Design of a Force-Controlled Cartilage Bioreactor

FC Bioreactor

ME 352 | Final Presentation

Client & ME Faculty Consultant: *Dr. Henak*

BME Faculty Consultant: *Dr. Campagnola*

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Agenda

Introduction

Motivation
Initial Problem Statement
Guiding Research
Client Need and Design Specifications

Final Design

Housing
Actuation

Conclusions and Recommendations for Future Work

Introduction

Motivation

Initial Problem Statement

Guiding Research

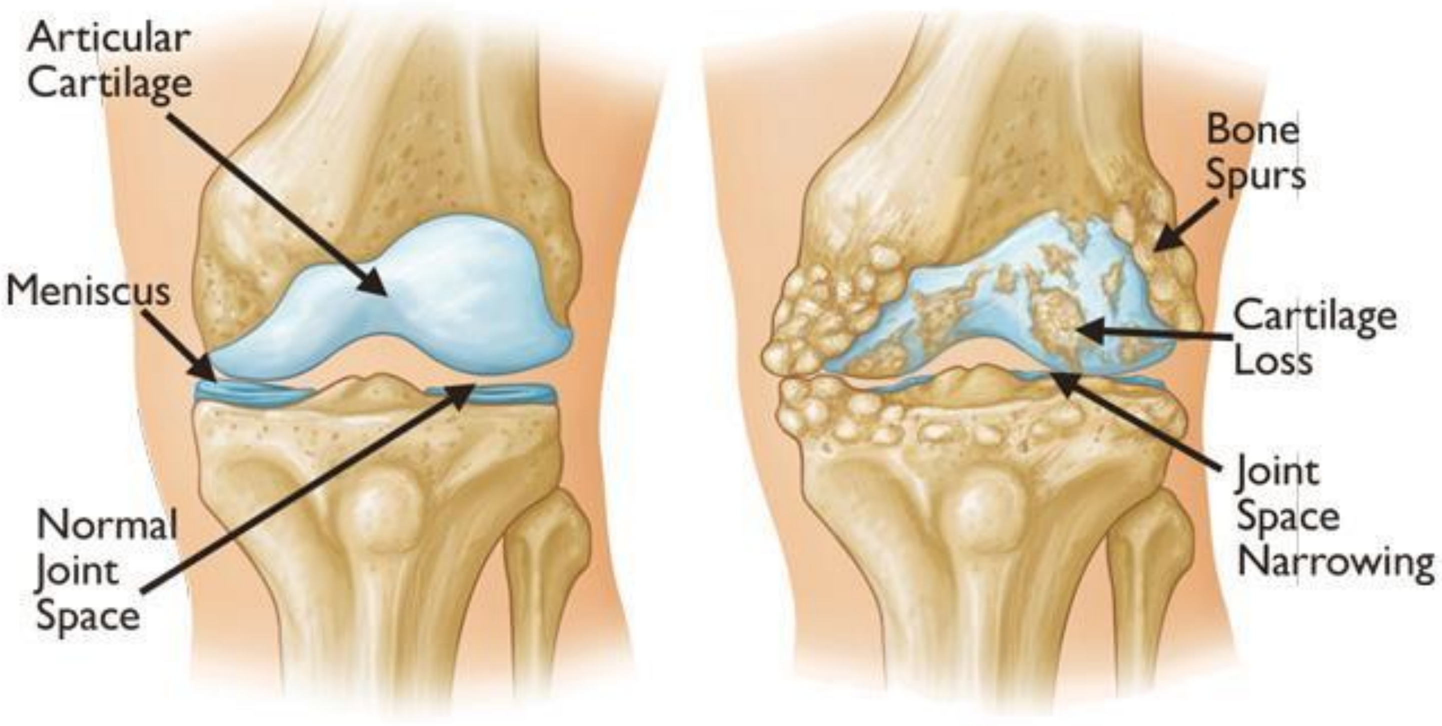
Client Need and Design Specifications

A look into the global impact and background of osteoarthritis (OA)

Osteoarthritis (OA) impacts 7% of the global population.

More than 22% of adults older than 40 are estimated to have knee OA.

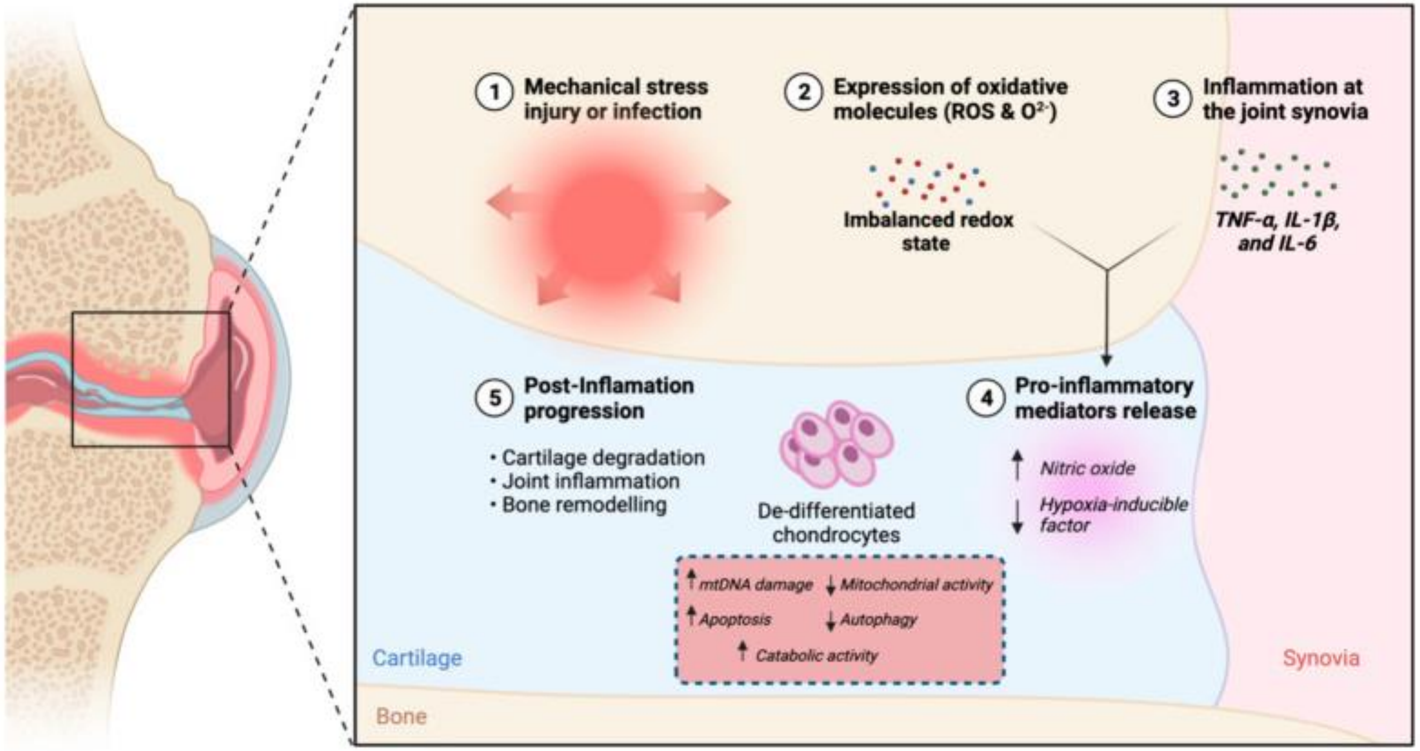
The mechanisms underlying OA disease progression remain largely unknown



Depiction of cartilage degradation in knee OA.

[1]

Cartilage disease state is mechanically mediated

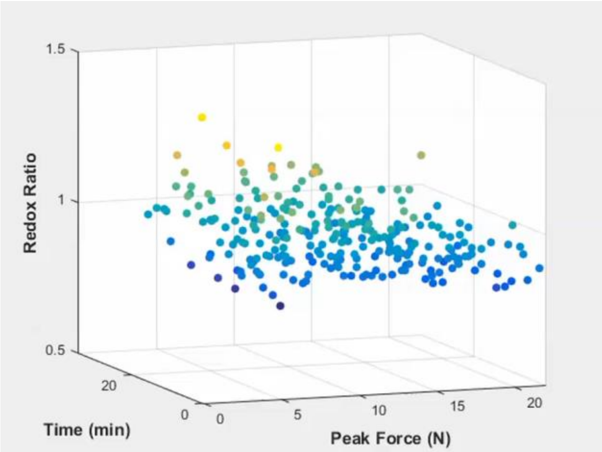


Mechanical loading has been implicated in metabolic dysregulation, which in turn plays a significant role in OA progression.

Mechanical Loading $\xrightarrow{?}$ **OA**

[2]

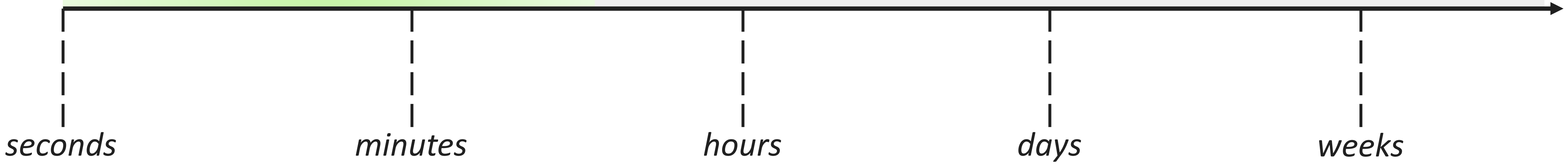
The long-term metabolic response of cartilage to loading has not been characterized



Walsh, S. K., Skala, M. C. & Henak, C. R. Real-time optical redox imaging of cartilage metabolic response to mechanical loading. Osteoarthritis and Cartilage 27, 1841–1850 (2019).

The Henak Lab has characterized the metabolic response to mechanical loading on short timescales.

To acquire the full history of how mechanical loading can induce OA, <u>greater timescales must be investigated</u>



[3]

The Henak Lab investigates the relationship between cartilage metabolism and disease state

To research the link between long-term mechanical loading and cartilage metabolic balance, **Dr. Henak has requested a device capable of applying cyclic loading* to a cartilage explant culture over several days or weeks.**

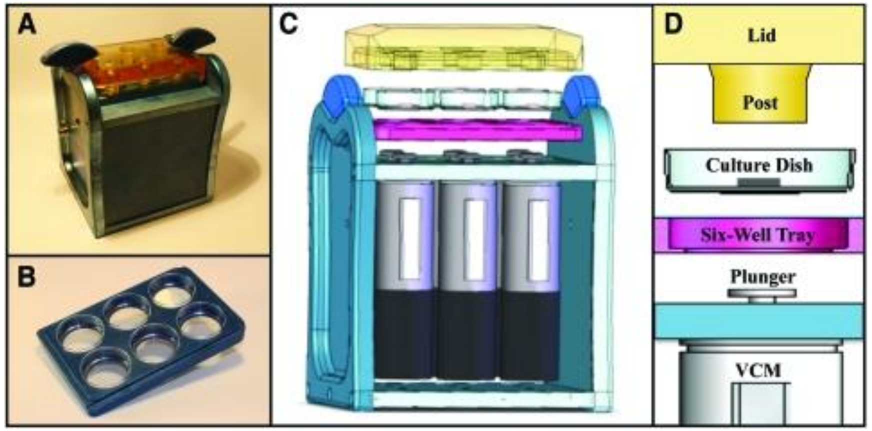
*Due to the poroelastic properties of cartilage, this loading must be force-controlled to avoid sample lift-off.

Industry and literature guided work

Industry

Not relevant – displacement-controlled or fail to apply uniaxial stress

Literature



1.

Lujan, T. J. *et al.* A novel bioreactor for the dynamic stimulation and mechanical evaluation of multiple tissue-engineered constructs. *Tissue Eng Part C Methods* **17**, 367–374 (2011).

Provided a force-controlled displacement – informed design

https://www.flexcellint.com/

https://www.cellscale.com/

ASTM F813-20 guides biocompatibility/cytotoxicity concerns.

Client need was directly translated to design specifications

Incubator-Safe

Fits within 20 x 21 x 25 [in^3] incubator

Can operate within 37 ºC, humid environment

Aseptic technique friendly

Physiological Force Output

Capable of inducing 20% ε_{engr} on cartilage samples

Applied displacement must be force-controlled

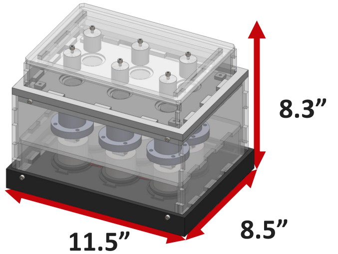
Cyclic loading profile (0.1 – 10 [Hz])

Budget-Friendly

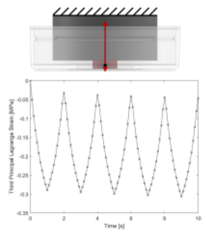
In total, housing, actuators, and circuitry must cost ≤ $5000

Guided by…

Material Selection & Design



Finite Element Analysis, Analytical Calculation, and Circuitry Prototyping



$$\sigma_z = \frac{F_{current}}{A_{ref}} = E\varepsilon$$
$$F \approx 6\ N$$
$$E = 1\ [MPa]$$
$$\varepsilon = 0.2$$
$$A = \frac{\pi}{4}(6\ mm)^2$$

Mindful, Well-Considered Design

	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

A more comprehensive, specific design specification matrix can be found in the supplementary slides.

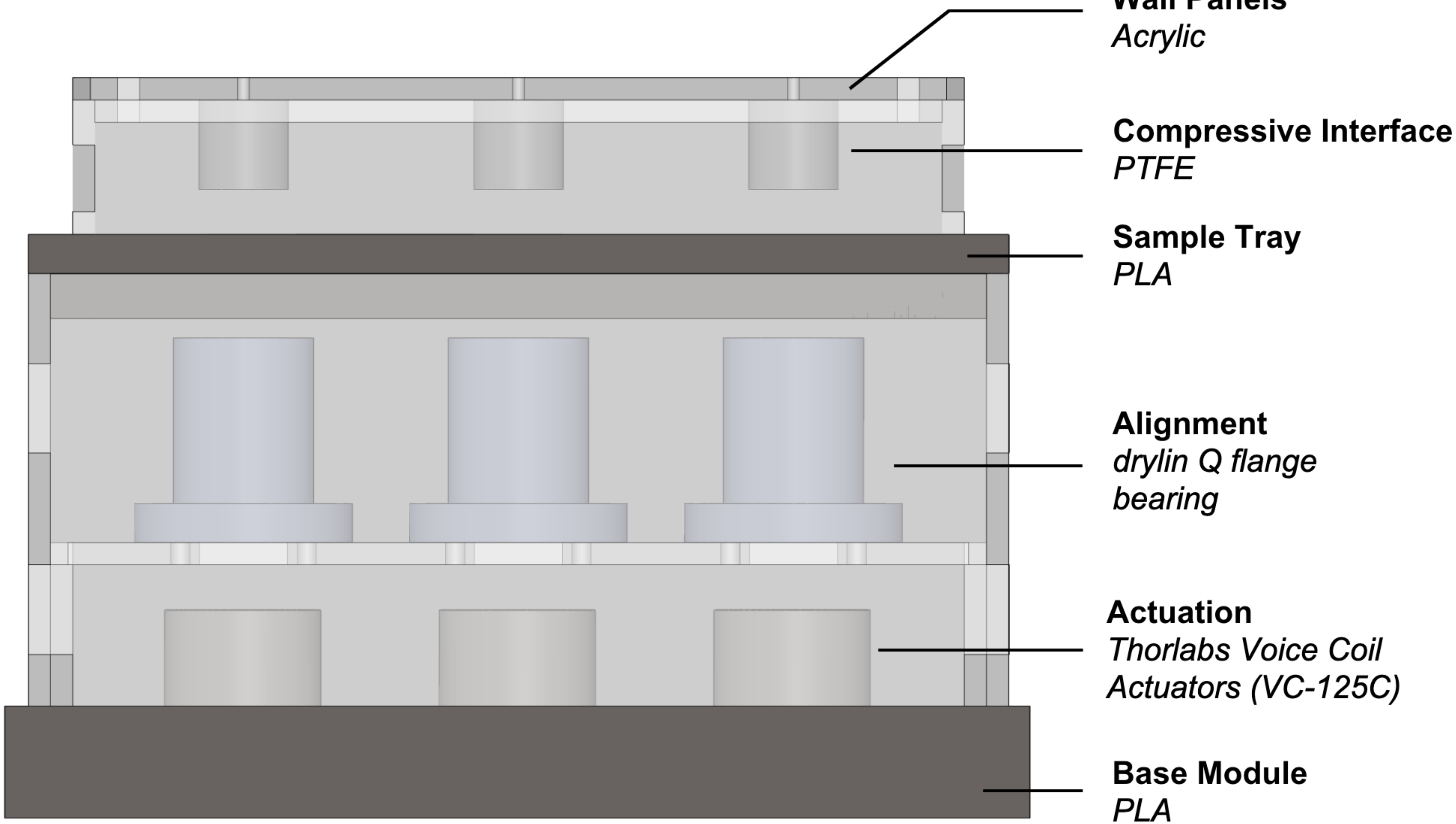
Final Design

Overview

Housing

Actuation

Overview



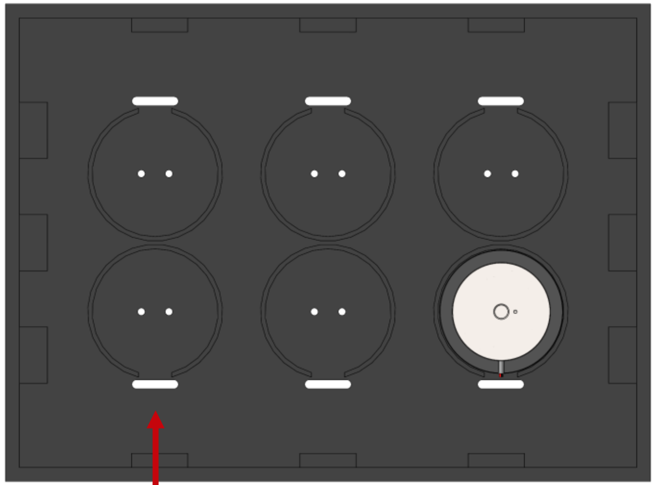
Wall Panels
Acrylic
Compressive Interface
PTFE
Sample Tray
PLA
Alignment
drylin Q flange bearing
Actuation
Thorlabs Voice Coil Actuators (VC-125C)
Base Module
PLA

Housing | *Base*

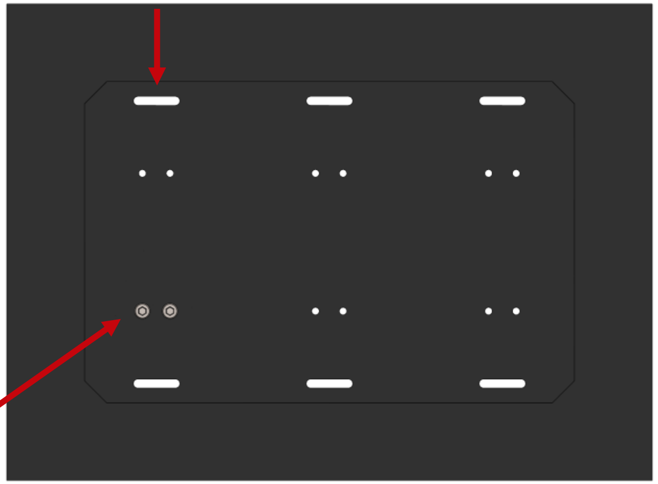
Material: PLA

Module Purpose: ***Secure** and fasten bioreactor*

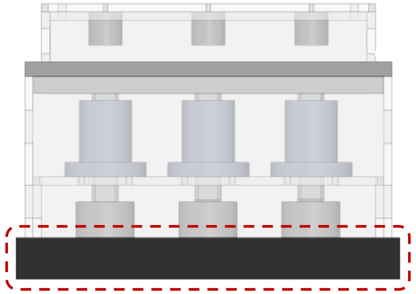
Acrylic paneling fastened to base via M4 bolts.



VCA wires are lined through ports and gathered at one exit in the module



Each VCA can be secured via 2x M4 cap screws

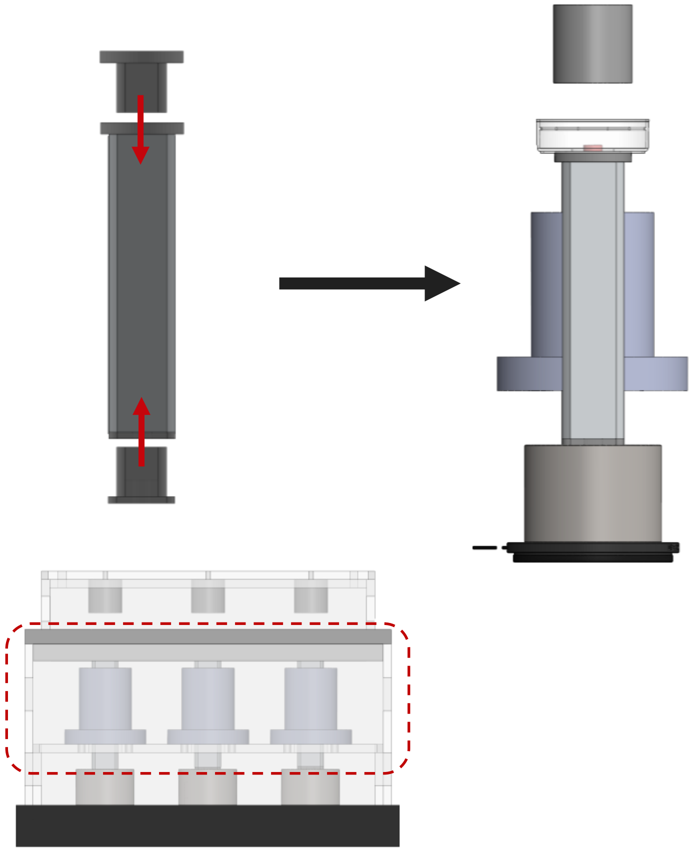


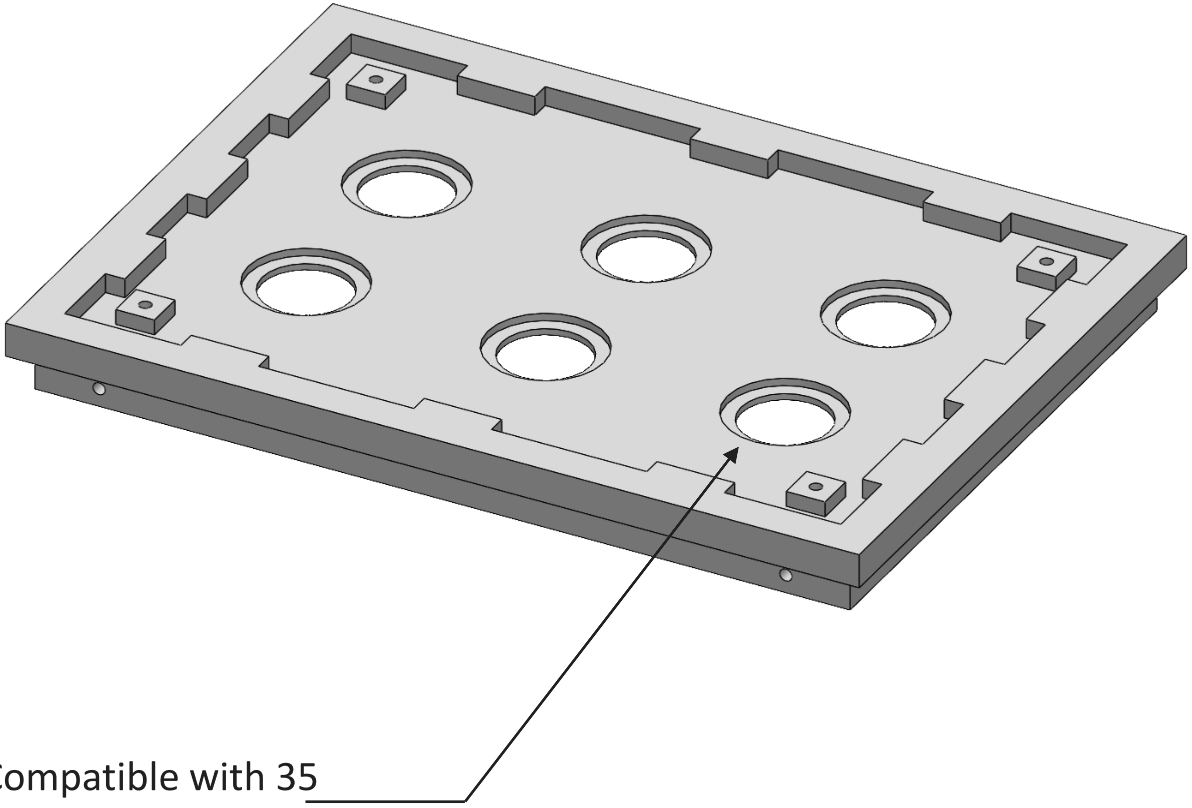
Voice Coil Actuator (VCA) provides force profile and is housed within the base.

Housing | *Alignment & Sample Tray*

Material: BioMed Clear (Mating Components) & Anodized Aluminum; PLA

Module Purpose: ***Align*** *actuation,* ***prevent rotation*** *& shearing, and* ***link actuation*** *to sample compression.*

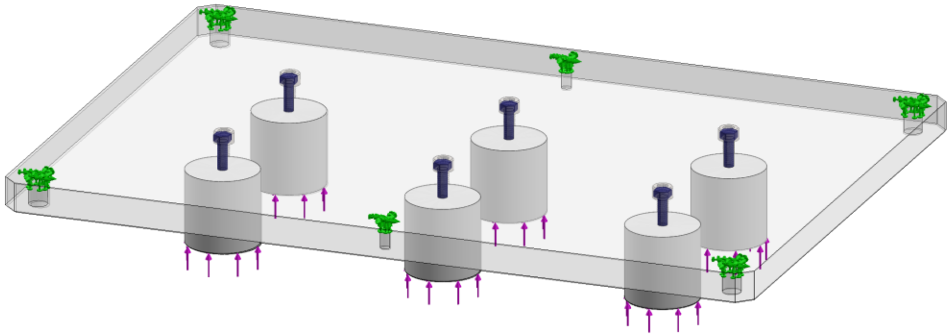


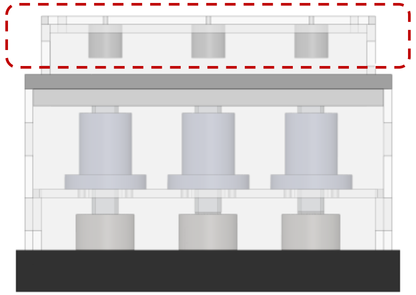


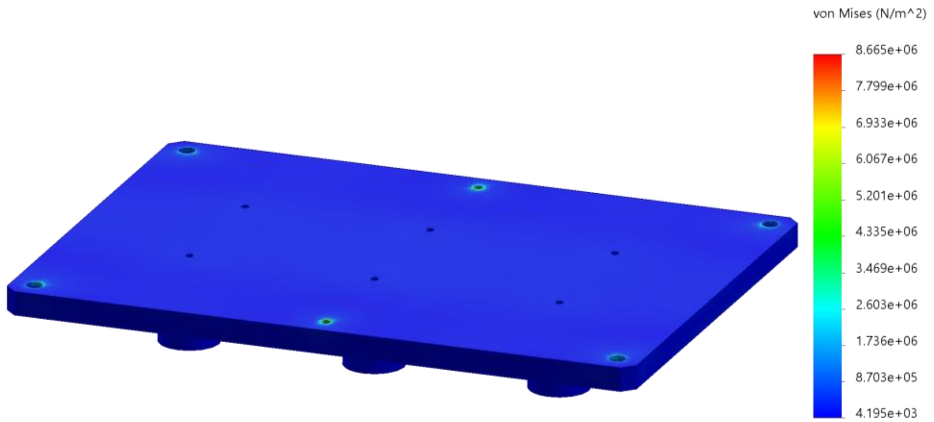
Housing | *Compressive Lid*

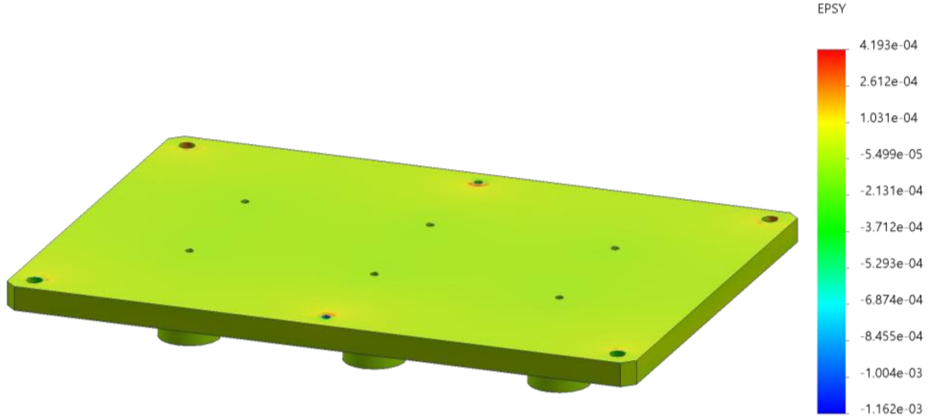
Material: Acrylic (Laser-Cut) & PTFE

Module Purpose: ***Compress*** *cartilage samples.*









Minimum F.O.S. of 3.3 at Max Loading Condition (Maximum Normal Stress Failure Criterion)

Actuation | *Voice Coil Actuators (VCA)*

Product: ThorLabs VC125C/M

$\boldsymbol{F} = q\boldsymbol{v} \times \mathbf{B}$

Lorenz force equation

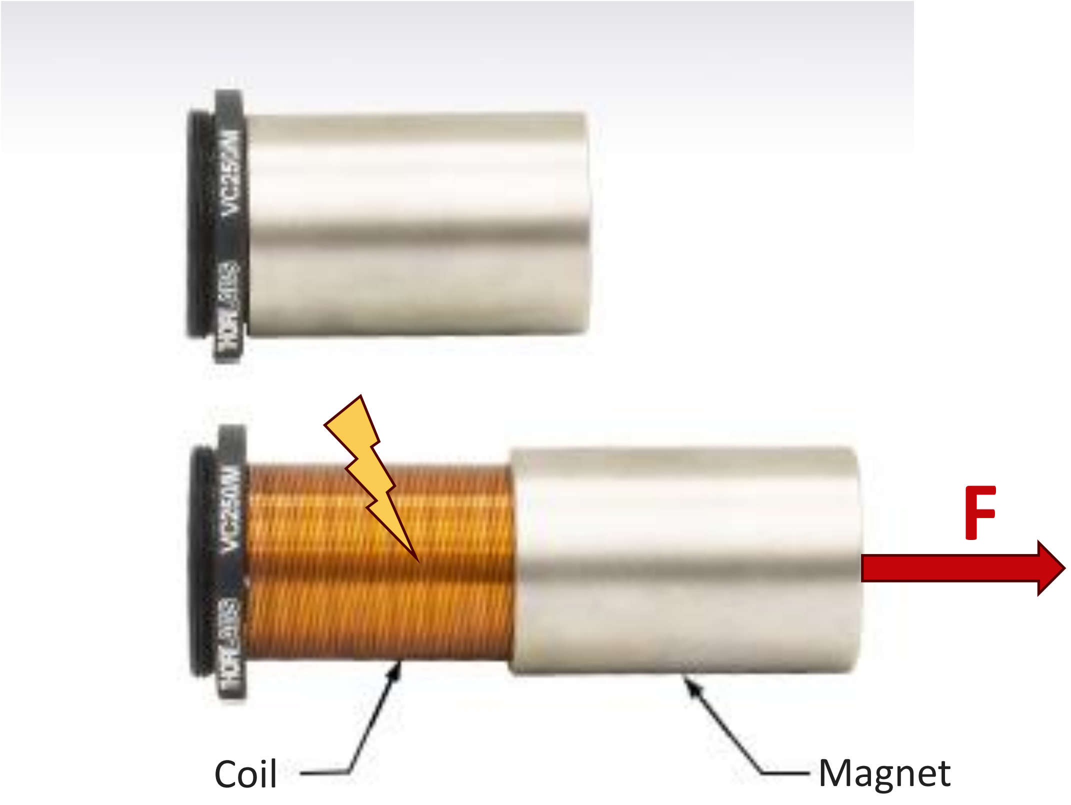
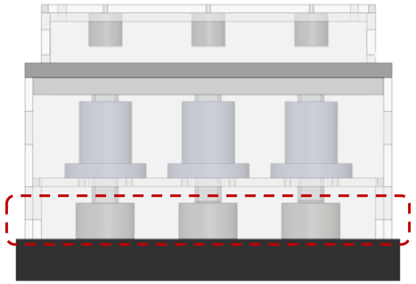


Image: ThorLabs

Image: ThorLabs

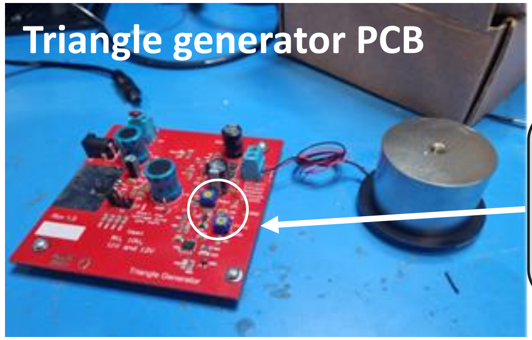
Force Constant	12.4 N/A
Travel	12.7 mm
Req'd Duty Cycle	50%
Max Operating Temp	230F/110C



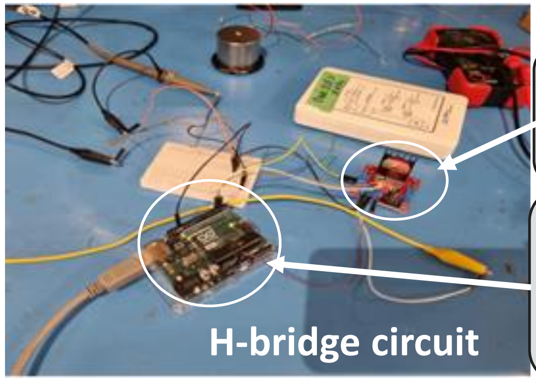
Actuation | *Circuitry*

Circuitry and electronics to power and control our actuators

Criterion	PCB	H-Bridge	Transistor
Functionality (15)	1 (3)	5 (15)	5 (15)
Ease of Use (10)	2 (4)	3 (6)	4 (8)
Space (10)	2 (4)	3 (6)	5 (10)
Price (5)	5 (5)	1 (1)	1 (1)
Total (40)	**16**	**30**	**34**

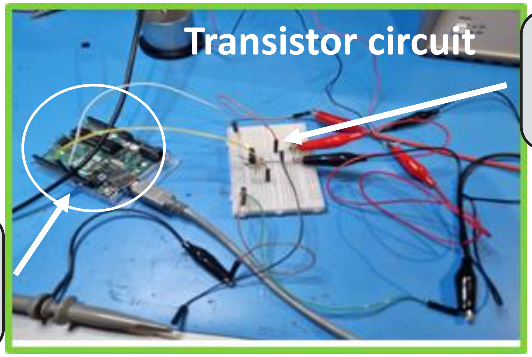


Potentiometers control voltage/force output and frequency



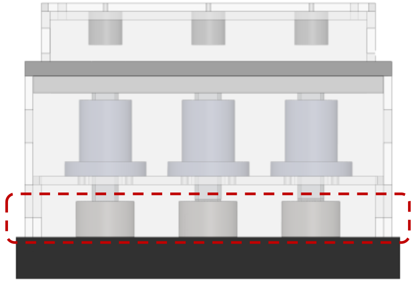
H-bridge operates actuator

Arduino and power supply settings control force output



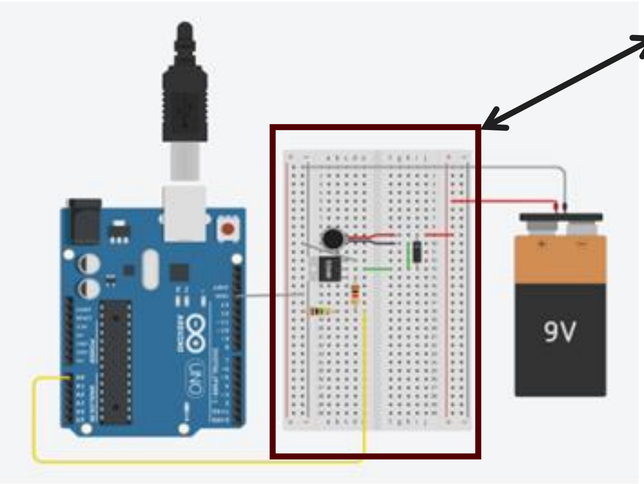
NMOS transistor operates actuator

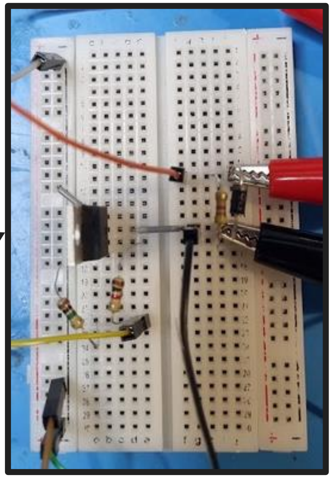
Arduino and power supply settings control force output

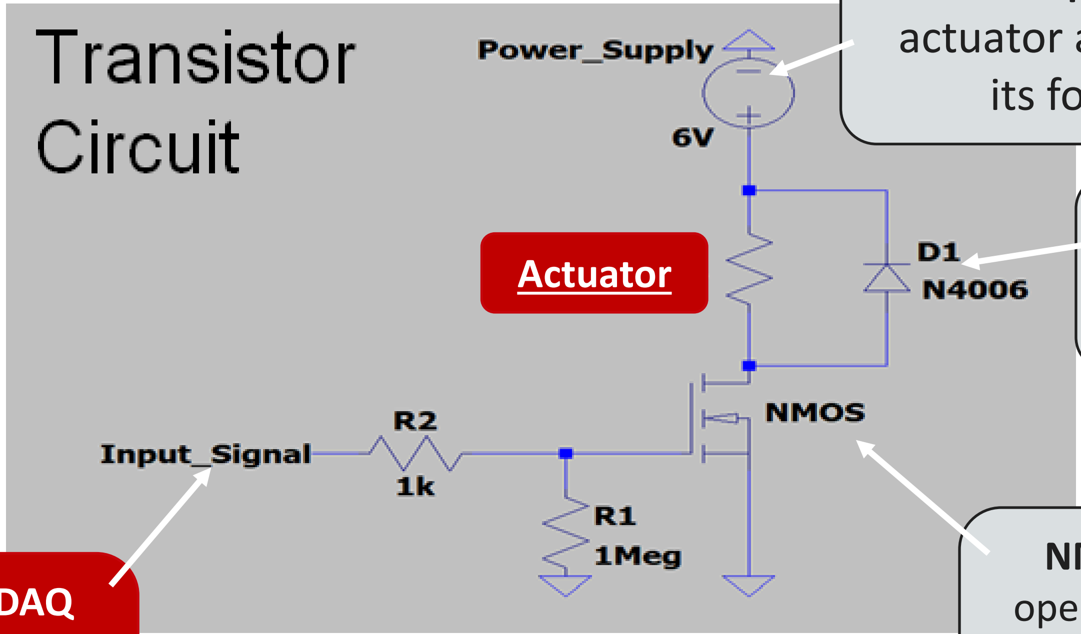


Actuation | *Circuitry*

Transistor circuit







Actuator

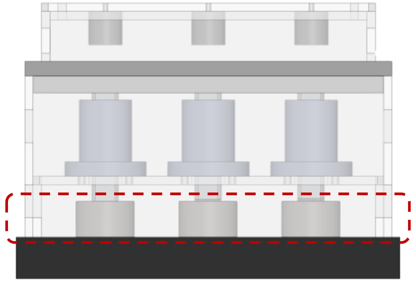
Power supply powers the actuator and determines its force output

Diode protects the actuator and transistor

Arduino or **NI DAQ** provides the input signal, controlling frequency

NMOS transistor operates the VCA by performing on and off switching

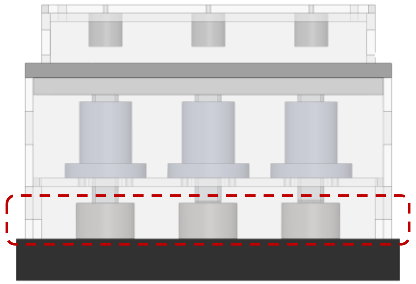
Cost: $550 ×6

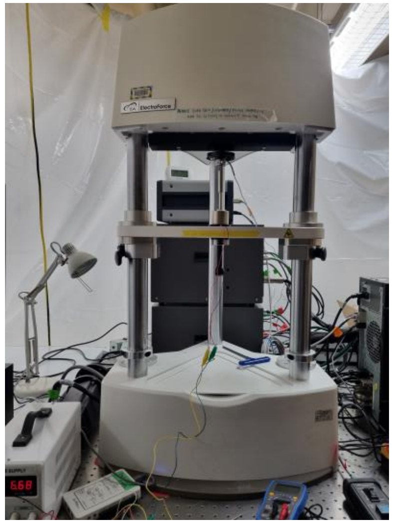


Actuation | *Circuitry Testing*

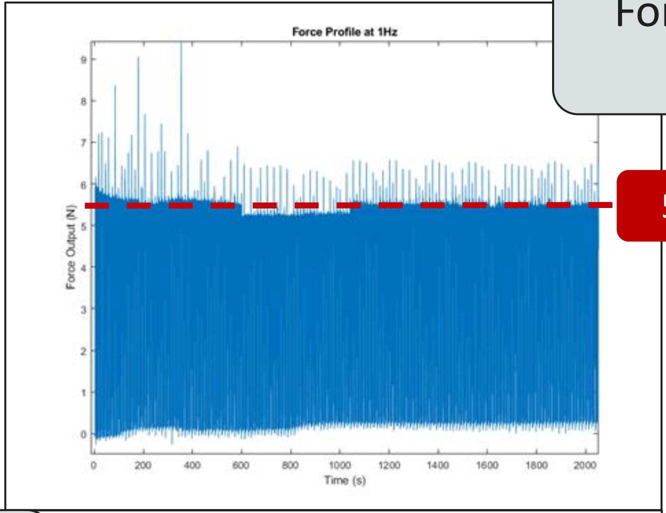
Load cell testing to validate the actuator to our design specifications

- Correct, desired force (i.e., 5.5 N)?
- Consistent force profile over time?
- Overshoot?



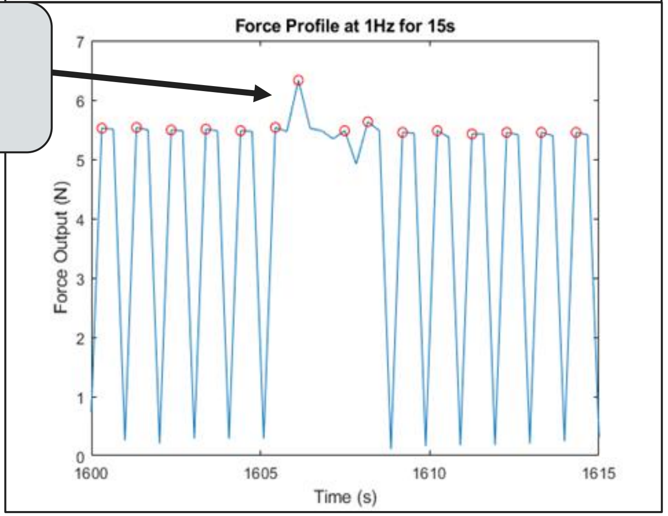


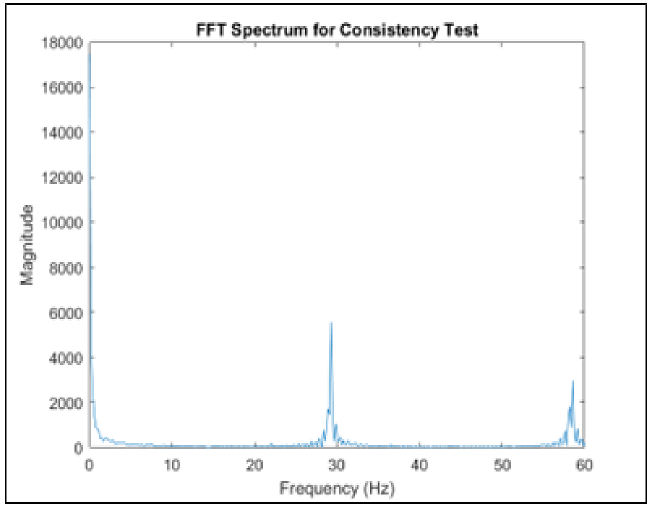
Force profile is relatively constant over time



5.5 N

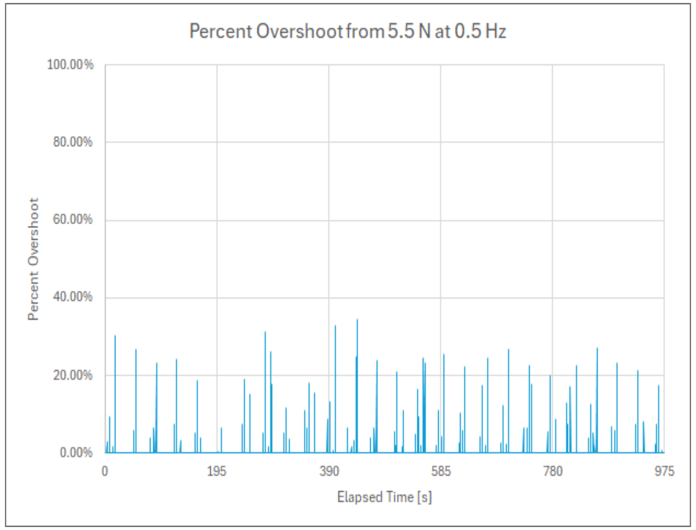
Overshoot occurs

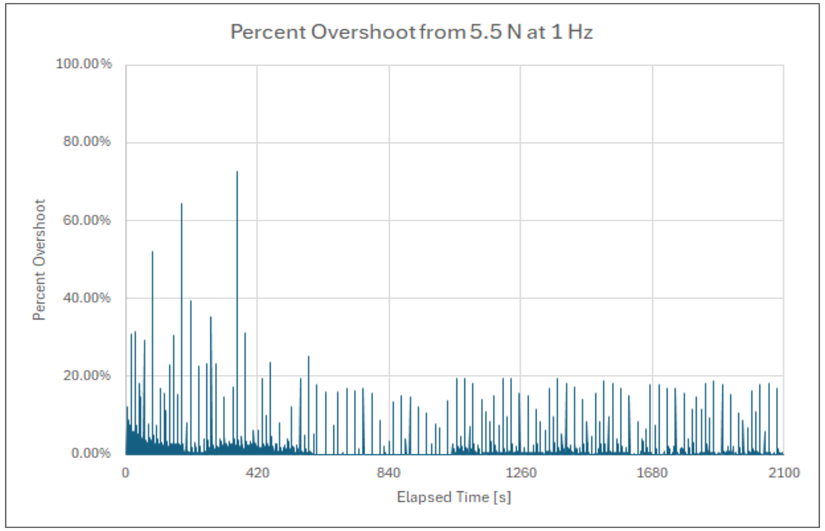


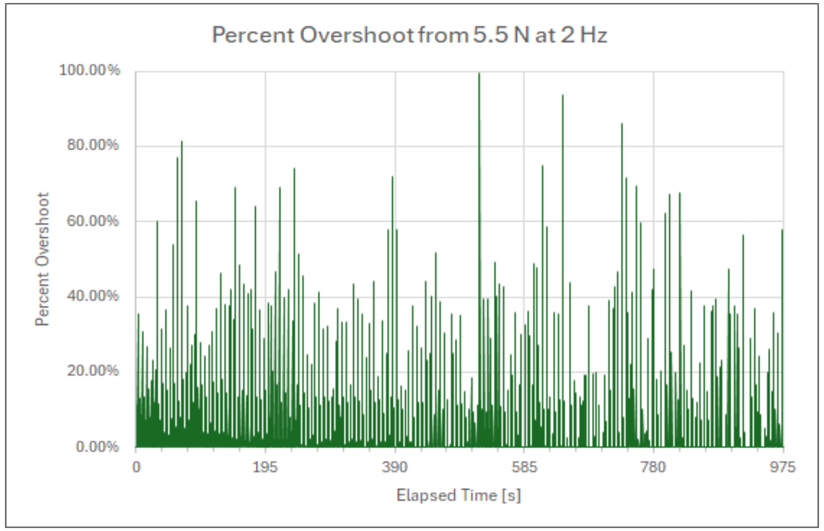


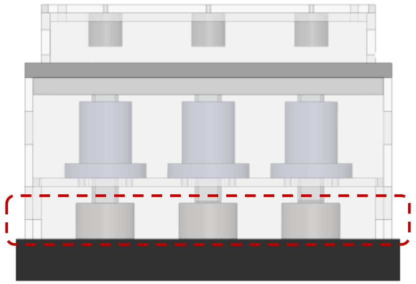
Actuation | *Circuitry Testing*

Quantifying percent overshoot from our target value of 5.5 N





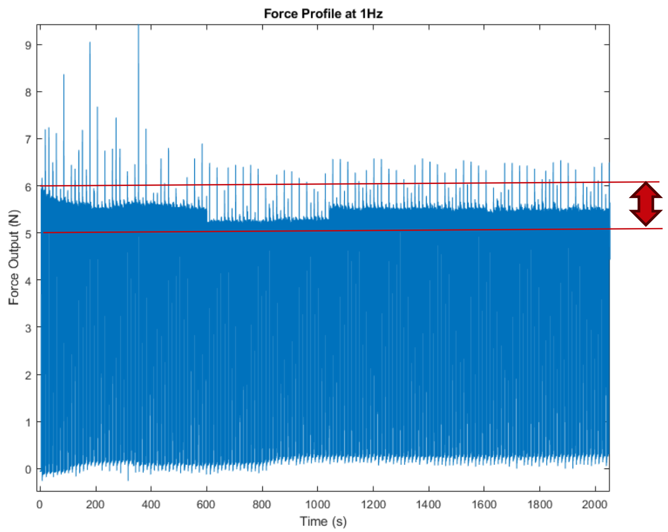




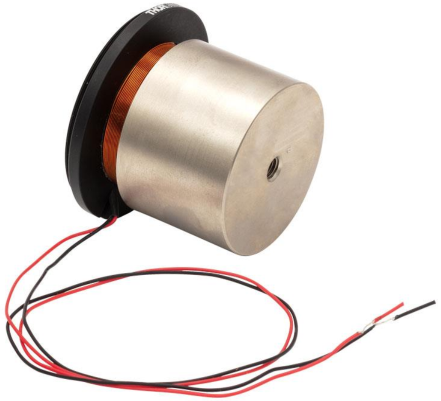
Overshoot	0.5 Hz	1 Hz	2 Hz
Avg.	11.44%	2.12%	9.84%
Std. Dev.	9.14%	4.52%	14.65%
Max	34.58%	72.78%	99.51%

Conclusions and Recommendations for Future Work

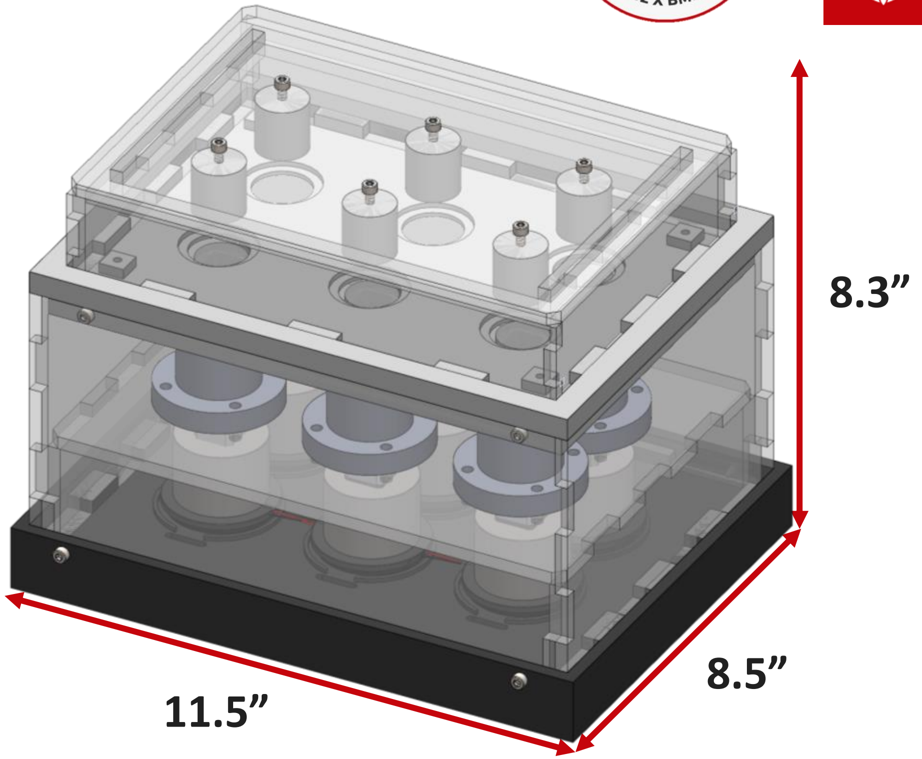
Specification Validation



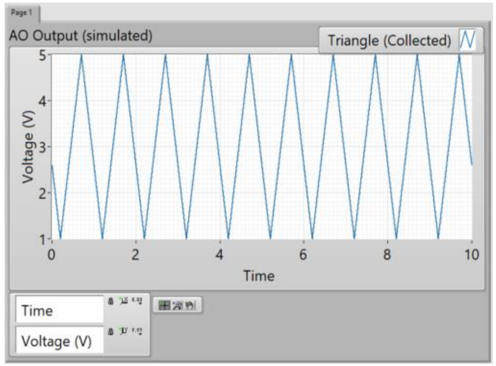
Average force output 5-6 N



Force-controlled



Biocompatible PTFE interface



Triangle-like force profile

- Smaller than 20 x 21 x 25 in^3
- Can be wiped down with ethanol
- Materials functional at 37C

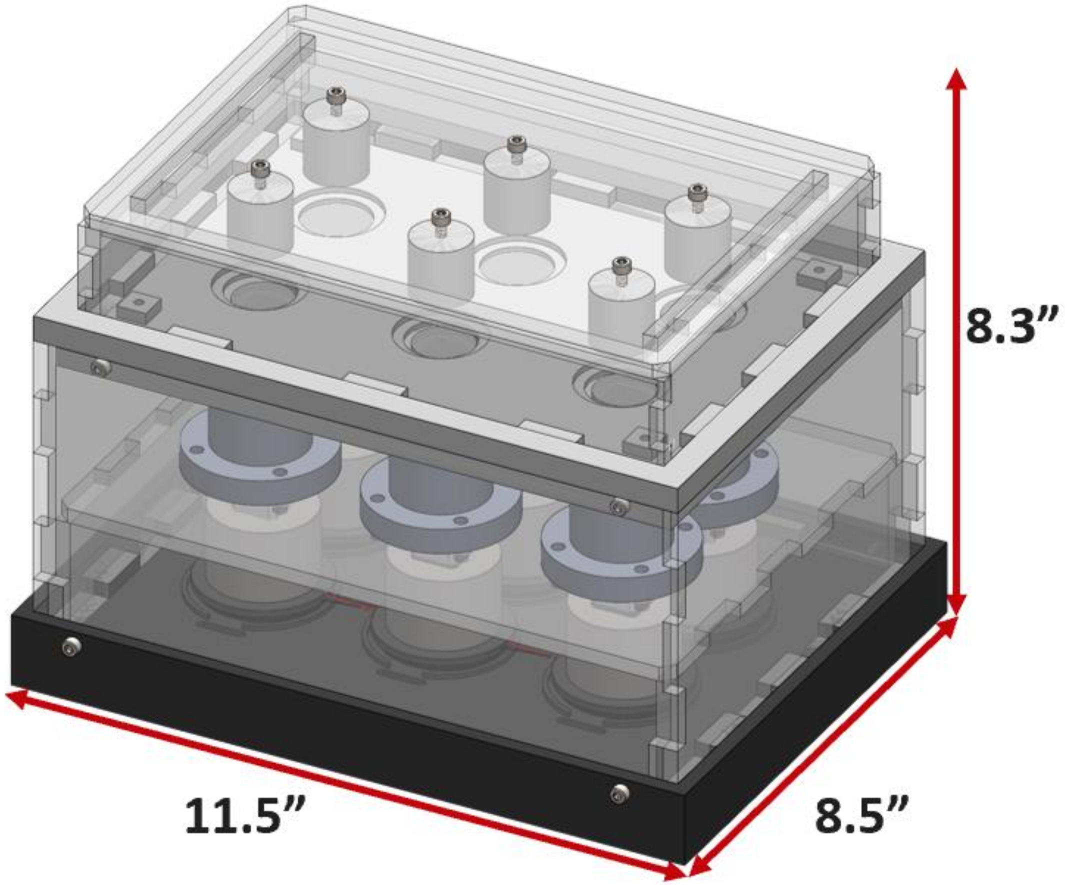
Final Cost: $730.22

Scaled up to six samples: $3777.72

Conclusions & Future Work

Designed and built a 1D actuator and circuit system to specifications

Built a housing prototype that can be used for experimentation



Next Steps

1. Test the unit in an experimental setting with full assembly
2. If testing goes well, order and print the components to scale up the bioreactor to include remaining samples
3. Machine the housing out of aluminum (hire TeamLab staff)

Acknowledgements

Our ME faculty advisor & client, Dr. Corinne Henak

Our BME faculty advisor, Dr. Paul Campagnola

Our TA, Patrick Dills

Thank you!
Questions are now welcome.

Funding from NSF-BMMB-2237707 is gratefully acknowledged

References

1) Yao, Q. et al. Osteoarthritis: pathogenic signaling pathways and therapeutic targets. Sig Transduct Target Ther 8, 1–31 (2023).
2) Mohd Yunus, M. H., Lee, Y., Nordin, A., Chua, K. H. & Bt Hj Idrus, R. Remodeling Osteoarthritic Articular Cartilage under Hypoxic Conditions. *International Journal of Molecular Sciences* **23**, 5356 (2022).
3) Walsh, S. K., Skala, M. C. & Henak, C. R. Real-time optical redox imaging of cartilage metabolic response to mechanical loading. Osteoarthritis and Cartilage 27, 1841–1850 (2019).
4) "Thorlabs - VC125C/M Voice Coil Actuator, 12.7 mm Travel, SM2 External Thread, Metric," www.thorlabs.com.

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	>6	N	Validate manufacturer specifications with testing	Must	MET
Induces 20% strain in (idealized) cartilage samples via uniaxial compressive stress	0.2	mm/mm	Use in-device load cell to determine deformation	Must	MET (via theoretical calculation and relation of force output)
Sufficient device actuation to allow for removal of sample dish	10	mm	attempt removal of sample dish	Must	MET
Low-friction compression/interface with cartilage sample	0.1	-- (coefficient of friction)	Manufacturer Specifications [19], [20]	Must	MET
Category 2: Incubator and environment					
Fit within incubator	(20 x 21 x 25)	inch	place fully fabricated box into incubator / measure	Must	MET
Able to withstand laboratory-grade sanitation procedures	---	---	Review of individual electronic technical specifications prior to use	Must	MET (ethanol)
Electronic components of actuator withstand incubator's simulated in-vivo environment	---	---	Review of individual electronic technical specifications prior to use	Must	MET
Cords of electronic components may be wired to external power sources	---	---	review of cord diameter and quantity	Must	MET
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	MET
Modular compressive pillars that are different shapes (e.g., indentors)	---	---	validate that the actuator applies the same force to the samples	Nice-to-have	NOT MET