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Research report

Automated Center-out Rodent Behavioral Trainer (ACRoBaT), an automated device for training rats to perform a modified center out task

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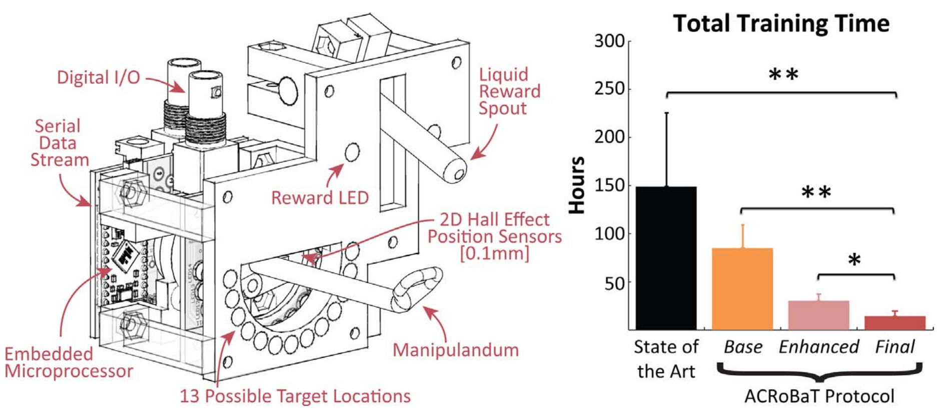
GRAPHICAL ABSTRACT



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1. Introduction

Animal models have long been a proxy for studying complex human behaviors such as decision making [1], perceptual discrimination [2,3], motor-skills [4], cognitive executive functions [5–7], learning [5,6], memory [5,6], and social behavior [8]. During the last century, as neuroscience has evolved to study the networked activity of neurons in the brain and spinal cord, much effort has been devoted to understanding the relationship between measured neural activity and external stimuli. However, studying complex processes such as decision-making, executive functions, and memory requires some measureable external behavior for researchers to quantify an animal's internal state.

*Abbreviation:*ACRoBaT, Automated Center-out Rodent Behavioral Trainer

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Thus, trained behavioral tasks have become the preferred domain for studying these systems.

Due to inherent variability of these trained behaviors, researchers must record many observations of each experimental condition. These conditions must be replicated precisely in order to reduce variability of results. To eliminate artifacts arising from laboratory specific protocols and/or experimenters [9], a myriad of automated behavioral chambers have been developed to standardize experiments and precisely record an animal's behavioral responses [5–8,10–20].

Studies of complex internal systems have historically used non-human primates due to their similarities in cortical structures [21] to human brains and complexity of their possible responses. Due to regulatory and funding hurdles, large scale primate experiments are prohibitively difficult to complete [22,23]. Recent rodent experiments have revealed surprising cognitive ability as they have accomplished tasks previously thought only completable by primates [24]. Rodents can learn probabilities of reward ratios in various game theory experiments [25–27], discriminate visual objects [28], perform multi-sensory integration [29], apply rules learned in different contexts [30], succeed in sensory discrimination [31], and manipulate a 2D joystick [32].

These complex tasks, however, often require precise timing, such as the manipulation of a lever or nose poke, or measurement of position in an arena. For rodents, automated behavioral chambers designed to control the precise timing and measurements of each element of the task can eliminate the tedious and error prone bias of human monitoring [9].

Automated rodent chambers often use several classic paradigms to record behavioral outputs. These include requiring animals to pull levers [7], retrieve pellets [13,14,19], or move in the cage, and utilize an array of sensors including video capture [15], infrared beams [33], nose-pokes, licking ports and/or joysticks. One of the most complex motor tasks developed for primates is a center-out reaching task [34]. This task has begun to be adapted for rodents [32], and we build on this work here by modifying the task, automating the training, and demonstrating success in many animals.

Our Automated Center-out Rodent Behavioral Trainer (ACRoBaT) device (Fig. 1) provides a fully automated 23-step algorithm to train naïve rats to perform a modified version of the classic center-out task. Custom hardware allows 13 possible target locations arranged in a bottom half circle, and we show training data from 18 rats learning a three-target choice task (Results Section: 3.4). We employ several key strategies to accelerate the learning process, including:

1. Adaptive Target Selection to prevent development of repetitive motor patterns during the target search portion of the task
2. Adaptive Timeout to introduce a dwell requirement for target selection
3. Soft Start and Intermittent Rewards to increase motivation throughout the sessions

These algorithms are fully instantiated on each device, while the experimenter can modify parameters and log relevant variables as needed when connected to a desktop computer. Human interaction is limited to selecting the current training step and then placing the animal in a behavioral arena for an hour-long training session. The ACRoBaT device has a flexible code framework for modifications so that the system is easily extendable via open source software. Built from 3D printed components, we believe this device can be easily adopted by labs and can drastically reduce the labor required for high-throughput rodent research, providing a low cost, open source tool for complex neuroscience experiments to our community.

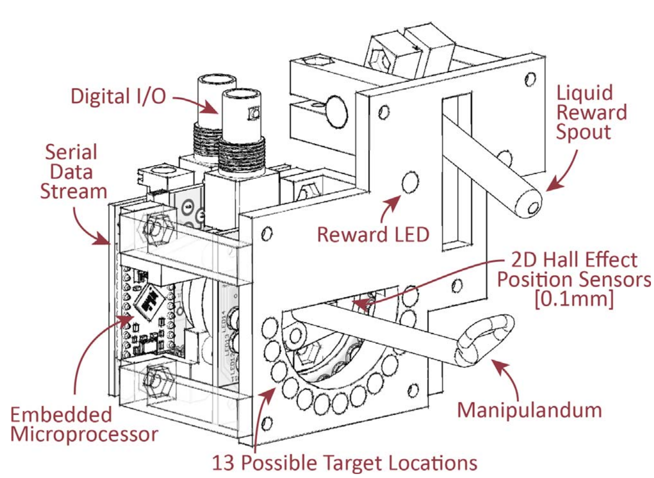

Fig. 1. CAD drawing of the ACROBAT device.
Two custom PCBs fastened to a 3D printed housing are attached to the front of the cage or arena. A half ring of 13 LEDs are controlled by MAX6966 LED driver chips on the front PCB. The rear PCB handles the capacitive sensor attached to the liquid reward tube, inputs from the 2D hall-effect joystick, connections for the Arduino Pro-Micro running custom C code and digital BNC connections (additional I/O ports). A small 3D printed joystick protrudes into the cage or arena and can easily be manipulated by a rat, with a spring return to the home position. Entire form factor is approximately 10 cm × 7 cm × 5 cm (width × height × depth). Although the device can operate autonomously for training, it must be tethered to a computer via a USB cable to log relevant variables at 100 Hz to a text file.

2. Material and methods

An automated 23-step training protocol and device (Fig. 1) has been developed for training naïve rats to grip a joystick with their paw and move in a two dimensional work space (bottom half of a circle). This protocol requires minimal human oversight, enabling an accelerated training timeline of 2–4 weeks. Visual cues provide sensory feedback about the target location during exploratory motions of the handle. After completing the training, animals will move the handle to and dwell in a specified window about the correct target for 1.25 s to obtain a liquid reward (Fig. 2B).

The Automated behavioral arena is built with 3D printed components to allow for easy modification and scaling to parallel training (Fig. 2). A military grade Hall Effect 2-axis joystick captures paw position within 0.1 millimeters and a capacitive sensor indicates animal contact with a liquid reward spout. Both sensors interface via custom PCBs to an Arduino microcontroller. A finite state machine (FSM) processes all variables (Fig. 3) to track animal progress and dispense rewards via a peristaltic pump. To log behavioral data variables, each device can be tethered to a desktop computer running a custom C++ program. When teathered, data is streamed via a serial connection at 100 Hz to a CSV text file on the desktop computer.

2.1. Animals

Adult female Long-Evans rats (Charles River, 200–300 g) were chosen for their ability to perform complex tasks [35]. Animals were group-housed during training (1–3 animals per cage). To habituate animals to the arena and human handling, we initially gave solid sugary food rewards (Kellogg's Froot Loops or Reese's Choco Puffs). We set the housing room light cycle to a 12 h day/night cycle, shifted such that the housing and behavior room was dark from 9am-9pm. This permitted training/testing to take place during the animals' active, dark cycle. We allowed *ad libitum* access to food throughout the training, but completely restricted animals from water in their home cages. We gave free water for ½ hour each day of restriction following completion of their training/testing sessions. For correctly completing a trial during the behavioral task sessions, we administered drops of apple juice as a liquid reward (0.05 ml). On weekends, we gave each animal free access to water. We weighed animals each day of restriction to ensure adequate growth for young animals and maintenance of body weight for older animals. All procedures were approved by the University of Washington IACUC.

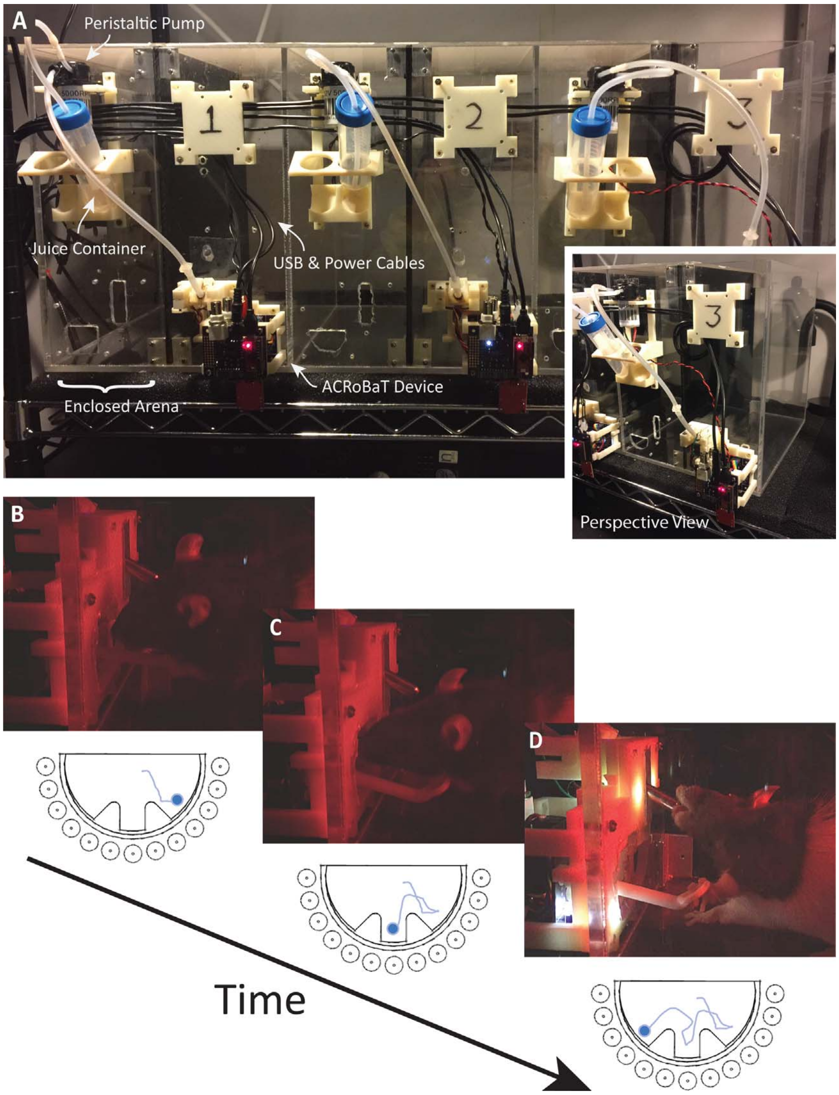

Fig. 2. Arena Assembly and Behavior.
PART A: Three behavioral arenas set up for automated training. Each self-contained arena has an ACRoBaT device near the floor of the enclosed training space, a peristaltic pump to deliver apple juice rewards, and a power and USB cable to connect the ACRoBaT device to a computer for data logging.
PART B–D: Example images of a rat manipulating the joystick to each of the three targets. Trajectories below show example progress through the workspace during a single trial (see Supplemental Videos 1–3 for more examples).

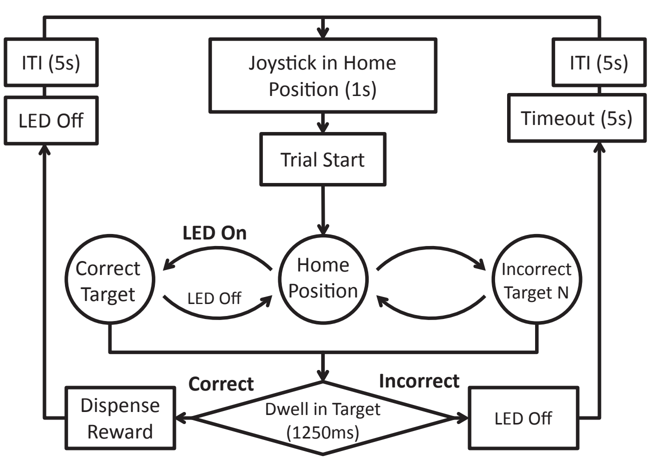

Fig. 3. Flow chart of the finite state machine (FSM) of final stage of task training. Block diagram shows the progression through each stage of a single trial. Trial starts once joystick remains in home position for more than 1 s, and concludes when animal dwells in a target for more than 1.25 s. If the target is correct, a liquid reward is dispensed, and the Inter-Trial-Interval (ITI) allows a new trial to start after 5 s. If the target was incorrect, an additional timeout penalty of 5 s is applied. These values are specified for our particular experimental paradigm, but each are customizable for a variety of applications. In our protocol for example, several variables including dwell in target time and LED turn on time, are modulated to progressively to increase task difficulty over time.

2.2. Behavioral arena and task design

A clear rectangular acrylic box (12" length × 8" width × 18" height) was outfitted with an ACRoBaT device, including joystick, housing and Arduino board. A pump dispenser and liquid reward tubes were mounted to the front of the arena (Fig. 2A). Range of motion for the joystick was a semicircle with a 4 cm radius, centered on the front wall 5 cm from the floor of the arena. The liquid reward sipper tube was centered in the arena, positioning the joystick predominately on one side of the animal. This encouraged the animal to use a single forepaw to manipulate the joystick. The ACRoBaT connected to the computer via a micro-USB cable. A 12V+ barrel jack cable powered the device, and a two-wire cable connected the pump to the ACRoBaT. Two additional BNC ports are available for synchronizing each to external hardware such as motion capture or neural recording devices. LED's on the ACRoBaT indicated trial start/stop times as well as the timeout periods following incorrect trials. The arena was lit with only red lamps in a darkened room to aid the experimenter in observing the animals. A lid was placed over the arena to prevent the animal from jumping out, and contained small holes for fresh air and to prevent condensation build-up.

While a traditional center-out task would have included a full circle of targets, we arranged our targets in a downward semi-circle. This was done because the rats were unable to push the joystick above their heads given the placement of our joystick in front of the animals. A traditional center-out task would also present the cue prior to start of joystick movement rather give a feedback signal while the animal is exploring the targets. All animals learn to move to a cued target as part of the training protocol detailed below. They then progress to search for 'hidden' targets. If the cued version of the task is desired, however, our flexible code framework can easily be modified to train animals to move to and dwell at the pre-cued target.

The ACRoBaT task encourages but does not completely restrict paw usage, for manipulating the joystick. Here we present data collected in left-handed arenas, with joystick on the left side of the sipper tube. We have included device designs with the joystick on either the left or right side of the sipper tube if desired (Results and Discussion: Section 3.6).

2.3. Software and data analysis

Each ACRoBaT device is run by its own Arduino microcontroller. Programmed with custom C code, they can independently handle all training steps. Additionally, to log behavioral data and training variables, each device can be connected to a C++ logging program on a personal computer via a serial interface. Many arenas can be independently controlled by a single desktop computer, limited only by the number of USB ports and computer RAM. Seven ACROBAT devices were simultaneously connected to a 3 GHz processor with 4GB of RAM, and no dropped data points, lag issues or serial disconnections were observed.

Behavioral variables were sampled at 100 Hz and logged in a text file. The log file consists of a comma separated value (CSV) file containing program variables. All post processing was performed in Matlab (The Mathworks). For all statistical tests, a two-sample *t*-test was used with $p < 0.01$ considered significant.

2.4. Training protocol

Each training session lasted approximately one hour or 200 trials, whichever came first. Sessions generally started at the beginning of the dark cycle and/or at the end of the dark cycle (either once or twice a day) to maximize motivation. Animals were placed into the behavioral arena, while the researcher selected the appropriate training step using the software on the personal computer. The 23 steps (Table 1) are divided into four distinct phases, and we specify each training step in detail below (Supplemental Video 2 illustrates example trials in each of the 4 phases). Each step is fully implemented and automated, so the researcher needs only to select the training step for each session and then can return after the hour of training is complete.

2.4.1. Pre-training

- **Step 1:** If animals were obtained from an outside vendor, we acclimatized them after transport for a minimum of one week [5], giving ad libitum food and water. Handling animals during this time helps speed up the acclimation process.
- **Step 2:** After the one week acclimatization period, we began liquid restriction, increasing by 4 h increments per day (day 1: restriction for 4 h, day 2: restriction for 8 h, etc.) until water is restricted at all times except when the animal is performing the task, and for 30 min following training completion each day.

2.4.2. Training

We trained each animal according to the protocol detailed below. Sessions lasted approximately one hour, during which time the automated device handled all interactions with the animals. We only needed to place the animal in the cage and select the initial training step. Table 1 details the criterion for successfully completing each training step and advancing to the next automated step.

2.4.3. Replace LED cue (stimulation, odor, audio or other)

At this point, the fully trained animal can perform an *n*-target modified center out task. They are actively searching for the correct target, and using the illuminated LED to identify the correct target before deciding on which target to ultimately select. If the end user would like to train a classic center out task (cue presented prior to start of trial, rather than as feedback), a simple setting in the code can be changed (see documentation in Results and Discussion Section 3.6).

As an optional extension to this protocol, steps 17–23 enable the end user to use audio, odor, pharmacological, optical, tactile or intra-cortical micro-stimulation (ICMS) instead of LED cues as desired by the experimental system under study (data not included).

3. Results and discussion

We have successfully trained 18 rats with various modifications to the training procedure to assess the improvements in performance. Three rats trained without our motivational and adaptive timeout strategies, three rats trained using motivational and adaptive timeout strategies, and 12 rats trained with both strategies and a high-resolution 2D hall-effect joystick.

3.1. Strategy I: Adaptive target selection

We discovered that training time substantially decreased by using an Adaptive Target Selection strategy. Rats have a difficult time with delayed gratification and easily develop "habits" or "patterns" which they robustly follow even if counterproductive to achieving the reward. In order to encourage them to break these habits and continue searching for a new target (i.e. stop repeatedly going to a single target), subsequent correct targets were selected based upon recent performance. For example, if the animal had a choice between targets A and B, and they had correctly selected target A only 30% of the time during the last 20 trials, there would be a 70% chance target A would be selected as the next target.

3.2. Strategy II: Adaptive timeout

We also discovered that progressively requiring longer dwell times resulted in much quicker learning of the dwell portion of the task. The Adaptive Timeout strategy successfully trained rodents to dwell in a particular target for a reward, rather than just receiving an instantaneous reward for reaching the correct target (Fig. 4). Each time the rodent completed five trials successfully, the time requirement to dwell for reward increased by 25 milliseconds and the dwell time requirement to trial timeout by dwelling in an incorrect target decreased by 50 milliseconds. This gradual progression substantially reduced the number of trials and sessions needed for completion of training compared to the large stepped increases of 150 milliseconds in our original protocol (Methods Section 2.4.3, Step 11).

3.3. Strategies III & IV: Soft start and interspersed easy trials

We employed two motivational strategies to encourage the rat to continue engaging with the task for the duration of the session. The Soft Start strategy sets the initial correct dwell requirement to 250 milliseconds and incorrect dwell requirement to 5 s for the first 20 trials. When used in the final steps of the training procedure, these easy trials provided initial motivation for animals to engage with the task. These were especially helpful when the task difficulty increased. The Interspersed Easy Trials strategy sets 10–20% of the subsequent trials to easy trials. These easy trials had a correct dwell requirement of half of the current value. These easy trials helped maintain motivation [36] over the course of several hundred trials of each session even during very challenging task conditions (Fig. 4).

Table 1
ACRoBaT Protocol.

Step #	Criterion for Completing: Trial	Training Step
Phase 1: Acclimation and Move Joystick		
1	Lick sipper tube for 20 milliseconds to complete the trial.	After a single session with at least 100 trials, step is complete.
2	Lick sipper tube 10 times to complete the trial.	After a single session with at least 100 trials, step is complete.
3	Move joystick handle 2 cm from center in any direction to complete the trial. Dominant target preferred by the animal (Left or Right) identified.	After one session of at least 100 trials, advance to next phase.
Phase 2: Cued to Move Joystick to One of Two Targets		
4	Move joystick to only the non-dominant target to complete the trial. Correct target indicated by illuminated LED during entire trial, while incorrect target is not illuminated. No penalty for moving joystick to incorrect target. (Physical dividers for guiding movement to the correct target are optional during Phase 2 steps.)	After one session of at least 100 trials, advance to next step.
5	Move joystick to only the previously identified dominant target to complete the trial. Correct target indicated by illuminated LED during entire trial, while incorrect target is not illuminated. No penalty for moving joystick to incorrect target.	After one session of at least 100 trials, step is complete.
6	Move joystick to the correct target (Left or Right) to complete the trial. The correct target is randomly selected per trial and indicated by illuminated LED during entire trial. The incorrect target is not illuminated. There is no penalty for moving joystick to incorrect target.	After two consecutive sessions with at least 100 trials each, step is complete.
Phase 3: Cued to Move Joystick to One of Three Targets		
7 (optional)	Introduce another target (Center, Top Left, or Top Right, etc.). Move joystick to the new target to complete the trial. Correct target indicated by illuminated LED during entire trial, while incorrect targets are not illuminated. No penalty for moving joystick to incorrect targets.	After one session of at least 100 trials, step is complete.
8 (optional)	Move joystick to randomly selected correct target (either Left, Right, Center, etc.). Correct target is indicated by illuminated LED during entire trial, while incorrect targets are not illuminated. No penalty for moving joystick to incorrect targets.	After two consecutive sessions with at least 100 trials each, step is complete.
	Repeat Steps 7 & 8 for each additional target. Method tested for up to three targets.	
Phase 4: Find Target and Select by Dwelling with Joystick		
9	Move joystick to find randomly selected correct target (Left, Right, Center, etc.). The correct target illuminates via LED only when joystick is in target, while incorrect targets' LEDs are never illuminated. Animal must dwell in correct target for 250 milliseconds to receive a reward, and a timeout period initiates if animal dwells in an incorrect target for more than 30 s.	After a session completed with at least 100 trials and accuracy of above 75% (two targets) or 66% (three targets), step is complete.
10	Same as Step 9, except the timeout period initiates after dwelling for 5 s in an incorrect target. Soft Start and Adaptive Timeout strategies begin at this step (Results & Discussion Section: 3.2 and 3.3).	After a session completed with at least 100 trials and accuracy of above 75% (two targets) or 66% (three targets), step is complete.
11–15	Same as Step 10. For each successive step, the correct target dwell time starts at 400 ms, 550 ms, 700 ms, 850 ms, and 1000 ms respectively. At the same time, for each successive step, the incorrect target dwell time begins at 4 s, 3 s, 2 s, 1.75 s and 1.5 s. These values change during the session as animal accumulates correct trials according to the Adaptive Timeout strategy (Results & Discussion Section: 3.2; Fig. 4). During **Steps 12–15**, the Intermittent Reward strategy is employed (Results & Discussion Results 3.3 section).	After a session completed with at least 100 trials and accuracy of above 75% (two targets) or 66% (three targets), step is complete.
16	During the final task, the animal must dwell for 1250 milliseconds in correct target to receive a reward and timeout period initiates if the animal dwells for 1250 milliseconds in any incorrect target.	After a session completed with at least 100 trials and accuracy of above 75% (two targets) or 66% (three targets), step is complete.
Phase 5: Replace LED Cue with Stimulation, Odor, Audio or Other		
17–23 (optional)	Same protocol as Steps 9–16, except using a different cue other than the LED's such as odor, audio tones, electrical or optical stimulation, tactile cueing, etc.	See Steps 9–16

3.4. *Training times*

Each additional training strategy resulted in a significant reduction in total training time and improved overall performance. All rats were trained to select one of three targets, and all but one animal completed the protocol. Eighteen rats, divided into three groups, demonstrated effects of motivational and learning strategies (Fig. 5). Group 3, employing strategies I–IV in addition to using a high resolution joystick, performed significantly better than Groups 1 (employing strategies I & IV) and Group 2 (employing strategies I–IV using a lower resolution joystick). All groups required significantly less training time than the current state of the art complex rodent behavioral task [6]. The number of trials per session ranged from 100 to 200 and sessions generally finished within one hour (Fig. 6).

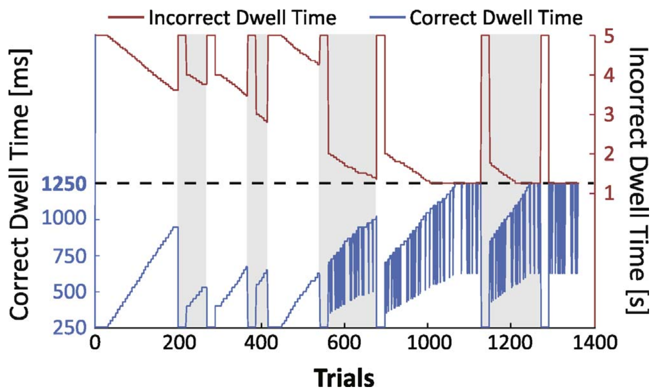

Fig. 4. Adaptive Timeout Strategy.
Initially, the dwell requirement to select the correct target is much lower than the dwell requirement to select an incorrect target. The incorrect dwell requirement starts at 5000 milliseconds and decreases at a rate of 50 ms per 5 correct trials. The dwell requirement to select a correct target begins at 250 milliseconds and increases at a rate of 25 ms per 5 correct trials. Each day begins with 20 easy sessions with dwell requirements at 250 ms and 5000 ms to encourage the animal to engage in the task. As the animal progresses in the training, the subsequent initial dwell requirements for the correct and incorrect targets are set higher and lower, respectively. During later training levels, we provide 10–20% easy trials to improve motivation. During these easy trials, the dwell requirement for selecting a correct target was halved (sawtooth blue curve from trials 580–1400). Note the different scales on the two y-axes. Alternating grey and white boxes denote training sessions.

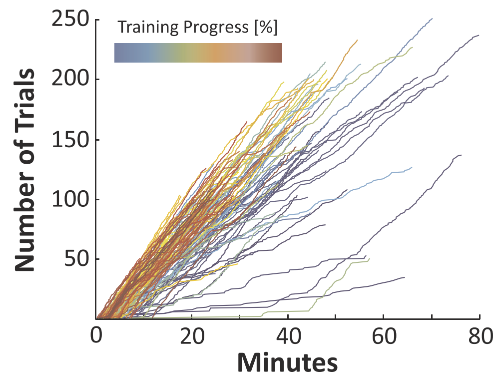

Fig. 6. Trial successes from a single example animal.
Usual sessions last one hour, and animals quickly progress to achieving 5 trials per minute. Typical sessions accumulate 150–200 trials. Animals will sometimes satiate prior to the completion of an hour and then sessions end early. For visualization, sessions occurring early in training are colored blue while later sessions are colored red. Note that as the training progresses, this animal achieves more trials in a shorter period of time. This is remarkable as the trial difficulty is also much higher later in the training protocol.

3.5. Home cage training vs. dedicated behavioral arena

Many recent automated training protocols [6,15,19,36] are moving towards in home cage training. The reduced effort of moving the animals from their home cage to their behavioral arena each day and the ability to train all day are attractive. We have no doubt that our ACROBaT protocol could be easily adapted for home cage training. For our current experiments using tethered stimulation, however, we found it advantageous to have a separate arena for training. If the animals need a tether to connect to implanted devices, daily handing provides an easy transition from training to performing the task with a tether.

Context is another important factor. Animals become aware that liquid rewards are only available when placed in the behavioral arena. Lack of water in their home cage motivates them to perform the task when placed in the behavioral arena. If continually exposed to a task in their home cage, animals might train infrequently or may become distracted between trials, rather than training until satiation. The current state of the art rodent decision-making task [6] also showed only minor improvement in efficiency with home cage training, suggesting limited benefits of training in the to home cage.

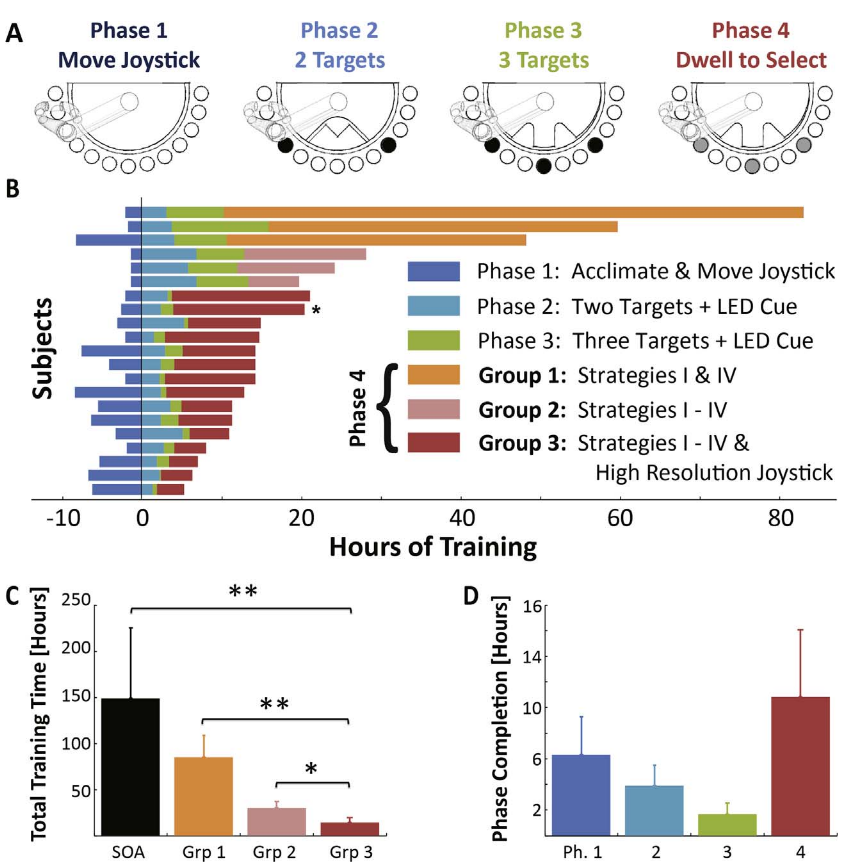

Fig. 5. Results of ACRoBaT device training performance.
PART A: Each animal progresses through four different phases, comprising 3–6 levels. Phase 1 requires the rat to move the joystick towards any of the open circle targets. Phase 2 cues the rat via illuminated LEDs to move the joystick to either left or right targets (randomized per trial). Phase 3 adds a third possible target (center). During Phase 4, LED cues are removed and the rat is required to search for the correct target. The target LED illuminates only when joystick is in the correct target (randomized per trial). The rat must dwell in a target for 1.25 s to make a selection. A liquid reward is given for correct target selections. If the target selected is incorrect, the rat must wait an additional five seconds before starting the next trial.
PART B: Total training times in hours for 18 animal subjects. Each of the three groups completed the first three phases before completing their individual final training paradigm. Groups 2 & 3 both used training strategies I–IV. Here the amount of time allowed in the incorrect target (before trial ends in an error) is initially much greater than the selection dwell time, and then gradually decreased as correct trials accumulate in a given session. Group 3 used a high resolution joystick (2 degree of freedom hall-effect sensor) rather than a traditional 2D resistor joystick. A single animal (*) was excluded during this final phase due to poor learning rates.
PART C: Average training times from naïve to fully trained for the three groups. Group 3 learns the task significantly faster than each of the other groups, and an order of magnitude quicker than the state of the art (SOA) rodent decision making paradigm (a Y-bar left/right decision making task [6]). Error bars reflect one standard deviation. A two-sample *t*-test was performed between Group 3 and each other group. * p = < 0.01, ** = p < 0.001.
PART D: Average time spent on each training phase for Group 3. Time to learning the cued joystick behavior requires only a few hours, while learning to search for targets and dwell to select requires about 11 h. Error bars reflect one standard deviation from the mean.

3.6. Dissemination

So that the community could take advantage of our device, we have assembled a complete list of parts required (Supplementary Materials: Bill of Materials) and assembly instructions (Supplementary Material: Instruction Manual). Please visit http://depts.washington.edu/moritlab for appropriate links to download user manual, source code, 3D model files, and PCB board designs.

4. Conclusion

Complex behavioral tasks for studying processes such as memory, decision-making, and perception have long required primates due to their ability to produce complex responses. Financial, regulatory and labor costs have limited researchers to experiments with small sample sizes and long experimental timelines. Our novel rodent training device, ACROBaT, eliminates many of these hurdles by improving on the state of the art complex behavioral task and dramatically lowering the time and labor costs needed to batch train large numbers of animals. We demonstrate several strategies for significantly improving training times, and delivered a robust protocol free from human bias in monitoring or evaluating performance. By automating each aspect of the trained task, we have enabled rodents to perform a task approaching the complexity of primates, with two to four-week training times in an open-source and flexible environment. This open source, low cost, automated training device lowers many entry barriers for complex behavioral research and can be used for a wide range of applications.

Conflicts of interest

The authors have no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.bbr.2017.11.031.

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