Animal Ventilator for Gated Hyperpolarized Helium MRI

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Abstract

The use of hyperpolarized 3-helium as a contrast agent in functional magnetic resonance imaging (fMRI) is an emerging technique for diagnosing diseases or abnormalities in the respiratory tract. Current methodology allows for fMRI scans to be taken during inhalation of helium every fourth breath. A device and/or method is needed to function as an oxygen ventilator and serve as a means to integrate hyperpolarized helium into the respiratory tract of small animals on every breath. This report a design that delivers user defined volumes of gas variable frequencies. Current designs, background, and future work is also discussed.

§1 Problem Statement

Create or redesign a small-animal ventilator capable of delivering constant volumes of hyperpolarized 3-helium and oxygen gas (1-20 mL) at user-specified frequencies (1-100 cycles/min) for safe and compatible use in fMRI.

§2 Intro

Imaging the respiratory tract using traditional MRI methods is very difficult. Our client, Dr. Sean Fain of the Medical Physics Department at the University of Wisconsin – Madison, is using hyperpolarized 3-helium as a contrast agent for fMRI imaging of the respiratory tract. A device is needed to deliver helium and oxygen into a small animal respiratory tract simultaneously, as to allow for imaging of the tract on every breath. This device will help to save our client and other researchers valuable scan time and allow other types of experimental variables to be implemented quickly and easily.

§3 Background

Helium MRI

Medical imaging systems are useful in diagnosis and physiological verification. Helium Magnetic Resonance Imaging is a fairly newer technique. It utilizes the same scanner as the conventional MR Imaging, except instead of tuning the scanner to Hydrogen, it is tuned to Helium (48.6 MHz). Therefore, the scanner receives the signal that is coded specifically from Helium. The Helium is typically inhaled while the MR scanner performs the imaging. The anatomical structures usually imaged with Helium MRI are the respiratory channels and lung systems. During the onset of inhalation, it is possible to see the Helium traveling down the trachea in humans (see Figure 1).

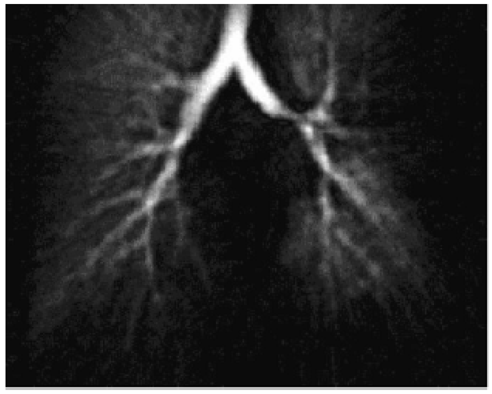


Figure 1. Helium MRI during onset of inhalation. Bright areas indicate regions inhabited by the Helium (1).

The traditional MR scanner receives signal from the hydrogen already in the body. The Helium, however, needs to be hyperpolarized (3-He) in order to be used in this process. The hyperpolarization gives the Helium a heightened spin state. However, oxygen has a paramagnetic effect that destroys the polarization of 3-He. Therefore, great care is taken to avoid mixing the two gases prior to the scanning.

Client Study

If 3-He MRI can accurately detect airways and air spaces, one could postulate that respiratory diseases such as asthma could be diagnosed with the use of this process. Ideally, 3-He MRI will successfully reveal information that will lead to diagnoses of respiratory diseases. Doctors will be better able to assess the patient's condition by viewing accurate images of their airway channels and lungs.

This idea is under study by Dr. Sean Fain from the University of Wisconsin Medical School, department of Medical Physics, and his team of researchers. Using an animal model, respiratory diseases are induced to achieve the anatomical effects of a respiratory disease, such as increased airway resistance. Once this is done, 3-He MRI will be performed to confirm the anatomical altercations experienced by the animal from the induced conditions.

The current model administers three breaths of oxygen to the animal and upon the fourth breath of 3-He, the MRI scan is done. The total scan time is currently around 8 minutes per animal. If there was a way to administer 3-He in every breath so that a scan could be performed every breath, the scan time could decrease by a factor of four. However, as stated previously, mixing 3-He with oxygen causes the Helium to lose its polarization. A study was done to quantify the signal loss from mixing oxygen and 3-He and revealed that the total signal loss was less than 5% from that of using a full breath of only 3-He when mixed immediately prior to inhalation (1).

§4 Current Design

The current method of 3-He delivery utilizes two independent systems; the MRI-1 Ventilator, and a modified linear stage-mover device that propels the helium breaths. The entire unit can be visualized in the block diagram shown in Figure 2.

The entire configuration is run from a single computer. This computer controls the MRI scanner and the ventilator setup so that the images can be collected simultaneously as the helium breath is delivered. The ventilator can be controlled either manually or from the

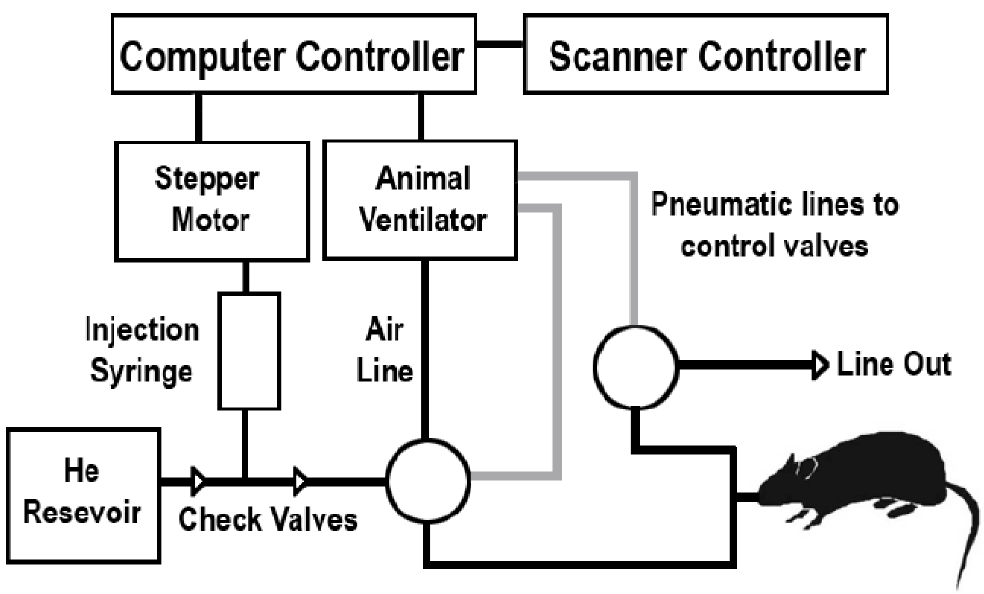


Figure 2. Current setup of gas injection system used by client.

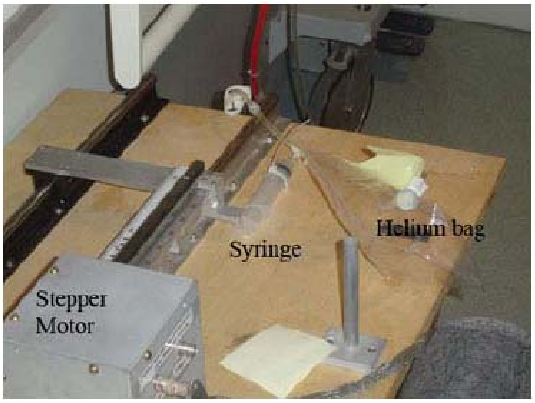


Figure 3. Syringe and 3-He reservoir bag.

computer controller and the stepper motor is controlled by an existing LabView program.

Helium is delivered via the pumping of a 10 mL syringe mounted to a 4'x 2' board. Also on this board is a large stepper motor, controller unit, and linear slide (Figure 3). The stepper motor rotation causes the linear slide to move a specified distance depending on the desired tidal volume to be delivered. The syringe is attached to the linear slide and He gas is delivered to the tubing connected to pneumatic valves that lead to the animal. As the plunger is pulled back into position, gas is moved from a helium holding reservoir, through a one-way check valve, and into the syringe to be stored until the next helium breath needs to be delivered.

The ventilator is used to not only to supply the air to the small animal, but also to serve as a control mechanism for the pneumatic valves (Figure 4). The pneumatic control lines are pressurized at about 40 psi and drawn from the wall outlet. When a breath is to be delivered, the control lines exert a pressure on the pneumatic valves, opening them and (depending on the breath) allow the passive air line or the helium line to enter the tracheal tube for inhalation or allow for passive exhalation from the animal.

Figure 4. Current ventilator with gas lines (red) to run pneumatic valves.

The ventilation system now in place works. However, it is very large and does not allow for helium to be delivered on every breath. It is suggested to change the current setup from the previously described system to one that integrates He and O2 into every breath. The block diagram in Figure 5 shows a suggested redesign of the setup.

In this design, the passive air supply is turned into a driven air source and powered simultaneously with the helium supply. This way, a known ratio of He and O2 can be delivered on every breath. The ventilator is still used, but in this case only to control the pneumatic inhalation/exhalation valves.

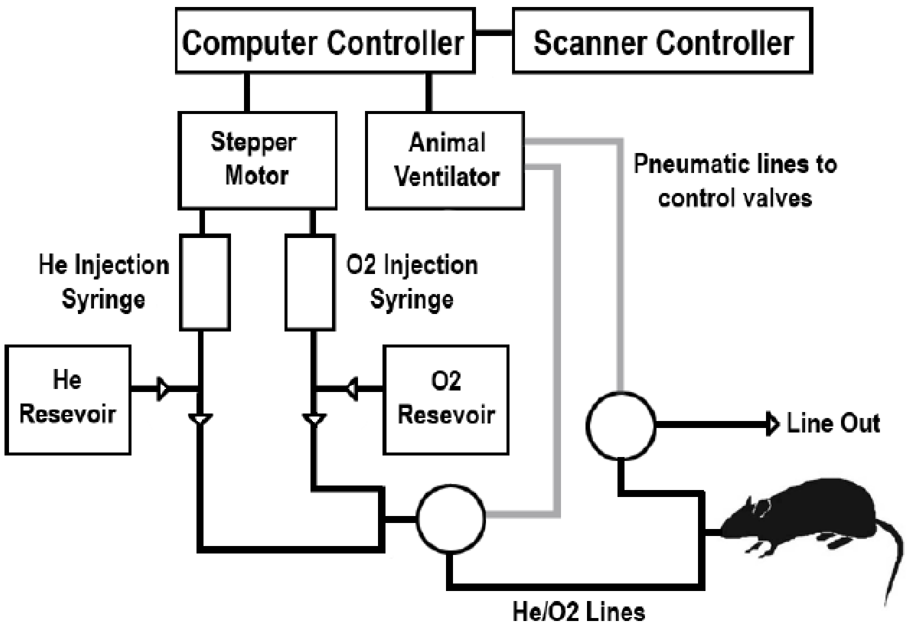


Figure 5. Modified setup desired by client.

§5 Literature Search

A literature search for ventilators capable of functioning in the way the client desires showed that there are few, if any, ventilators that describe a way of administering the desired mixture of gasses. Ventilators similar to USPTO patent 5,107,830 or the setup described in 5,752,506 might be used as a reference, however by themselves, do not describe an appropriate mechanism. Some patents were found that describe similar methods for using helium in ultrasonic applications in 6,375,931 and a method of administering contrast agents in MRI imaging was found in 6,963,769 but nothing combining the two. In the current design, a modified MRI-1 Ventilator manufactured by CWE, Inc. is used in combination with a homemade motor-syringe pump. In the setup currently used, any MRI compatible ventilator could be used. Such units can be found from Magmedix, Inc., Omni-Vent, and Datex-Ohmeda, to name a few.

§6 Final Design

After considering several other approaches to the design of the ventilator, it was concluded to style our design after the method currently in place. This was chosen because not only was it known that the system worked, but the software model was already complete and could be easily altered to fit the new design's requirements.

The current design of the hyperpolarized gas MRI animal ventilator can best be described as a motor-driven syringe pump (Figure 6.). The major components of the unit include; a base, four rods, two rod supports, two sliders, an axel/gear component, and the motor, controls and casings. The hardware allows for the movement and the software will deliver the desired control.

Hardware

The first step in the construction of the device was milling of the high-density polyethylene (HDPE) parts purchased from McMaster-Carr. The base is made of a 12"x 8" x ½" HDPE sheet. The 5/8" diameter aluminum rods are supported by HDPE rod supports with four holes centered ½" and 1" in from the sides. The rods are set in the HDPE supports with a #6 brass peg and plastic epoxy. The rod supports are held on the base with epoxy and brass wood screws.

On the aluminum rods sits a HDPE slider. The slider's length contains two holes, in which the rods slide. One slider is built to accommodate the larger gear and the other to accommodate the smaller gear. This accommodation had to occur in order for the axel to remain horizontal and in contact with both sliders. Grooves in the sliders were made to fit 1/8”, 38 pitch gear racks, cut to fit and mounted with epoxy.

Beneath the slider units are the plunger mounts. These are bent pieces of 1/8” aluminum with a tapped hole drilled in the side. In the hole, a brass thumbscrew is used to pinch the plunger and bind the plunger of the syringe to the sliders. Each syringe is mounted to the base with a zinc-coated U-clamp. The clamp is made to fit ½” tubing, and fasten the syringes in place on the base with nuts from beneath the base.

The axel is currently made of stainless steel (which is hoped to be eventually replaced with aluminum). The ½” rod was lathed down to ¼” to accommodate the inner diameter of the large gear. At one end, a ¼” hole with set screws was made to attach onto the stepper motor shaft. On the other end, a hole was made to so that a threaded brass screw could fit in, on which the smaller gear is mounted. Finally, another piece of ¼” steel rod was screwed to sandwich the small gear into place. A HDPE upright ensures the gears have contact with the sliders at all times.

Once the base unit was set up, the motor and other electrical parts were assembled. Electrical components of the device are all enclosed in a 6” x 6” x 4” aluminum enclosure to prevent interference of the MR images. Cords running to and from the device will also need to be enclosed in metal shielding; however, the actual material has not been selected.

All drawings and dimensions can be found as 2D line drawings in Appendices B-F.

Software

The motion is controlled by a stepper motor system comprised of three components: a stepper motor, a controller/driver board, and a computer. This system provides a user interface through the computer to control the properties and motion of the stepper motor. This setup allows both manual and automatic control of the motors speed, acceleration, timing and position.

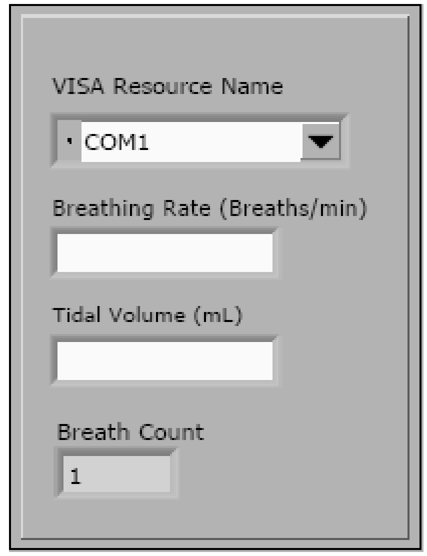


Figure 7. Custom LabView Virtual Instrument

The stepper motor is a standard NEMA size 17 motor controlled by a DCB-241 controller/driver board. The motor shares a 24V 1.2A unregulated DC power supply with the controller. The controller receives ASCII commands via serial communication with a computer, and the driver delivers corresponding pulses to the motor to produce the desired movement.

Our setup uses a computer interface to provide commands to the controller in real time. The computer interface consists of a LabVIEW VI (Figure 7.) that allows the user to select the syringe size, and enter breathing rate and tidal volume of the subject. An algorithm converts the desired tidal volume into a linear distance for the syringe plunger, which is directly related to the number of steps per motor cycle (breath). The motor moves at a constant speed of 1000 steps/second, so the number of steps per breath determines the time it takes to deliver each breath. The appropriate breathing rate is then achieved by inserting a delay between breaths (if necessary). The program returns an error if the indicated breathing rate exceeds the maximum for the indicated tidal volume. The block diagram for the LabView program is included in Appendix G.

§7 Future Work

Our future work will consist of two major stages. First, we will need to test the prototype. This testing will include testing to see if the device is able to deliver the desired oxygen to helium ratio as defined earlier in the paper. Also, we will test our LabVIEW program to verify that we will be able to deliver variable tidal volumes, depending on the different rats that will be used in the study. Since the respiration of the rat will be completely dependent upon our device, the stepper motor must be able to inspire and expire at a very high rate.

One of our concerns is that the stepper motor we are currently using may not have enough torque to operate at the speed needed. After testing the device, a new stepper motor may be implemented in order to meet the speed requirements. Another of our concerns is 3-He and O_2 mixing within the dead space. This poses a potential problem for two reasons. First, if the two gasses mix significantly, or for a long period of time, we may lose the polarity of the ^3He, rendering it useless as a contrast agent. Second, significant mixing will destroy our desired 80% 3-He, 20% O_2 ratio, leading to asphyxiation of the subject, or low-contrast images. To test for gas mixing, we plan to image the delivery tubes of the final design while it is running. This should allow us to see any mixing as a loss of contrast in the image. A similar experiment could be performed with colored gas or smoke, but may be more difficult to see.

Once we have confirmed that our device is able to deliver the correct oxygen to helium ratio deliver variable tidal volumes within the allotted time for each breath, scans will be performed on the test rats using our proposed set up. The images obtained while using our device will be compared to previous images that were taken without our device. This side-by-side comparison will allow us to see if image quality improved between the two setups. Furthermore, we will be able to see whether or not taking a scan every breath is more beneficial to the study as compared to one scan every four breaths.

§8 References

1. Hedlund, LW; Moller, HE; Chen XJ; Chawla, MS; Cofer GP; Johnson, GA. *Mixing oxygen with hyperpolarized He for small-animal lung studies*. NMR Biomed. 2000 Jun;13(4):202-6. PMID: 10867697 [PubMed - indexed for MEDLINE

2. *USPTO Patent Search.* 1 Sept 2005. United States Patent and Trademark Office. 1 March 2006. < http://www.uspto.gov/patft/index.html>

Appendix A. Product Design Specifications

Project Design Specification

February 17, 2006

Team Members: Matt Smith, Micah Brown, Chris Wegener, Ashley Anderson

Function:

The function of our device is to deliver a set ratio of a helium/oxygen mix in order to image the airways and lungs of an anesthetized rat within an MRI machine. Currently, the scanning time is longer since the helium contrast agent can only be administered once every four breaths. By incorporating the oxygen into each breath, our client will be able to image every breath and therefore reduce the scan time by a factor of four.

Client Requirements:

- *Must be compatible with MRI scanners. However, since the injection system will be outside the magnet bore, ferromagnetic materials are permissible as long as they are away from the magnetic field.*
- *Oxygen/Helium must be at a ratio of 20%:80%*
- *Title volume of breaths must be variable and controlled by computer*
- *Must minimize the time the oxygen and helium are mixed to reduce the amount of helium depolarization.*

Design Requirements:

1. Physical and Operational Characteristics

a. Performance Requirements- The device must be able to inject a set title volume of 0%:80% oxygen/helium mix into an anesthetized rat every breath.

b. Safety- The device's ferromagnetic components must be outside the magnetic field created by the MR scanner in order to reduce the danger of attraction and presence of artifacts in the scans. Also, the device may not cause any harm to the animals being tested.

c. Accuracy and Reliability- Device must be able to deliver set title amount and set oxygen/helium ratio every breath continuously for the entire scan time (average scan time is 3 minutes)

d. Shelf Life- The device must last up to 5 years, for the entire duration of the client's study.

e. Operating Environment- Must be operated outside the magnetic field of 1.5T produced by the MR scanner. Must be able to withstand daily cleaning with industrial strength disinfectants for sterilization purposes.

f. Ergonomics- The device should be easily transported, set-up, and torn down to reduce the total scan time on the animal.

g. Size and Shape- The device will be incorporated into a 1' cubic box. This will reduce the weight of the device, as well as make setting up the device very easy.

h. Weight- No more than 20 lbs. in order to make the device easily transported.

i. Materials- Ferromagnetic materials are allowed to be used in this design, as the device will be outside of the magnetic field. Aluminum and other light metals will be used to reduce the weight of the device.

j. Aesthetics – It doesn't have to look pretty, function is more important.

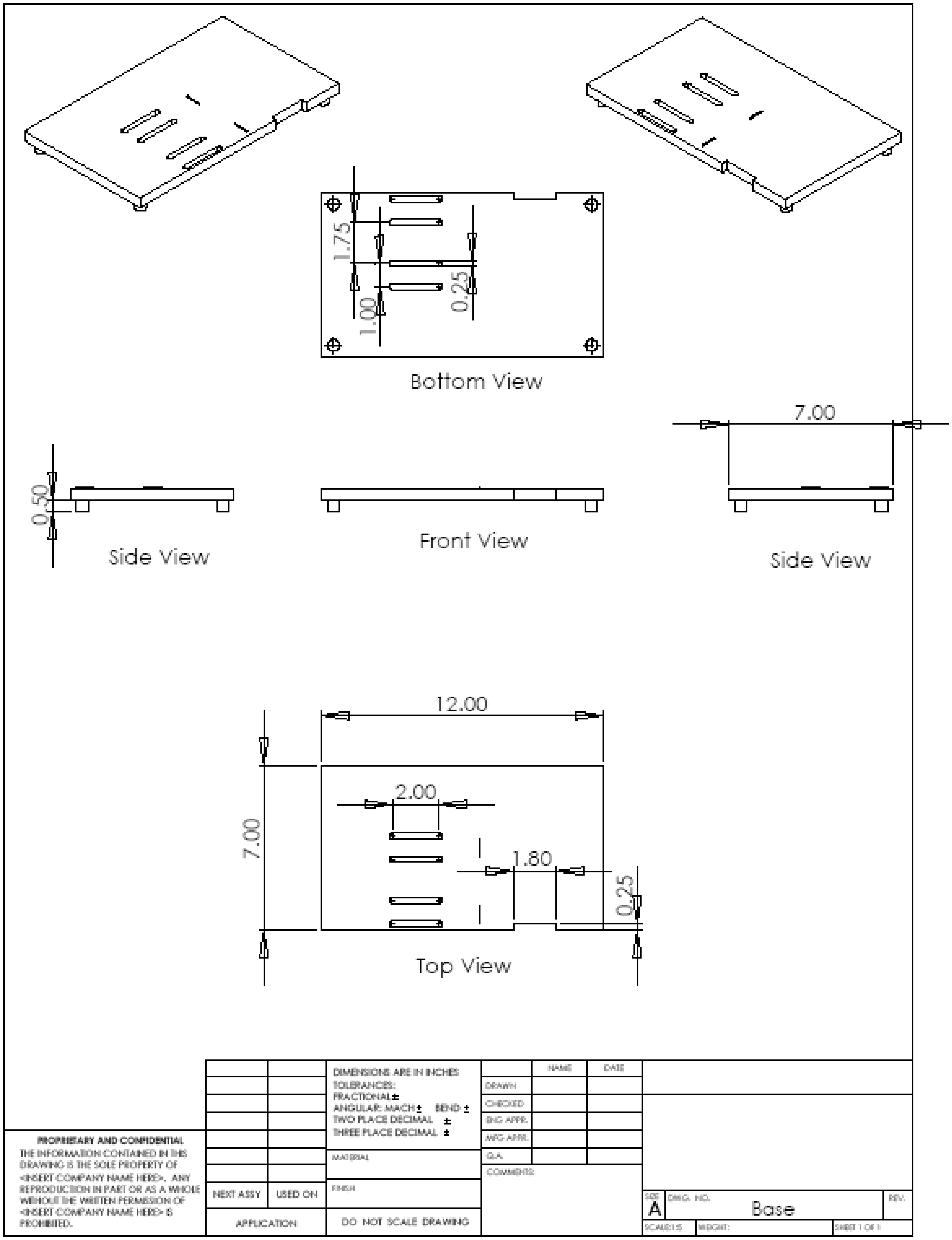
2. Product Characteristics:

a. Quantity – Only one device is needed.
b. Target Product Cost- The device should stay within the client budget of $1,000.

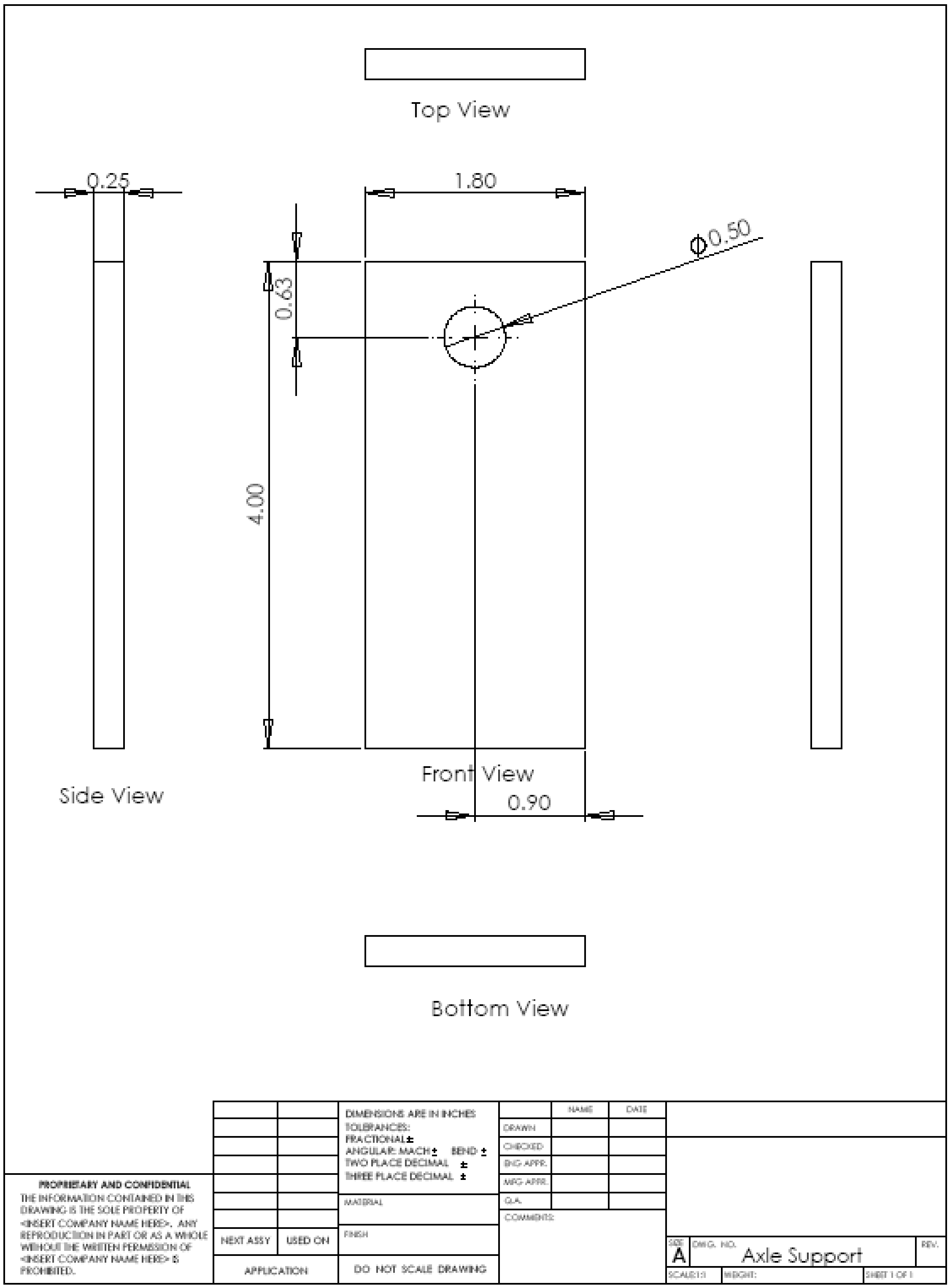
3. Miscellaneous:

a. Standards and Specifications- The device should comply to the guidelines setup up by the FDA for medical instruments. Further information is available online at the FDA's website, but it's too extensive to specifically list. The device is subject to performance and safety standards without exemption, for its classification.
b. Patient-related concerns- The patient in this case is an anesthetized rat. The device must not harm the animal in any way.
c. Competition-No known devices exist for the injection of a helium contrast agent to be used for the imaging of a rat's airways and lungs.

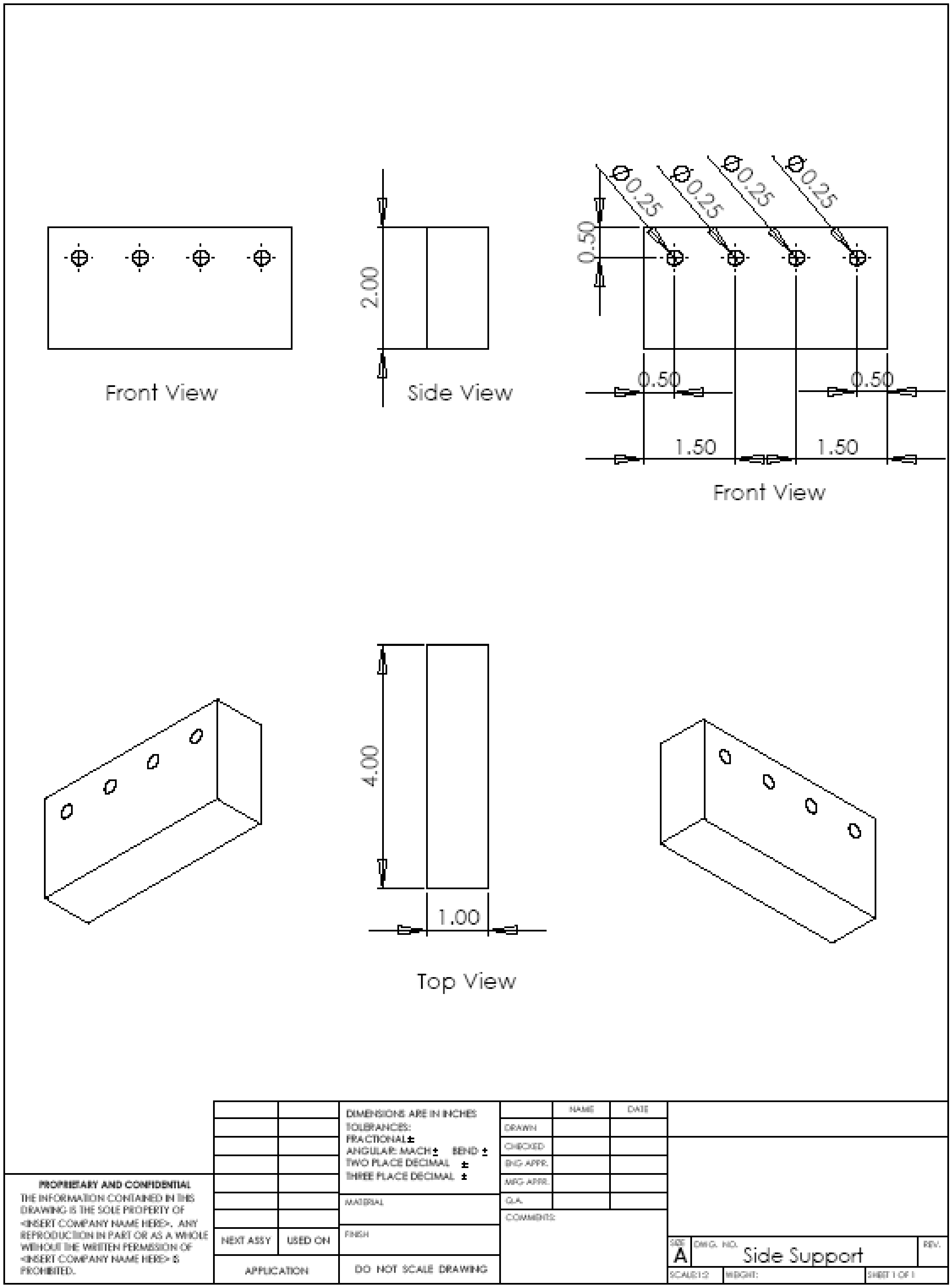
Appendix B. Base



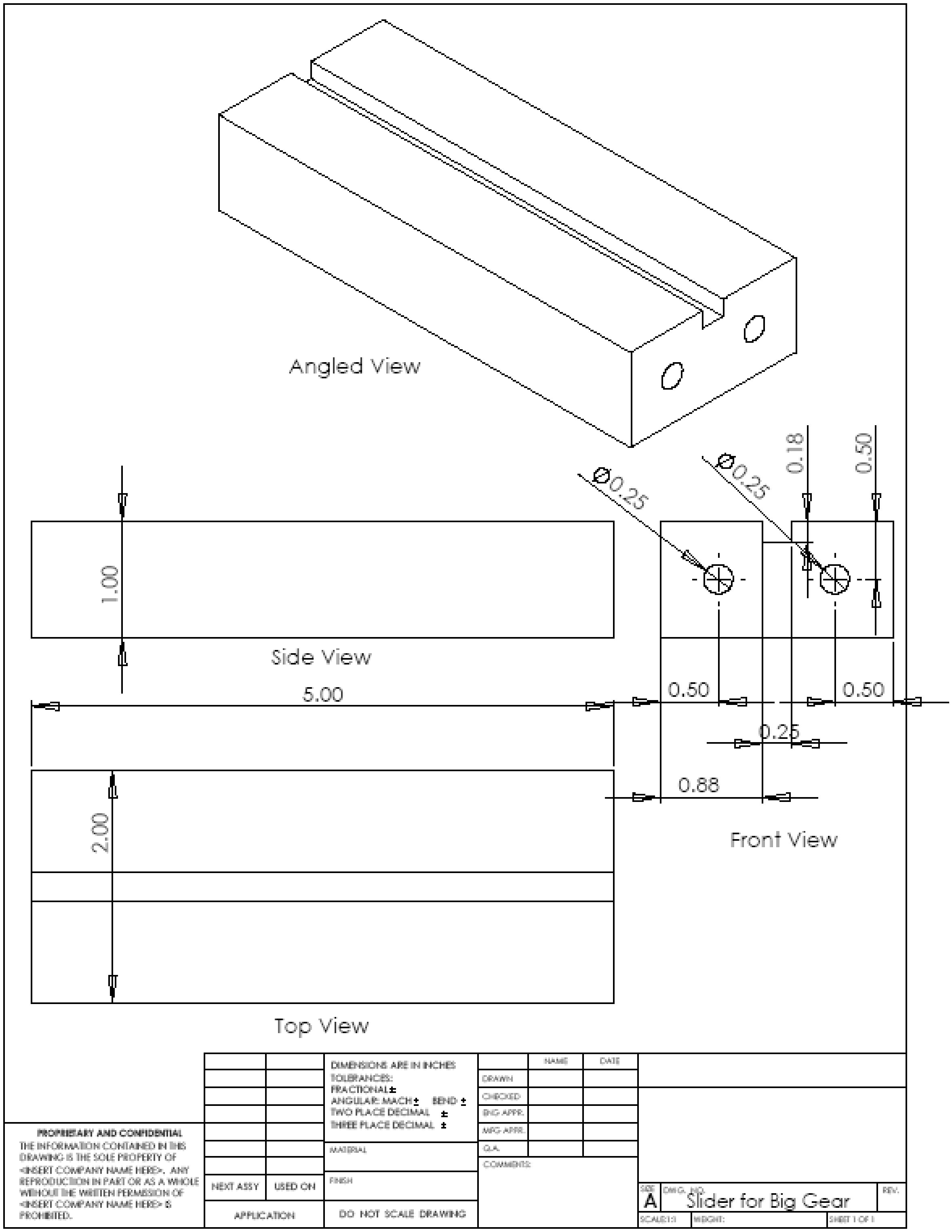
Appendix C. Axle Support



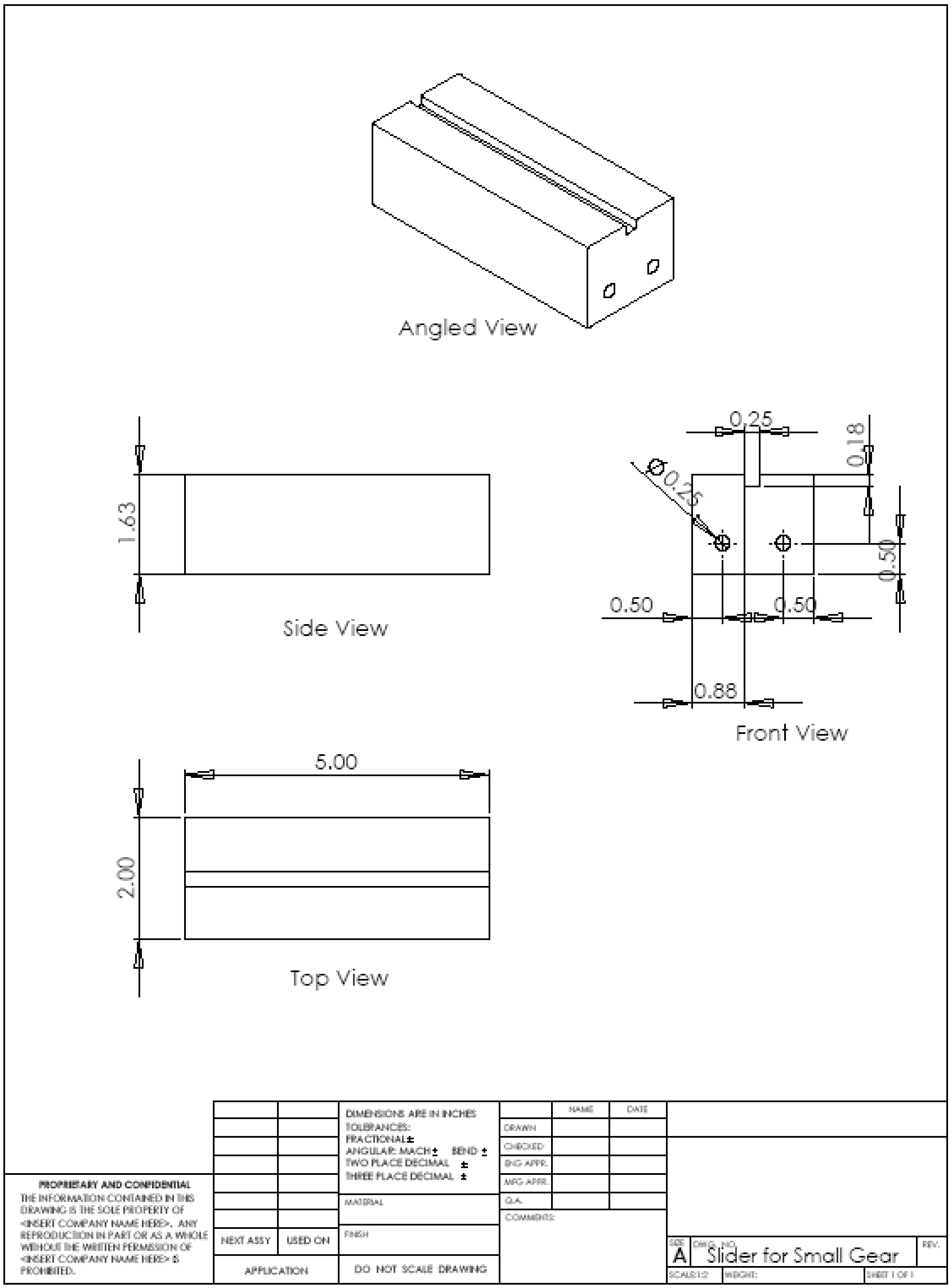
Appendix D. Slide Support



Appendix E. Slider 1



Appendix F. Slider 2



Appendix G. LabView Block Diagram