# Preliminary Report

BME 200/300

October 10, 2018

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# Abstract

Ophthalmology research often requires the viewing of photoreceptor cells in the back of the eye. In order to successfully image all of the subject's photoreceptors, the eye of the subject must be rotated about two axes. Traditional stages for microscopic viewing provide easy solutions for translational movement, but lack the features necessary to rotate while keeping focus on the subject. Our client desires a device which can provide rotational movements around two axes and translational movements in all three dimensions. Different sized subjects will need to be viewed on the device without compromising its movements or accuracy. The final device shall concentrate on increasing the possible motion while keeping the center of all rotations focused on the pupil of the subject.

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# I. Introduction

According to the World Health Organization as of October 11, 2017, there were 253 million people living with vision impairment, 36 million of which were completely blind while the other 217 million had moderate to severe blindness. It is approximated that by 2050 there could be upwards of 115 million people who are blind. This is mostly attributed to a growing population and also an increasing age of the existing population. [1]

Scientists are researching the sources of visual impairments by using microscopy and other optical techniques. Imaging the eye is a technically demanding procedure.[2] The image subject needs to remain stationary while photos are being taken to account for the uneven topography of the eye surface.[3] Both lateral and rotational movement with high precision is also required.

A biomedical optics and biophotonics laboratory currently uses a u-shaped container with a bite bar to stabilize their image subjects which are typically laboratory mice and a thirteen-lined ground squirrel. In their attempt to visualize the photoreceptors of the eye which lie most posteriorly to the pupil, they are using a TMC vibrationless table and an AOSLO microscope.

## *Existing Devices*

### TMC Vibration Control CleanBench

This bench isolates the microscopes and other lab equipment from vibration for more accurate results. The table top (stainless steel) has a honeycomb design such that equipment with screws on the base can thread into the table. It uses Gimbal pistons to maintain vibrational equilibrium. [4]

### Kent Scientific Infrared Warming Pads

While imaging, living specimens are heavily sedated so they require warming pads to maintain constant body temperature. The current pads measure 15.2 cm x 20.3 cm x 0.64 cm and have a removable sleeve and a rechargeable battery. The pads generate infrared waves (which animal bodies absorb 90% of) to heat the specimens. Temperature ranges from 20 to 40 degrees Celsius.[5]

### AOSLO Microscope

Adaptive Optics Scanning Laser Ophthalmoscope (AOSLO) can capture high-resolution images of the retina. It can image individual photoreceptor cells, retinal pigment epithelium cells, microscopic capillary vessels, and the nerve fiber layer. The process is quite complex, but it is important for our design that a prism on the microscope must be placed within 1 mm of the eye.[2]

## *Competing Designs*

*Figure 1: The figure above depicts a Posi drive from Deltron. It is a modular microscope attachment for stage translation (XYZ).*

Posi drives (Figure 1) are devices that allow for XYZ positioning, 12” of travel, and “provide[s] both accuracy and excellent positional repeatability” [6]. This device is, “fitted with lead screw and anti backlash nut and [is] supplied with a motor adaptor and coupling” [6]. In terms of the device that our team is looking at, we could take some of the aspects of the translational movement. However, this device provides none of the rotational movement that our client requested.

*Figure 2: The figure above depicts a Micrometer Positioning Stage from Deltron. It is a modular microscope stage capable of fine XYZ translation.*

Similar to the Posi Drives, The Micrometer Positioning Stage (Figure 2) allows for movement in the XYZ direction, but only allows 0.25” to 2.0” of travel. This device comes in either, “linear ball slide [or] linear crossed roller slide technology” [6]. Because of the small limit of travel, the device is extremely accurate and moves efficiently. However, the device cannot move a subject any further than 2.0” which could come as a disadvantage if the client to needs to move the stage any further.

*Figure 3: The figure above is a rotary stage from the company Standa. It allows for fine radial translation (rotation about the z-axis).*

The Rotary Stage of Big Platform 7R170-190 (Figure 3), provides 360-degree rotation about the z-axis; something that could be very useful when it comes to turning the subject while keeping the eye center. The device can rotate to an, “accuracy of 1 degree, and [so] finely to adjust them within 10 degree by micrometer” [7]. This precision is exactly what our client is looking for to make a device that is accurate and easy to position. Another interesting aspect of this device is that it has preset holes that could be used for different modular stage components.

## ***Problem Statement***

While doing research on photoreceptors in the retina of an eye, images are frequently viewed through a stationary device. In order to view all of the photoreceptor cells, the eye in conjunction with a translational/rotational device needs to rotate with at least five degrees of freedom, preferably with six to accommodate for different viewing angles from the microscope. A device must include translational and rotational movements while keeping the center of focus on the pupil.

# II. Background

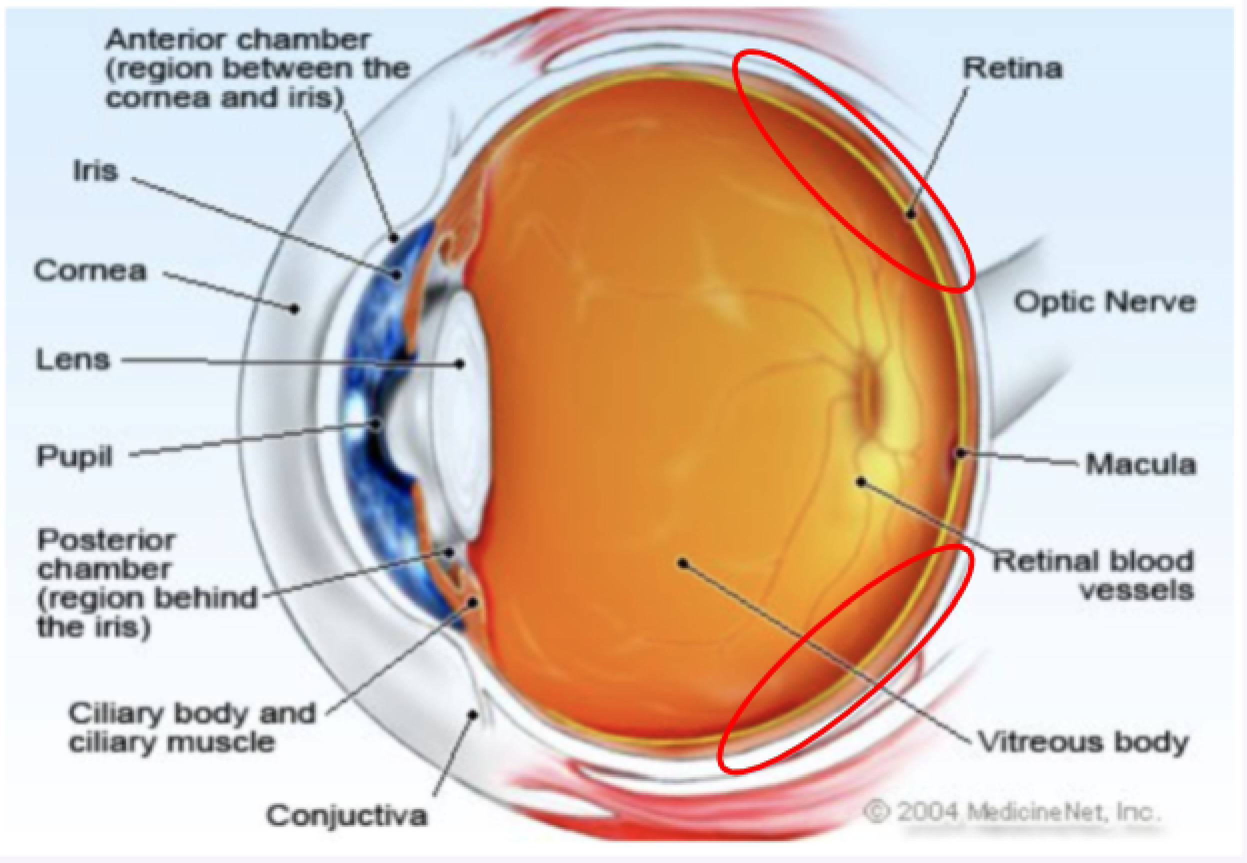

*Figure 4: The figure above is a detailed diagram of the human eye.*

The goal of our design is to image the retina, which, as shown, is in the very back of the eye in relation to the pupil. One should note that the eye has a curved geometry, so in order to see the whole back of the retina, it is necessary to image the eye with something other than a stationary view. By putting the eye at different angles in relation to the imaging device, it is possible to see the rest of the retina, specifically the parts of the retina marked with the red circles.[8]

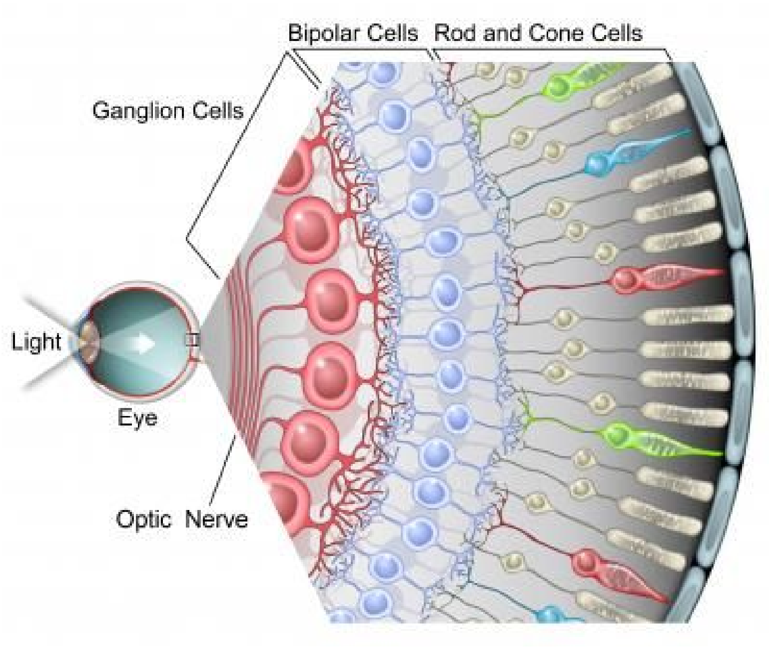

*Figure 5: The figure above is a more detailed and zoomed in version of the retina of the eye.*

The most important thing to notice about figure 5 is the number of photoreceptors situated on the retina. The photoreceptors span throughout the whole retina forming an arc on the back of the eye. Due to this, a stationary stage can only situate the imaging device to see a portion of the photoreceptors. If you rotate or translate the stage so the top or bottom of the retina can be seen, researchers will have an easier time imaging these photoreceptors.[9]

The goal of Dr. Rogers' research is to study the photoreceptors to develop a deeper understanding of the causes behind blindness or visual impairment. The photoreceptors which consist of either rod or cone cells receive stimulus from light energy. Photopigments which are integral to the photoreceptor are made of an opsin and a chromophore. The opsin and the chromophore work in tandem to absorb photons, flip the 11th and 12th carbon atoms from a cis to a trans conformation, and in turn trigger a transduction cascade. Sodium channels open due to the transduction cascade and hyperpolarization results creating a graded potential. This graded potential travels along the photoreceptor cells to the bipolar cells which then continue the graded potential to the ganglion cells. An action potential is initiated at the Ganglion cells which travels to the optic nerve and ultimately to the brain for signal interpretation [3]. Sources of blindness can come from a breakdown in any of the above stated physiological steps.

## *Client information*

Dr. Jeremy Rogers is a researcher and assistant professor in the biomedical engineering department at UW-Madison. He has extensive training and experience in optical sciences and imaging. Throughout his research, Dr. Rogers images photoreceptors in the eyes of many different specimens.

### *Design Specifications*

The stage must have 5 degrees of freedom (i.e. if the x-axis is in the direction orthogonal to the pupil, then rotation about the y and the z is required along with translation on all three axes) and must translate with 100-micron precision. Scientists need to rotate the specimens to focus on ~ 1-micron objects. It must include interchangeable stage mounts for different viewing subjects (detached human eye (2.4 cm diameter, 7.5g), a thirteen lined ground squirrel (33 cm long and 227g), and a white mouse (12.5 - 20 cm long and (12 - 30g)).[10][11][12]. The device shall contain non-absorbing surfaces and must be assembled in a way that limits the number of small creases so that it is sterilizable between uses via alcohol wipes.

Because this is a custom device being used in a research setting that does not store human patient data; there are no international or national standards by which to abide. The device must operate optimally in normal room temperature, pressure, humidity, etc. for approximately 500 hours of use. The device shall weigh under 5 kg and stand less than 15 cm tall to fit conveniently on the lab bench. The device shall withstand drops of 1.0 meter without breaking into shards. The project budget is $250.

## III. Preliminary Designs

### *Design 1: The Park*

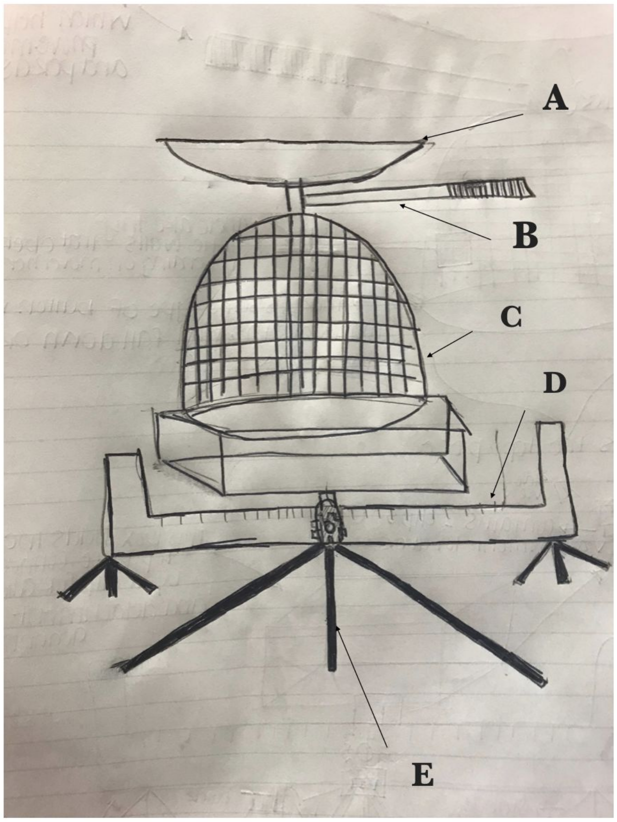

*Figure 6 A: Detachable bed with a small neck (2 cm). B: Handle which acts as a ratchet allowing precise movements ( 8 cm long). C: Dome base, with a grid system and individual walls which allows movement forward but not backward (7 cm diameter). D: Gear track which allows for movement in the XY direction (15 cm). E: Tripod attachment used for stability and translation in the Z- direction (varies).*

It is important in this design to consider that it is similar to the structure of a gear stick within a car. When thinking about the way a car drives it has a function which allows for the gear stick to go forward, lock-in, and then prevents movement backward. This function allows for the device movements to stay put in place on the specific grid system. The top piece consists of a dome, with a grid-like system, and a bed with a smaller neck and a handle that acts as a ratchet. This piece is then mounted onto a box, which is connected to two different clips. One clip is attached to gear track which swings left and right to allow for translation in the XY direction. Then there is a tripod connection which is used for stability and translation in the Z-direction.

## *Design 2: The Rigamortis*

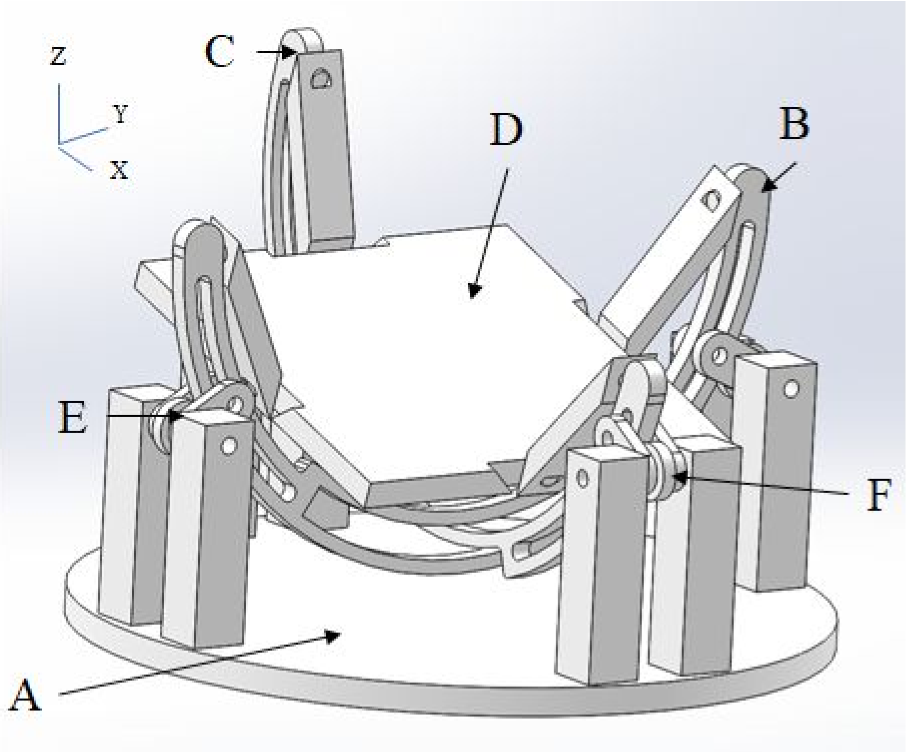

*Figure 7. A: Circular base which can rotate around the z-axis. B: Curved arm which provides rotation around the x-axis. C: Curved arm which fits inside arm B and provides rotation about the y-axis. D: Table attached to arms B and C whose center sits 5 cm below the focal point for rotation in all three directions. E and F: Gears to move arms C and B respectively.*

The Rigamortis design places emphasis on keeping the center of rotation on a fixed focal point, while allowing maximum rotation. Specifically, the device allows 45 degrees of rotation around the x and y-axes and 360 degrees around the z-axis. The axes of all three motions intersect at a fixed point in space 5 cm above the center of the subject table. This makes it so the rotations will always be centered on that point.

Curved guide arms provide rotation around the x and y-axes in The Rigamortis design. The arms are semicircular with a 12 cm radius. The upper 45 degrees on each side will contain gear teeth which match up with gears attached to the base supports. These gears enable the user to rotate the device about the x and y-axes. The gear between the base support arms has 20 teeth, and if the curved arms were completely circular and continuous, it would be a 200 tooth gear. Thus, one rotation of the base gear gives 36 degrees of rotation for the table. This can be further reduced with additional gear combinations, which will become fine and coarse adjustment knobs. In the bottom of one guide arm is a slot which allows the other arm to slide within it. Due to this slot, the arms can have the same radius, but not crash into each other at the bottom.

The spacing between the table and focal point allows for the creation of individualized modular devices for a specific viewing subject. Different sized subjects can have their own specific holder to attach to the table in order to bring the pupil of the eye of that subject to the focal point of rotation. This holder will be attached manually by the user with velcro, magnets, adhesive, suction cups, or some other method which allows the user to move the device to a specific translational position on the table. Each holder shall also include a small mechanism for adjusting the height. With those mechanisms in place, the holder can be translationally adjusted in the x, y, and z directions, giving The Rigamortis 6 degrees of freedom.

## *Design 3: The Rocking Chair*

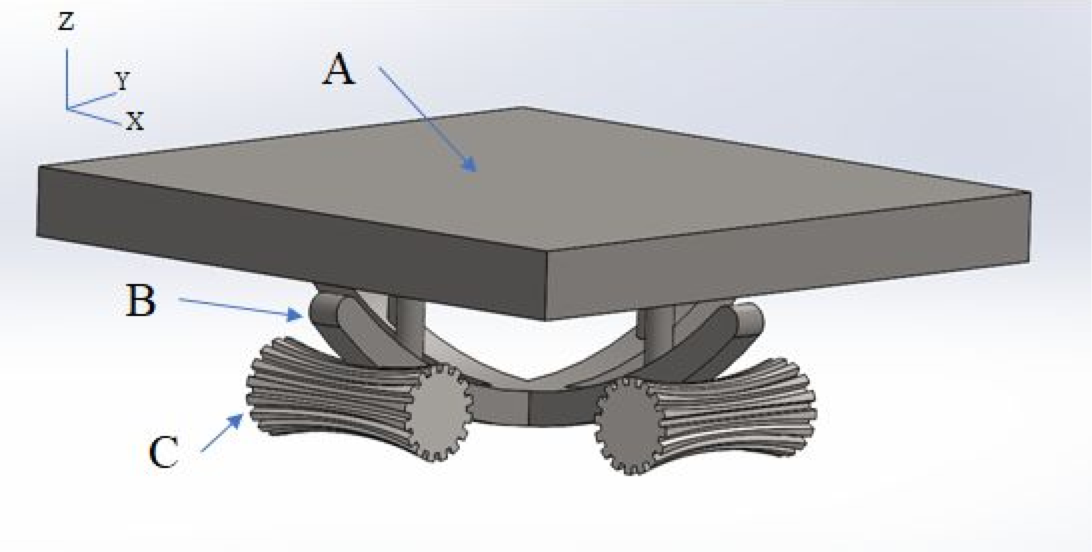

*Figure 8. A: Table for the subject holder. B: A curved gear track which transmits the rotation of a gear (C) to the table (A). C: A curved gear which can rotate to move the table (A) which also allows the gear track (B) to slide when rotating in the opposite direction.*

The rocking chair design features a large, wide, square stage that rests atop a curved gear rack. Two curved gears control the rotation about the x and y-axes. When one rotates (acting as a gear), the other allows the teeth on the curved gear rack to slide. Like the Rigamortis, this allows rotation around the x and y-axes while keeping the focal point 5 cm above the center of the table. This design would have the same modular holders for different subjects to translationally position the pupil of the eye in the focal point of rotation.

The flaw in this device is that the pitch diameter of the gears changes between their center and outsides. Since the number of teeth does not change, the gear's module (diameter/teeth) is not constant, so it will no longer line up with the track below the table. In reality, this would allow only a few degrees of rotation before friction between gear teeth would lock the movement.

# IV. Preliminary Design Evaluation

## *Design Matrix*

| Design Aspect | Weight | **Design 1: The Park Rank (1-5)** | Weighted Rate | **Design 2: The Rigamortis Rank (1-5)** | Weighted Rate | **Design 3: The Rocking Chair Rank (1-5)** | Weighted Rate |
|---|---|---|---|---|---|---|---|
| Precision | 35 | 3 | 21 | 4 | 28 | 4 | 28 |
| Usability | 25 | 3 | 15 | 5 | 25 | 2 | 10 |
| Height | 15 | 4 | 12 | 2 | 6 | 2 | 6 |
| Amount of Rotation | 10 | 2 | 4 | 3 | 6 | 1 | 2 |
| Ease of Build | 5 | 3 | 3 | 3 | 3 | 3 | 3 |
| Cost | 5 | 4 | 4 | 5 | 5 | 5 | 5 |
| Safety | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| **Total:** | **100** |  | **64** |  | **78** |  | **59** |

Our design matrix, shown above, was used to evaluate our three preliminary designs: The Park, The Rigamortis, and The Rocking Chair. Before fully grading each of our designs, our design specifications were ranked from highest to lowest importance. The design specifications were defined as follows:

**Precision**: Precision is defined as how accurately the device keeps the center of rotation during rotations. While this was originally defined in the product design specifications as a measurement in microns, an accurate reading would not fully be determined for each device until they were fabricated. The precision ranked for each device was thus determined based on the ability to keep the eye at the center of rotation.

**Usability**: Usability can be defined as how easily you can adjust the rotational and translational movements of the device. The rotational precision has to be less than a degree.

**Height**: Height is defined by the requirement that the device is less than 15 cm. Shorter devices will score higher in this category because they allow for more workable room under a microscope if image subjects are viewed from above.

**Amount of Rotation**: The amount of rotation indicates the degree a device can rotate around the focal point in comparison to two different axes (e.g. pitch and roll). This criterion was based upon rotational dimensions of each design provided.

**Ease of build**: Ease of build is defined as how easy it is to produce a prototype and how easy it would be for someone else to fabricate and manufacture the device.

**Cost:** The cost is defined by a budget of $250. Devices which cost less to produce and test will score higher in this category. This price reflects the allowable budget for fabrication, testing, and product development.

**Safety:** Safety is defined as how well the device limits harm to the user(s). This criterion entails safety for both the mice who are acting within the holding device and the researchers are operating the anesthetic and imaging procedure.

As shown (from top to bottom), the aspects of our design that were of most importance were: precision, usability, and height (weights 35, 25, 15, respectively). These three were followed closely by amount of rotation, ease of build, cost, and safety (weighted 10, 5, 5, 5, respectively). The specifications were then distributed by weight, with the aspect of greatest importance having the highest weight and the one of least importance with the lowest weight. Then, as a group, we ranked each design from one to five by design aspect.

Designs 2 and 3 scored highest in the precision category because the focal points remain constant for all device rotations. Design 2 scored highest in the usability category because its gear design provides the highest and most user-friendly degree of rotational control and the best method of rotation. This is due to the fact that the gear ratios can be adjusted to allow for both fine and coarse adjustment of rotation. Design 1 scored highest in the height category because the tripod base can be adjusted to a lower height than the other designs. Design 2 scored highest in the amount of rotation category because it allows between 45 degrees of rotation. Designs 2 and 3 scored highest in the cost category because they include all 3D printed parts, which keep them well below the $250 budget. All three designs scored five out of five for safety because all gears are contained, there are no sharp edges, the devices are inflammable, and there are no other significant sources of danger. Therefore, Design 2: The Rigamortis, finished with the highest score of 78 when ranked against the other two designs. Based on its score in the design matrix, and after discussing further with the team, we decided that The Rigamortis was best suited to be our proposed final design.

# V. Fabrication/Development Process

## *Materials and methods*

After the design was developed, the parts were rendered in SolidWorks. They will be 3D printed using ABS. 3D printing is the best construction option because it is cheap, easy, customizable, and compatible with SolidWorks. Compared to other available 3D printing plastics (e.g. PLA) ABS is the best plastic to use because it is cheap, easy to print, durable, impact-resistant, and does not dissolve in alcohol or bleach. [13][14]

## *Testing*

There are several factors that will be responsible for the success of the modular stage device. Each condition will be validated by running single variable tests.

Rotation of 45 degrees is necessary to successfully capture images of all photoreceptors in the eye. We will run tests on the rotational range of the device using radial measurement tools in SolidWorks. The underlying assumption of this test is that the physically printed prototype will be a replicate of the SolidWorks design. Once the device is 3D printed, the device will be tested manually. The team will simulate the movements that will occur during microscope imaging to ensure that, like the SolidWorks design, it has the desired rotation.

MTS stress testing will be used to determine if the device can hold the desired weight of 2.0 kg. The MTS machine will be preset to stop at 2.0 kg of applied stress and the resulting graph will be collected for analysis. If the device can hold this weight, it can then be concluded that it will sustain the weight of all image subjects. A full stress-position curve will be collected to determine the ultimate load the device can handle. Young's modulus will be measured for this stress-position curve. The MTS machine in the team lab will be used to measure the full stress-position curve.

The material to be used must withstand environmental conditions of -10 to 50 degrees Celsius and 20% to 90% humidity. Additional research will be conducted on the material properties to determine whether these fluctuations will provide any change in device functionality. The device will be observed qualitatively for 30 minutes under typical operating conditions. Typical operating conditions will be those of the laboratory room in Dr. Roger's Lab. The functionality of the device will be tested by placing 2.0 kg on the device and rotating the gears prior to entering laboratory conditions and after 30 minutes have passed.

The device is required to be sterilizable via 70% alcohol wipes. This test will be executed by pouring a saline solution that is mimetic of urine and 70% alcohol wipes will be used to clean the spill. Qualitative observation will be used to determine whether the surface is rid of the contamination.

The ergonomics, sterilizability, and functionality of the device including the modular bed attachments will be tested using qualitative feedback from Dr. Rogers and related faculty. A set of unbiased questions will be asked of each member testing the device. Each question will rate the user on a scale of 1-10 for each aspect of the device.

## VI. Results

In our future results, the MTS test will provide us with a stress-position graph. During the MTS test, we will find the position of the graph with the highest peak for 2.0 kg. That data will then be compared to the total force that the device can handle which is generated using Young's modulus. From that information we can then conclude a factor of safety for our device. From this information, we can then infer how much stronger our system is from the intended weight.

After giving a survey to Dr. Rogers and related faculty, we will comprise the answers that we receive and then average out the answers to each of the questions. These results will give us reliable feedback on our design and hint at where it could improve.

The relevant data we have now is from SolidWorks. The data from SolidWorks showed us that the movement and rotation of our device were made along the desired axis. From this, we will be able to conclude that our design has the ability to rotate around a focal point with less than a degree difference. The accuracy will be confirmed to fit Dr. Rogers needs. These results have allowed us to modify our design and to meet as many design criteria as possible.

The most salient feature from our results so far is our device's rotation within 45 degrees with less than one-degree difference. These results allow us to infer that we will meet all of our design criteria necessary for our device.

## VII. Discussion

Based on the results in SolidWorks we will know the degrees of freedom, the weight, the correct movement, and the micron precision. We can conclude this based on comments that other SolidWorks users have had. Users say that they have experienced accurate printing while using SolidWorks (3D). We can assume that the ABS will be able to withstand the environment. [15]

The ethical conduct that must be considered for this device is the use of animals under anesthetic drugs. The device must account for these guidelines. This means that it must have places for both a warming bed and space for specific equipment regarding those drugs. The warming bed will be used to keep the animal warm during anesthesia. This is important because the animal, while under anesthesia cannot monitor its own body heat.

One significant change made to the design in SolidWorks was making the curve skinner by adding the slot in the middle where they intercept. The original design had it stacked below the slot for the gears. By making it separate from the slot gears, it allows for the thickness to of the curve to decreases. Along with this change, we made the base circular so that it can rotate with as a gear in order to gain 360-degree rotation in about the z-axis.

Another change that was made to the design in SolidWorks was changing the arms into vertical columns and adding separate supports to attach to the guide slots. This allowed the device to work simply and efficiently. In past versions, the gear slot was not tangent to the attachment point of the arm. This caused restricted mobility in the rotation which was inefficient for our design.

Because we are using SolidWorks for a majority of our testing, some sources of error could arise during our rotation, detachable bed, and movement testing. There could be a miscorrelation between any of our digital results and our results after we eventually 3D print our device. Specifically, with the gears on our device in SolidWorks may not be perfectly aligned which would affect the movement once the device is printed. If there is an error in the SolidWorks design, it is possible that our 3D printed design will have that error as well. This risk is important to take note of because we do not want to spend more money than is required to print our device.

## VIII. Conclusions

The use of a modular stage is important to all microscopy practices. Microscopy is used to visually analyze many different cellular structures and mechanisms including those of the photoreceptors in the eye. The team has been tasked with creating a microscope stage that can operate with five degrees of freedom about the human eye. The five degrees of freedom would include all three translational movements and two rotational degrees of freedom. Three distinct designs were developed to satisfy the client's need; The Rigamortis design was chosen as it scored highest in the design criteria matrix. The Rigamortis features movement capability with six degrees of freedom using a combination of curved racks with sliding tracks fitted to rotating gears. The team will design the device to allow for rotational precision of 100 microns and translational precision of 1 mm. ABS will be used via 3D printer to fabricate and assemble the working parts of the device. Testing will begin after fabrication and optimizing adjustments will be made after each round of testing.

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# X. Appendix

## Product Design Specification

### Rodent Rotation and Translation Stage Device

### 20-Sep-2018

Jamison Miller, Cory Van Beek, Alexus Edwards, Aaron Patterson, Kevin Koesser

## Function:

A stage to more precisely position a subject's eye at the center of rotation for easier capture of photoreceptors via microscope.

## Client requirements:

- 5 degrees of freedom: If the x-axis is in the direction orthogonal to the pupil, then rotation about the y and the z is required along with translation on all three axes.
- Minimum stage adjustment with 100-micron precision.
- Modular design that allows interchangeable stages for different viewing subjects.
    - Subjects include a detached human eye (2.4 cm diameter, 7.5g) [1], a thirteen lined ground squirrel (33 cm long and 227g) [2], and a white mouse (12.5 - 20 cm long and (12 - 30g) [3].
- Sterilizable between uses via alcohol wipes

## Design requirements:

***1. Physical and Operational Characteristics***

*a. Performance requirements:*

- The device should operate with 5 degrees of freedom keeping the center of rotation about the eye.
    - Degrees of freedom: If the x-axis is in the direction orthogonal to the pupil, then rotation about the y and the z is required along with translation on all three axes.
- The device shall be able to support a weight of 2.0 kg.
- The device will be used on average for 1.0 hour per day in a sterile environment by operating technicians.
- The device shall allow for interchangeable stages that accommodate different sized subjects.

- The device shall allow a warming device to keep the viewing subject at body temperature.

*b. Safety:*

- The device shall be sterile and protect the operating technician from animal contamination.
- The device shall withstand drops of 1.0 meter without breaking into shards.

*c. Accuracy and Reliability:*

- The device will be manipulated by hand such that a microscope can focus on a photoreceptor as small as one micron.
- The device shall support a minimum translational motion of 100 microns.

*d. Life in Service:*

- The device shall maintain optimal function through 500.0 hours of use.

*e. Shelf Life:*

- The device shall maintain optimal function through 10.0 years in storage at room temperature.

*f. Operating Environment:*

- The device shall operate between -10.0 and 50.0 degrees celsius.
- The device shall operate between 20.0% and 90.0% humidity.
- The device shall be non-absorbable for water and bodily fluids.
- The device shall be non-photosensitive.

*g. Ergonomics:*

- The device shall provide simple rotational and translational movements of the stage.

*h. Size:*

- The device shall not have crevices or open gaps that inhibit cleaning and maintenance.
- The device shall not exceed the following dimensions: 30.0 cm x 30.0 cm x 50.0 cm.

*i. Weight:*

- The weight shall not exceed 5.0 kg, to provide easy accessibility and movement throughout the lab space.

*j. Materials:*

- The device shall contain non-absorbing surfaces and must be assembled in a way that limits the number of small creases.
- The materials cost must be within a budget of $250.

*k. Aesthetics, Appearance, and Finish:*

- Aesthetics, appearance, and finish are not important in this device as it will be used and operated in a research setting.

### *2. Production Characteristics*

*a. Quantity:*

- 1 unit is needed

*b. Target Product Cost:*

- The project budget is $250, which includes the costs of manufacturing and testing a prototype. Similar existing products cost over $4,500 [4].

### *3. Miscellaneous*

*a. Standards and Specifications:*

- This is a custom device being used in a research setting; there are no international or national standards by which to abide.

*b. Customer:*

- The customer would prefer this device be modular for the use of interchangeable stages to account for varying imaging subjects.
- The customer wants the device to connect to the stabilization table.

*c. Patient-related concerns:*

- The device must be sterilizable by alcohol wipes between uses.
- There is no storage of patient data involved in this device.

*d. Competition:*

- Narishige Mag-2 head holding device with angle adjuster for mice [5].
- US Patent #5337178: Tiltable Optic Microscope Stage [6].
    - This stage gives three degrees of freedom. The patent mentions that translational adjustments may be required after rotational movement.

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