

Device for the Presentation of Olfactory Stimuli to Monkeys

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Problem Statement:

The olfactory stimulation device is designed to assist in research designed to compare the ability of young and aging monkeys to make correct, discriminatory selections of specific odors and tastes. The device must have the capacity to conduct experiments using either tastes or smells with equal ease. The device must be able to present two different samples to the monkey: one that contains a taste or smell stimulus of variable concentration, and another that contains no stimulus. The monkey will have the option to select the positive (correct) stimulus after testing both options. If the correct choice is selected, the monkey will receive a reward; the reward should be hidden behind a door corresponding to the stimulus selection. Upon choosing one door, the other one will be inactivated by a locking mechanism. The apparatus should be readily movable between cages, and all interactions between the monkey and the device should occur either inside the testing cage or within reach of the caged monkey. The device needs to be lightweight, yet durable and reliable.

Background:

Researchers wish to study the abilities of animals to taste and smell. Animals of particular interest to sensory researchers are primates, due to their close physiological relationship to humans. Information gleaned from primate research often has significant parallels in human physiology, which makes this type of research very valuable. It is hoped that the results of this research may one day help increase our understanding of how the human brain senses and interprets taste and olfactory stimuli.

One of the methods used by researchers to study the sensory performance of monkeys is the two-bottle preference test. This test examines whether a monkey prefers to drink from a water bottle or from a bottle containing water that has been sweetened with sugar. The two-bottle preference test is a simple test that yields clear data: it is easy to infer which fluid the monkey prefers from the volume consumed (Danilova, 2002). However, this test cannot be used to determine whether the monkey can distinguish between, say, 1% sugar and ½ % sugar solutions. It also cannot be used to determine preferences in odors.

Research has shown that sensitivity to smells and tastes changes over the life of the monkey; there are significant differences between the sensory abilities of young and old monkeys (Hellekant, 2002). Different age groups of monkeys more easily sense certain smells or tastes. Our clients wish to perform experiments that would work at or near the “threshold concentration” – the lowest concentration of a substance that the monkey can still positively

detect. The two-bottle preference test provides qualitative information of the monkey's sensory abilities, but conclusions are limited to simply whether the monkey prefers one taste or smell to another. The testing method does not provide any quantitative data. In order to obtain quantitative data, a different testing method must be used. First, experiments should be performed using near-threshold concentrations of scents or tastes. Also, the animal must be trained to make an intentional choice, choosing one and only one stimulus from a simultaneously presented pair. An experimental design integrating both of these factors would yield quantitative measures of an animal's olfactory and tasting abilities, rather than only qualitative results produced by the two-bottle preference test.

The goal of our project is to develop a system that can be used to perform an olfactory discrimination test with Rhesus monkeys (*Macaca mulatta*) as subjects. By the word "system," we imply the creation of an apparatus able to carry out the experiments designed by our clients. Other olfactory discrimination experiments have been carried out with humans, reptiles, pigeons, dogs, and other species of primates (Hubener, 2001). Two different experimental methods have been used to study olfactory performance in test subjects. The first method, introduced in 1992 and used in a 1998 study, simulated natural foraging behavior to determine olfactory performance in monkeys when multiple choices were presented simultaneously. The experimental method was called "multiple-choice discrimination." (Hubener, 1998) The later experimental method is termed "two-choice discrimination"; this method was used in a 2001 study to determine the olfactory sensitivity of pigtailed macaques for the odors of peanuts, *iso*-amyl acetate (a banana-like smell), and *n*-pentanoic acid (a component of primate body odor) (Hubener, 2001). Our client, Goran Hellekant, wishes to perform experiments using a new apparatus that would make use of the two-choice discrimination method in the testing of both olfactory and tasting abilities in Rhesus monkeys.

The two-choice discrimination method can be described as follows: The animal is offered a choice of two stimuli, one being "positive," and the other one being "negative" – in the sense that the positive stimulus indicates a "correct" choice, and the negative stimulus infers an "incorrect" choice on the part of the monkey. The two stimuli are presented simultaneously, yet distanced apart from one another. The animal may investigate one stimulus at a time; yet, it also move freely back and forth between the stimuli for further investigation. The stimuli are presented on an apparatus that provides a reward for the correct choice – an example apparatus would be a box containing a reward inside, with the stimulus placed on the lid of the box. For a two-choice discrimination test, one would hope to use a technically-simple testing apparatus, in order to make the connection between a positive stimulus and a reward is as readily obvious as possible.

When using primates as experimental subjects, extensive training of the monkeys is necessary. First, a monkey must be trained to operate the experimental apparatus itself. This involves teaching the monkey how to effectively sample the stimulus (whether through smelling or tasting), how open the door or box, and finally how to access the reward. It becomes clear at this point that there exists "beauty in simplicity" – the more straightforward the apparatus, the faster the monkey can become proficient in its use. If proficiency in operation is gained rapidly, then experiments can begin earlier. Valuable time is therefore saved.

After the monkey has mastered the operation of the experimental apparatus, the monkey must be taught to associate a certain stimulus with a corresponding reward. Finally, the monkey must learn to preferentially choose the positive (correct), rewarded stimulus over the negative stimulus. In the 2001 study that used a two-choice discrimination method, the macaques required between 480 and 900 trials before acquiring the skills necessary to complete the experiment as designed. In performing a two-choice discrimination experiment, the learning process is the most time-consuming; from the above example, the number of trials required to teach the necessary behaviors equates to a time period of between fifty and ninety days.

According to the description of experiments that our client wishes to perform, the monkey would be offered two different stimuli, either in the form of scented paper strips (in the case of odors) or bottles filled with flavored fluids (in the case of tastants). Each stimulus would have a “door” or other opening associated with it: a covered, recessed space into which a reward would be placed in the case of a correct choice, and no reward in the case of a wrong choice. By sampling the odors and/or tastes, the monkey would be taught to choose one of the two doors based upon its preference between the stimuli. A correct choice would earn a reward, and an incorrect choice would be met simply with the lack of a reward (as opposed to a punishment). In either case, the initial choice of the monkey would have to be final; a mechanism must be in place to prevent the monkey from either opening both doors simultaneously, or from opening the other door after already making a choice.

Alternative Solutions:

Alternative 1: Electronic Design

This design is fully electronic and is operated by the user via the use of push-buttons or screen touch interfaces. The stimuli would be incorporated into rotating discs that would be shuffled for a random time interval by the push of a button. The apparatus would use electronic circuits to transmit and display information from both the human operator and from the monkey. The monkey would choose the sample that he wants by pushing a button. As soon as the button is pushed, both choices would retract on sliding drawers; if the choice was correct, a third door would open with the reward on it. If the choice was incorrect, no drawer would open. The stimuli-discs would be placed on trays that rotate in a manner similar to that of a CD changer. The electronic apparatus would record the choices of monkey and print out a copy of the results at the end of a testing session.

Alternative 2: Mechanical Design

This design is very simple and meant to be operated by any person regardless of knowledge or experimental experience. The stimuli are presented in two locations (one on the left side and one on the right) with corresponding reward drawers located beneath the stimuli. The monkey chooses one of the stimuli by pushing in on the door. There is a mechanism inside to lock the doors; as one door is pushed, a semicircular piece of wire is also moved. As the wire moves, its angular orientation changes, and it falls (from the force of gravity) into a “groove”. Once in this groove, the wire cannot move because the groove prevents it from altering its

orientation. In the locked position, a pad attached to the other end of the wire now presses up against the back of the other door, preventing it from being opened.

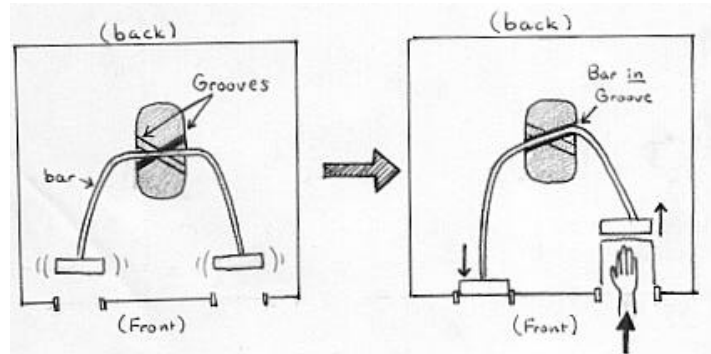


Figure 1: Diagram of how a wire locks the second door upon the opening of the first (Kolpin, 2002).

The area where stimuli are presented allows for easy interconversion between tastes and smells. For tastes, there are clamps upon which drinking bottles can be attached. For smells, these bottles can be removed, and strips of paper containing the odors can be easily inserted in their place. This device is simple, yet achieves all of the desired goals within its simplicity. Anyone can use it, and its use is easy to learn for both operator and monkey.

Alternative 3: Revolving Presentation Design

This design is also mechanical in nature, but uses a vertically-oriented revolving mechanism to present stimuli to the monkeys. On the cage-facing side of the device, the two doors for stimulus presentation would be located directly above one another; meanwhile, the doors for distributing the reward (or lack thereof) would be located at the same vertical level on either side of the device. The stimuli would be affixed to a wheel inside the device; the operator could change the arrangement of stimuli on this wheel. In order to give a random pair of stimuli to the monkey, the wheel would be spun, and the presented stimuli would be those that corresponded to the location of the presentation doors when the wheel stopped.

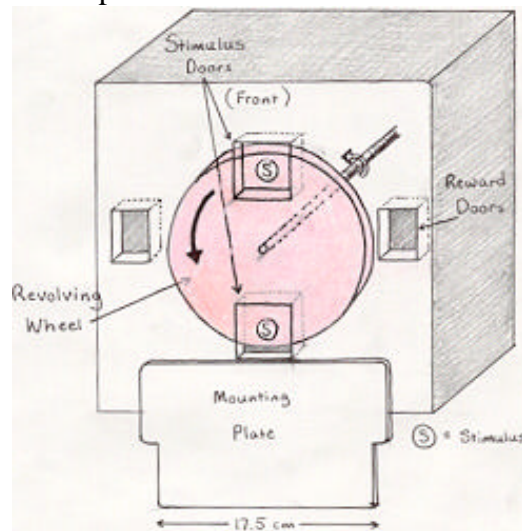


Figure 2: Drawing of the revolving wheel design (Kolpin, 2002)

This design presents the advantage that the stimuli would be offered in a truly randomized fashion. However, there are several drawbacks. First, the locations of the presentation and/or reward doors would not line up with the appropriate openings in the mesh of the monkey cage. Secondly, the arrangement of the presentation doors (in a vertical fashion), as well as the arbitrary assignment of the reward doors, is potentially confusing to the monkey. It is preferable to allow the monkey to choose between 'left' and 'right,' rather than between 'up' and 'down.'

Design Matrix:

	Electronic design	Revolving design	Mechanical design
easy for taste	0	0	+
easy for smell	+	+	+
simplicity	0	0	+
user friendly	+	0	+
durable	0	+	+
lightweight	+	+	+
movable	0	+	+
monkey friendly	0	0	+
easy to learn	0	0	0
attach cage easily	0	0	0
locking easy to do	0	+	+
TOTAL	3	5	10

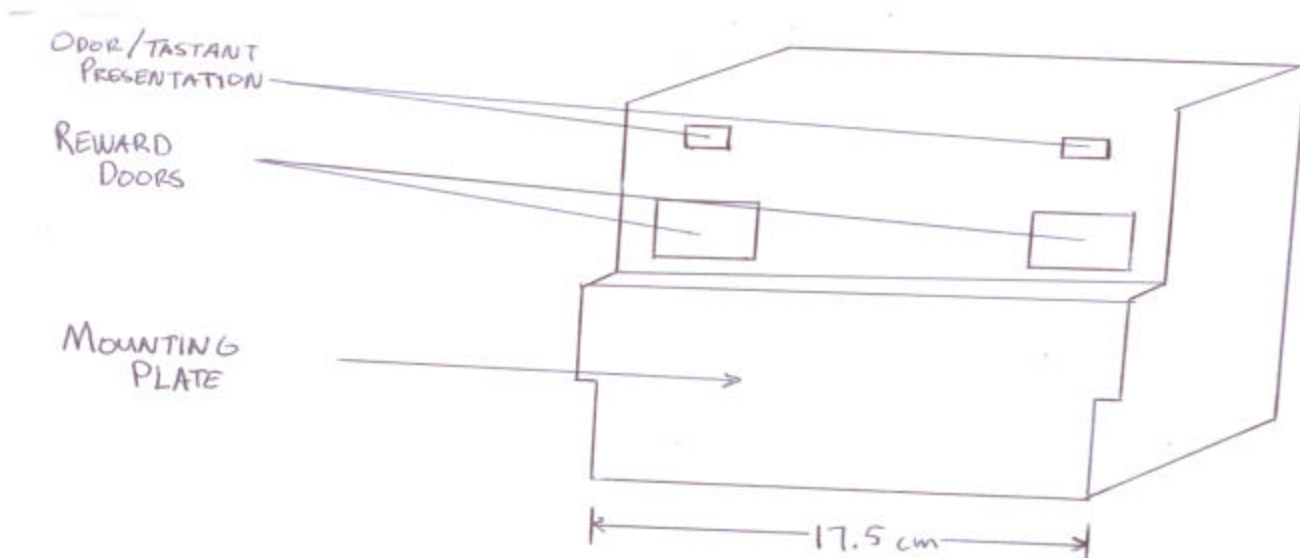
Selected design:

The design, shown below, which can be incorporated into "new," modern cages was chosen as our selected design. From conversations with our client, we have decided that a design that incorporates side-by-side reward doors with the odor/tastant presentation sites located directly above the rewards is the most applicable and functional design. All of the new cages in use at the Primate Center have a standardized feeding tray mounting plate (Appendix C), which secures the feeding tray to the cage. An identical mounting plate will be incorporated into the front of the device, which avoids concerns pertaining to mounting our device on a variety of cages – thanks to the current trend towards cage standardization. The new cage possesses larger holes in the cage mesh through which the caged monkey can easily reach to manipulate the device (see figure below). This eliminates the large problem associated with the monkey's inability to reach through the cage to perform the tests; a Rhesus monkey of almost any age or size will have no difficulty in extending its reach beyond the cage in order to operate the device. As was mentioned earlier, these "new" cages are fast becoming a standard in laboratory settings; therefore, this design could be easily applied in any lab utilizing these modern cages.

The specific design of the monkey-device interface was selected for both its simplicity and ability to incorporate a tasting bottle – the latter is a feature that client requires. This design is superior to the other designs in both these regards. The vertical revolving door design,

presented as the third design alternative, could not be developed to incorporate a fluid-tasting bottle, which is used to deliver a liquid stimulus to the monkey. This is due to the revolving design. The design that presents stimuli in a side-by-side fashion can easily incorporate drinking bottles by securing them internally within the box, with the nozzles of the bottles protruding through the odor/tastant presentation doors. Also, the horizontal arrangement of the four large mesh holes makes the implementation of the vertical revolving door impossible. Thus, the design that presents stimuli in a side-by-side manner becomes the obvious choice.

The top of the device is recessed inward to avoid contact with the sliding door of the cage during insertion. The device will be mounted so that the two reward doors will be located directly in front of the far right and left large, two-inch mesh holes of the cage. The doors reserved for stimulus presentation will be located directly above the reward doors. These stimulus-doors will be placed high enough so that they rest above the sliding door tract, and between the thin one-inch mesh holes directly above the door tract.



**Figure 3: Schematic drawing of the basic shape of our selected design (Potter, 2002).
Any dimensions not specified above are still considered arbitrary.**



Figure 4: Photograph of “new” cage with a feeding tray mounted directly below large mesh holes (Campbell and Potter, 2002).

Future Work:

In the future, we hope to make improvements to our basic design, to make it better serve the needs of the client. One such improvement that we are planning to make is the incorporation of a blinking indicator light. The design would be exactly like the selected design presented in design alternative two, except that there would be a blinking light present to indicate when a correct choice is made. The presence of the light, a visual signal, helps facilitate the monkey’s learning process of mentally associating a particular stimulus with a reward. Experiments have shown that monkeys, like humans, are highly visually-oriented animals; they rely most heavily on their vision to provide them with information about the environment. Thus, the presence of a blinking light may drastically shorten the time period necessary to train the monkeys how to perform the test. The light would serve only to indicate that the monkey made a correct choice; the experimental results themselves would not be affected. This design feature would likely be best incorporated into a second-generation prototype, once the basic structure of the apparatus has already been constructed and tested.

Appendix A:

Product Design Specifications (March 13, 2002)

Title: BME 301 - Olfactory Stimulation of Monkeys

Group Members : Sarah Kolpin (leader), Kevin Campbell (communications), Heather Shaner (BSAC), Wyatt Potter (BWIG).

Function: Apparatus should provide quickly interchangeable pairs of stimuli to a caged monkey. It should then allow the monkey to choose between two possible solutions, each corresponding with one of the stimuli. The device must then provide a reward for the correct solution.

Client requirements:

- a. The device should allow for the presentation of both tastants and scents to the monkey (not necessarily simultaneously).
- b. The tastants will most likely be standard water bottles, and the scent will come from filter paper.
- c. The device should present the monkey with two options for an action that will allow the monkey indicate its choice in tastant/scent.
- d. These two options must clearly separate and must clearly correlate to a specific stimuli.
- e. After monkey has chosen one smell/tastant, choice should be final.
- f. A reward should be provided for the correct solution; an incorrect solution will earn no such reward.
- g. A light should also indicate that the correct choice has been made. It must be possible to turn off this light mechanism for the duration of testing.
- h. Apparatus should be readily moveable from cage to cage.
- i. The apparatus should work at two height levels: about 1 foot from the ground, and about 5 feet from the ground.
- j. The device must easily accommodate an operator who is responsible for switching stimuli and moving the device from cage to cage.
- k. The replacement of stimuli between tests must be out of sight and smell range of ALL monkeys within the immediate vicinity (i.e. testing room).

Design requirements:

1. Physical and Operational Characteristics
 - a. *Performance requirements:* Device should operate continuously, should handle extreme forces from angry monkeys. It should not break or fail if dropped or knocked off of the cage. The device should withstand moisture, fecal matter, and urine.
 - b. *Safety:* Product should not cause harm to monkeys. There should be no risk of monkeys to electrocution, shock, extreme heat or cold, fast-moving blunt objects, or pinching of fingers.
 - c. *Shelf Life:* Device should be functional indefinitely, stored in temperatures ranging from 0°C-37°C.

- d. *Operating Environment:* Temperature range should ideally be around standard room temperature and pressure; the device should handle large amounts of dust, humidity, vibration, resist all corrosion (due to water and/or monkey urine), should be easily handled by people and monkeys.
 - e. *Size:* The device should have dimensions that will allow it to slide into the available feeding bin slot on the front of cage (about 6 inches by 10 inches). The device will attach to the outside of the cage and be a size that is easily manipulated by both the caged monkey and the operator. The monkey should not have to strain his reach to operate the device or receive its reward.
 - f. *Weight:* Should not weigh more than 20 lbs; optimum weight should be around 10 lbs.
 - g. *Materials:* Materials should consist mostly of metal. This metal could be stainless steel or aluminum. Any material that is either subject to corrosion or easily breakable should not be used.
 - h. *Aesthetics, Appearance, and Finish:* The device should not be colorful, highly reflective, or distracting in any way to the monkey. One or two indicator lights may be attached to the cage-facing side of the device to indicate to the monkey when a correct choice has been made. Another light or indication device should be on the back of the device to inform the operator if monkey has or has not made a choice yet. No particular finish is required.
2. Production Characteristics
- a. *Quantity:* Begin with one prototypic device. If successful, several machines will be made, to be used simultaneously.
3. Miscellaneous
- a. *Customer:* All recommendations from client will be incorporated into design.

Appendix B: Sources

Campbell, Kevin and Potter, Wyatt: Digital images of monkey cages, taken on (?????)

Danilova, Vicktoria (Vika): Personal conversation held on February ____

Danilova, Vicktoria (Vika): Visits to the UW Primate Center on February ____, ____,
and March 12, 2002.

Hellekant, Göran: Personal conversations held on February ____ and March 1, 2002.

Hubener, Fabienne and Laska, Matthias: “Assessing Olfactory Performance in an Old
World Primate, *Macaca nemestrina*” Physiology and Behavior, Vol. 64, No. 4, pp. 521-
527. © 1998 Elsevier Science, Inc.

Hubener, Fabienne and Laska, Matthias: “A Two-Choice Discrimination Method to
Assess Olfactory Performance in Pigtailed Macaques” Physiology and Behavior, Vol.
72, pp 511-519. © 2001 Elsevier Science, Inc.

Kolpin, Sarah: Drawings of locking mechanism and of Alternative Design Three.

Potter, Wyatt: Schematic drawings of selected design and of mounting plate (see Appendix C)

Appendix C: Schematic of the mounting plate:

