Engineering Design Integrated Tissue Engineering Course Module: Scleraxis Tendon Bioreactor Project

Dr. Tugba Ozdemir, South Dakota School of Mines and Technology

Dr Ozdemir is an Assistant professor in Biomedical Engineering Department at South Dakota School of Mines and Technology. SHe completed her PhD in 2013 at The Pennsylvania State University Biomedical Engineering Department. She completed postdoctoral research in University of Delaware Materials Science and Engineering Department and University of Pennsylvania Clinical Studies and Advanced Medicine Department respectively. Her research interest includes development of biomaterials for regenerative engineering of craniofacial tissues. Her engineering education work has been published in biomedical engineering and biomaterials journals for the past few years and currently heavily interested in bridging the classroom and laboratory using her courses.

Ms. Jillian Irene Linder, South Dakota School of Mines and Technology

Jillian Linder is a Master's Student at South Dakota School of Mines and Technology. Jillian has worked as a Teaching Assistant in the Biomedical Engineering Department for two semesters under Dr. Ozdemir. She also has worked with Middle Schoolers at Mission Middle School in Bellevue, Nebraska, to run a makerspace classroom during summer school to help build and encourage students to get into engineering.

Erdal Şenocak, Tokat Gaziosmanpaşa University

He is a professor of chemistry education. He has been teaching chemistry at the undergraduate and graduate levels for fifteen years. His interests include how people learn science/chemistry, problem-based learning, and nanotechnology education. He works with educators from kindergarten to undergraduate to help them learn how to teach science effectively in their schools. He had also spent a year as a visiting scholar at Purdue University. In that period, he collaborated with researchers to design an instrument to determine kindergarten students' understandings of the scientific inquiry process.

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Abstract

Increased exposure to engineering design projects during undergraduate engineering education has gained attraction over the past years. In addition to the capstone senior design course offerings, Biomedical Engineering programs increasingly incorporate standalone engineering design courses into the curriculum as early as freshman year. These promising attempts emphasize the importance of reinforcing engineering design practices. However, it is still a challenge to accommodate engineering design projects into field-specific courses. Tissue Engineering is a multidisciplinary field that synergizes biomaterials, cells, and bioreactors to recreate damaged or missing tissues. Bioreactor design in the tissue engineering course curriculum is taught primarily by introducing existing studies to the students and discussing the reported outcomes of the design. Due to the significant time and specialized infrastructures (due to sterile and complicated instrumentations used in Tissue Engineering) needed to model, build, and test the tissue engineering bioreactors, integrating a design component into a Tissue Engineering course is a difficult task. In this study, we developed a five-week Tissue Engineering Bioreactor Design and Development Project enabling students to follow all stages of the engineering design process (identification of the problem, prototype development, testing design, design optimization, and sharing the solution). Teams of 4 students were presented with a case scenario where they were expected to develop a “Scleraxis Tendon Tissue Engineering Bioreactor (TTEB)” with the design criteria specified as autoclavable, mammalian tissue culture-compatible, and an ability to apply at least 50% cyclic stretch on enclosed cell-seeded biomaterial scaffolds.

After acquiring a discretionary budget available upon initial prototype presentation, teams fabricated TTEBs and evaluated their designs. In order to overcome the time limitations associated with the iterative nature of the prototype optimization step, we incorporated LEGO® bricks for the initial prototype development step followed by the actualization of the final prototype utilizing maker space tools (3D printers and laser cutter) and testing their final design. The five-week activity started with an introductory lecture on the “engineering design process”, “rules on keeping an engineer's notebook”, and “introduction to the five-week project”. In week 2, the case study was introduced followed by developing a LEGO® prototype by utilizing potential solutions, determining the dimensions and maker space tools required, lists of materials, and potential price range to fit within the budget. In week 3, each group presented the potential design solution with a product development timeline, parts list, and a proposed budget for the judges. Weeks 4 and 5 consisted of independent activity of each team towards developing and testing the final prototype and presenting the final design to the judges. Following the presentations, students submitted their engineering notebooks alongside answering the post-activity surveys. From the activity, it is expected that students learn many important aspects of engineering design and apply engineering design strategies to develop tissue engineering bioreactor prototypes. The activity may also give students the opportunity to improve their understanding of Hooke’s law and its applications to tendon bioreactor design.

Introduction

Tissue Engineering (TE) is an emerging subfield of Biomedical Engineering[1]. TE utilizes stem/primary cells, biomaterials, and signals to recreate damaged or missing tissue[2]. Several successful tissue engineering products exist, and the field is continuing to expand towards promising options to replace the need for organ donations[3]. Incorporation of nanomaterials[4] and tissue engineering[5] research were successfully implemented in the past as outreach activities. As the field expands, standalone tissue engineering courses are becoming part of the standard engineering curriculum[6]. To make TE into a curriculum, it requires a broad amount of knowledge to be condensed into a single course. Current courses commonly lack design projects for the students due to the time constraint within a semester and needing to cover a lot of material. This is similar to other Biomedical Engineering elective courses; students get a lot of broad knowledge but very little depth due to how complicated these electives can get. In a survey, 135 undergraduate students were asked "*Would you be interested in extending your knowledge of tissue engineering and regenerative medicine?"* and more than 85% of the students answered yes to the question[6]. The concepts of tissue engineering and regenerative medicine are interesting to the BME students. Due to the applied nature of TE, teaching fundamental theoretical knowledge with application-driven experiments remains to be a challenge[7, 8]. For instance, the development of TE bioreactors for mimicking physiological forces is an important engineering component of TE, however design and fabrication of a TE bioreactor requires significant training and lab hours which are challenging to incorporate into a TE course and laboratory. It also requires a lot of infrastructure and materials to develop a good TE design course [9].

Design is a large part of engineering, and we need more of it. We need to teach students how to critically think through the design process. Engineering design is a systematic, imaginative, and progressive approach to problem-solving. The steps involved in the design process are problem identification, idea generation, model development, and redesign. Several recent undergraduate engineering design activities utilized LEGOs® as suitable tools to realize design ideas into an initial prototype[10-12]. LEGO® design aims to improve group problem-solving, shared learning, and collaboration through making and creating in a relatively short amount of time. The purpose of our TE design activity is for the students to solve a TE-related design problem while applying the knowledge they gained during the TE course. Thus, our research question is: "Can biomedical engineering students design a functional tissue engineering bioreactor in a five-week module utilizing simple LEGO® prototypes and a maker space on campus?" In the fall of 2024, the engineering design activity was conducted with thirteen undergraduates taking the Cell/Tissue Engineering and Laboratory course. We created a small five-week module to encompass all necessary parts of engineering design, formulate a design based on given criteria, plan and prototype the design, present findings, propose a method to overcome limitations, and successfully come up with a prototype that can function with the desired criteria. This allows students to improve hands-on skills and encourage engagement with the material. During the engineering design process, students worked in a group to solve the design problem, using scientific and technical information, students designed a product prototype and shared the prototype design[13].

Methods

Learning Objectives

Class engineering design projects like those we implemented in this study may help fulfill many student outcome analyses related to ABET accreditation needs. For instance, ABET outcome number 5 was fulfilled during the initial design process and feasibility testing of the prototypes. During their design projects, students communicated with each other, and with faculty, both on campus and off campus, they communicated their design ideas with companies thus fulfilling

ABET outcome number 7. Students from the beginning to the end of the project worked in teams and learned how to manage their project plan tasks and meet objectives thus fulfilling ABET outcome number 4. At the end of the design process, students tested the maximum stretch applied to the biomaterial samples and compared their bioreactor design with the Tenosynth model bioreactor thus fulfilling ABET outcome number 2. Finally, during the preparation of engineering notebooks students actively gathered new knowledge through independent literature search thus fulfilling ABET outcome number 9[14]. The design module of the bioreactor has the majority of the ABET outcomes built-in (Appendix 1).

Suggested Prior Knowledge About Building the Module

In this study, we used a previously developed educational tendon stretch device[5] to show as an initial model. Utilizing computer-aided design software geared towards building LEGO® models, we reproduced the existing stretch device (Appendix 1). The list of pieces needed to build an initial model is provided (Appendix 5) for instructors interested in incorporating a LEGO® module into their curriculum. Utilization of LEGOs® made it simpler to build an initial prototype, students also reported that it was fun and allowed them to quickly build an initial prototype.

Instructor Recommendation

This module was part of a senior elective course (3 credit lecture, and a 1 credit laboratory) where a significant amount of knowledge required to build a tissue engineering bioreactor prototype was introduced in the lecture portion of the course. The required knowledge students learned for this course was stem cells, biomaterials, tissue organization, and signals: mechanical, biochemical, and physical cues, that are required to differentiate stem cells. Students were also taught the components of bioreactors and how they are built to grow tissue *in vitro*. In terms of the infrastructural requirements to perform this module, a dedicated design lab is needed with 3D printers, laser cutters, and basic machining tools.

We also provided the student groups with a small budget to buy the basic materials with the help of an internal faculty development grant. This is so students get the chance to manage their own budget, plan for the timely arrival of materials, choose the correct materials for the design space tools, and report how successfully they managed the budget.

Scleraxis Bioreactor Module Structure

This project was set up to be completed in a five-week period. The first week we divided students into groups of four to five students, ending with a total of three groups. Then we introduced a current bioreactor to stretch tendon scaffolds and introduced the desired modifications for it and the basic requirements needed. In the second week, the students were asked to design their own bioreactor on paper, present it to the class, and then make a technical drawing of their design. The third week was to prototype the design using LEGOs® and order the materials needed to build it within the given budget. The fourth week was dedicated to building their designs, and the fifth week was dedicated to testing them to the desired specifications given. Based on the feedback we recommend the instructors consider adding an additional two weeks to allow students to build and test the final prototype.

Design Project

In the first week, students were introduced to their problem through a case study example detailed in Appendix 1. Briefly, student groups were expected to improve the design of an existing tendon tissue engineering bioreactor (TenoSynth) by making it tissue culture suitable, autoclavable and being able to create a 50% stretch on the biomaterial scaffolds pre-seeded with cells. The next generation bioreactor will be called Scleraxis. After being introduced to the TenoSynth, we asked the students to assemble it completely and test it with a makeshift tendon biomaterial. We asked the students to then brainstorm as a class to come up with possible solutions for some of the issues and roadblocks that were present in the TenoSynth. The students then split into groups to discuss what each individual group wanted to make and come up with a drawing which would be presented to the class. In the following weeks, students built their prototype first with LEGO® pieces followed by utilizing the maker space and their tools, available free on campus. They tested their prototype and identified places that needed improvements.

Students Assessment

Students developed an engineer's notebook detailing the elements of the engineering design process. Each component was evaluated using a rubric designated for assessing engineering design steps. At the beginning of this project, students were given a rubric made by NASA (Appendix 2), which they would be judged based on 5 criteria: identifying the problem, building a model or a prototype, testing and evaluating the design, optimizing the design, and sharing the solution. To fully encapsulate this, students were required to each make and keep an online engineering notebook as they went through the lab. They were given a template and a previous year’s notebook as an example to follow. The template included sections asking for identifying the problem, background research, modeling, and prototyping, testing and evaluating, optimizing the design, and how their design compared to what was required of them. A sample engineering notebook entry is shown in Appendix 3.

Course Evaluation

Students were asked for input throughout this lab section, asking how they felt about time constraints, certain requirements given, and how well they thought their project was going. They were also given, at the end of the semester, a course evaluation survey (Appendix 4), which utilized Likert scales to judge their performance and how well they believed the module was set up. The questions for each survey were determined through discussion with a science education faculty member.

Statistics

The mean and standard deviations were found for each question and rubric criteria, which were then plotted. The N of this module was 13.

Ethics Statement

Prior to the study, all participants signed the consent form included in Appendix 6. IRB request for exemption is filed to South Dakota State University (IRB-2024-27).

Results

Figure 2 represents the side-by-side comparison of the LEGO® and final prototype of each group. Group 1 chose to build a bioreactor by stretching the scaffolds through a magnetic sliding mechanism operated by a lever arm connected to a motor. When autoclaving their magnets, they lost the magnetism due to the heat of the autoclave. This design was intended to keep the moving pieces outside the cell culture media submerged environment. During the LEGO® prototype design the group had difficulty finding appropriate LEGO® pieces to design their idea, so they built a nonmagnetic version. Group 2 chose to utilize an elliptical gear located on the shaft operating the connected gears on each side, which then held the rods proposed to the scaffold, shown in Figure 2B. The elliptical gear was connected to the shaft of the motor which was placed outside the culture chamber. Group 2 combined both their 3D printed gears and LEGOs® in the initial LEGO® design, which they could not attach their rods to, so they missed the design flaw of the rods being unsecured. Group 3 built a prototype similar to an existing product. Their proposed design mechanism worked without scaffolds attached to it, however, they concluded with scaffolds attached, the operating magnets would not be strong enough to hold the scaffolds in place. Therefore, they proposed to optimize the magnetic mechanism in future designs. In addition, the chosen acrylic was not heat resistant, and the magnets also demagnetized in the autoclave. In their LEGO® design, they wanted to represent how their external gear works with a contactless magnetic gear network. The students' grades for engineering notebooks are shown in Figure 3. Each rubric criteria represents one step in the engineering design process and is out of 20 points. Based on grade averages students had an average of 17.69 ± 4.39 for identifying the problem. They averaged 16.15 ± 5.06 for building a model or prototype and achieved an average of 17.69 ± 4.39 for Testing and evaluating the design. They averaged 17.69 ± 4.39 for optimizing the design and averaged 16.92 ± 4.80 for sharing the solution. For all the rubric criteria students' averages either meet or exceed expectations according to the rubric. The students were evaluated on the class module based on a Likert scale survey out of ten points, with questions listed in the table in Figure 4. The data is the average of the student survey responses, which are shown in Figure 4. Based on the survey, students' willingness to do the project again was 8.46 ± 1.26. Next, we asked if the LEGO® portion was encouraging or not and the average was 6.46 ± 1.56, and the question on the likelihood of using LEGO® in other design projects was 6.08 ± 2.02. Next, we asked how adequate the duration of the project was, the average was 3.35 ± 1.77. Further, we asked how useful it was to perform this module in the maker space and how the maker space finalized their design. The student averages were 9.42 ± 0.64. Finally, we asked how helpful designing a TE bioreactor was using the knowledge they acquired in the classroom portion, the average was 7.85 ± 1.07. The results of the Likert scale survey out of five points on evaluating students' personal reflections are shown in Figure 5 with the list of questions in the table below. Based on the survey students' confidence in being a tissue engineer averaged 4.15 ± 0.38. Also, students' confidence in designing a tissue engineering bioreactor averaged 4.15 ± 0.80. Students' confidence in using the maker space and their tools in other projects, like a capstone or senior design project, averaged 4.77 ± 0.44. The next question surveyed students' opinions about themselves being good at engineering and averaged 4.0 ± 0.82. When we asked students about their confidence in applying their theoretical knowledge in tissue engineering the responses averaged 4.23 ± 0.44. Next, we asked about their ability to work in a team to accomplish a goal, the results averaged 4.77 ± 0.44. The next question surveyed whether they could successfully come up with a project, follow through, and present their findings, which then averaged 4.77 ± 0.44. Finally, we asked if they felt good at problem-solving, and the results averaged 4.54 ± 0.52.

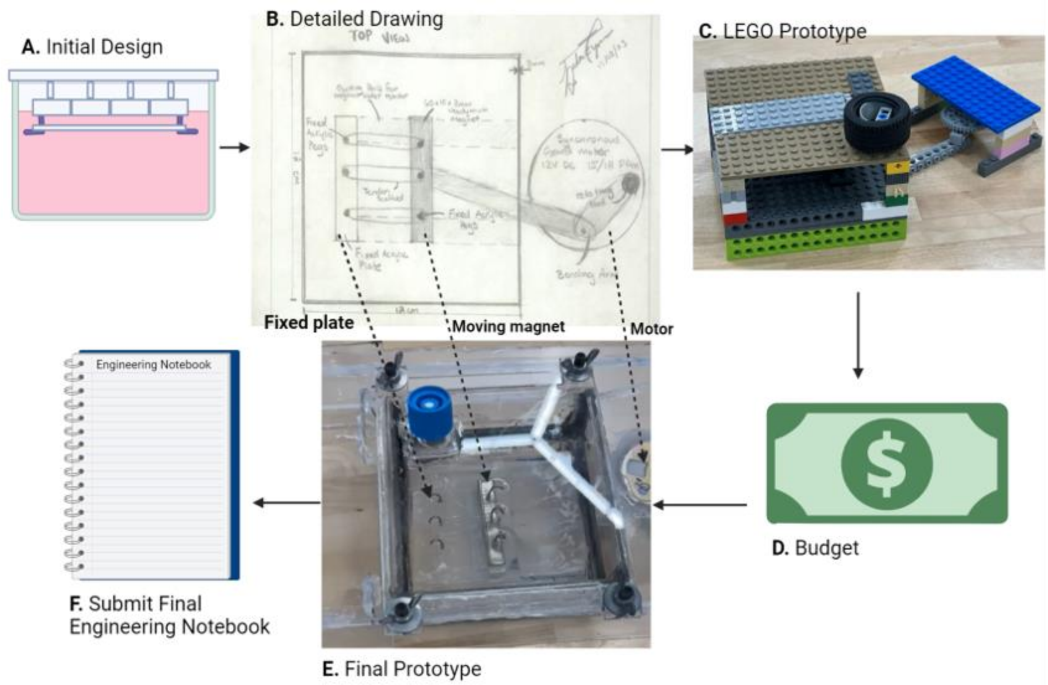
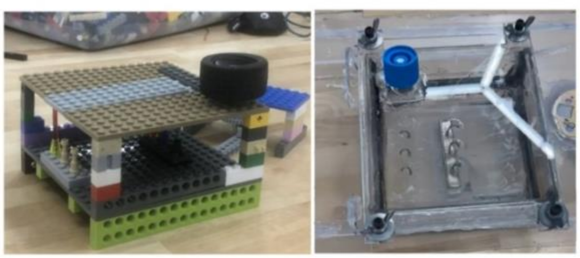
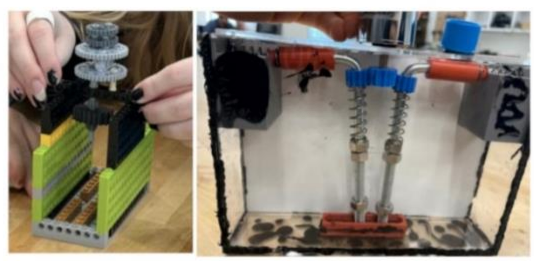


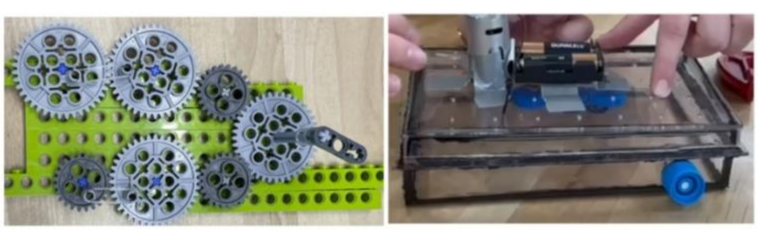
Figure 1: A flow chart describing the steps involving the Scleraxis bioreactor module. (a) Students started by hand drawing their proposed design after initial research. (b) More detailed technical drawings were prepared by students describing working principles and potential pieces. (c) A LEGO® initial prototype. (d) Students were given a budget and started ordering the parts needed to build their bioreactor. (e) A final prototype. (f) Engineering notebooks were submitted after testing.



A. Group 1 LEGO Prototype and Final Design



B. Group 2 LEGO Prototype and Final Design



C. Group 3 LEGO Prototype and Final Design.

Figure 2: Comparison of LEGO® prototypes and final prototypes built in the maker space by each group. (a) Group 1 used a sliding mechanism operated by a motor, which created a stretch on scaffolds through interfacing magnets. (b) Group 2 used a 3D printed camshaft and gear to stretch the scaffold tied onto rods that were placed perpendicular to the moving gears. (c) Group 3

designed a contactless magnetic gear network that proposed to stretch the scaffolds held inside the chamber with magnets.

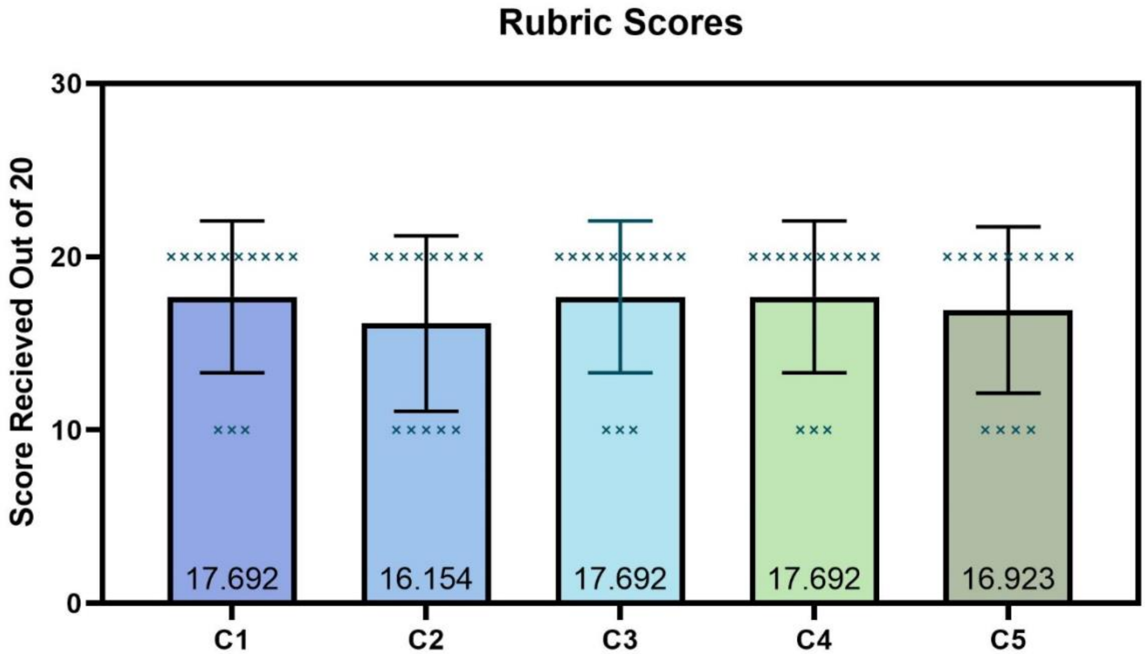


Figure 3: Summary of the grades from engineering notebooks for each rubric criterion. X values are individual student scores for each rubric criterion. The mean of each criterion is at the bottom of each bar (n=13).

Table 1: The rubric criteria we judged the students from.

C1	Identifying the Problem
C2	Building a Model or a Prototype
C3	Testing and Evaluating the Design
C4	Optimizing the Design
C5	Sharing the Solution

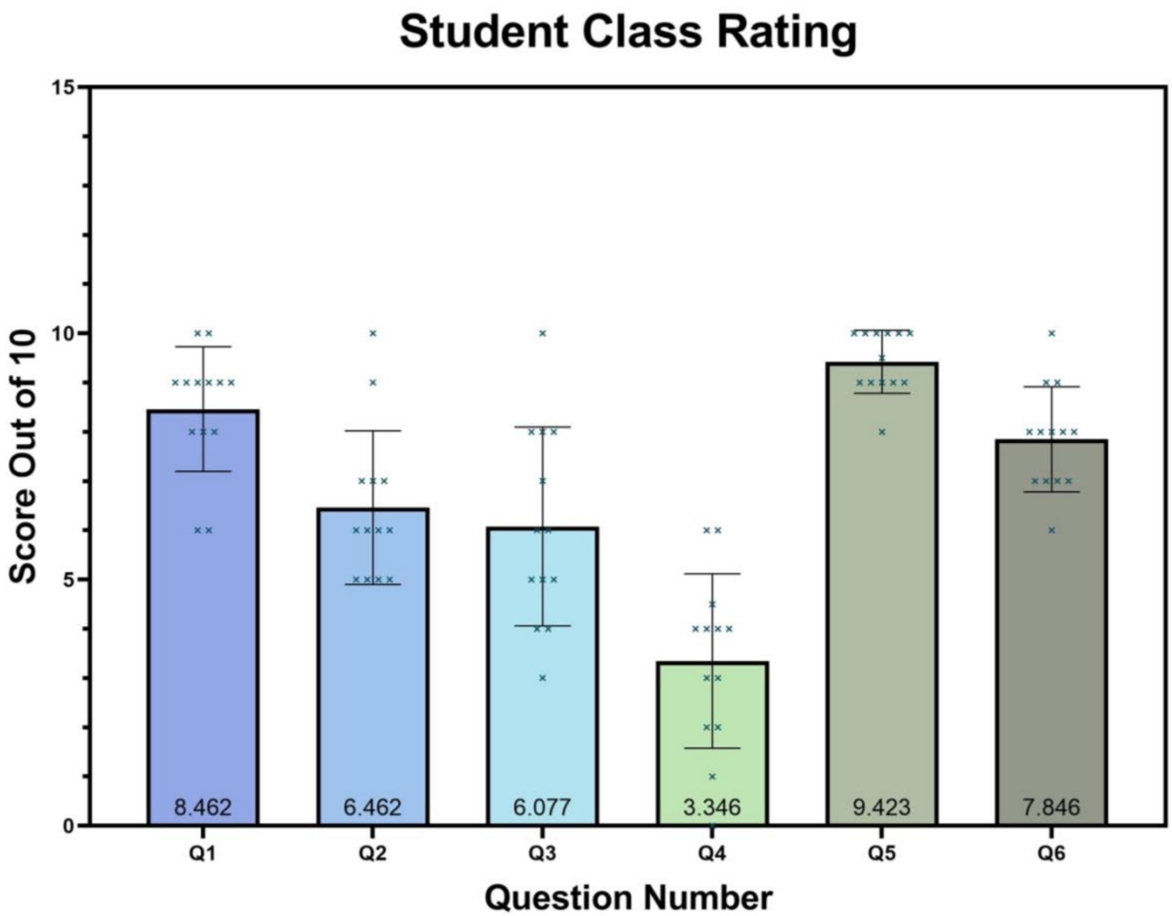


Figure 4: Summary of the results from surveys questions reflecting on the class module for the bioreactor. Data is represented as mean±standard deviation (n=3). Mean for each question is included at the base of each bar. X values are individual student scores for each survey question. The mean of each survey question is at the bottom of each bar.

Table 2: The questions given to students for assessing the classroom and the module for the bioreactor.

Q1	How willing would you like to do a project like this again?
Q2	How encouraging was the LEGO® portion to conceptualize your design?
Q3	How likely would you use a LEGO® portion in other projects that you are working on to help in design?
Q4	How adequate was the duration of the project?
Q5	How useful was it to use the maker space in the finalized design?
Q6	How helpful was designing a tissue engineering bioreactor with the knowledge you learned in the class portion?

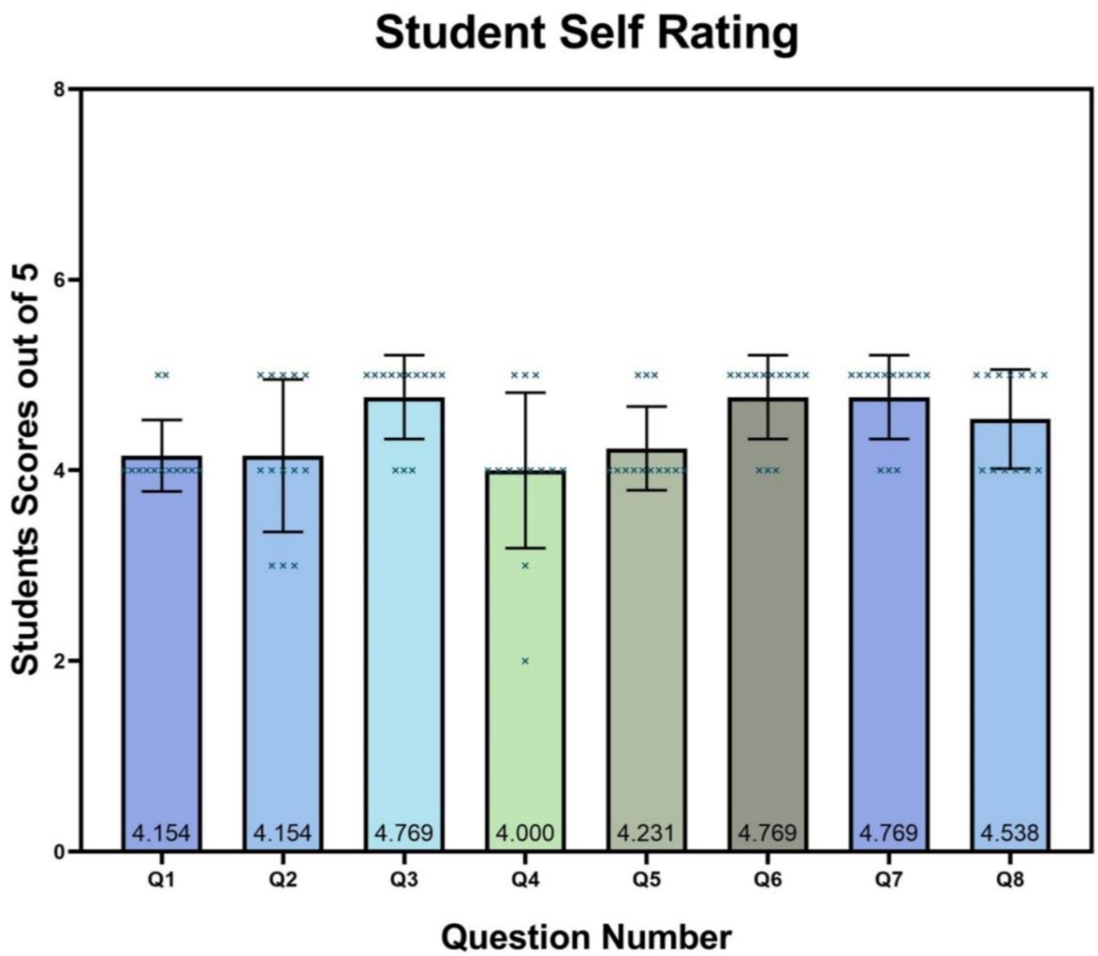


Figure 5: Summary of the results from surveys questions reflecting on the student's personal development in engineering. Data is represented as mean±standard deviation (n=3). Mean for each question is included at the base of each bar. X values are individual student scores for each survey question. The mean of each survey question is at the bottom of each bar.

Table 3: The questions asked to the students to assess how they felt about being an engineer after the module.

Q1	Now I feel confident in being an engineer, specifically in tissue engineering.
Q2	I feel confident in designing a tissue engineering bioreactor.
Q3	I feel confident using the maker space and their tools in other projects to help further my designs.
Q4	I am good at engineering.
Q5	I am confident in applying my knowledge in tissue engineering.
Q6	I am able to work in a team to accomplish a goal.
Q7	I can successfully come up with a project, follow through, and present findings.
Q8	I am good at problem solving.

Discussion and Conclusion

In this study, we created an in-class design module to introduce tissue engineering bioreactor design to undergraduate biomedical engineering students. In a five-week module, students designed a tendon bioreactor and built a LEGO® prototype, followed by an actual prototype utilizing the maker space tools and a given budget. Finally, test the final prototype. Three student groups each built independent bioreactor; one with a magnetically driven lever arm, one with a gear shaft driven sliding rods, and one with contactless magnetic gear works to stretch the tendon biomaterial scaffold placed in a culture chamber. Student performance was assessed using an engineering notebook, submitted at the end of the semester based on a rubric assessing the engineering design process steps. At the end of the module students' opinions on both module performance and their personal reflections were assessed using a Likert scale survey. Based on our findings biomedical engineering students enjoyed this activity and found it useful. However, the module duration was found to be inadequate based on the personal reflections survey. Students' confidence in engineering-based skills (design application of knowledge, problem-solving) were all improved. In the future, we want to extend the module's duration to a semester-long project based on the feedback and observations of students during the design module. Students can work on the design longer and better prepare for prototype making, prototype testing, and optimization of parts.

Appendices:

Appendix 1. Testing and Implementing Alternative Prototype Designs Using LEGOs® for Tendon Cyclic Stretch Bioreactor Model

Review of Case Objectives

Students can;

- identify a problem that can be solved through an engineering design process.
- decide the tissue engineering content knowledge required to solve the problem (i.e. calculating the elastic modulus of a rotator cuff tendon).
- develop a variety of possible solutions to the problem (i.e. developing a tendon bioreactor device to apply physiological stretch on the tendon).
- test possible solutions and evaluate test results (i.e. calculating how much stress tendons need to generate the desired physiological stretch).
- use an iterative testing procedure to optimize a selected preliminary design (i.e. modifying the bioreactor layout to implement the calculated stress on the existing device and test it on a sample material).
- create the final design and communicate it to an external audience

ABET outcomes that align with case objectives

- An ability to identify, formulate and solve complex engineering problems by applying principles of engineering, science and mathematics;
- An ability to communicate effectively with a wide range of audiences;
- An ability to function on a team whose members together provide leadership, create collaborative and inclusive environment, establish goals, plan tasks and meet objectives
- An ability to develop and conduct appropriate experimentation, analyze and interpret data, and use engineering judgement to draw conclusions;
- An ability to acquire and apply new knowledge as needed, using appropriate learning strategies

Engineering Design Problem

You have just graduated from college and have started working as a biomedical engineer at Boston Dynamics to develop a robotic device to apply physiological stress onto tissue engineered tendon scaffolds. One of the products in the pipeline is TenoSynth, a potential robot assisted living implant for athletes with shoulder disability. As an engineer, you are expected develop the stretch device by going through the engineering design process. The company has an existing stretch device as shown in Figure A1. It can handle 4 biomaterials scaffolds and the amount of stretch is the same for all the scaffolds. <u>*As the human shoulder has tendons with varying degree of length, collagen density and therefore spring constant, the company wish to construct a new bioreactor which could reflect the physiological scenario better than the current design. The requirements they want in this project are the materials are bioinert, be able to have a 5% CO2 air exchange, autoclavable, and enclosed to protect against contamination.*</u> It should also be able to apply a 50% stretch without using human applied power. It should also be able to be made using a laser cutter with the pieces designed exclusively in Google Sketch. The engineering design process is a series of steps that engineers use to come up with a solution to a problem. You will be given an engineer's notebook which includes instructions to guide you in the engineering design process. The notebook is specially designed for engineers to record thoughts and report technical information while solving a design problem. You will test the feasibility of your design using LEGO® pieces before machining and testing the new design and optimize your prototype.

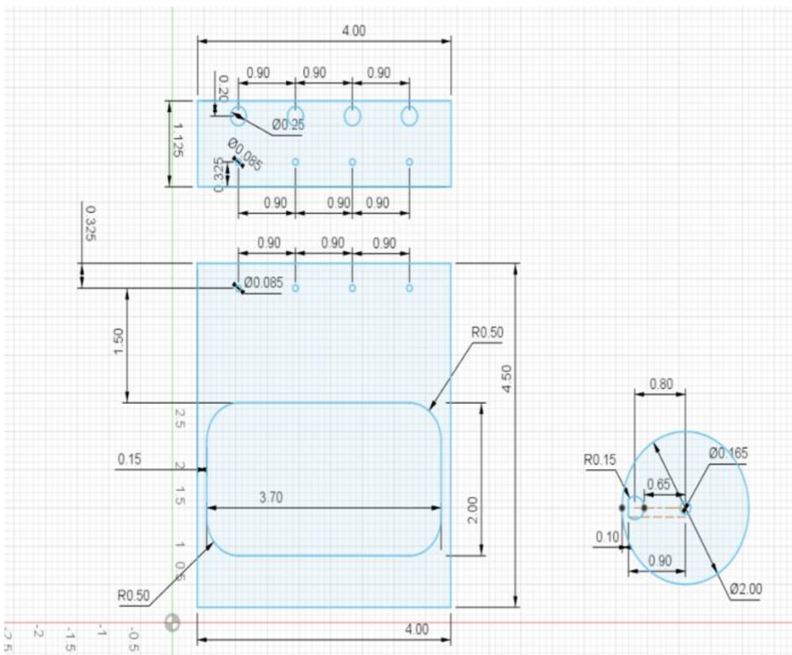


Figure A1 The schematic of the existing tendon stretch device with dimensions.

Appendix 2. Engineering Design Rubric:

Jet Propulsion Laboratory
California Institute of Technology

Teacher Answer Key

Engineering Design Rubric

	Does not meet expectation (1 point)	Approaches expectation (2 points)	Meets expectation (3 points)	Exceeds expectation (4 points)
Identifying the Problem	Relevance and context of problem is unmentioned. Scope and constraints are poorly defined resulting in unclear direction for investigation.	Relevance and context of the problem is included, but vaguely defined. Scope, criteria for success and constraints are included but only superficially.	Problem is specifically defined in a relevant way with context. Criteria for success are defined. Investigation considers relevant constraints.	Problem is specifically defined, as are root causes. Constraints are identified, specific, and testable.
Building a Model or Prototype	Constructs only one concept or solution to the problem.	Describes multiple solutions although without principles to guide how they address the problem at hand.	Multiple concepts or solutions are proposed with justification based within the constraints of the problem.	Multiple concepts or solutions are proposed with not only justification from constraints, but from external research.
Testing and Evaluating the Design	Evidence for design success is unsupported by testing.	Evidence for design success is weakly aligned to metrics that represent criteria and constraints.	Evidence for design success is well aligned to metrics that capture the criteria and constraints being explored.	Considers multiple metrics that align to several relevant criteria and constraints.
Optimizing the Design	Makes no iterative modifications to test changes in performance.	Makes changes to original model, but the changes are not iterative or are not guided by evidence from data.	Uses iterative modifications based on evidence from data.	Uses iterative modifications based on testing and justifies final design from data.
Sharing the Solution	Documentation of results does not cite references and lacks crucial information.	Documentation is organized but contains very little evidence and suggestions for further work.	Documentation communicates design strengths and weaknesses and makes recommendations for further work.	Documentation communicates design strengths and weaknesses. Evaluates tradeoffs between relevant constraints.
				Total / 20

Appendix 3. Student Engineering Notebook:

Building a Scleraxis Tendon Bioreactor
ENGINEER'S NOTEBOOK

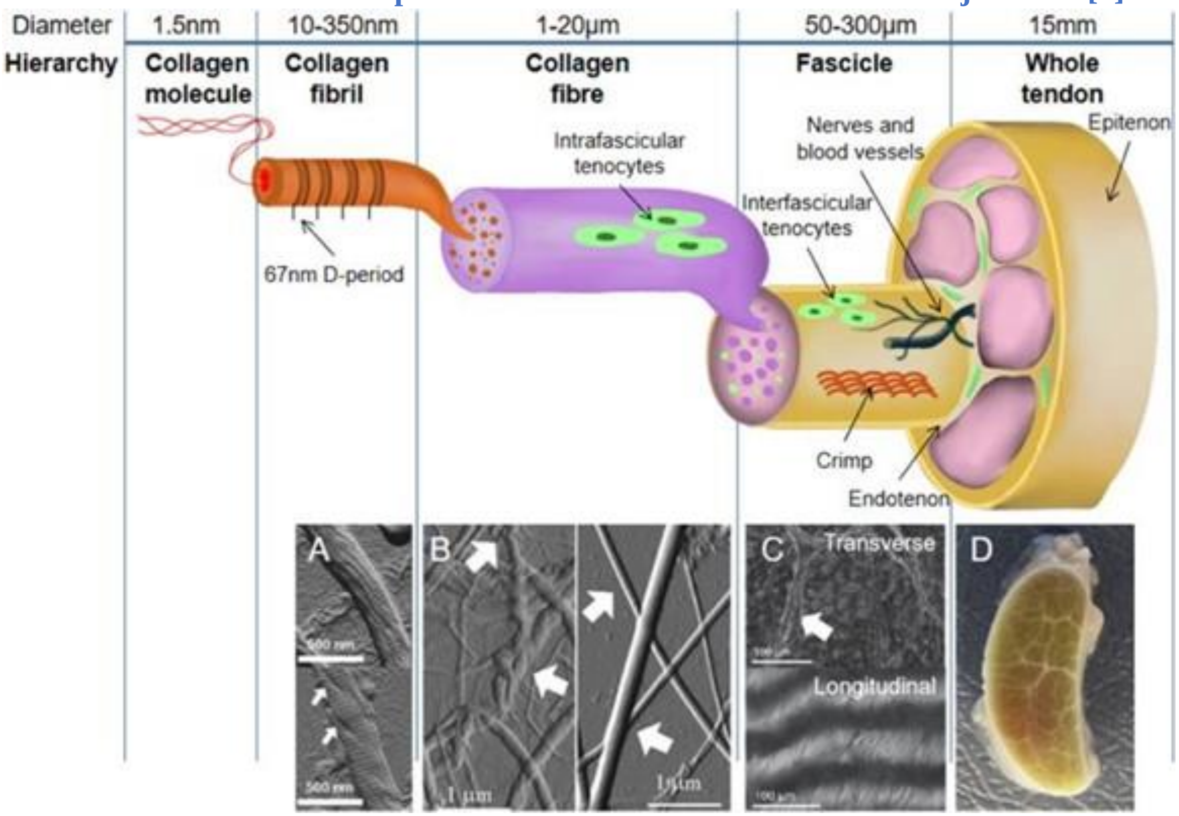
Student Name: STUDENT NAME

Follow the instructions below to complete the LEGO® bioreactor design process as an engineer. Reflect your thoughts and technical information as much in your notebook as you can while following these steps. The notebook will be customized during the design process by the engineers to record thoughts and report technical information while solving a design problem. Please use this notebook as you design a LEGO® bioreactor.

STEP 1: Identify the Problem

At this step, the research problem in engineering process and the characteristics of the target design will be identified.
What is your research problem? **Construct a bioreactor that simulates stretching of tendon scaffolding within a human shoulder. This research problem involves improving on an existing design that the company is currently using. The company wishes for a construct that can reflect the physiological scenario better than the current design in use.**
List the requirements for your target design: • **Materials Must be Bioinert** • **Able to have a 5% CO2 air Exchange** • **Must be Autoclavable** • **Must be Enclosed in Order to Protect Against Contamination** • **Should be able to Apply a 50% Stretch Without Using Applied Human Power** • **Bioreactor should be Made Using a Laser cutter with the Pieces Designed Exclusively in Google Sketch** • **Able to Hold Multiple Scaffolds**
Describe any potential obstacles or restrictions to the target design: **Some potential obstacles and restrictions include: bioreactor must be constructed using $100 or less, workable prototype must be completed within five weeks, parts needed that are ordered online may take too long to arrive in order to meet deadline, working on project outside of scheduled class time may be required in order to meet deadline, testing for bioinertness may not be possible due to time constraints, fatigue failure analysis (how long will device last before it fails) will not be conducted due to time constraints, having a lower budget limits the amount of device iterations that are possible to achieve the most possible optimization.**

STEP 2: Background Research

At this step, please decide which tissue engineering knowledge will be applied to engineering process and for what reason LEGO® will be utilized.
List the tissue engineering knowledge you need to complete the target design: **Tendons have a hierarchical organization ([Fig. 1]). A connective tissue sheath called the epitenon encloses the periphery of the tendon. The subunits of the tendon are the fascicles, which consist of numerous collagen fibers that are bound together. Fascicles are irregular in shape and vary in diameter, ranging from 150 to 500 µm , having a complex interweave arrangement. Surrounding the fascicles is a connective tissue compartment termed the interfascicular matrix (IFM), also called endotendinous connective tissue (endotenon), which contains blood vessels and nerves. The endotendon divides the tendon into the fascicle subunits and connects with the epitenon. Tenocytes secrete the ECM and growth factors to maintain tendon homeostasis. According to the location distribution of fibroblasts, the cells distributed in the IFM area are termed interfascicular tenocytes, while the cells distributed in the fascicle area are termed intrafascicular tenocytes. Fluorescence staining against connexins 32 and 43 showed positive results in mature tendon cell-cell junctions[1].** 

Improved treatments for tendon repair are therefore required. A promising approach is through tissue engineering (TE), which aims to restore functionality by combining cells and a biodegradable scaffold to give rise to a fully-functional replacement tissue. As a cell source, mature tenocytes have key limitations, principally their scarcity and associated donor site morbidity, which equate to low cell number for use and the requirement for extensive *in vitro* expansion that leads to phenotypic drift, and decrease the tenogenic activity. The majority of current TE approaches therefore use adult tissue-derived mesenchymal stromal cells (MSCs), particularly those derived from bone-marrow and adipose tissues as a cell source that is relatively easy to obtain, can undergo extensive replication, and are able to differentiate along the tenogenic lineage. For TE, the cells are combined with a biomaterial scaffold, often in combination with growth factors (GFs), to induce tenogenic differentiation and matrix deposition. Although stem cell-based tendon TE holds great promise, success depends upon robust and efficient differentiation of stem cells into mature and functional tenocytes, which remains challenging. Various approaches to induce tenogenic differentiation from stem cell populations have been reported, but a wide range of conditions are used and there remains a lack of consensus on the fundamental aspects of an effective tenogenic protocol [2].

Continuum constitutive laws are needed to ensure that bio-artificial tissue constructs replicate the mechanical response of the tissues they replace, and to understand how the constituents of these constructs contribute to their overall mechanical response. One model designed to achieve both of these aims is the Zahalak model, which was modified by Marquez and co-workers to incorporate inhomogeneous strain fields within very thin tissues[3].

Musculoskeletal tissues are highly sensitive to their mechanical environments. Mechanical forces not only maintain skeletal tissue homeostasis, but they also guide tissue development. Disruptions in the loading environment during development often lead to pathological conditions. For example, in neonatal brachial plexus palsy (NBPP), damage to the brachial plexus during birth leads to shoulder paralysis and results in a number of shoulder pathologies in children, including bony defects, a decreased range of motion, and ultimately a loss of limb functionality in the most severe cases. This condition affects approximately 1 in 100 births, making it one of the most common pediatric shoulder disorders [4].

Describe for what purpose and how you will use the LEGOs®:

We are using the Legos to get a better visualization of various prototype concepts. Legos offer an inexpensive way to test various preliminary prototypes quickly. Many great inventions and designs come from starting out the process in this manner. When it comes to engineering, it is better to fail fast to save on time and resources. This step is way to mediate future issues and failures down the road when the team has possibly reached a point of "no return."

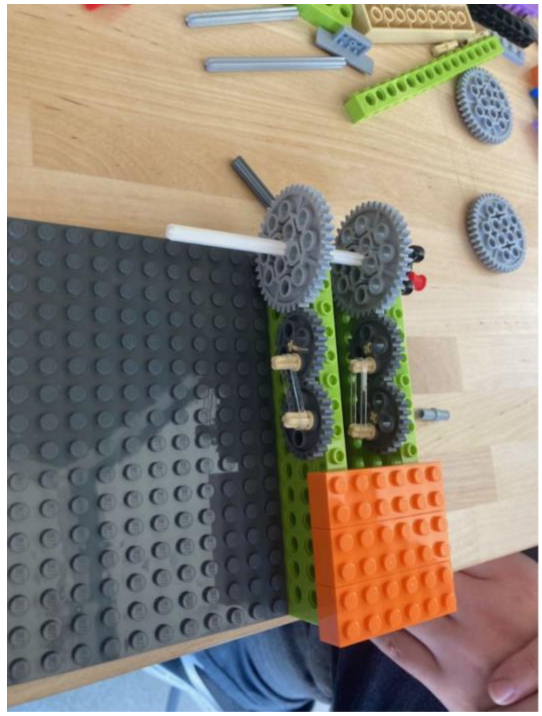
STEP 3: Build a Model or Prototype

At this step, list your design solutions/prototypes. When listing your solutions/prototypes, consider the criteria the design should meet. While listing your designs, keep in mind the restrictions of your research problem. You can also use drawings while listing your design solutions.

Design solution 1: **Stretch-O-Mag**

The first design concept consists of a setup that can stretch three shoulder tendon scaffolds. The enclosed biorector consists of a sliding magnet at the bottom that will stretch the tendons from roughly 1” to 2.25” achieving the 50% stretch. The magnet within the bioreactor will be attracted to another magnet outside and undernieth the bioreactor. This magnet will be moved mechanically by two arms connected to a 8V motor. The tire in the on top of the reactor will be a lid from a T-25 media flask that will facilitate the 5% CO_2 gas exchange along with media exchange. The materials should all be autoclavable to ensure sterilization. The container components will be cut using the laser cutter in the makerspace lab at Mines. This design seems to be the most novel compared to the other design.

Design solution 2: **Gear and Peg Concept**

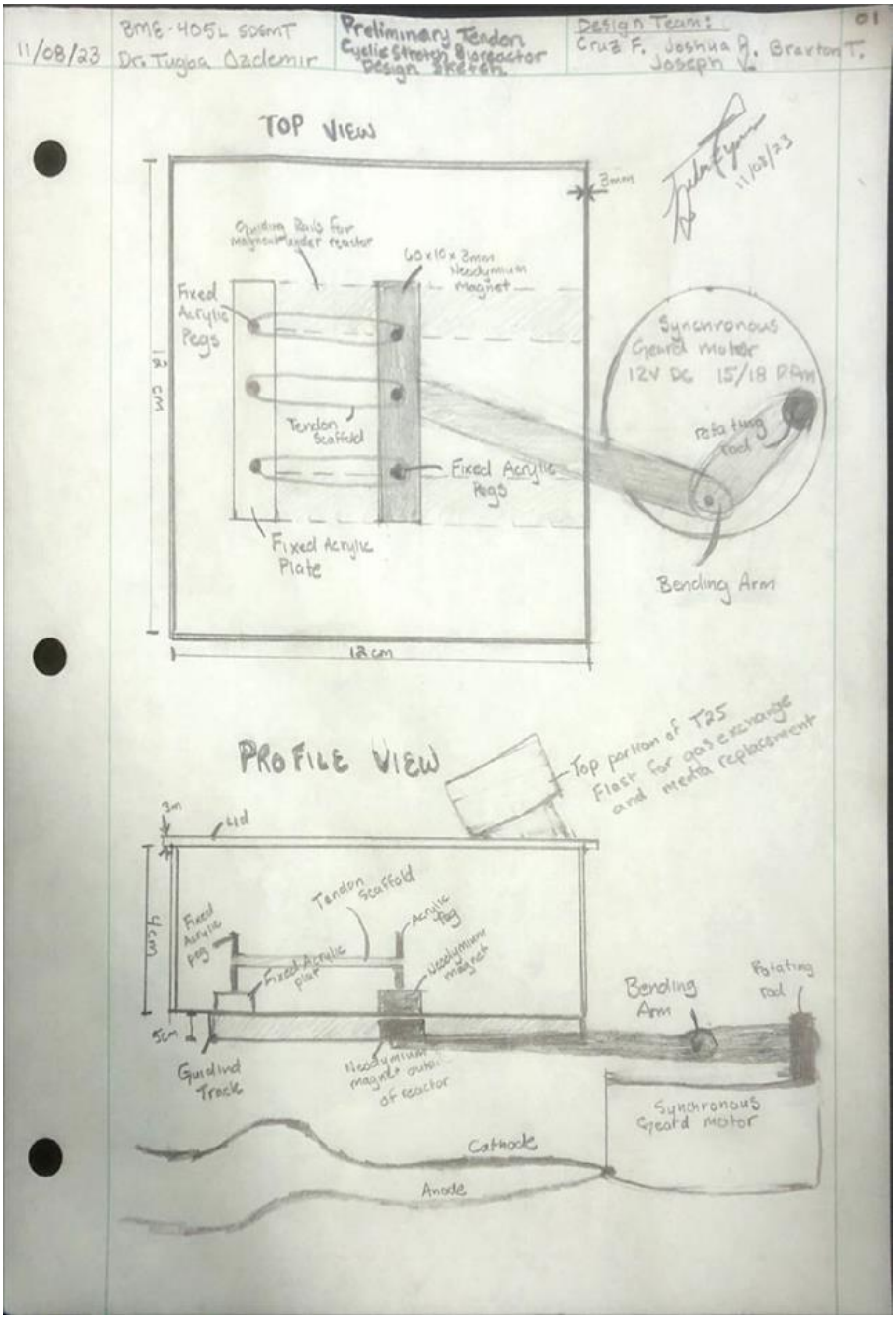



This is a design concept that another team working on this project had modeled. Tendon scaffold stretch is completed by wraping the scaffold around the two pegs which are connected to gears. The benefits of this model is that the streching of the tendon scaffold more accurately mimics the movement of the tendon in a human shoulder tendon. The amount stretch on a tendon made went from 0.33" to 1.5% achieving the 50% stretch constraint. The gears will be hooked up to a small 8V motor allowing for non-human intervention. Compartents can be added to increase the amount of scaffolds the reactor can hold to greater than three. This design seems bulky and does not utilize the space of the bioreactor efficiantly.

STEP 4: Test and Evaluate Prototype

At this step, test your designs. Evaluate the test results and identify your best design solution. Present your supporting arguments and success criteria before selecting the best design.

Best design solution: **Stretch-O-Mag**



Reasons:

The Stretch-O-Mag is not only the most novel out of all the ideas that the teams came up with, it also seems capable of having the most benifits. In the place of gears there is a single sliding magnet which will help prevent contamination by eliminating uneccassary surface area that comes with using gears. Also by increasing the amount of space in the bioreactor by getting rid of the grears, this makes it possible to had more tendon scaffold if needed. The T-25 media flask alows for 5% gas exchange and easy access to replace media as needed. Also, it demonstrated the most tendon stretch. Materials being used for the design are also relatively inexpensive.

ITEM:	**Description:**	**Cost:**
Motor	CHANCS DC Turntable Motor, Synchronous Geared Motor TYC-50 12V DC 15/18RPM 4W Low Speed CW/CCW Direction for Hand-Made, School Project, Model or Guide Motor	$15.90
Magnets	MIKEDE Strong Rare Earth Neodymium Magnets, Heavy Duty Bar Magnets with Double-Sided Adhesive, Powerful Pull Force, Perfect for Fridge, Garage, Kitchen, Science, Craft, Office, DIY 60x10x3mm 6pack	$15.99
Glue	Lactile Epoxy Glue (148 deg C)	$7.99
Screws and Wing Nuts	Four screws and wingnuts for closing the lid (4x)	$3.08
Acrylic (Plexiglass)	16" x 24"	$15.99
	Total:	$58.95

STEP 5: Optimize the Design

At this step, retest your best design and then interpret the outcomes. Before retesting your best design, note what changes you've made.

What was improved (optimized) in the selected design/Retest outcomes:

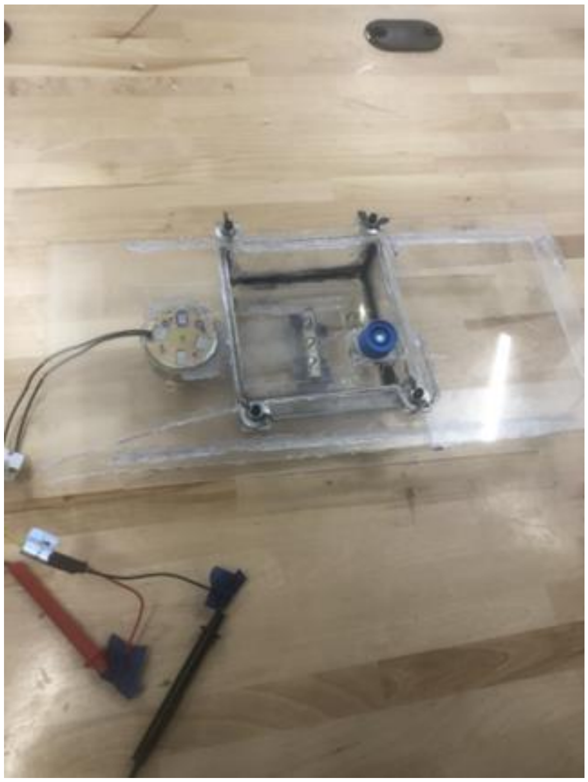
- **Smoothed Down the Magnet Track with Sand Paper: To make magnet slide smoother and more even across bioreactor. Result: Magnet was observed to have a much smoother movement throughout sliding process.**
- **Voltage Increased: To make help insure a more consistant movement. Result: Arm moved at a consistand velocity of 2.25 seconds per rotation**

- **Decided that Sterilization Could only be Done via UV Light or Plasma Sterlization: This will prevent the loss of magnitization that occured through the autoclaving. Result: Magnents will work the way they were designed and calibrated to**
- **Created a Stand to Hold Bioreactor: To stablize the bioreactor and prevent it from moving while the arm and rotating. Result: Bioreactor no longer moves/shifts while the arm is rotating meaning it is okay to leave by itself without the need to worry if it "walks"**
- **Recoated the Seams with Epoxy: To ensure that the bioreactor properly holds media. Result: The media stays within the bioreactor with zero leakage observed.**

STEP 6: Share your solution

At this step, create your final report which will include the information from your design process, the tissue engineering knowledge you used, the strengths/restrictions of your final design, and any suggestions for further work.

Describe how your best design came to be:



The Stretch-O-Mag was intitially tested using Legos just ensure the dimension would work out and to observe if the design was even feasable. This design was a favorite amongst the team because reduced the chances of contamination due to it not using gears, it increased the available space within the bioreactor allowing for more tendon scaffold attachments and obervational access, it was the most novel, and seemed to meet all design contraints. The only issue the team found with this design was the fact that the magnets were not able to go through the autoclave and maintain its magnetic strength. After creating the prototype a few components were optimized in order to increase its effeciency and increase the likelihood that all design requirements were met. The team then tested the required contraints and found that it met all design contraints except for it not being autoclavable.

Do you have a perfect design in the end? Explain your reasoning briefly.

We do not have a perfect design. Our final prototype, though it works, should continue to be optimized and changed. It is not unreasonable to have several prototypes of the same design with each one being an improvement on the last. With more time and resources, our team feels like this could potentially be a standard for building a bioreactor for shoulder tendon scaffolds. It is cheap to make, mimics the movement of the tendon within the shoulder accurately enough, and meets all requirements except it not being able to be autoclaved. This project is the first steps into potentially making a novel and effective bioreactor for shoulder tendon scaffolding. Alot more work, optimization, and testing needs to be completed; however, this prototype is a promising first step.

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Appendix 4. Survey to Students:

Class and Lab Rating

How willing would you like to do a project like this again?

0 - Hated it and never want to do another project like it.	1	2	3	4	5 - Didn't hate but didn't want to do again.	6	7	8	9	10 – Would do again and would recommend others to do it as well.

How encouraging was the LEGO® portion to conceptualize your design?

0 – Cumbersome, and more of a hinderance in learning.	1	2	3	4	5 - Neutral on helpful, could have used it or not.	6	7	8	9	10 – Helped solidify the plan and idea in a tangible form before making a prototype.

How likely would you use a LEGO® portion in other projects that you are working on to help in design?

0 – Not at all, wouldn't be useful/applicable	1	2	3	4	5 - Neutral, would be helpful for somethings	6	7	8	9	10 – Very likely, would be used in almost every aspect of design

How adequate was the duration of the project?

0 – Very bad, rushed on everything and did not have enough time to complete anything.	1	2	3	4	5 - Could have been better, rushed on some parts, or too much time	6	7	8	9	10 – Very Good, didn't feel rushed or had enough time to complete everything.

How useful was it to use the maker space in the finalized design?

0 – Not useful, More of a hassle to use than doing it on your own	1	2	3	4	5 - Neutral, helpful in some areas, not in other.	6	7	8	9	10 – Very useful, every part of the design was made using the space.

How helpful was designing a tissue engineering bioreactor with the knowledge you learned in the class portion?

0 – Not helpful, didn't combine the knowledge with lab at all.	1	2	3	4	5 - Neutral, helpful with some material.	6	7	8	9	10 – Very helpful, incorporated all elements of the class to the lab.

Free Response Section, give your honest answers. I'm not looking up your student ID numbers it's just to make sure each person turned it in.

1. Did you do any other design activity this semester? How did it compare to this lab?

2. What is the most striking impact of this activity?

3. Which part did you enjoy the most?

Rate yourself after completing the lab and class, comparing yourself to the beginning of the semester.

1 - Not at all, 3 - Neutral, 5 - Very well

Now I feel confident in being an engineer, specifically in tissue engineering.	1	2	3	4	5
I feel confident in designing a tissue engineering bioreactor.	1	2	3	4	5
I feel confident using the maker space and their tools in other projects to help further my designs.	1	2	3	4	5
I am good at engineering.	1	2	3	4	5
I am confident in applying my knowledge in tissue engineering.	1	2	3	4	5
I am able to work in a team to accomplish a goal.	1	2	3	4	5
I can successfully come up with a project, follow through, and present findings.	1	2	3	4	5
I am good at problem solving.	1	2	3	4	5

Entrepreneurial Skills: how did you demonstrate each of the C's? Use drawings, words, or whatever you need to express each one.

Curiosity

Connections

Creating Value

Appendix 5. List of LEGO® Pieces:

All of these pieces should be given to one group, multiply the amounts for each group there is:

- 10 Technic gears with different teeth amounts
- 30 An assortment of lengths of one wide LEGO® bricks
- 20 An assortment of lengths of one wide Technic LEGO® bricks
- 5 Rubber bands
- 20 Technic pegs
- 20 Technic axels for the gears
- 30 Assortment of flat LEGO® pieces to allow for sliding mechanisms.
- 1 Flat LEGO® build plates, about 32x32

Appendix 6. Student Consent Form

You are invited to participate in a study of teaching and learning impact of an engineering design component integration into [redacted] Cell and Tissue Engineering course[redacted] We hope to learn information about how teaching and learning take place in the class—information that will help future teachers of such courses to improve their teaching. The outcomes of the study may include such items as published articles, books, online resource materials for teachers, conference presentations and workshop materials.

The study will not take any extra time from you except what your teacher requires as part of the course. Your name will never be used in any outcome of the study. All your work will be anonymous. There are no known risks for you in this study. The rewards include an opportunity to benefit from your own self-reflection on your learning and to help future teachers who will be teaching Tissue Engineering class throughout the world and consider incorporating engineering design components into their syllabus.

If you agree to participate, some of your course material, including the engineering notebook, or some personal interviews (all used without name) will be used in the study, along with similar materials from students.

Your decision whether or not to participate will not affect in any way your future relations with your teacher or your institution. If you decide to participate, you are free to withdraw your consent and discontinue participation at any time without penalty. If you have any questions, please contact the project's Principle Investigator, [redacted]

Please sign this form, submit one copy to Dr Ozdemir and keep the other copy for your records. You are making a decision whether or not to participate. Your signature indicates that you are a student enrolled in this class and have decided to participate, having read the information provided above

Please PRINT your name clearly

Signature

Date

Your Professor's name

I am at least 18 years old: _______YES. ________NO

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