AUTOMATED TRAINING APPARATUS

Preliminary Report

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Background:

A wide variety of biomedical research relies on animal models; these models reveal causal relationships between biological mechanisms and behavioral symptoms applicable to human pathology[1]. Animal-based studies can predict drug effects, develop alternative therapeutics for the treatment of human diseases, hone in on higher order cognitive and learning phenomena, and inform decision across a variety of other biological areas[2].

While a powerful tool, animal models are extremely difficult to duplicate – both between laboratories and within labs themselves. In fact, studies considering the reproducibility of rodent behavioral studies show that the experimenter who handles the rodent introduces variability that cannot be eliminated by physiological methods or by standardizing the genetic backgrounds of the rodents. This human influence most often occurs when the handler transports the rodent between the home cage and training area. The transportation diminishes the validity of experiments, as the day-to-day behavior of a rodent changes with its level of contact with the handler on that day. The handler's gender can also influence how the rodent acts during their training sessions, further contributing to uncontrolled variability[3]. Handling of the animals between training sessions can induce stress in the rodents and impact their cognitive performance during training[1].

In addition to combatting variability arising from direct human/rodent contact, researches encounter difficulties when running studies that rely on specific temperature, humidity, light, or sound. Labs often house multiple rodent cages in close proximity; therefore, altering one cage's environment for a study concurrently impacts all other cages and experiments. The proposed "Automated Training Apparatus" address these issues, eliminating both handler-induced and cage environment variability by entirely automating the training process in the home cage.

Project scope:

Client: Keith Hengen, a professor of biology at Washington University in St. Louis.

Need: Dr. Hengen's lab needs to more efficiently gather informative neuronal network data by decreasing the amount of time and manual labor required for training rats under differing experimental conditions.

Scope: To address the Hengen lab's need, we will design a rat cage that facilitates experimental individualization and automation of data collection; the cage will be sound proof, incorporate automated light and feeding control, allow for potential visual experiments and rat response indication, have an opening for a monitoring camera, and will also fit onto the shelves housing the lab's current rat cages. A software package will enable control of the rat's sound, light, feeding, and visual stimuli, and allow for exportation of this data in usable data types. This specialized cage and controlling software will be functional and available to Dr. Hengen by April 30, 2019.

Design Specifications:

Design Component	**Metric (inches, unless indicated otherwise)**
Overall Cage Design	7” x 14” x 12”
Support Beam (x6)	1” x 1” x 12
Front Wall Base	6” x 14”
Front Wall Sliding Top (x2)	7” x 6”
Back Wall	14” x 12”
Light Containment Cover	Outer Dimensions: 22.5” x 14.5” x 16”
	Inner Dimensions: 20” x 12” x 13.5”
Display Screen (x2)	6” x 4” x .03”
Water Port Opening	Radius: 0.25”
	Location: 3.5” x 3” from front bottom left corner
Water Dispenser	Radius: 0.40”
	Height: 4”
Food Dispenser	Triangular face: 3” x 4” x 5”
	Length: 6.5”
Temperature	23°C
Beam Break Sensor (x2)	0.8” x 0.4” x 0.3”
Capacitor Sensor (x2)	4.4” x 0.25” x 0.2”
Temperature/Humidity Sensor	1.05” x 2.32” x 0.53
Arduino Uno (x4)	2.1” x 2.8” x 0.5”
LED Strip	19.7” x 0.6” x 0.2”

Existing Solutions

Manual Training: Manual training methods comprise the current research standard. The handler will come in at specified times during the day and transfer the rodent from the home cage to the training area. Depending on the type of study, the handler may have to fix the rodent's head in a specific position. Common studies on food restriction vs. water restriction for training rodents frequently apply head fixation. Affixing the rodent's head in a certain position for training once every day traumatizes the animal to a degree, impacting its experimental performance. In effort to monitor the rodent's consumption, handlers in studies restricting food and water introduce further variability by opening the cage and removing the remaining food or water for measurement and comparison with initial amounts.[4]

Alternative Automated Training: To counteract the deficiencies of manual methods, a few research groups have successfully employed specialized automated rat training regimes. These include teams headed by Weimin Zheng at the Neurosciences Institute in San Diego, CA, and Daniel Leventhal at the University of Michigan.

With the goal of more efficient study of neuronal activity in response to auditory cues, Zheng fully automated rodent behavioral testing. As shown in Figure 1, a custom-made, acoustically transparent system housed the rats under study – this system comprised a cage with three paneled walls to let sound through, and one modular operation wall[5]. A lever resided on the bottom of the operation wall which, when pushed, granted rats food pellets as reward from a distributing level locate above. A rat could also stick their nose into a nose-hole centered in the operation wall, initiating the reveal of another hidden lever. This automated system successfully taught rats to identify an auditory sensory cue, and then to press the correct lever indicated by the cue – either the standard lever or the version requiring nose-hole initiated operation – to redeem a food reward.

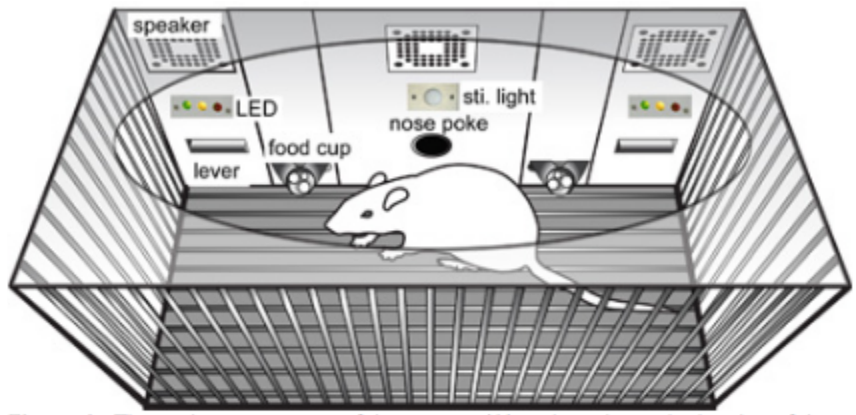


Figure 1: Schematic drawing of the Zheng Lab custom-made auditory operant chamber.

Zheng's chamber indicates that non-manual methods can feasibly train rats for neurological study; however, the need for developing a Hengen Lab-specific system remains. The acoustically transparent cage discussed received tones delivered in a sound-proof booth, necessitating the three paneled walls to permit the sound to enter. In Dr. Hengen's case, lack of access to a sound-proof room and desire to train rats in multiple, closely-situated cages underlies the need for a more confined soundproof environment for a cage. Additionally, the use of levers requires unnatural movements from the tested rats – these rodents learn lever-pushes slower than simpler indication systems, such poking a capacitor with their nose. Lastly, Zheng researchers customized the chamber to their needs and software setup, limiting its versatility and application in labs with pre-establish testing systems.

Daniel Leventhal's group explored automated rat tested with an emphasis on a single-pellet reaching system and high-speed video capture for the study of fine motor control[6]. Depicted in Figure 2, their system delivered single reward pellets for rats to grasp with their forepaw, detecting reaches with real-time computer vision that triggers video acquisition. They show that rats acquire the automated task with similar results to manual training, and demonstrate the feasibility of simultaneous optogenetic measurements.

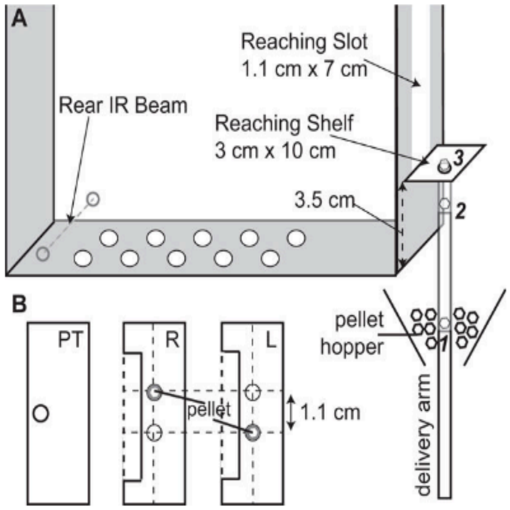


Figure 2: Schematic diagram of the Leventhal Lab skilled reaching chamber. (A) The skilled reaching chamber and pellet delivery mechanism. (B) Reaching shelf configurations, viewed from above, for pre-training (left), and right and left paw training (middle and right respectively)

Components of this system – such as video capture and automated food dispensing – overlap with the Hengen lab's general needs, but lack the lab's desired water control and non-reaching feeding system. Dr. Hengen will eventually incorporate optogenetics into his neurological measurements; the Leventhal group affirms the possibility of this addition. A set of silent, computerized fans ventilate the Leventhal chamber, and a wheeled, soundproof cabinet lined with acoustic foam houses the apparatus. Custom LabView software integrates all features, allowing for total operant control. The training system developed for Dr. Hengen and lab will include similar ventilation, soundproof capabilities, and software.

Marketed Solutions: Patents exist for various designs of rodent cages. However, each only comprises of a few of the aspects desired by the Hengen lab. Two primary categories define these cages: those regulating the environment of the rodent, and those capable of training the rat to perform a task. The integration of these two concepts has not yet reached the market, allowing for a unique opportunity for the proposed design.

One such cage that regulates environment was created by Ingley, Hahn, and Battles. This animal containment device includes a top wall, bottom wall, three permanent side walls, and a fourth wall that allows for replacement with a monitoring module as seen in Figure 3. The monitoring module includes multiples sensors in a package transferable from cage to cage for the regulation of properties such as cage temperature, humidity, oxygen concentration,

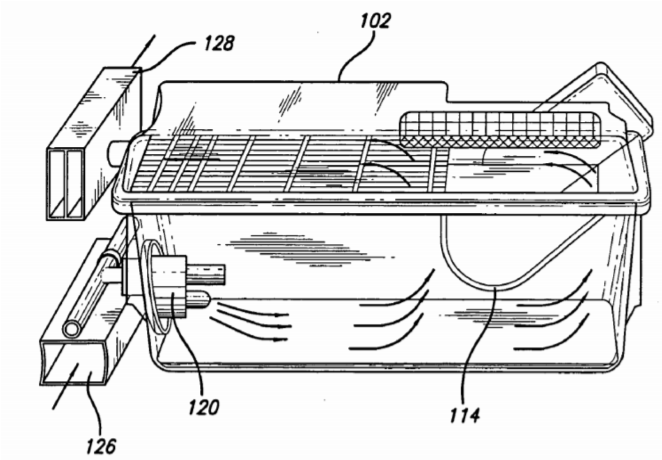


Figure 3: The cage. Designed by Ingley, Hahn, and Battles, demonstrates the solid-wall design with the additional monitoring module attached on the left wall for increased monitoring of cage conditions.

nitrogen concentration, and carbon dioxide concentration. The monitoring module connects to a monitoring system that triggers the sending of a system alert to the caregiver whenever values exceed their given threshold set by the researcher. The walls of the cage comprise another unique aspect of this design. For economic purposes, wire bars traditionally structure the walls of a rodent cage However, this limits the types of animals a cage can contain. This design instead incorporates walls constructed from a translucent, photosensitive material. Although solid, the translucence of these walls allows for constant monitoring by caregivers. The photosensitive properties also enable precise regulation of the amount of light in the cage.[7] Primarily, this cage allows for the regulation of air quality and light penetration into the cage but still lacks any influence on the animal's behavior.

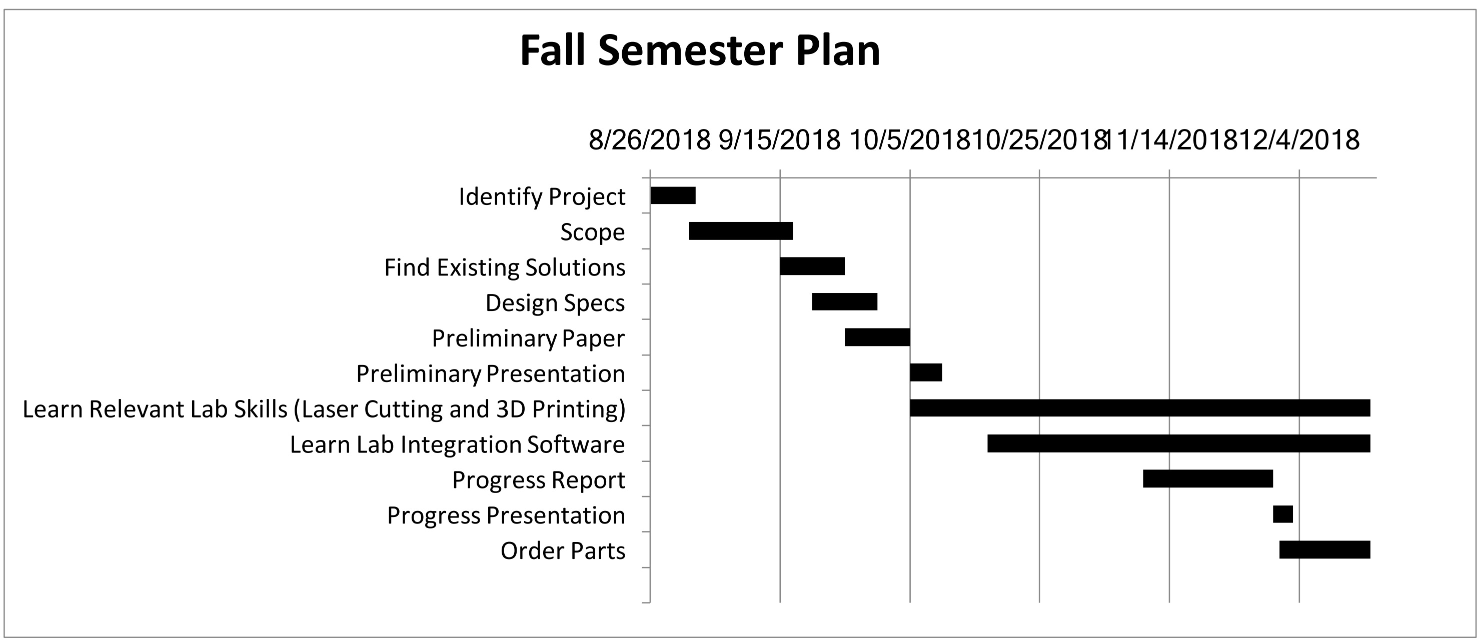
Conversely, Gondhalekar and Brunner designed a training arena with the sole purpose of training a rodent and observing its behavior. Rather than tailoring a cage or home for the rodent, their training setup requires the removal of the rodent from their home cage and placement in the training arena before initiation of training. The arena is designed as a maze with an electronically programmable floor capable of constructing various obstacles and passageways. This programmable floor can be automated to proceed through a training protocol of increasing difficulty based on the subject's ability to traverse the maze. By recording the amount of time required for the rodent to reach the center of the maze, the programmable floor can anticipate the need for a shift to a more challenging maze design and adjust itself accordingly[8]. This existing maze design is very efficient in testing rodent memory; however, fails to satisfy the need for behavioral conditioning for neurological studies.

While each effective at their individual purposes, the separation of home and training in the discussed designs influences experimental results. Because rats reside in a single cage while being trained in a separate setting, removal from their home cage on a regular basis for the training process stresses the animals. The proposed Automated Training Apparatus confronts this issue by joining the home and training arenas.

Design Schedule and Gantt Chart

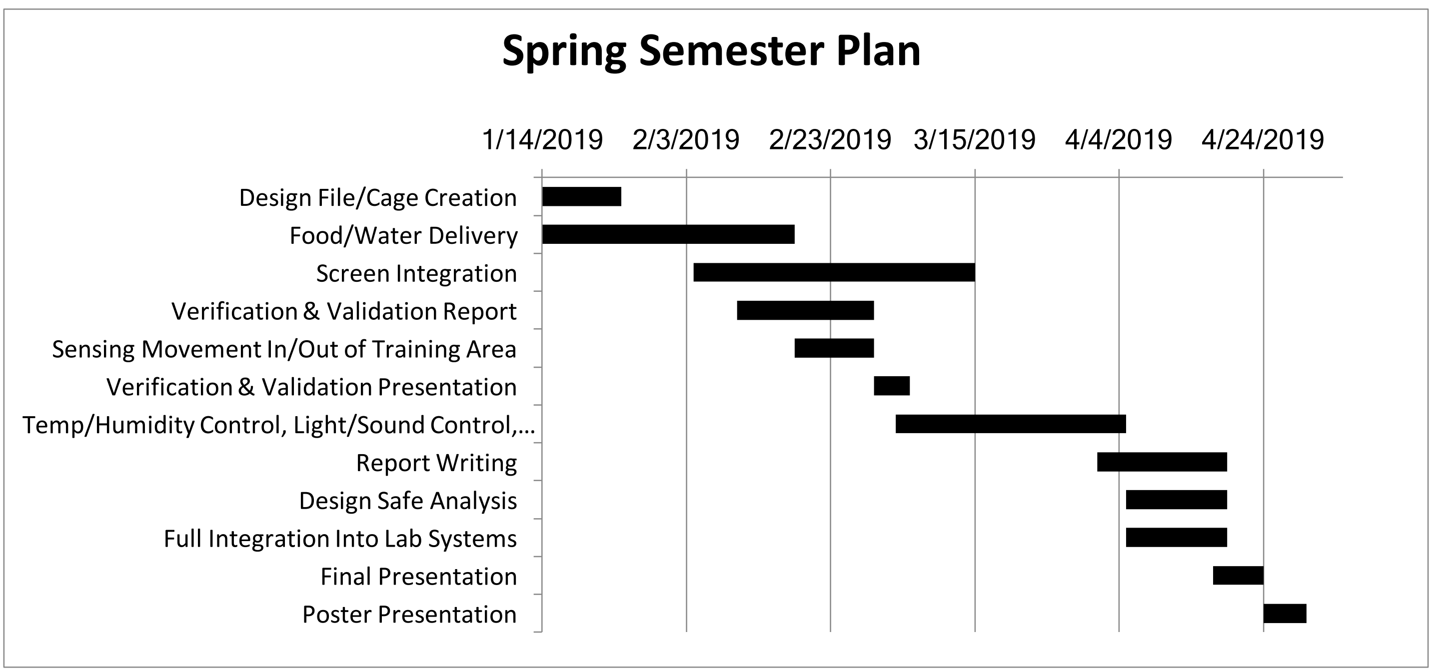
Fall Semester:

Task	Start	End	Duration (days)
Identify Project	8/26/18	9/2/18	7
Scope	9/1/18	9/17/18	16
Find Existing Solutions	9/15/18	9/25/18	10
Design Specs	9/20/18	9/30/18	10
Preliminary Paper	9/25/18	10/5/18	10
Preliminary Presentation	10/5/18	10/10/18	5
Learn Relevant Lab Skills (Laser Cutting and 3D Printing)	10/5/18	12/15/18	71
Learn Lab Integration Software	10/17/18	12/15/18	59
Progress Report	11/10/18	11/30/18	20
Progress Presentation	11/30/18	12/3/18	3
Order Parts	12/1/18	12/15/18	14



Spring Semester:

Task	Start	End	Duration (days)
Design File/Cage Creation	1/14/19	1/25/19	11
Food/Water Delivery	1/14/19	2/18/19	35
Screen Integration	2/4/19	3/15/19	39
Verification &Validation Report	2/10/19	3/1/19	19
Sensing Movement In/Out of Training Area	2/18/19	3/1/19	11
Verification & Validation Presentation	3/1/19	3/6/19	5
Temperature, Humidity, Sound, and Light Control, Drug Delivery	3/4/19	4/5/19	32
Report Writing	4/1/19	4/19/19	18
Design Safe Analysis	4/5/19	4/19/19	14
Full Integration into Lab Systems	4/5/19	4/19/19	14
Final Presentation	4/17/19	4/24/19	7
Poster Presentation	4/24/19	4/30/19	6



Breakdown of Responsibilities:

	Ellie	Sara	Zoe
Research	X	X	X
Client Communication			X
CAD Modeling		X	
Finding and Ordering Parts	X		
Cage Construction	X	X	X
Food/Water	X		X
Screen	X	X	
Sensing			X
Temp/Humidity			X
Light/Sound	X	X	
Presentation 1			X
Presentation 2		X	
Presentation 3	X		
Testing And Integration	X	X	X
Instructions	X	X	X
Report	X	X	X

References:

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8. Gondhalekar, V., & Brunner, D. (2003). U.S. Patent No. US20030024482A1. Washington, DC: U.S. Patent and Trademark Office.