# Somatosensory Stimulus Apparatus for Rodents

UW BME Design (400)

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# Abstract

Currently, no methods exist to test the efficacy of sciatic nerve repair on rodent models based on responsiveness to hindlimb somatosensory stimulation. The proposed device produces somatosensory stimulations through vibrations induced on the hindlimb of a conscious rat. By isolating the stimulation to either left or right hindlimb, the subject is presented a two-alternative forced choice (2AFC). A healthy rat is trained to conditionally respond to the stimulus by indicating on which limb the stimulus was felt. Once the rat is trained, the nerve is surgically deafferented and repaired. During recovery the rat is presented with the same 2AFC at various time points to determine the length of recovery of sensory function.

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# Introduction

## Impact

In adult mammals nerve repair is very difficult when they have been completely severed, if not nearly impossible. The clients of this project are studying surgical options to repair these damaged nerves in the Peripheral Nervous System (PNS). Their work is focused on analyzing the success of these surgical procedures to determine how effective the treatment was in repairing the neurological connection that was lost, or damaged. This work could translate into surgical procedures to help humans who have had their neurological connections damaged or severed, regain the control and sensations that they may have lost otherwise. The human body already has the ability to regrow certain nerve connections in the PNS specifically . This regrowth starts through a process called Wallerian Degeneration, and is followed by axon regeneration. This process is only possible in the PNS and if the distal portion of the axon is not too far from the cell body [1]. In a scenario where the Wallerian Degeneration leaves the axon too far to reattach to the cell body, a surgeon can come in and help to guide the regrowing axon to the cell body. If this solution can be shown to have a significant positive impact on the regeneration of nerve connections in rats, it could one day be implemented to help regrow human nerves as well.

## Problem Statement

The two clients for this project are currently researching surgical nerve repair in rats, more specifically repair of the Sciatic nerve.  This is the nerve that innervates the buttocks into the leg and foot. This nerve is highly important in connecting the muscles of the leg and foot to the spinal cord and brain [2]. Thus, after surgical repair of this nerve, the success of the surgery must be assessed by stimulating this nerve, and observing the rats ability to distinguish the individual stimuli in each hindlimb. The clients are looking for a non-invasive, non harmful way to stimulate this nerve in rats having undergone sciatic nerve repair surgery.

## Current Devices/Methods

A device that can independently stimulate a rat's hind limbs does not currently exist on the market. However, there are some devices that have been used in past studies to apply vibrations to rats.

In one study, standard housing cages were affixed to a vibrational shaker (V408 Shaker, Brüel and Kjær North America, Duluth, GA) (fig 1) [3]. Rats were introduced to the cage and vibrations were applied to the cage. This design does not satisfy the clients requirements because the vibration was applied to all four limbs at once, and the clients want to stimulate only one hindlimb at a time.


Fig 1. A LDS V408 Permanent Magnet Shaker from Brüel & Kjær. Image taken from https://www.bksv.com

Aside from vibrationally stimulating the hindlimbs of rats, our device will also have to house rats for the duration of testing. There are several products on the market which are used to house rats during behavioral testing.

First, the Rat Passive Avoidance Cage from Coulbourn Instruments (fig. 2) is used to condition rats to stay in certain areas. The cage (20"W × 10"D × 12"H) is divided into two rooms separated by a door: a dark room and a light room. The dark room has opaque walls, preventing outside lights from entering the room while the light room has clear plexiglass walls that allow ambient light to enter the room. The rat is naturally inclined to enter the dark room, however by providing an electric stimulus, the rat can be conditioned to remain in the light room. This product can give us a starting place for determining the size of our design.

Fig 2. A rat passive avoidance cage by Coulbourn Instruments. Image taken from https://www.coulbourn.com

Second, the Rat Touchscreen Chamber by Lafayette Instrument Company can be used for multiple applications (fig 3). The cage features a touchscreen with which the rat can interact, and several slots that can be used for pellet dispensers, levers, lights, and other stimulatory devices. This device can inform us on how to collect information from the mouse during training. We may want to use a touchscreen, or to use lasers to determine if the rat get the desired response to the given stimulation.

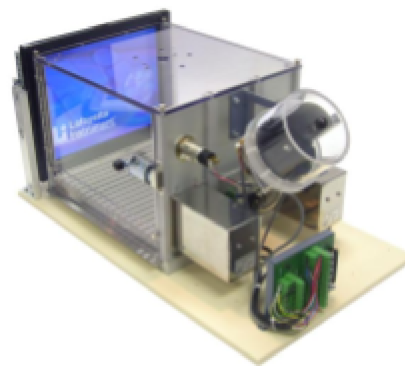


Fig 3. A Rat Touch Screen Chamber from Lafayette Instrument Company. Image taken from http://lafayetteneuroscience.com

# Background

## Research

### Relevant Physiology and Biology Research

Damage to nerves in adult mammals have very different regeneration possibilities depending on where in the nervous system they occur. A damaged nerve in the Central Nervous System (CNS), is almost completely incapable of regenerating due to the neuroglia, in the CNS. Astrocytes in the CNS, after a nerve is damaged, form a barrier around the damaged nerves, which turns into astroglial scar tissue. In addition to the blockage of nutrients due to the astrocytes, and astroglial scar tissue, the myelin of the CNS releases growth-inhibiting proteins which block any regrowth of a nerve in the CNS [1]. However, in the PNS, damaged nerve cells undergo Wallerian Degeneration, a process which protects a portion of the damage peripheral nerve with Myelin, while the debris of the damaged section is cleared by macrophages. Wallerian degeneration is followed by axon regeneration, in which growth-promoting factors are released by the myelin and cell body, and help to guide the regrowing axon back to the cell body [3]. There are situations in which the nerve is unable to reach the cell body it was originally attached to, in these situations surgical modifications can be used to lead the axon back to the cell body.

Vibrational stimulation has been tested in different ways to study the effects it has on different rodents. In one study looking at behavioral changes in female mice when subjected to different frequencies of vibration showed that the mice exhibited the most noticeable transient responses at frequencies between 70-100 Hz., and at an acceleration of 1.0 $m/s^2$ [4]. Another study which looked at the vibrational frequency threshold for mice and rats found that rats, after being tested at a range from 0 - 600 Hz., would attenuate with vibrations around 50 Hz., whereas a humans resonant frequency is between 9-16 Hz [5]. This was an expected result since rats are smaller than humans their resonant frequency was expected to be significantly higher than that of a humans. These different studies will be used to help determine the range of vibrational frequencies that will be available to the clients during their testing.

### Design and Prototype Production Research

Initially, the team's research focused on finding a component which could provide an isolated, user-defined vibrational stimulus to the hindlimb of a rodent. The various devices and device specific results of this research can be found under Preliminary Designs and Preliminary Design Evaluation.

Another future interest will be the hardware and software used to interface between the scientist selecting a desired frequency of stimulation and the motor itself. An Arduino™ Due Baseboard may be used for this.

A further future focus of design research is the rodent enclosure. The enclosure should be made out of a non-porous material for sanitation purposes. It should also create a watertight seal between the bottom of the enclosure and the platform through which the rodent experiences vibrations to it's hindlimbs. Additionally, it should ensure that any mechanical or electrical components housed underneath the enclosure are not subjected to stresses, strains or biological waste created by the rodents.

## Client Information

Dr. Aaron Suminski is a scientist with the University of Wisconsin, Department of Biomedical Engineering. He collaborates with Dr. Aaron Dingle, a post-doctoral researcher, with the University of Wisconsin, Department of Surgery, Poore lab. The Poore lab's research focus is clinical and experimental microsurgery, with an emphasis on peripheral nerve regeneration and repair. Together they are researching the effectiveness of various treatments and methods of nerve repair.

## Design Specifications

According the Project Design Specifications (Appendix A), the experiments are usually conducted in a laboratory. The design should be able to set up on a benchtop and weight less than 12 kilogram for the convenience of the clients. Since the experiment only includes 1 rodent at a time, the size of the cage should be approximately 30 cm x 30 cm x 30 cm. Moreover, the device should be waterproof and sanitinizable because the rodents may urinate during the experiment.

The main purpose of the clients' experiment is to check whether the rodent can receive the stimulation through its left foot or right foot. At the current stage, vibration will be a proper way to do the job. Thus, the device should be able to stimulate one of the rodent's legs using vibration. Other parts of the rodent's body, such as belly and the other foot, should not be stimulated. The vibration should have controllable intensity and frequency. A computer can be used to adjust these parameters. For the safety of the rodents, the device should not generate intense vibration that injures the rodents.

# Preliminary Designs

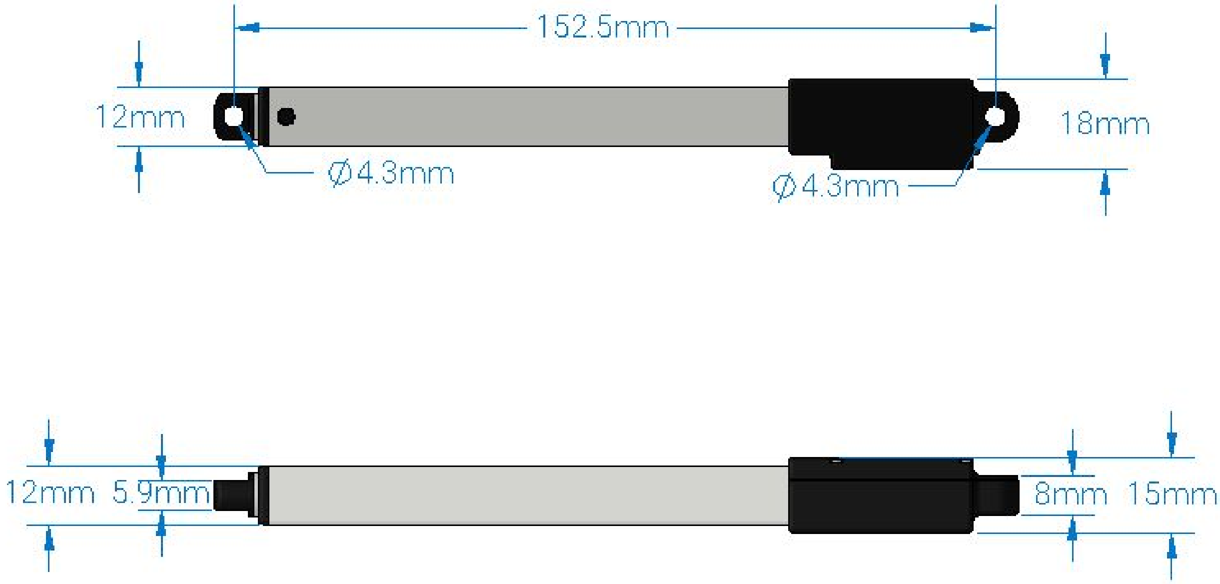
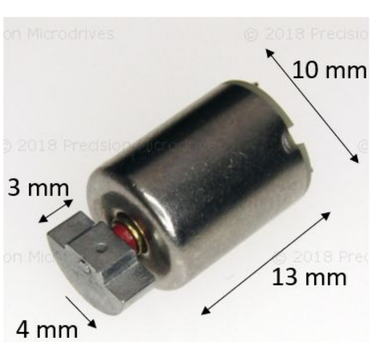



**Figure 4**. Linear actuator capable of one-dimensional movement [6].

The device shown above (Figure 4) is a linear actuator with its dimensions. It can produces a simple linear motion using a rod and screw. When it is fully extended, the full length of this linear actuator can reach 252.5 mm. It can be used to generate the vibration of interest by programing how far the rod goes out and how long the delay is. The cost of this device is 69.99 USD.


**Figure 5.** Micro Vibration Motor for Cell Phone. Motor has a fixed frequency of vibration that is achieved by rotating an unbalanced weight at the head of the unit [7].

The cell phone micro vibration motor (Figure 5), has a body size of 4 mm x 8 mm(D*H) and a total length of 13mm. Its head has a unbalanced weight. By spinning the head, the motor can generate vibration. It can only generate vibrations with fixed frequency. Thus, to create a vibrational platform with a controllable frequency, three of such motors are needed to be placed under one platform, with frequencies of 150 Hz, 87 Hz and 58 Hz. Frequencies other than those three are unreachable. The cost of such motors is 1 to 3 USD each.



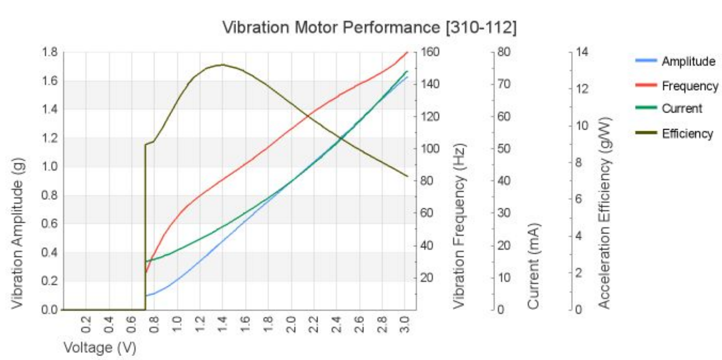




**Figure 6a.** (left). Precision vibration motor with variable frequency. Motor has a variable frequency of vibration that is achieved by rotating a semi-circular weight at the head of the unit. **Figure 6b.** (right). Frequency vs Voltage plot supplied by manufacturer [8].

The precision vibration motor is another unbalanced weight vibration motor (Figure 6a). Its body is cylindrical with a diameter of 10 mm and a full length of 13 mm. It has a unbalanced head, working similarly as the cell phone micro vibration motor. Different from the cell phone micro vibration motor, the frequency of the vibration generated by this motor can be adjusted by changing the input current. The frequency can range from 30 Hz to 150 Hz (Figure 6b). Thus, only one of such motor will be enough to build a vibrational platform. The cost of this motor is 26.25 USD.

# Preliminary Design Evaluation

## Design Matrix

**Table 1**. Design Matrix used in selecting a motor to create a surface vibration. The design matrix considered various categories ranging from “segregation of stimulation” to “cost” and assigned each category a weight based on importance to the project. Three devices, a linear actuator [6], a micro vibration motor [7] and a precision vibration motor [8] were evaluated on a range of 1 through 5 in each criteria. This evaluation was multiplied by the weight of the criteria. The product with the highest total sum of weighted criteria was chosen to be incorporated in the design.

| Criteria | (Weight) | Linear Actuator  | | Micro Vibration Motor  | | Precision Vibration Motor  | |
|---|---|---|---|---|---|---|---|
| Segregation of stimulation | 25 | 5/5 | 25 | 4/5 | 20 | 4/5 | 20 |
| Frequency range | 20 | 3/5 | 12 | 3/5 | 12 | 5/5 | 20 |
| Ease of integration | 15 | 3/5 | 9 | 2/5 | 6 | 3/5 | 9 |
| Size | 15 | 3/5 | 9 | 4/5 | 12 | 5/5 | 15 |
| Ease of acchieving desired effect | 5 | 5/5 | 5 | 3/5 | 3 | 4/5 | 4 |
| Cost | 5 | 3/5 | 3 | 5/5 | 5 | 4/5 | 4 |
| **Total** | **85** | | **63** | | **58** | | **72** |

The team and client prioritized the development of a component which would create a variable, user-defined vibration. Other design aspects of the project will be evaluated at a later point. For a detailed description of design matrix criterion see Appendix B.

Design criteria were chosen and weighted based on engineering practicality, as well as the desires of the client. Fundamental to this project is the segregation of stimulation - the ability to only stimulate one hindlimb. All devices could perform this task. However, the linear actuator could be programmed to precisely deliver changes in length, with user defined periods and delays. The vibrational motors relied on the circular movement of a weight to create a vibration, which would thereafter have to be transferred to a platform; introducing variability and potential sources of error.

Additionally, the devices had to operate within a desired frequency range. The precision vibration motor's manufacturer provided a voltage vs frequency diagram covering the desired ranges. The linear actuator could produce vibrations on the lower range of the spectrum. The micro vibration motor could only vibrate at a specific frequency. This would have meant purchasing multiple micro vibration motors with various rotations per minute (rpm) and turning them on and off separately.

Ease of integration considered the difficulty of engineering an interface between the device and the rodent. The linear movement of the linear actuator is a more simple interface than integrating a part that relies on circular movement.

The final product would have to be sized to fit on a lab-bench, or compact enough to easily be moved between lab spaces and an animal housing spaces. Therefore, the individual components should be as small as possible. The order of components from smallest to largest is: precision vibration motor, micro vibration motors, and linear actuator.

Ease of achieving desired effect was a subjective measurement of the ease in which the device could be programmed or modified to vibrate at the desired frequency. All devices would be able to vibrate within the desired range, however the linear actuator would be the easiest to program.

Finally, cost was the last metric on which devices were compared. The micro vibration motors were cheapest and the linear actuator was the most expensive option.

## Proposed Final Design:

Precision Microdrives ™ Model No. 310-112 outperformed the other options of creating a vibrational stimulus and was therefore selected as the motor in the proposed final design. It operates within a frequency range of 30 - 150 Hz, with an input of 0.75 - 3.0 V.


**Figure 7.** Precision Microdrives ™ Model No. 310-112. The motor chosen for use in the proposed final design. The motor's adjustable frequency, as well as small size and low cost made it the preferred source of vibrational stimulation.

# Fabrication and Development Process

## Materials

A Precision Microdrives™ Model No. 310-112 (10mm Vibration Motor - 13mm Type) was used as the vibrational stimulus. An Arduino Due Baseboard will create a variable voltage output. A plexiglass enclosure will be used to house the rodent. Plexiglass will be used as the platform which receives the vibrational stimulus.

## Methods

In order to create two separate vibrational platforms using the precision microdrive motor, two separate connections were proposed. The first is a two bar linkage to the base of the platform, as seen in Figure 8. This allows the rotation of the head of the motor to spin the bar connected to the motor in a complete circle, while the second bar will create a sinusoidal vibration in the platform. With the current dimensions of the linkage the amplitude of movement in the platform will be 2 mm. Additionally, the dimensions of the sketch are not fixed for the motor above since quotes for the motors have only been requested thus far.

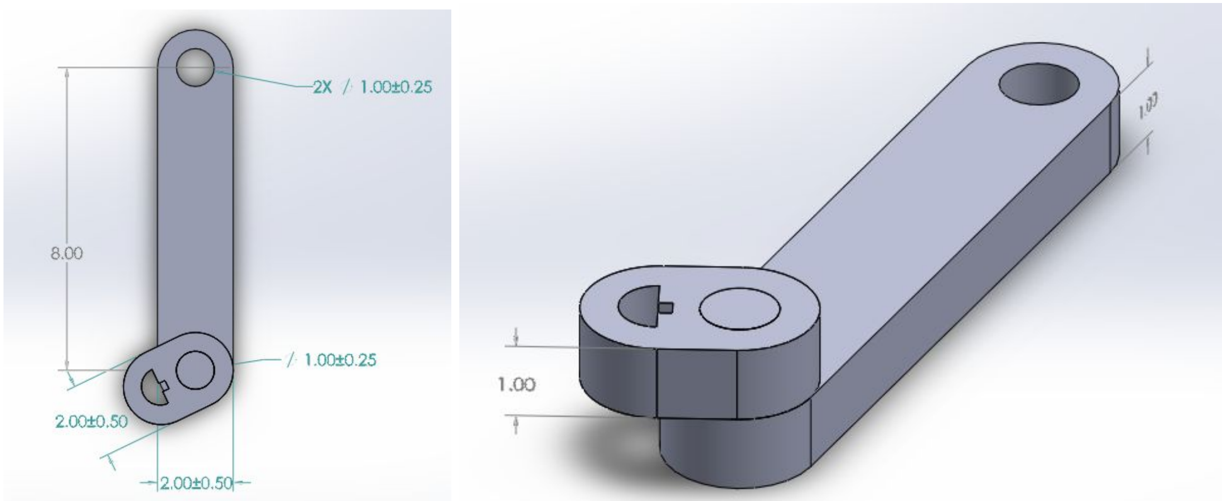



**Figure 8 A, B:** These CAD images show a model design for a potential way to vibrate the platform to stimulate the Sciatic nerve in the rats. The measurements shown are in millimeters, and the total amplitude of the vibration is 2 mm.

The second method of vibration would be attaching the motor itself to the bottom of the platform. The issue with this method of attachment is whether or not the amplitude of the vibration will be large enough to cause a stimulation in the rats hindlimbs. The other potential problem is whether or not the frequency of vibration in the motor will translate to the vibration of the platform itself. However, until the team has received quotes and ordered the motor these questions will remain unanswered.

## Final Prototype

At this early stage of the project, the team is mainly working on the circuit, code and cage design. Fabrication process will begin after the plan is finalized. Currently, the final prototype is not available.

## Testing

Testing will be performed under the supervision of our clients. The nature of the testing that will be conducted is not currently known. However, it is clear that the testing will determine if healthy rats are able to sense vibrations in their hind limbs from our device. The rat will be placed in the cage and will be trained via positive rewards to assume the correct position. Then the rat will be trained to respond to the vibration by selecting the corresponding option.

Additional testing will be performed to determine the frequency and amplitude of the vibration applied to the platform by the motor. These data will be used to calibrate the software to provide accurate vibrations.

# Results

No results to date. Expected results are a voltage to vibration frequency calibration curve that will be used to write software to program the arduino.
Once animal testing begins, results will show which vibrational frequencies the rodents were most responsive to.

# Discussion

Ethical considerations in the design come with use of rodents as test subjects. Unless absolutely necessary the client did not want any type of pain or injury to be induced on the rats during the attempted stimulation of their surgically repaired nerves. Another ethical consideration would be duration of the tests and ensuring that the rats are not subjected to any harmful conditions for an extended period of time. However, the tests that will be run with this device will be relatively short vibrational tests to determine the frequency best suited for stimulation, and then tests to measure the success of the surgeries.

# Conclusions

Designed for the experiment of the clients, the device should hold one rodent and stimulate one of it hindlimbs by vibration. According the references, the team believes that a vibration with a frequency ranging from 50 Hz to 150 Hz will be appropriate to stimulate the rodent without injuring it. Three devices are proposed that can generate vibrations at this frequency range. They are Linear Actuator, Cell Phone Micro Vibration Motor, and Precision Vibration Motor. To evaluate the possible performance of these devices, the team decides to rate each motor according to segregation of stimulation, frequency range, ease of integration, size, ease of achieving desired effect and cost. The scores are put into a design matrix and Precision Vibration Motor gets the highest total score. The team decides use Precision Vibration Motor in the design to create the vibration and will be working on how to integrate this motor in the final device.

## Future work

Future work will involve purchasing the Precision Microdrives ™ Model No. 310-112 and a microcontroller for the motor. Once obtained, we will write software to control the motor and receive information from the user. This will also involve creating an interface between the microcontroller and the user, so that information can be clearly communicated to control the motor.

Furthermore, we will design, purchase materials for, and construct the cage that will house the rat, motor, and microcontroller.

# References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# Appendix

## A. Preliminary Design Specifications

**Function:**

Peripheral nerve injuries are common, debilitating and costly. Approximately 2.8%-5% of all trauma patients in the US sustain such an injury. Many peripheral nerve injuries are a result of amputations, which affect an estimated 185,000 people in the US each year. Prosthetics are continually improving, but a large issue that remains is the patient's lack of tactile perception. Many researchers, including Dr. Aaron Dingle, are designing devices to solve this problem. The functional outcome of these devices can be assessed in humans by asking the patient questions, but this technique is not an option in animal models. Rats are commonly used as animal models as a precursor to human subject testing. In order to receive functional outcome data from rats, a healthy rat can be trained to respond in a certain way to a somatosensory stimulus. A peripheral nerve can then be surgically cut and the novel device implanted. The device can then be used to apply what should be recognized as the same somatosensory stimulus the rat was trained with. Observations on the percent of correct reactions can be used to determine success.

This project aims to design the somatosensory stimulation device used to train the rats. The device should be able to apply a graded stimulus to at least two limbs individually. The device will consist of a cage or cage insert as well as a microcontroller to control the stimulus grade.

**Client requirements:**

- Must house one rat
- Must be able to individually stimulate each hind limb of the rat
- Must be completely controlled by a computer (no user input other than to start the device and configure settings)
- Must be sterilizable
- Mouse must be visible while in the cage

**Design requirements:**

**1. Physical and Operational Characteristics**

a. *Performance requirements:* Multiple experiments may be run per day. The device should be capable of repeated use and cleaning between trials.

b. *Safety*: The device should not harm the animals in any way.

c. *Accuracy and Reliability*: The device should accurately and reliably produce a graded stimulation of the user's choice.

d. *Life in Service*: Trials would last approximately 15 minutes in duration.

e. *Shelf Life*: A 10 year shelf life is prefered.

*f. Operating Environment*: Room temperature (25℃) and pressure (1 atm).

g. *Ergonomics*: The rodent should have enough room to rear on its hind legs and interact with the forward facing wall.

h. *Size*: No smaller than 30 cm x 30 cm x 60 cm. No larger than 120 cm x 120 xm x 120 cm

i. *Weight*: No heavier than 11 kg.

j. *Materials*: Plexiglass.

k. *Aesthetics, Appearance, and Finish*: Must be able to observe test subject through wall material.

**2. Production Characteristics**

a. *Quantity*: One unit.

*b. Target Product Cost:* < $100

**3. Miscellaneous**

*a. Standards and Specifications*: The device should be approved by the UW-Madison Research Animal Resources and Compliance (RARC) center.

*b. Competition*: None

# B. Design Matrix Full Description

Each motor was rated according the the following criteria (weights in parentheses):

1. **Segregation of Stimulation** (25): The degree to which the vibrational stimulation is localized to one hindlimb of the rat. A score of 5 would imply that any vibration applied to one hind-leg platform would be undetectable in the other hind-leg platform. A score of 3 would imply that when vibration is applied to one hind-leg platform there is a measurable

vibration in the other hind-leg platform between 0 and 0.1 times the amplitude of the applied vibration. A score of 1 would imply that when a vibration is applied at one hind-leg platform there is a measurable vibration at the other hind-leg platform between 0.5 and 1 times the applied vibration.

2. **Frequency Range** (20): How closely the vibration range of the motor matches the desired vibration range. A score of 5 would imply that the motor has a range larger than but including 70 Hz to 100 Hz. A score of 3 would imply that the motor has a range of 70 Hz to 100 Hz but has limited resolution within this range. A score of 1 would imply the motor does not produce vibrations within the 70 Hz to 100 Hz range.
3. **Ease of Integration** (15): The ease of creating an interface between the motor and the rat. A score of 5 would imply that the interface could be designed within two weeks. A score of 3 would imply the interface could be designed within a month. A score of 1 would imply that it would take more than one month to design the interface.
4. **Size** (15): The design must be able to fit on a laboratory bench and hold one adult rat. The cage has a minimum size of 30 cm × 30 cm × 60 cm. A score of 5 would imply the motor could be used with a cage of dimensions 30 cm × 30 cm × 60 cm. A score of 3 would imply the motor could be used with a cage of dimensions 35 cm × 35 cm × 60 cm. A score of 5 would imply the motor requires a cage larger than 40 cm × 40 cm × 60 cm.
5. **Ease of Achieving Desired Effect** (5): The ease of controlling the motor. We will need to create code that will manipulate the motor. A score of 5 would imply that there is a sufficient amount of documentation on how to control the motor. A score of 3 would imply that there is a some documentation on how to control the motor. A score of 1 would imply that there is little to no documentation on how to control the motor.
6. **Safety** (5): The safety of the design. The design should not harm or cause discomfort for the user or rat. A score of 5 would imply that there is little to no chance that the rat or user will be harmed. A score of 3 would imply that there is some chance that the rat or user will be harmed. A score of 1 would imply that there is a high likelihood that the rat or user will be harmed.