

MRI-Compatible Olfactometer

BME 301

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Abstract

In order to accurately deliver timed increments of 6 odors to a subject during an fMR scan, an MRI-compatible olfactometer is needed. This olfactometer will primarily be used for research purposes in the laboratory of Dr. Vivek Prabhakaran; however, it is a potentially marketable device for researchers who do not have the time or resources to build their own olfactometers. The design for this olfactometer is compact, provides a hand controllable flow rate of odor up to 2.5 L/min, programmable switching of odors, and meets the majority of the client's design requirements. Due to its reliability and portability, it has good marketability and is a viable option for both the client's lab and other labs doing olfaction research.

Problem Statement

Olfactometers are present in most olfactory research laboratories. This device allows the researcher to more accurately perform experiments that require an odor delivered to the subject. In our client, Dr. Prabhakaran's experiment, the odor must be delivered in a cycle: odor for 30 s, followed by clean air for 30 s. The duration of time the odor is delivered can be varied depending on the experiment. This odor delivery must occur during an fMR scan of the patient's brain in order to monitor brain activity during the experiment. Currently, the researchers in Dr. Prabhakaran's laboratory are using "smell sticks" to deliver the odors. The subject is instructed when to put the smell stick to their nose and when to take it away. This procedure poses major accuracy issues. One of the main requirements of the olfactometer is to deliver the odors at precise intervals. If the subject does not begin actively sniffing the smell stick at the correct time, the experiment may have considerable error. Also, a potential issue with the smell stick is that if the subject moves his or her head slightly (2 mm), the fMR image will be ruined.

Motivation

The problems with the current method of using smell sticks provide an opportunity for design of an olfactometer device to deliver the odors directly to the subject. This device will allow the researcher to more accurately carry out their fMRI experiment. Some research topics which may have use for an MR-compatible olfactometer are Alzheimer's disease, obesity, and perfume.

Background Information

fMR Imaging

Blood oxygen level dependent (BOLD) functional magnetic resonance imaging (fMRI) is used to monitor brain activity. The fMRI measures the oxygen delivered to neurons by hemoglobin. Active neurons require more oxygen, which causes blood flow to increase in areas of increased neural activity. The MR machine detects oxyhemoglobin differently than deoxyhemoglobin. This difference in detection allows the fMR image to display the brain's neural activity.

The images produced by the fMRI machine during an experiment are called activation maps. These maps of the brain show where the brain activity is

increased during a stimulus, such as an odor. A simple experiment alternating between a visual stimulus and dark every 30 s creates an activation map (Figure 1).

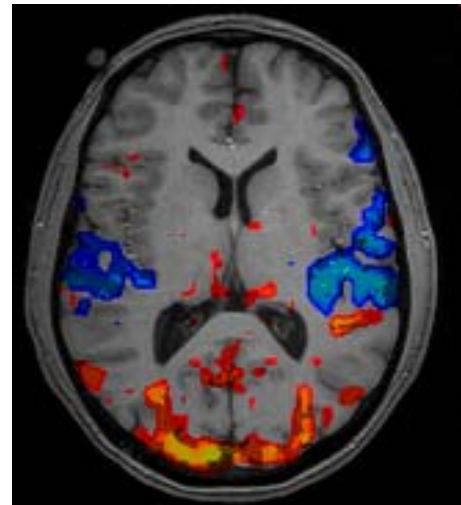


Figure 1. Activation Map of a simple fMRI experiment (<http://www.fmrib.ox.ac.uk/education/fmri/introduction-to-fmri/what-does-fmri-measure>)

Olfaction Research

Olfaction is a relatively recent area of research, although there are some very important discoveries being made in this line of work. Alzheimer's disease could be diagnosed earlier by a loss of the sense of smell. Obesity studies have shown that the sense of smell is closely linked to the sense of taste, and olfaction researchers are discovering treatment methods for obesity based on that fact. In patients who are going through cancer treatments, the delivery of pleasant odors during treatment procedures has proven to relax the patient. The perfume industry also uses olfactory methods to determine if a scent is pleasant to people before marketing the perfume.

Experiment

The olfactometer will be used in an fMRI experiment to deliver odors in timed intervals. The interval times will vary from 20 s of odor cycling with 20 s of clean air (Figure 2).

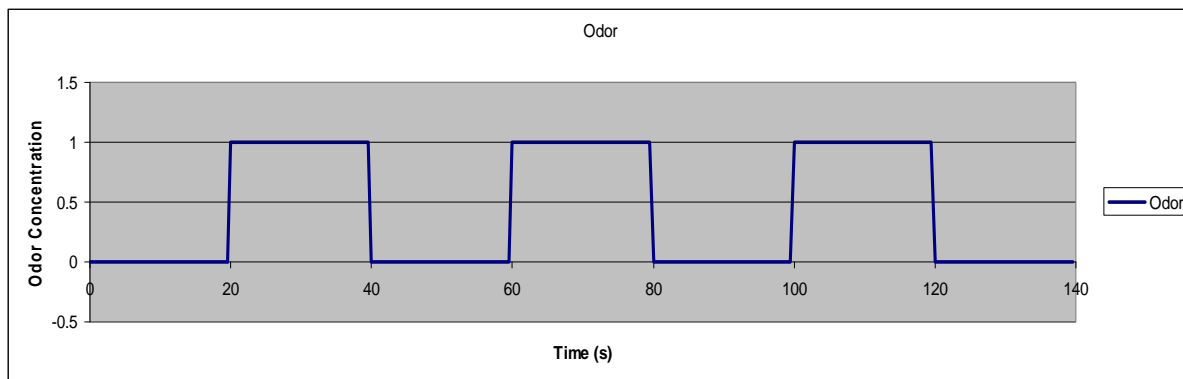


Figure 2. Example of odor delivery in the experiment versus time.

Literature Search

There have been many olfactometers constructed at different hospitals and universities for research purposes. Although many past researchers have designed and constructed olfactometers for their laboratory, no olfactometer was found in the literature search that is commercially available. Researchers at Harvard University and McLean Hospital constructed an olfactometer for their own fMRI studies (Figure 3).

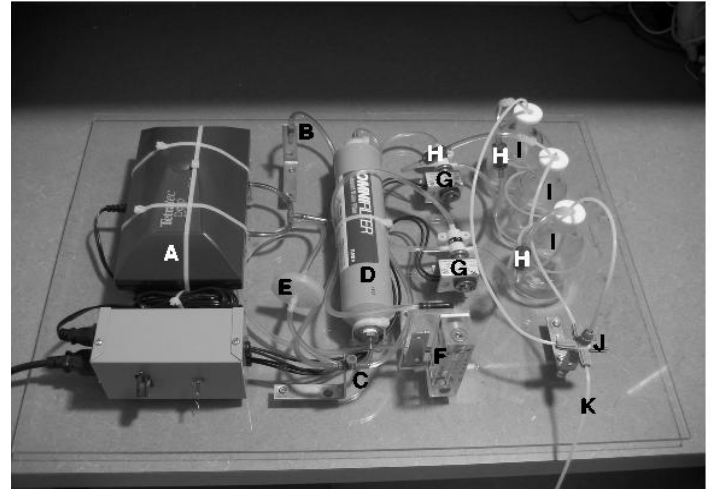


Figure 3. An olfactometer used at Harvard and McLean Hospital (<http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1602106>)

The olfactometers that have been created for researchers at different hospitals and universities are all similar in theory, but differ in the features they have to measure the odor and air. Also, there are a limited number of olfactometers that have been developed to be MR compatible.

Design Specifications

Our client wants to use our olfactometer as the primary means of delivering odors to test subjects undergoing an fMRI scan. As such, the olfactometer must be compatible with the MRI environment. This means that any part of our design that is in the MRI suite must not have any ferromagnetic components; if the best design necessitates the presence of some sort of ferromagnetic material within the MRI suite, this material must be kept at a safe distance from the magnet, about 5 m. Any ferromagnetic components caught in the MRI's magnetic field will

create an extremely dangerous environment for both the experimenter and the test subject, and will almost certainly cause a great amount of damage to the olfactometer itself.

In order to maintain a tolerable testing environment and obtain accurate results, our client would like to be able to control the temperature of the odors delivered to the test subject. The odors will be delivered at approximately 37.5 °C, or body temperature. The reason for this is twofold. First, this temperature will prevent discomfort for the test subject. It is possible that odors delivered too hot or too cold will irritate the test subject, and inevitably leads to inaccurate results. Second, the client wants to keep odors delivered to the test subject at body temperature in order to prevent activation of the hot and cold receptors of the nose and face. The purpose of the client's study is to investigate which parts of the brain are involved in olfaction; this is accomplished via the fMRI scan. Olfaction is directly tied to the first cranial nerve, while the hot and cold sensors are directly tied to the fifth cranial nerve. If the fifth cranial nerve is stimulated too much, it will cause an fMRI reading due to the temperature of the odors, and not of their olfactory qualities.

Our client would like the olfactometer to have inputs for six different odors. These odors will be prepared as liquids and then absorbed into pellets; these pellets are what actually contain the odor delivered to the test subject. Our design must therefore be able to support six different odor pellets. These odors must be kept separate from each other to avoid contamination, and the container for them must either be disposable or washable if it is to be used more than once.

Our client would like to be able to control the olfactometer via the computer that controls the MRI machine. He would like the ability to program which odor is released at a certain time, and the duration that odor is delivered to the test subject. As such, a program needs to be created that can control the flow of air through the olfactometer and can dictate which odor is delivered

at a given time. This program should readily interface with E-Prime, the program the client currently uses to control the fMRI. This ensures that the olfactometer runs in conjunction with the data gathered from the fMRI, allowing for the most accurate results possible.

The olfactometer design must be compatible with our client's current experiment. Most notably, this means the design must be compatible with the active sniffing method of odor delivery. Active sniffing is a technique that has test subjects consciously smell the environment around them. This differs from other olfaction experiment techniques that deliver odors directly into the test subject's nose, eliminating any chance of missing the odor. In order to comply with the active sniffing technique, the odor should be delivered to and contained in an area surrounding the test subject's nose. This area should be sequestered from the outside environment, and should have conditions that can be dictated through the use of the olfactometer. However, the design should be compatible with a cannula as well to make it more versatile for other experiments.

Final Design

Airflow Design

The airflow of the olfactometer was designed to deliver a predictable flow rate to the subject while maintaining control over the experiment and allowing for efficient switching between the odorized and nonodorized conditions. Figure 4 shows that to accomplish this, a pump drives air through two filters and into a flow controller. After the flow controller, the air lines divide off in seven directions. One line is a clean air bleed line that allows for quick odor clearance and a level of consistency when the odors are turned off; the other six lines come from a six-to-one solenoid valve wheel that controls which odor is on at a given time. These lines run

to syringe filters which contain the odor the experimenter wishes to test. These syringe filters are attached to an eight-to-one check valve manifold, which then leads to a nasal cannula. All tubing and valves are made of or coated with polytetrafluoroethylene (PTFE), or Teflon. This ensures that the tubing will not retain any residual odors, and gives the olfactometer an added measure of longevity and reliability.

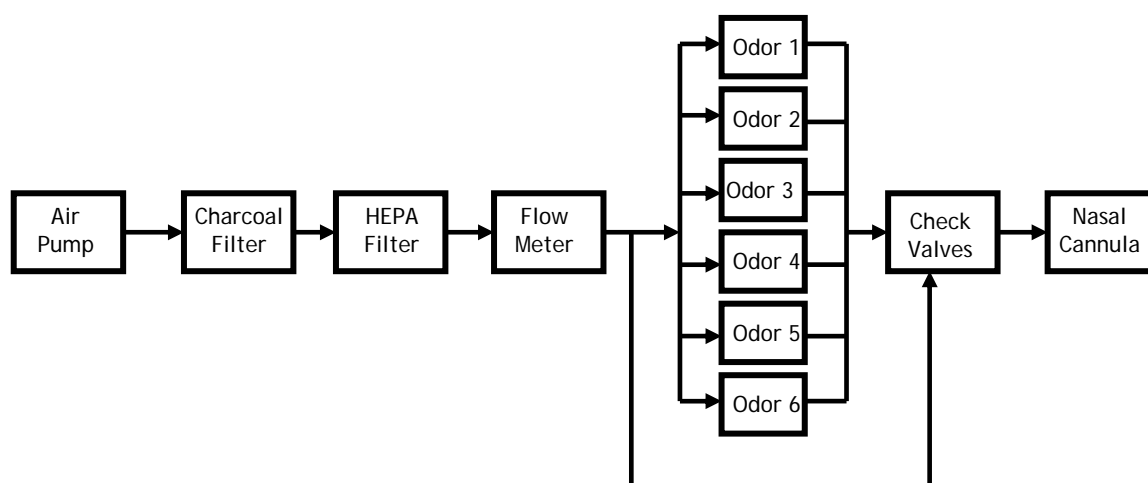


Figure 4. Block diagram of olfactometer airflow

The airflow for the olfactometer begins with a pump. The Elite 801 Air Pump by Hagen has been selected to serve as the pump for this design (Figure 5). This specific pump is a small diaphragm pump intended for air driven aquarium filters; thusly, it suits the needs of this design perfectly. It outputs about 21 kPa at 2500 mL/min and costs \$7.99, making it an inexpensive and effective solution (www.hagen.com). In addition, the Elite 801 is very small (about 60 cm² in surface area) and light (about 300 g in mass) which aids in keeping the portability of the olfactometer.



Figure 5. Elite 801 Air Pump by Hagen (www.hagen.com)

The air driven by the pump must be filtered to ensure complete control over the odorants reaching the test subject. To accomplish this filtering, two different filters are used: a charcoal filter and a High Efficiency Particulate Air (HEPA) filter. These two filters serve two different purposes. The charcoal filter acts as an air purifier. It removes any undesirable residual odor that may be present in the ambient air around the olfactometer, thus providing clean, odor free air for the experiment. Despite its utility, it is possible for the charcoal filter to input charcoal dust into the air past the filter. The HEPA filter removes any particulates that may have entered the air via the charcoal filter, thus ensuring that the air leaving the olfactometer is both odor-free and safe to breathe.

The OmniFilter R200 Refrigerator Icemaker Water Filter was selected for the charcoal filter. This filter has the desired qualities of a charcoal filter, plus an extremely long life: it is rated to filter 14,763.106 liters before failing, which, when used in conjunction with the Elite 801 air pump, gives it a minimum use life nearly 100 h (filters.filtersfast.com). The OmniFilter R200 Refrigerator Icemaker Water Filter is thusly ideal for use with the olfactometer.

The HEPA filter selected for the olfactometer was the Whatman HEPA-VENT filter from Cole Parmer. This filter is rated to remove 99.97% of airborne particles greater than 0.3 μm in diameter (Cole Parmer 2009). In addition, this filter has barbed ends, making it ideal for use in series with the charcoal filter and making it small enough to fit neatly into the olfactometer.

Once the air in the olfactometer has been fully filtered, the flow is measured and a level of control is added. This is accomplished through the use of a flow meter/controller. The flow meter selected for the olfactometer can accurately measure flows up to 2.5 L/min, perfect for use with the Elite 801. It can also effectively control the flow rate through the system, giving the experimenter another level of control over the experiment.

After the air flows through the opened solenoid valve from the group of six valves, it travels through Teflon tubing from the control room and to the MRI scanner room. There it flows through a syringe filter that contains the odor. Two to three small sponge-like pellets are placed in the liquid odor for at least 12 h, and then they are placed into the syringe filter. As the air flows through, it picks up the odor in gas form from the pellets, while the pellets add no resistance to the flow. The six tube lines from the solenoid valves then meet at a manifold system. The entrance to the manifold is governed by check valves to make sure the airflow travels in the correct one-way path. The six check valves then output the airflow to one Teflon line. Finally, this line connects to a nasal cannula that is properly fitted to a subject undergoing the fMRI experiment.

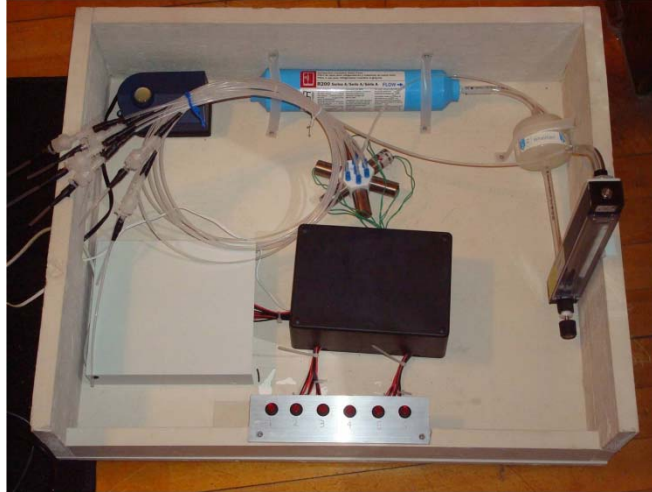


Figure 6. Finished olfactometer showing pump, filters, flow meter and valves

Figure 6 shows the mechanical aspects of the olfactometer in finished form. Flow begins at the upper left portion of the box and travels left to right, through both the charcoal and HEPA filters. It then turns downward through the flow meter with hand controller, and then back up and to the left to the valves and the clean air bleed line. The housing for the circuitry can be seen in the middle, with wires running to a power relay, LED pushbutton switches, and the solenoid valves.

Electronic Layout

The electronic layout of the design consists of all components necessary for solenoid operation. Since there are six solenoids (one per each valve), six single unit designs are cascaded in parallel with a single power source in series. Each unit consists of a manual pushbutton switch with an LED indicator, a computer-controlled switch, and the solenoid load itself (Figure 7).

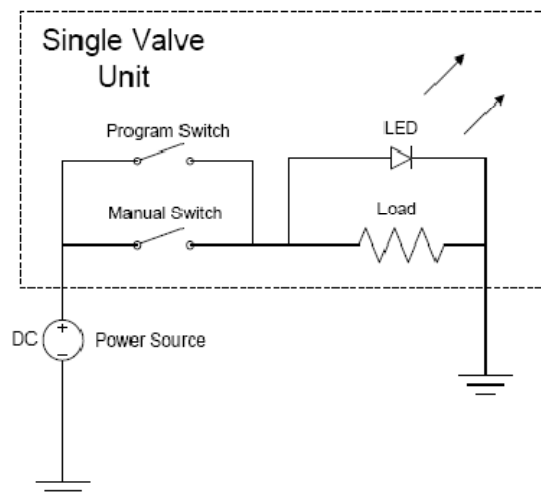


Figure 7: Single valve unit with power source. Six units are cascaded in parallel (one for each valve) with the power source in series.

Each solenoid valve requires 12 VDC at 2.6 W (Cole Parmer 2009). An AC/DC converter is used to satisfy this requirement; the model chosen plugs directly into a wall outlet and supplies 12 VDC with up to 500 mA. This converter supplies enough power to operate up to two valves at a single time if necessary.

The manual pushbutton switches are convenient for making quick assurances. They are an easy way to check for proper air flow and odor prior to beginning an experiment. The LEDs inside each switch turn on when the solenoid is activated (from the manual button or the power relay switch). They are rated to turn on at 1.7 V. Since they are arranged in parallel with each load, the 12 V across each solenoid during activation will not easily burn them out. If the LED were to burn out in the future, the circuit would still be operational but there would be no visual indication of the valve's status (this would not be a large concern since the valves emit a strong audible click when they open and close).

The most complicated piece of the unit is the Switch & Sense 8, a data acquisition (DAQ) power relay board device. The Switch & Sense 8 uses a microcontroller with a USB port for

digital input/output. Unlike most other DAQ devices, however, its output is devoted to eight power relays. These power relays are the program switches seen in Figure 7. The Switch & Sense 8 is compatible with LabVIEW as well as many other common programming languages, including Visual Basic and C++. It requires a wall outlet to operate and driver installation before first use (www.measurementcomputing.com).

Program

The program, written in LabVIEW, is the brain of the olfactometer. It directly interfaces with the client, so adequate reliability and user-friendliness was considered when it was written. The program works with the Switch & Sense 8 to activate and deactivate the power relays according to the client's desires.

Figure 8 shows the front panel of the program. The first control is the cycle duration. This controls the number of seconds in one cycle period. The second control is the duty cycle, which determines the percentage of the period for which the solenoid valve is on. For instance, a 50% duty cycle devotes half the cycle to odor and the other half to clean air. The next parameter is the total number of cycles for the experiment. The user can select from 1 to 6 cycles, and the 6 odors can be chosen for each cycle below this input.

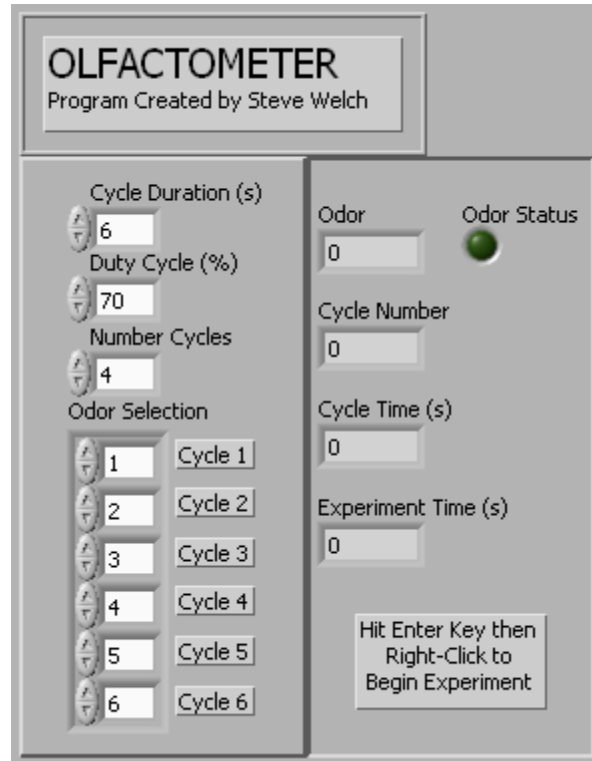


Figure 8. LabVIEW program front panel interface. Program allows customization of olfactory experiment setup.

One of the client requirements is to synchronize the program with EPRIME, which is another program used to create experiments with the fMRI machine. In EPRIME, the user begins the experiment with a mouse left-click. The LabVIEW program takes advantage of this fact; to begin the experiment, the user presses the enter key, then left-clicks the mouse. This works even if LabVIEW is minimized on the computer screen. The aim is to set up the LabVIEW experiment, then minimize this program to set up the EPRIME experiment. When both are ready, the user can hit the enter key, then use the left-click on the mouse to begin both experiments simultaneously. Due to its inherent programming and interface with the Switch & Sense 8, an experiment cannot be conveniently aborted after initialization. The easiest way to

abort an experiment if necessary is to unplug the Switch & Sense 8, then wait for the program to run to completion.

In addition to the controls on the front display of the program, the program also displays a number of indicators to reassure the user the experiment is running properly. The odor of the current cycle is displayed at the top of the indicators, with a status light indicating if it is being delivered or not. As previously mentioned, the LED indicators on the pushbutton switches also light up when the corresponding odor is being delivered. Another indicator includes the number of the cycle the experiment is currently in along with the elapsed time in the cycle. This indicator resets to zero every cycle change. Finally, the total experiment time is indicated, which only resets to zero when a new experiment begins.

Testing

The preliminary testing of the final prototype that was accomplished showed that the very basic functions of the olfactometer were working to specification. Primarily, we tested the air flow of the olfactometer to verify the air flow followed the correct path of the circuit designed for the olfactometer. This testing was done by testing the air flow from the pump after each of the separate components had been added. The air flow through the olfactometer always followed the correct path as shown in Figure 4. The air flow was also monitored using the flow meter to verify there was not significant fluctuation in the air flow at any time.

In order to verify the LabVIEW program created was working according to specification, several different combinations of odors, cycle durations, and number of cycles were used. These factors were varied, and the program was tested to verify the switches opened at the correct intervals to deliver the correct odor. The olfactometer was also tested to verify no odor was delivered when all of the switches were closed.

The manual switches were also tested on the olfactometer to verify that manually using the switches would open and close the valves correctly. All of the valves opened and closed correctly with the corresponding switch. Also, when the switches are on, the LED on the corresponding switch must be turned on, and when the switch is off, the LED must be turned off. Testing of the switches verified that all of the switches were functioning correctly and the correct odor was delivered with the corresponding switch.

Although preliminary testing provided very good results for the functionality of the olfactometer, much more testing must be accomplished to further quantify the efficiency of the odor delivery. Testing using the fMRI procedure will determine the speed at which the olfactometer can switch between odors. This can be tested by monitoring the activation map during odor delivery. The map will display the location of the brain activity during the time of delivery of an odor, and the activity should switch locations with the delivery of a different odor. The testing using fMRI will test the ability of the olfactometer to switch between odors in less than 1 s.

Testing must also be done to measure the flow and pressure of the air flow through the olfactometer circuit. This testing can be carried out by using a calibrated flow meter to measure the flow, and using a pressure sensor to measure the pressure of the air going through the circuit. This testing will need to be completed after the olfactometer has been set up in the MRI suite at the hospital with the correct length of tubing running into the MRI suite. This testing will verify the air pressure and flow are constant while being delivered to the subject.

Ethical Considerations

This olfactometer will be used to deliver odors to subjects who are participating in research trials. The odors delivered to the subject must be at a safe concentration for the subject so they are not receiving too much odor. The device must be comfortable for the subject to use, while still delivering odors at the correct intervals and allowing the researcher to collect accurate data from the experiment. Also, since this device is being used with an MRI machine, there must not be any nonradiotranslucent material within the designated distance to the MRI machine. If any metal were to come too close to the MRI machine, there is potential for serious injury to the subject, clinician, researcher and MRI machine.

Future Work

Although most of the major design and construction of this olfactometer prototype has been completed, there are tasks that still need to be accomplished. The check valve system will be implemented in order to ensure no odor from other odor canisters enters the pathway of other odors, or the clean air line. This check valve manifold also allows all of the tubes from the odor canisters to be connected into one multiport connector to send a single tube line to the cannula at the subject.

Along with connecting the tubes to a multiport connector, the correct length of tubing will need to be cut to run from the MRI control room, where the olfactometer will sit, to the MRI scanner itself, where the subject is. This line will be connected to a nasal cannula, or a closed mask system to ultimately deliver the odor to the subject.

The program interface created to control the olfactometer was created using LabVIEW. The program that the researchers at the hospital use currently to control their experiments is E-

Prime. The LabVIEW program must be synchronized with the E-Prime software by writing a simple program to initiate the LabVIEW program after starting EPRIME. If the LabVIEW program cannot be synchronized with E-Prime, the program to interface the olfactometer will need to be written using the E-Prime software.

A major component of the future work is to develop a system within the olfactometer that controls the temperature and humidity of the air flowing through the circuit. Several ideas have been suggested for the implementation of temperature and humidity control, but a method must be chosen and designed before being implemented in order to control these factors.

Aesthetically, the device can be made smaller and easier to carry by creating a smaller box for the olfactometer components. The box will need a lid to prevent damage to the olfactometer. The box should be constructed out of a lighter weight material than wood in order to decrease the weight of the olfactometer and make the device more ergonomic.

Product Design Specifications: MRI-Compatible Olfactometer

Team Roles:

Team Leader:	Steve Welch
Communications:	Ryan Kimmel
BWIG:	Kaitlin Brendel
BSAC:	Joe Decker
Last Update:	May 8, 2009

Function: The purpose of this design is to deliver timed amounts of olfaction stimulants to a test subject undergoing an fMRI scan.

Client Requirements: • Must be user friendly • Must have replaceable parts • Must be automated • Must have quick setup time • Must be MRI compatible

Design Requirements: • Constant temperature and humidity • Have up to four odor canisters to 37.5 °C. • Control air pressure to 1 atm. • Easily portable, must weigh less than 15 kg. • Must fit within limited table space. Roughly 1 m × 1 m. • Must have a computer interface. • Must present odor for controllable amount of time in a mask or cannula • Must have ability to control the flow rate • Easy to set up • USB connection
• Compatible with EPRIME
• Must be able to go to the no-odor condition in under one second • Must not retain any residual odors • Must be compatible with the “active sniffing” technique • Must be able to determine when odor reaches subject

1. Physical and Operational Characteristics

a. Performance Requirements: The olfactometer must operate for a desired time sequence. For example, the odor could be sent for 30 s, and then clean air must be sent for 30 s. There will be four complete sets of an odor sent to the cannula and clean air sent to the cannula.

b. Safety: The air pressure must not be strong enough to cause discomfort or dizziness to the patient. Therefore, the pump should not exceed 21 kPa.

c. Accuracy and Reliability: A high degree of repeatability is required. Flow rate must be constant and controllable. The temperature of the liquid odors must be kept at 37.5 °C, and the humidity must be kept under 20%.

d. Life in Service: Parts should be made replaceable, increasing the service life indefinitely. The cannula must be replaced after each test, and parts will be replaced primarily following accidents.

The olfactometer will be used daily for at least 30 min at a time.

e. Shelf Life: The olfactometer should last in storage as long as the shelf life of the commercially available parts used (the valves, pump, flow meter, etc.). A ten-year life span would be desirable.

f. Operating Environment: The olfactometer will be used in an ordinary MRI environment. All of the components that are near the MRI scanner must be compatible so that they do not interfere with the magnet that operates with a magnetic field of 2 T and at a Larmor frequency of 42.57 MHz/T.

g. Ergonomics: The olfactometer should require as little human interaction as possible while still remaining reliable and user friendly. The users should be able to quickly control the desired flow rates and timing, and then proceed with the experiment.

h. Size: The olfactometer must be small enough to fit on a 1 m × 1 m tabletop. It must be easily transportable between buildings.

i. Weight: The liquid controller must be light enough to be carried up and down stairs and between buildings by an average person. Therefore the weight should be less than 15 kg.

j. Materials: Materials must not interfere with the magnet of the MRI scanner. The tubes that follow the odor canisters should be made out of Teflon so they do not retain any odors. The canisters should be made of polyethylene so they could be easily cleaned.

k. Aesthetics, Appearance, and Finish: The olfactometer should be designed with functionality in mind, and aesthetics are of secondary concern.

2. Product Characteristics

a. Quantity: One unit will be needed.

b. Production Cost:

Estimated budget: \$750.00 - \$1250.00

I ITEM COST

Quantity	Item	Price per Item	Total Price
1	Housing tray	\$10.00	\$10.00
Cole-Parmer: http://www.coleparmer.com/			
1	6-way solenoid valves	\$498.00	\$498.00
1	Flow meter (direct read)	\$40.00	\$40.00
3	1/8" (3.75 mm) Teflon tubing	\$27.50	\$82.50
1 (10 per pack)	Tefzel cones	\$23.50	\$23.50
1 (10 per pack)	Polypropylene fittings	\$20.00	\$20.00
1 (10 per pack)	Tee fittings	\$9.25	\$9.25
1 (10 per pack)	Barbed fittings	\$21.25	\$21.25
1	HEPA-VENT capsule	\$55.00	\$55.00
Fisher Scientific: http://www.fishersci.com/			
1 (10 per pack)	Swinnex syringe filters	\$68.00	\$68.00
Measurement Computing: http://www.measurementcomputing.com/			
1	Switch and Sense 8	\$299.00	\$299.00
Radio Shack: http://www.radioshack.com/			
6	LED button switches	\$1.99	\$7.94
1	12 VDC Adapter	\$21.99	\$21.99
1	Printed circuit board	\$3.49	\$3.49
1	Project enclosure	\$5.99	\$5.99
1 (30 per pack)	Nylon wire ties	\$4.49	\$4.49
1	Heat Shrink Tubing	\$3.99	\$3.99
Discount Filter Store: http://www.discountfilterstore.com/			
1	OmniFilter R200	\$9.42	\$9.42
Pet Guys: http://www.petguys.com/			
1	Elite 801 air pump	\$6.49	\$6.49
JRS Medical: http://www.jrsmedical.com/			
4	Nasal cannulas	\$0.84	\$3.37
TOTAL:			\$1197.67

3. Miscellaneous

a. Standards and Specifications: No standards or specifications are required.

b. Customer: The olfactometer will be used by faculty members in the department of radiology and neurology on the UW-Madison campus. The customer prefers E-Prime for easy integration into already existing programs. An air pressure system will drive odors into the cannula.

c. Competition: There are currently no devices on the market that meet all of the client's requirements.

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Behav Res Methods, 2006 May; 38(2): 307–313

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www.mccdaq.com.

University of Oxford fMRI Centre Web Page.

<http://www.fmrib.ox.ac.uk/education/fmri/introduction-to-fmri/what-does-fmri-measure>