedious and require a lot of programming of the microcontroller. Varying current was then investigated as a solution. One method would be through an H-bridge where it acts like a transistor, switching the circuit on and off at a high frequency. The H-bridge would receive a DC input, where the H-bridge would output a sinusoidal wave. This method, however, would not be possible without a feedback loop from a load cell and a current regulator. Due to the nature of having a feedback loop and a load cell, the overall price of the electronics side would become increasingly costly. In addition, the programming and circuit setup would require a different housing design to accommodate the different positions each component will need to be. To tackle this problem, an in-house circuit board is therefore ideal as it is compact and has the possibility and capability of producing different wave profiles.

To make a circuit board that caters to our needs, the team worked closely with a professor from the biomedical engineering department, Dr. Amit Nimunkar, and a professor from the electrical engineering department, Dr. Mark Allie. Since Dr. Allie had a board in hand that can generate triangle waves, we decided to move forward using a DC adapter with different resistor-capacitor values. The triangle wave generator is soldered onto a PCB board using various components such as resistors, potentiometers, capacitors, and power amplifiers. The board is also powered through a wall adapter, capable of outputting up to 15V, instead of using a signal generator or microcontroller. This can be seen in **Figure 10** below with a different number of functions and resistors-capacitor combinations. The power input utilizes a wall adapter that outputs a peak DC voltage of 15V. Then by changing the resistor values, we can generate and output 9, 10, 11, and 12V, respectively. This can change by varying the resistor soldered on the PCB. Following that, we can effectively change the amplitude and frequency by changing the value of the potentiometer. The amplitude potentiometer can vary between 0-1V of the set DC value, and the frequency potentiometer is able to go as low as 0.1Hz, up to 20Hz. The output will be connected to the voice coil actuator, but as seen below, a resistor is hooked up for ease of testing.

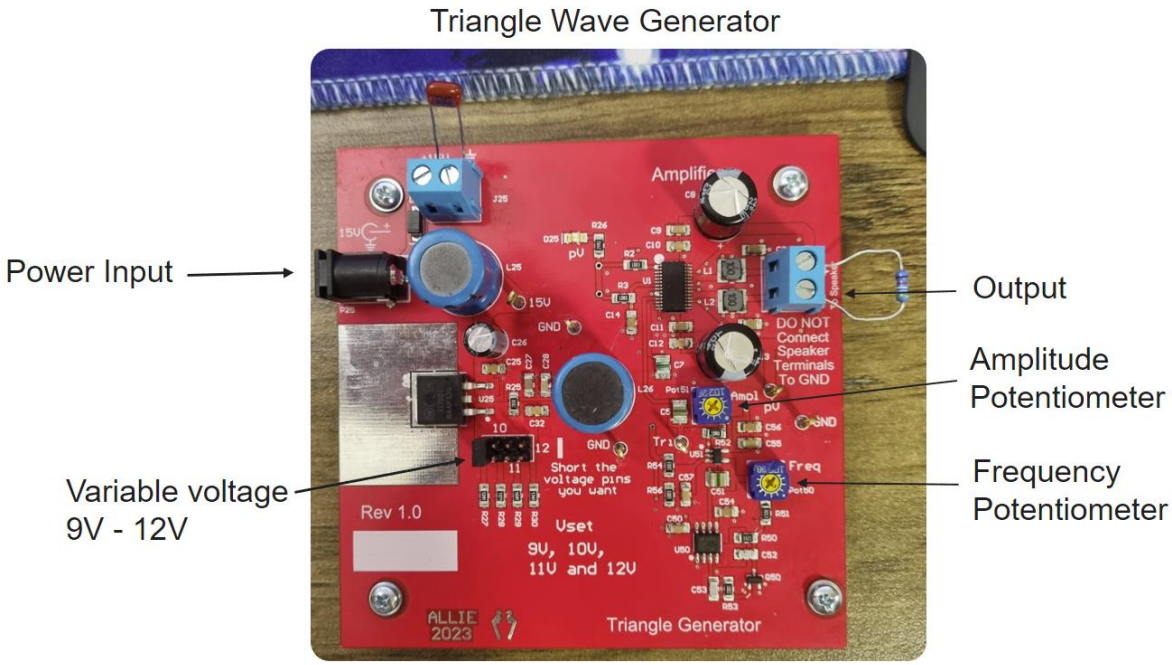


Figure 10. PCB board designed by Dr. Mark Allie.

Testing and Results

After testing the PCB board using an oscilloscope, the results obtained are shown below in **Figure 11**. It was noted that the wave profile is similar to that of a triangle wave but looks more like a capacitor's charging-discharging wave as the peaks are not sharp but smooth. It was also observed that the frequency of the wave is 2.63Hz with an amplitude of 8.73V.

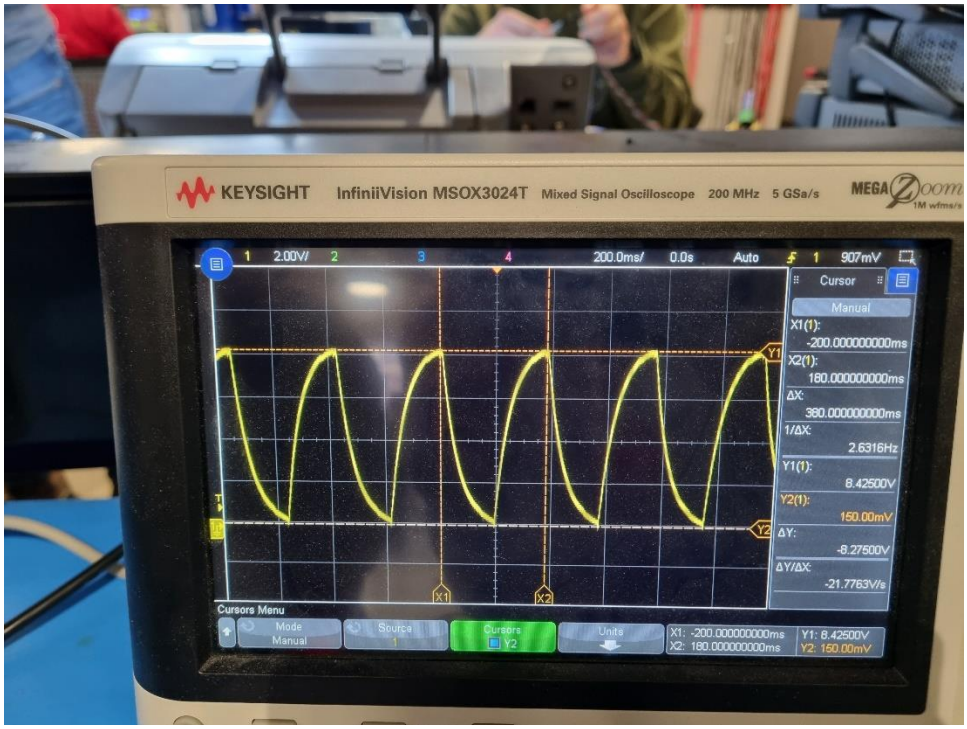


Figure 11. Wave profile observed when hooked up to oscilloscope.

While the frequency was within the requirements of 0.1-10Hz, we were not able to obtain a frequency lower than 2Hz as the circuit board automatically turns off below 2Hz. This is due to the safety feature built into the resistors and amplifiers to protect against any damage to the circuit components. To bypass this safety feature, an older model of resistors and amplifiers will need to be purchased and implemented to obtain a frequency of 1Hz.

Housing

With the actuating mechanism and device selected, a housing system could be developed that integrated all the bioreactor's components. Reexamining the exploded view of the prototype (**Figure 12** below) will provide an effective structure for illustrating the purpose of the housing's individual components.

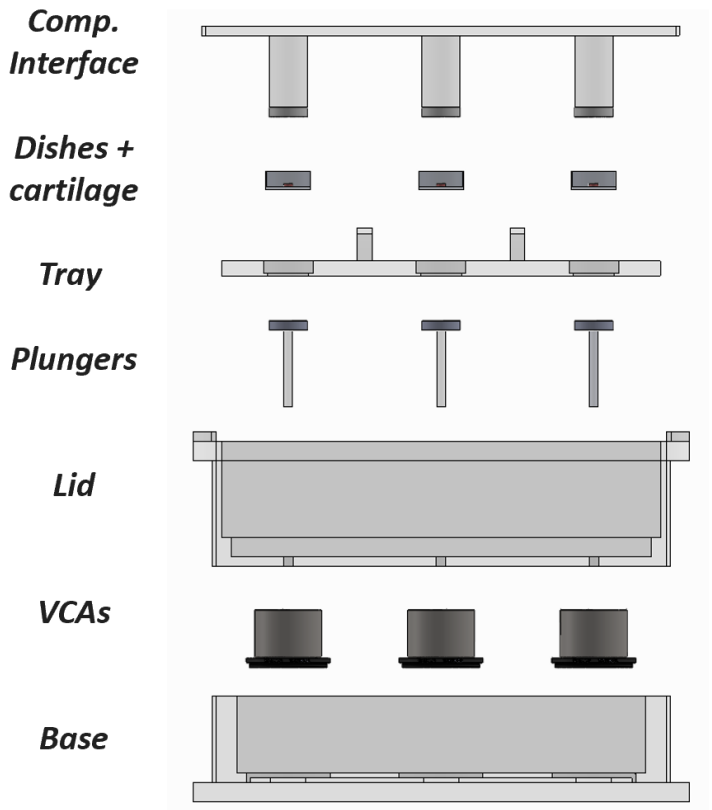


Figure 12. Exploded view of the bioreactor with its components labeled.

The housing base includes the actuators and electronics and is kept isolated from the rest of the bioreactor. This is to mitigate exposure to the humid bioreactor environment, as well as to isolate the electronics from the cartilage samples to minimize contamination. Future edits may be made to isolate the base more by adding a seal. The housing unit is the experimental chamber where the actuation will transpire. Future edits to the unit may involve opening up the sides to more freely interface with the humidity and to add holes for culture media replenishment.

The culture dishes which house cartilage samples rest in pits in a tray. The bottom of each pit has a cutout that is just wide enough for a plunger that is connected to the VCAs to pass through, connect with the underside of the culture dish, and propel it upward into the compressive interface. When the experiment is over, all samples can be removed easily at once by removing the compressive interface housing lid, grabbing the two handles on the sample tray, and lifting. Future edits will include a mechanism to latch down the compressive interface housing lid to prevent it from lifting off with actuation of the samples.

The housing will be 3D printed with Biomed Clear V1 resin, which is biocompatible. Even though nothing in the housing will touch the samples, it should still be ensured that exposure to contaminants is minimized.

Conclusion

To enable effective research on cartilage metabolism over longer time scales (i.e., several days to weeks), Dr. Corinne Henak has requested the design and fabrication of a force-controlled cartilage bioreactor that applies cyclic compressive loading. To serve Dr. Henak's needs, the team has designed a prototype bioreactor consisting of the housing and all its components (e.g., compressive pillars with low friction, biocompatible interface, plungers, electronics casing) and outlined circuitry to drive the VCAs; the current design satisfies all design specifications and remains under the $5000 budget. The prototype bioreactor will consist of a 3D-printed BioMed Clear V1 casing which houses six compressive pillars with PTFE interfaces, six Thorlabs VC125C/M VCAs, PCBs, a six-well sample dish tray to provide ease of sample retrieval, six plungers to interface the VCAs with the sample dishes, and a separate housing to better isolate the VCAs and other electronics from the conditions in the incubator and autoclave. Preliminary oscilloscope tests on the provided triangle wave generator PCB verified its ability to generate a roughly triangular 8.275 V output at 2.63 Hz. Into the next semester, the team aims to finalize and fabricate the CAD housing schematics, machine the PTFE compressive interfaces and configure them within the housing, update and finalize the circuitry and electronics, and validate the force output, determining appropriate custom inputs with Henak Lab load cells.

Appendix A: Design Specification

Table A-1: Client needs (i.e., customer requirements) and engineering design specifications for the force-controlled cartilage bioreactor.

Client Needs					
Client Need Statement					
To investigate the relation between cartilage redox balance and disease state, the Henak Lab requires a method of applying physiologically relevant mechanical stimuli (which is known to influence said redox state) to articular cartilage samples over the long-term; to meet this need, Dr. Henak has requested the fabrication of an incubator-housed device capable of replicating in vivo compressive stimuli profiles over the desired timescales.					
List of client needs (in their words)					
Low-to-no friction on contacting pillar surface					
Linear actuation applying ~20% strain to 6mm x 2mm (diameter x height) cartilage samples					
Constant force, not necessarily constant strain, applied across all samples					
Device must be capable of providing a variety of force profiles					
Incubator-compatible					
Specification description	**Target**	**Unit**	**Test method**	**Rank**	**Met**
Category 1: Device Function					
Device to apply & control linear actuation with controlled force capable of actuating compression mechanism	>25	N	Validate manufacturer specifications with testing	Must	
Induces 20% strain in (idealized) cartilage samples via uniaxial tensile stress	0.2	mm/mm	Use in-device load cell to determine deformation	Must	
Sufficient device actuation to allow for removal of sample dish	10	mm	attempt removal of sample dish	Must	
Low-friction compression/interface with cartilage sample	0.1	-- (coefficient of friction)		Must	

Category 2: Incubator and environment					
Fit within incubator	(20 x 21 x 25)	inch	place fully fabricated box into incubator / measure	Must	
Able to withstand laboratory-grade sanitation procedures	---	---	Review of individual electronic technical specifications prior to use	Must	
Electronic components of actuator withstand incubator's simulated in-vivo environment	---	---	Review of individual electronic technical specifications prior to use	Must	
Cords of electronic components may be wired to external power sources	---	---	review of cord diameter and quantity	Must	
Category 3: Additional Functions					
Modular compressive pillar attachment (i.e., to allow for 6, 12, 24, etc. well plates to be used)	---	---	N/A	Nice-to-have	
Modular compressive pillars that are different shapes (e.g., indentors)	---	---	validate that the actuator applies the same force to the samples	Nice-to-have	
Re-feeding mechanism (i.e., to change sample media automatically within incubator)	---	---	N/A	Nice-to-have	

Appendix B: Actuation Mechanism Design Matrix

To investigate the differences in the three actuator types that the team believed showed the most promise for creating the necessary force, a design matrix was made. Each actuator type—voice coil, pneumatic, and hydrostatic—was evaluated for cost, displacement, force output, force control, and general size and weight (footprint).

Voice Coil:

Cost	$520 / voice coil; not factoring in cost of current modulation/control
Displacement	12.7 mm stroke
Force	12.4 N/A force constant Peak continuous force: 15.5 N
(Force) Control	F = B x l – direct control over force input via Lorentz Force/Effect (i.e., current dictates for
Footprint	1.06 lbs; 2.2" base diameter

Summary: Excellent control over force; cost would limit number of samples. Approach validated in literature.

Pneumatic:

Cost	Waiting on quote – presumably far cheaper than voice coil due to constituent parts
Displacement	Customizable (12.5-300 mm)
Force	Reported linear relation between pressure & force: Push = DeltaP * 67.7; Pull = deltaP*60
(Force) Control	Air pressure regulation; need to compensate for frictional losses in shaft (~2% of force, according to company)
Footprint	~0.4 kg, depending on stroke; 14.3 mm base diameter

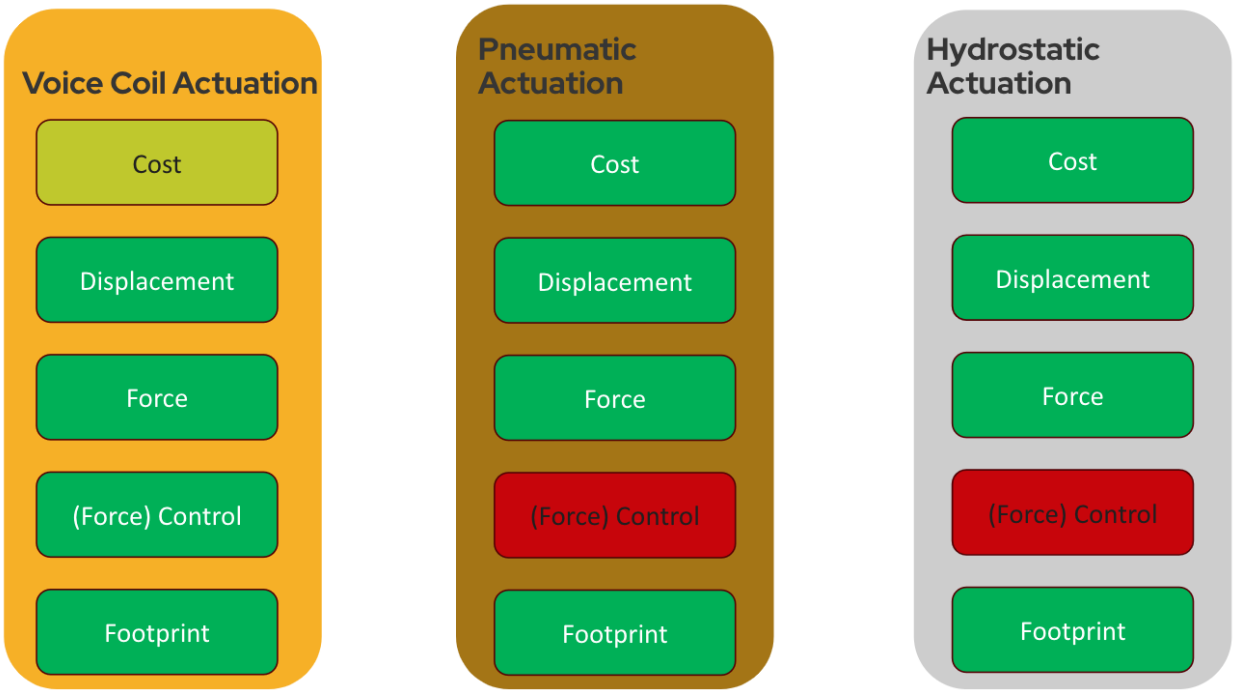
Summary: Control over force, given factor of friction (which would vary over time), would be difficult.

Hydrostatic:

Cost	Waiting on quote. Only one source of pressure control needed for membrane deflection, so presumably relatively inexpensive.
Displacement	Customizable (via changing deflection of membrane).
Force	Control via deltaP.
(Force) Control	Control over actuation is complex – requires accurate membrane deflection model in response to pressure change (which will also require modulation, similar to pneumatic). Attaching sample to flexible membrane could also be challenging.
Footprint	

Summary: Precise force control may be difficult, given variance in membrane deflection. Approach validated in literature & commercial application.

After examining how each actuator performed in each category, a definitive ranking emerged. Since proper force control is a high-priority specification, the VCA was selected despite the high cost.



Appendix C: Actuator Product Design Matrix

After selecting VCA as the actuation mechanism, a product could be selected. Four from Moticont and one from ThorLabs were evaluated. The Moticont products were suggested by a Moticont engineer over the phone and are as follows:

1. GVCM-025-038-01: a standard VCA that should hit all specifications appropriately.
2. GVCM-051-025-01: a sized-up VCA that costs more but may be a safer choice.
3. LVCM-032-025-02: a VCA without the linear bearing that Moticont plans on launching as a GVCM model in the next month, would have to wait to order. Will have an output between options 1 and 2.
4. DDLM-038-051-01: a direct drive linear motor (DDLM) which is powered by VCAs.

These Moticont actuators were contrasted with the ThorLabs product that seemed to fit the specifications, VC125C/M. The actuators were evaluated on these five criteria:

1. Force constant: how little current we can use to power it
2. Degrees of freedom (if coil is fixed): “shaky” magnet assembly or not
3. Resistance to heat: high continuous force/larger
4. Availability: could we order it tomorrow
5. Cost: single order + five at a smaller unit price

The properties of each actuator was assigned a color based on a red-green scale that contrasted its value to the other products. The matrix is shown below:

	ThorLabs	Medium GVCM	Large GVCM	Small (G)LVCM	DDLM
FC	12.4 N/A	9 N/A	6.9 N/A	3.9 N/A	7 N/A
DoF	3	1	1	1	1
Heat Tol	324g / 13.5N	102g / 11N	320g / 23.5N	127g / 9.3N	280g / 14N
Availability	now	now	now	~1 month	now
Cost	$3120	$5101	$4972	~$5000	$3413

Even though the ThorLabs actuator will have issues with horizontal translation that will need to be rectified later, it is the cheapest and fits all the other specifications well. As such, it was selected for the bioreactor.

References

[1] E. Yelin, S. Weinstein, and T. King, "The burden of musculoskeletal diseases in the United States," *Semin. Arthritis Rheum.*, vol. 46, no. 3, pp. 259–260, Dec. 2016, doi: 10.1016/j.semarthrit.2016.07.013.

[2] Q. Yao *et al.*, "Osteoarthritis: pathogenic signaling pathways and therapeutic targets," *Signal Transduct. Target. Ther.*, vol. 8, no. 1, Art. no. 1, Feb. 2023, doi: 10.1038/s41392-023-01330-w.

[3] S. K. Walsh, M. C. Skala, and C. R. Henak, "Real-time optical redox imaging of cartilage metabolic response to mechanical loading," *Osteoarthritis Cartilage*, vol. 27, no. 12, pp. 1841–1850, Dec. 2019, doi: 10.1016/j.joca.2019.08.004.

[4] M. H. Mohd Yunus, Y. Lee, A. Nordin, K. H. Chua, and R. Bt Hj Idrus, "Remodeling Osteoarthritic Articular Cartilage under Hypoxic Conditions," *Int. J. Mol. Sci.*, vol. 23, no. 10, p. 5356, May 2022, doi: 10.3390/ijms23105356.

[5] T. J. Lujan, K. M. Wirtz, C. S. Bahney, S. M. Madey, B. Johnstone, and M. Bottlang, "A novel bioreactor for the dynamic stimulation and mechanical evaluation of multiple tissue-engineered constructs," *Tissue Eng. Part C Methods*, vol. 17, no. 3, pp. 367–374, Mar. 2011, doi: 10.1089/ten.TEC.2010.0381.

[6] M. Wilson, "What is a Voice Coil Actuator?," Machine Design. Accessed: Dec. 11, 2023. [Online]. Available: https://www.machinedesign.com/mechanical-motion-systems/article/21278883/tsn-fueled-automation-amps-up-the-ev-value-chain

[7] "Voice Coil Actuators." Accessed: Dec. 11, 2023. [Online]. Available: https://www.thorlabs.com

[8] H. Magnetech, "VOICE COIL ACTUATORS VS MOVING MAGNET ACTUATORS," Magnets By HSMAG. Accessed: Dec. 11, 2023. [Online]. Available: https://www.hsmagnets.com/blog/voice-coil-actuators-vs-moving-magnet-actuators/

[9] C. Dynamics, "How Pneumatic Actuators Work," Cowan Dynamics. Accessed: Dec. 11, 2023. [Online]. Available: https://www.cowandynamics.com/blog/how-pneumatic-actuators-work/

[10] SEMCOR, "How Pneumatic Actuators Work | Pneumatic Actuator Uses & Applications," SEMCOR. Accessed: Dec. 11, 2023. [Online]. Available: https://www.semcor.net/blog/advantages-of-pneumatic-actuators/

[11] "FX-5000C™ Compression System." Accessed: Dec. 11, 2023. [Online]. Available: https://flexcellint.com

[12] "Thorlabs - VC125C/M Voice Coil Actuator, 12.7 mm Travel, SM2 External Thread, Metric." Accessed: Dec. 11, 2023. [Online]. Available: https://www.thorlabs.com

[13] H. B. Musgrove, M. A. Catterton, and R. R. Pompano, "Applied tutorial for the design and fabrication of biomicrofluidic devices by resin 3D printing." bioRxiv, p. 2021.11.23.468853, Mar. 28, 2022. doi: 10.1101/2021.11.23.468853.

[14] M. Bengisu, "Borate glasses for scientific and industrial applications: a review," *J. Mater. Sci.*, vol. 51, no. 5, pp. 2199–2242, Mar. 2016, doi: 10.1007/s10853-015-9537-4.

[15] E. Dhanumalayan and G. M. Joshi, "Performance properties and applications of polytetrafluoroethylene (PTFE)—a review," *Adv. Compos. Hybrid Mater.*, vol. 1, no. 2, pp. 247–268, Jun. 2018, doi: 10.1007/s42114-018-0023-8.