



Microscope Low-Cost Motorized Stage

Preliminary Product Design Specifications

Biomedical Engineering 300/200: Biomedical Engineering Design

Date: 10/20/2021

Client: John Puccinelli

Team Members: Mark Nemcek, Nate Burkard, Corey Steinhauser, Alex Nadolski, Caitriona Treacy, Charlie Fisher

Abstract

The biomedical engineering teaching labs at the University of Wisconsin-Madison have two inverted fluorescent microscopes. These microscopes are the Nikon Eclipse Ti-U and the Olympus IX71. Both of these inverted fluorescence microscopes are currently controlled using manual translational control knobs. These manual control knobs do not allow for automated imaging and automated stitching of images. Integrating a motorized stage allows for a range of functions including time-lapse imaging, automated tracking, and image mosaic creation. The current commercially available options for motorized hardware for the stages of microscopes are quite expensive. The goal of this project is to design, program, and fabricate a lower cost motorized stage to be used for inverted fluorescent microscopes to allow for automated imaging and automated stitching that can be integrated with the Nikon Elements imaging software in the teaching labs. The mechanism must cost less than \$100 and the resolution of the stage's movement should be around 1 μm .

Table of Contents

Abstract	2
Table of Contents	3
Body	3
Introduction	3
Background	5
Preliminary Designs	5
Design 1: Replaceable Stage	5
Design 2: Worm Drive	7
Design 3: Attachable Gearbox	8
Preliminary Design Evaluation	9
Fabrication Development Process	11
Conclusions	12
References	13
Product Design Specification	14

Body

Introduction

In the current biological research community, innovative technology and more efficient research methods has been essential for progress. Improving research methods with technology can make results more accurate and time-efficient. As important as improving research methods and technology is, it is equally important that the technology is easily accessible and at low-cost, for more people to be able to use. The more people with access to the efficient and affordable technology, the quicker the development of research will be.

Microscopes are a certain type of technology used to help researchers see microscopic organisms and other types of cell biology. They are a key visualization tool used throughout several areas of research and development of drugs. Combining microscopy and imaging allows for permanent images to be taken of a microscopic sample, to evaluate at later times. Although imaging for future use is crucial for gathering and presenting research, it is not always intuitive. The ability to understand the microscope and all it is capable of can be critical for maximizing the potential use of imaging microscopy. Creating a more intuitive type of imaging microscopy can speed up the research process and lead to faster results.

Furthermore, automating the imaging process will allow imaging with a click of a button. Computer software and motors that control the stage can take images and stitch them together creating a large image of the entire sample, while still being able to zoom in on particular parts of the sample to see them in full focus. While there are some versions of microscopes with automatic imaging capabilities, these designs are expensive and therefore not always accessible for research. A tool or attachment for a microscope is needed to add automatic imaging to current microscopes.

Current designs for an automatic imaging tool include more affordable replaceable stages made by research groups [1]. These designs are useful, but can be difficult to standardize over several different types of microscopes, since stage size can vary, and having a replaceable stage may not be the easiest to attach and remove. More expensive products made by companies called Echo and Prior Scientific also come up with solutions. The Echo in specific, has many useful imaging features including imaging and stitching, but comes as a whole new microscope, and costs around \$70,000 making it not feasible [2].

The biomedical engineering teaching labs have two inverted fluorescence microscopes, that use stages controlled by translational knobs. Manipulating these manual translational knobs to take images can be a tedious, and non-uniform process, making it an inefficient system to create sub-par images. Creating a cost-efficient method to automate imaging and stitching can benefit the BME teaching lab with a more efficient way to make accurate images.

Background

At the BME teaching labs there are two inverted fluorescence microscopes, the Nikon Ti-U and Olympus IX71. Fluorescence microscopy is ideal for imaging samples in biology labs because it allows the imaging of targeted, single cells using a naturally fluorescent protein or antibody as a fluorescence tag [3]. The Nikon Ti-U comes equipped with TI-SR Rectangular Mechanical Stages [4] and the Olympus IX71 comes with IX-MVR Mechanical stages [5]. Both stages can be controlled manually using the stage knobs in the x and y directions. Ideally, a motorized stage would be used because of its accuracy in movement and its capability for automated imaging. However, obtaining a motorized microscope stage can be very expensive. To image, software called Nikon Elements Basic Research is capable of processing, measuring, and analyzing images [6]. The integration of a motorized microscope stage with the Nikon Elements Basic Research software makes collecting imaging data easier and more time efficient, by allowing for automated imaging and stitching. An imaging device that can be easily detachable from the microscope will create a more affordable solution for a motorized stage with automating imaging and stitching. Our client for this design project, Dr. John Puccinelli, the Associate Chair of the Undergraduate Program at University of Wisconsin-Madison wants a device that can be easily attached or removed to the microscope and the movement must have a resolution of 1 μm . It must be integrated with Nikon Elements to be programmed to do a 30-minute automated imaging and stitching process. Finally, the device must be low-cost, within the budget of \$100. See Appendix A for the full Product Design Specification.

Preliminary Designs

Design 1: Replaceable Stage



Figure 1. The Replaceable Stage. This stage would replace the current stage. The joystick on the right controls the stage movement [7].

The first alternate design is the Replaceable Stage design. This design would entail the complete removal and replacement of the current stage. Currently, the stage has a manual knob that controls the Y-axis and X-axis movement of the stage. Instead of trying to build a motorized design that connects to these knobs, with the Replaceable Stage we would completely replace the stage. The benefits of doing this design idea are numerous. For one thing, if the group decided to fulfill this design, there would be complete freedom of how the stage was designed, how it moved, and how we incorporated the motor. This is in contrast to the other designs, which are limited by the current stages' knob mechanism. Unfortunately, this design also has some major drawbacks. Since there are two different types of microscopes, the Nikon Eclipse Ti-U and the Olympus IX71, that would mean the group would have to design two completely different stages with the specs and size of each individual microscope. This would be both expensive and time consuming. The expenses are partially due to the size of the stage being relatively large and the variety of materials that would likely be required to replace all functional aspects of the current design. Time constraints also prevent the design of the stage from being efficiently created and functional to the high standard of the current design.

Design 2: Worm Drive

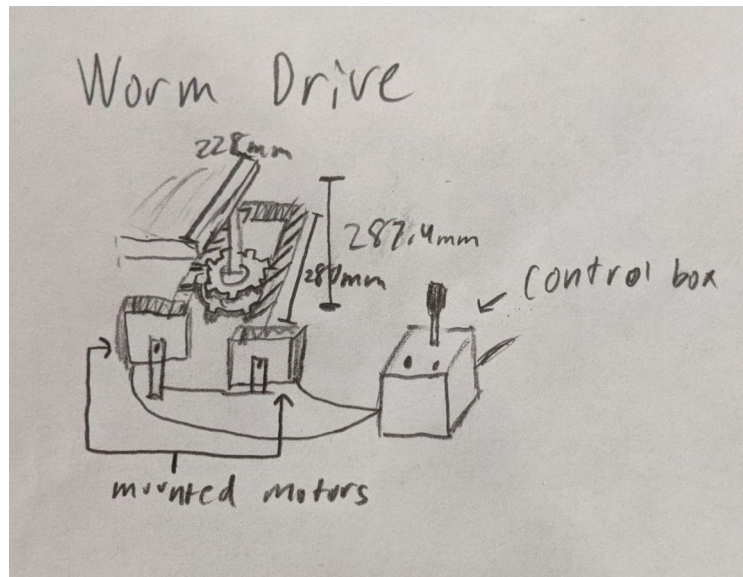


Figure 2. The Worm Drive consists of two worm gears attached to the manual shaft and controls the stage via rotation in the worm gears.

The second alternative design that the team is considering is called the Worm Drive. This design would attach to the current knobs that manually control the movement of the stage in the X and Y direction. This design uses two motors that are fixed in place. Both motors would rotate a long worm gear. One of the motors would be assigned to the X-axis knob and the other would be assigned to the Y-axis knob. As the motor spins the worm would spin the so-called worm wheel gears that are attached to the manual knobs. This design has many advantages. Firstly, since the manual knobs are very similar on both the Nikon Eclipse Ti-U and the Olympus IX71 microscope, it would be very easy to make one design that works with both microscopes. Secondly, this design would require a lot less expenses than that of the Replaceable Stage design. Since the group has a budget of \$100, it is important that the design not be overly expensive. Finally, this design would solve an issue that the previous group was having with their design. When the manual knob in the Y-direction is turned, the entire arm containing both knobs moves. Since the motors are not attached to the arm in this design and the worm gears allow for translation along the y axis without decoupling the gears from the worm wheels, this issue is mitigated. The worm gears also provide a very high degree of accuracy due to the high gear ratio relative to the size of the gears. While the Worm Drive does have many positives, there are also a

few negatives associated with this design as well. One negative of the Worm Drive design is that the team would have to undo some of the work done by the past group in order to go through with this design. The group would have to create all new gears and would not be able to use the current gears or motor attachment that are in place right now. It also has the issue of increased friction between the worm gears and the gears themselves due to increased surface contact[8].

Design 3: Attachable Gearbox

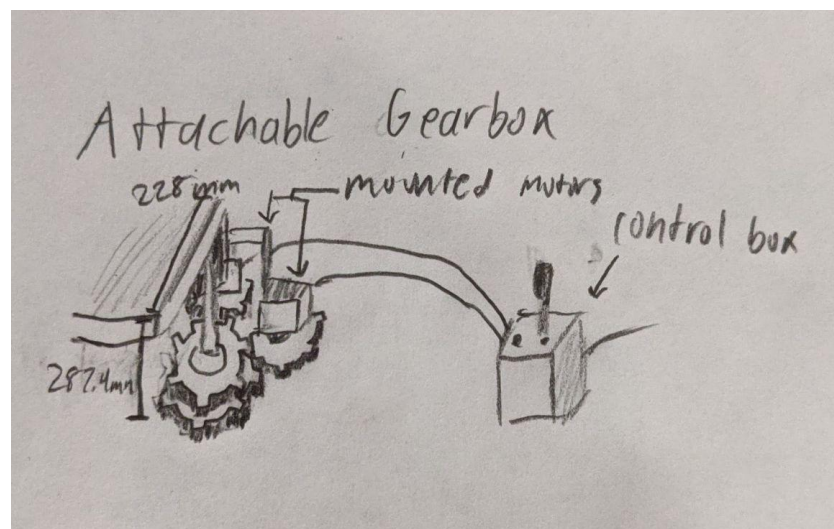


Figure 3. The Attachable Gearbox Design. The motor is attached to the stage on the left. The gears are attached to the stage knob and the motor shaft. The control box on the right has a joystick to control the stage.

The third and final design is called the Attachable Gearbox. This design is similar to the design which was previously being worked on by the past group. Similar to the Worm Drive design, the Attachable Gearbox uses two motors, one for movement in the X direction and one for movement in the Y direction. Unlike the Worm Drive design however, the motors are attached to the arm of the microscope which contains the manual knobs. These motors turn a set of gears, which are attached to the gear on the manual control knobs. Therefore, when the motors are activated there is control over both the X and Y direction of movement. This design has many benefits. One of the main benefits of this design is that the team would not have to design new gears or motor attachments. This would save a lot of time and energy. One main

disadvantage to this design is that as the stage moves in the Y-direction, the entire arm moves with it. This causes issues when it comes to wiring as well as the gears staying together. Unless the team can come up with an effective solution to this problem, it would be a major inhibitor for continuing with this Attachable Gearbox design. Another main disadvantage is the additional strain placed on the stage itself. Since the stage is not designed with additional attachments in mind, the addition of two fairly heavy stepper motors to the stage may interfere with prolonged functioning of the stage.

Preliminary Design Evaluation


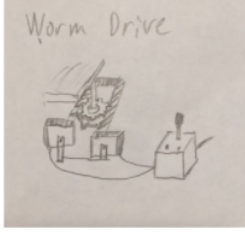
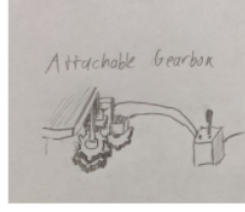
	Replaceable Stage		Worm Drive		Attachable Gearbox	
Design Criteria						
	Score	Weighted Score	Score	Weighted Score	Score	Weighted Score
Accuracy (25)	5/5	25	4/5	20	3/5	15
Cost (20)	1/5	4	3/5	12	3/5	12
Detachability (20)	2/5	8	4/5	16	3/5	12
Ease of Use (15)	3/5	9	5/5	15	5/5	15
Longevity (10)	5/5	10	4/5	8	5/5	10
Safety (5)	4/5	4	3/5	3	3/5	3
Ease of Fabrication (5)	1/5	1	3/5	3	5/5	5
Total (100)		61/100		77/100		72/100

Figure 4. The Design Matrix. The matrix evaluates the three preliminary designs (at the top) based on seven criteria (on the left). The boxes highlighted in yellow show which design scored best in each category. The Worm Drive Design scored the highest overall.

After narrowing down the team’s preliminary ideas for the design, a list of criteria was developed to evaluate the top three designs and compare them to one another. Accuracy was

given the most consideration in the design matrix due to the general importance of accuracy as it relates to mechanisms in the lab. The thought process here was that if a motorized state compromised the accuracy of the overall system, it would be of virtually no use in the lab.

The team also gave increased consideration to the projected cost of each project given the emphasis placed on the element of cost by the client. The main purpose of the project is to find a lower cost alternative to the options currently available, something that was important to reflect in the evaluation of the preliminary designs.

Detachability has to do with the ease with which the device would be able to be removed from the microscopes in the lab. This struck the team as significant because creating a prototype which requires complex changes in the structure of the microscope itself might result in increased complication and less ease of use. The idea here was that creating a device that could be easily interchanged between microscopes would likely yield the best results in terms of functionality in the lab.

Another measure that the team thought was important to consider with each design was how easy it would be to use. Given that this device is intended to be used in labs on campus, it is important that the product be intuitive and not complicated to use so that it can be utilized by all those who work in the lab rather than a select few with a specific skill set or training.

Longevity was given consideration in the design matrix due to the fact that the client had mentioned the desire for the product to “last forever,” but it was not given exceptionally high consideration because the team did not foresee any significant differences in longevity between designs. In terms of materials, each design requires similar parts, but the differences in longevity were attributed mainly to the possibility of shifting in the mechanism to cause malfunctions sooner in the Worm Drive design compared to the others.

Safety is something that should always be kept in mind for any design, but given that the nature of the project does not suggest a high-risk mechanism regardless of the design, it was not found suitable to give safety extraordinary weight in the design matrix. The thought here was that all design options in the matrix entail similar risks which are relatively low to begin with.

Ease of fabrication was a consideration that held importance to the team given the timeline for when the product will ideally be fabricated. The team thought it was worth contemplating how realistic it would be to fabricate each design as getting a physical prototype is a goal of the semester. However, ease of fabrication was not weighted as highly as the other

categories of evaluation due to the simple fact that just because a design is easy to fabricate does not mean that it is better in functionality or other, more important, aspects.

Proposed Final Design:

Based off of the design matrix, the group decided that the Worm Drive would be the fabricated design. The Worm Drive Design exceeded the score of the Attachable Gearbox in the design evaluation by a relatively small margin. This resulted primarily from the notion that Worm Drive design excelled in many of the criteria the group weighted most heavily in the matrix. In all three of the categories of accuracy, detachability, and longevity, the design scored a four on a five point scale. These categories were important because they reflected specific preferences voiced by the client. Namely, the need for the microscope to have a resolution between 1-10 μm , be detachable, and last forever. The Worm Drive design also scored joint first in cost effectiveness, and scored full points in ease of use. This is beneficial to the design because students will be using the microscope frequently, so it should be intuitive to maximize accessibility on campus. Through careful completion of the design evaluation criteria as it related to each preliminary design, it became apparent that the Worm Drive design was the preferred design for the team to proceed with.

Fabrication Development Process

Materials:

There are various materials necessary to create a functioning prototype of the Worm Drive Design. The first thing that the group will need is the worm drive gears themselves. The team is hoping to design these gears and 3D print them. If that is not an option, the group will look into buying worm drive gears that fit into our design. Next, the group needs two motors for the worm drive gears to be functional. These two stepper motors are provided by the past design group. Additionally, the group will need an Arduino Uno as well as wiring. These items are already owned by members of the group. Finally, the group will need a joystick device that will be used to control the movements of the stage. This will need to be purchased by the group.

Methods:

The group will either buy or 3D print worm drive gears. Next, the team will fabricate motor holders which correspond to the height of the gears on the manual knobs on the arm of the microscope. After fabricating the motors the team will attach motors to the motor holders and worm drive gears. Finally, the team will use an Arduino Uno Microcontroller to create a program allowing the joystick to control the motors.

Testing:

After a prototype of our Worm Drive design has been created, the group will perform various tests in order to assess the performance of the design. The team will test the accuracy of movement by setting the device to move a known distance, and then directly measuring to see if there is error in the movement of the stage. To test how well the final product can complete image stitching, the group will run an experiment that requires the use of image stitching, and assess the effectiveness.

Conclusions

The teaching lab in the Engineering Centers Building of the University of Wisconsin Madison has two inverted fluorescent microscopes. The group was tasked with creating a low cost motorized microscope stage for these microscopes. The current microscopes are controlled by manual translational knobs that must be spun to move the stage. These manual knobs do not allow for automated imaging or image stitching. The team decided on the Worm Drive for the final design. This design consists of two motors which each control one worm drive gear. One worm drive gear would control the movement in the x-direction and the other would control movement in the y-direction. Ultimately, the goal would be to have these motors be controlled by a joystick or other control mechanism and the resolution of the stages' movement should be 1 um. Moving forward, the group wants to 3D print worm drive gears to fit to the arm of the manual knobs. Additionally, the team will use two motors connected to an Arduino Uno Microcontroller. The Arduino Uno Microcontroller will be used to program a controller that can control both the x-direction and y-direction motor. Finally, the team will perform a series of tests to examine the efficacy of the design.

References

- [1] Bhakti, T., Susanto, A., Santosa, P. and Widayati, D., 2021. *Design of Motorized Moving Stage with Submicron Precision*. [online] Citeseerx.ist.psu.edu. Available at: <<https://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.589.55&rep=rep1&type=pdf>> [Accessed 15 October 2021].
- [2] Discover-echo.com. 2021. *Revolve Fluorescence Microscope by Echo*. [online] Available at: <<https://discover-echo.com/revolve>> [Accessed 15 October 2021].
- [3] K. Thorn, "A quick guide to light microscopy in cell biology," *Molecular biology of the cell*, 15-Jan-2016. [Online]. Available: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4713126/>. [Accessed: 20-Oct-2021].
- [4] "Nikon Inverted Microscope ECLIPSE Ti-U Ti-U/B Ti-S Ti-S/L100 Instructions," *eliceirilab.org*. [Online]. Available: <https://eliceirilab.org/sites/default/files/2016-09/Nikon%20Eclipse%20Ti-U%20Manual.pdf>. [Accessed: 19-Oct-2021].
- [5] "Instructions IX71/IX51 - University College Cork." [Online]. Available: https://www.ucc.ie/en/media/academic/anatomy/imagingcentre/icdocuments/OLYMPUSIX71_manual.pdf. [Accessed: 20-Oct-2021].
- [6] "NIS-elements: NIS-elements basic research," *Nikon Instruments Inc*. [Online]. Available: <https://www.microscope.healthcare.nikon.com/products/software/nis-elements/nis-elements-basic-research>. [Accessed: 11-Oct-2021].
- [7] Holmarc.com. 2021. *Microscope Translation Stage*. [online] Available at: <https://www.holmarc.com/microscope_translation_stage.php> [Accessed 15 October 2021].
- [8] Roymech.org. 2021. *Worm Gears - Roy Mech*. [online] Available at: <https://roymech.org/Useful_Tables/Drive/Worm_Gears.html> [Accessed 19 October 2021].

Appendix

Appendix A:

Product Design Specification

September 24th

Client: Dr. John Puccinelli

Advisor: Dr. Melissa Skala

Team Members:

Mark Nemcek (Team Leader) mtnemcek@wisc.edu

Nate Burkard (Communicator) njburkard@wisc.edu

Corey Steinhauser (BWIG) steinhauser2@wisc.edu

Charlie Fisher (BPAG) ctfisher3@wisc.edu

Caitriona Treacy (BSAC) ctreacy2@wisc.edu

Alex Nadolski (BWIG) rnadolski@wisc.edu

Function:

Inverted fluorescence microscopes are currently controlled using manual translational control knobs. These manual control knobs do not allow for automated imaging and automated stitching of images. Our goal is to design, program, and fabricate a motorized stage to be used for inverted fluorescent microscopes to allow for automated imaging and automated stitching that can be integrated with the Nikon Elements imaging software. The stage must cost less than \$100 and the resolution of the stages' movement should be around 1 μm .

Client Requirements:

- The movements of the stage should be able to be controlled by joystick or computer software.

- The program should be able to perform automated imaging and stitch images together.
- Team must create a motorized mechanism that moves and controls the stage.
- The movements of the stage should be within a resolution of 1-10 microns in x and y direction.
- There needs to be a fast and slow mode for the joystick.
- Should be powered by a wall outlet, and there needs to be a switch to turn the device on and off.

Design Requirements:

1. Physical and Operational Characteristics:

- Performance Requirements:* The product must be able to automatically take pictures, and stitch them together. This device will be used often, and should be easy to put on and remove as an attachment. Should be powered by a wall outlet, but needs to have a switch to turn the device off. The device should be able to take images and stitch it in a 30 minute cycle.
- Safety:* It is important for the team to keep moving elements of the stage enclosed, such as gears. Additionally, it is vital that any high-voltage elements be insulated and well organized, as to not cause any danger to the user.
- Accuracy and Reliability:* The stage should have an ideal movement resolution of around 1 μm . The client specifically requested that the stage have a resolution between 1 and 10 μm . Cannot drift during imaging cycles to prevent faulty imaging.
- Life in Service:* The microscope stage should be able to be used for as long as the microscope is in use. Since the microscopes have never had to be replaced in the past, the goal for our shelf life would be forever. A quantifiable goal would be at least 20 years of quality use.
- Shelf Life:* When not in use, the device should be stored at room temperature and in a dry environment. The device will not require batteries as it will use standard wall power to run.
- Operating Environment:* This device should be able to withstand similar temperatures to the microscope at 0°C - 40°C and less than 60% Humidity [1]. The device will be used inside

where it will spend most time at room temperature, so it does not need to withstand a fluctuating temperature or environment.

- g. *Ergonomics*: The mechanical elements should not be able to be manipulated manually and should only be controlled using the provided controller or designed software.
- h. *Size*: Should be able to be easily attached and removed and should not inhibit the movement of the stage in any direction. If we decide to replace the current stage plates, the new plates must not be taller than the current plates, otherwise the inverted fluorescent microscope will be inaccurate.
- i. *Weight*: The weight of the stage should be small enough that it does not affect the balance or the mechanical properties of the microscope.
- j. *Material*: There are not any restrictions, however typically light weight aluminum is used. Given the emphasis on keeping costs low, finding a material that functions well while also minimizing overall costs will be beneficial.
- k. *Aesthetics*: Stage should be black in color, so it does not reflect light from the inverted fluorescence microscope. Stage should not be too bulky, as it needs to be able to be used practically with a classroom.

2. **Production Characteristics:**

- a. *Quantity*: The client wants us to aim for an end goal of two units since there are two similar microscopes in the teaching lab, but he would be happy if we made one as long as it is functioning as desired.
- b. *Target Product Cost*: The product must be less than \$100. Client stated if necessary the group could go slightly over the target product cost, but does not expect this to be necessary.

3. **Miscellaneous:**

- a. *Standards and Specifications*: Microscope stages do not need FDA approval as they are device class 1, which makes them exempt [2]. Nikon Ti-U Inverted Fluorescence Phase Contrast Microscope Pred Ti2 is the microscope that we will be using. Standard microscope safety procedures should not be compromised by the product.

- b. *Customer:* Our customer would like us to have our design able to be controlled by a joystick as well as a computer program that can operate independently.

- c. *Patient-related concerns:* Needs to be intuitive so that students who use the teaching lab will be able to use it for years to come. With the ongoing pandemic, the device needs to be able to be easily cleaned.

- d. *Competition:* A couple of companies are selling work that is similar to our own. One of these companies is Zaber [3]. Some other companies doing this type of work are Prior Scientific [4] and Echo [5].

Works Cited: IEEE format

- [1] "ECLIPSE Ti2 SERIES: SPECIFICATIONS," *Nikon Instruments Inc.* [Online]. Available: <https://www.microscope.healthcare.nikon.com/products/inverted-microscopes/eclipse-ti2-series/specifications>. [Accessed: 22-Sep-2021].
- [2] "Product classification," *accessdata.fda.gov*, 20-Sep-2021. [Online]. Available: <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpd/classification.cfm?id=5177>. [Accessed: 24-Sep-2021].
- [3] *Zaber Technologies*. [Online]. Available: https://www.zaber.com/products/scanning-microscope-stages?gclid=Cj0KCQjwqKuKBhCxARIsACf4XuFgEuegCULlyzycG19HIr-bf7WOgpQ68wCHPqkBGRQRDXsFb2vVrIkaAIlpEALw_wcB. [Accessed: 23-Sep-2021].
- [4] "Microscope motorized stages, XY stages, precision stages," *Prior Scientific*. [Online]. Available: <https://www.prior.com/product-category/motorized-stages?gclid=Cj0KCQjw1ouKBhC5ARIsAH>

XNMI9_AsBqKR83FdP0QIOOnJo6ztnDI9AJOTtT2zUPyAKtAoAT4fysqFrSaAqnMEALw_wcB.
[Accessed: 24-Sep-2021].

[5] “Redefining microscopy for life science research,” *Discover Echo*. [Online]. Available:
https://discover-echo.com/?utm_source=google&utm_medium=search&utm_campaign=11380688541&utm_term=motorized+microscope+stage&utm_content=505993872680&gclid=Cj0KCQjw1ouKBhC5ARIsAHXNMI_3xPRL8j0lS98sKdirvi69QyfNvPLfS-GGZ8iVymvGb_1_qPeDi7caAgf1EALw_wcB#headerAnchor. [Accessed: 24-Sep-2021].