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UNIVERSITY OF **WISCONSIN-MADISON**

DEPARTMENT OF BIOMEDICAL ENGINEERING

A Thermoelectric Device for Brain Cooling in Mice

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Background

The function of sleep remains one of the greatest unsolved mysteries in modern science. A multitude of theories have been proposed regarding the necessity of sleep, but none have been substantively established.

Sleep is known to be an essential process of life, taking up almost 1/3 of the average human's lifetime. Furthermore, it is such a necessity that deprivation has been known to cause health problems in rats, leading up to death (Everson 1995). Additionally, the effects of sleep have been studied on a variety of life factors. Retaining homeostasis is a commonly accepted view, since studies have shown that lack of sleep hampers healthy metabolic activity and immune system response (Zager 2007). Furthermore, sleep has been linked to proper memory function—lack of sleep has been shown to correlate with cognitive impairment, decreasing by as much as 38% in comparison to a control (Turner 2007). However, these functions all provide effects of sleep; they do not examine the purpose of it.

A hypothesis has been proposed by Dr. Giulio Tononi that sleep is used for synaptic downsizing. Specifically, he states that “The synaptic homeostasis hypothesis claims that plastic processes during wakefulness result in a net increase in synaptic strength in many brain circuits; during sleep, synaptic strength is globally downscaled to a baseline level that is energetically sustainable and beneficial for memory and performance” (Tononi 2005). The client has started an experiment to test this hypothesis, using 2-photon microscopy to image synaptic activity in the brain in awake and sleeping mice. The client has proposed an additional experiment based upon the neural activity hypothesis.

The rationale behind the second experiment lies in the logic assumed by an increase in synaptic strength. If the hypothesis is correct, then wakefulness with a decreased level of synaptic activity will produce a longer time between sleep/wake cycles. Additionally, it has been shown that cooling of brain tissue will reduce synaptic activity (Benita & Conde 1972 ,Waleszczyk 2005). With this line of reasoning, the client wishes to selectively cool a region of the brain that is responsible for modulating the sleep/wake cycle. By doing so, he believes that he will be able to silence the synaptic activity, affecting the sleep cycle.

In order to carry out this new experiment, the client would like a device capable of cooling a 3mm hemispherical region of a mouse's brain. The device must be able to cool the tissue enough to silence neural activity, but not so much that tissue damage occurs. Furthermore, the device needs to allow the acquisition of an accurate EEG signal in order to confirm that synaptic activity has been suppressed.

Client Requirements

At the beginning of the semester, our client, Dr. Ugo Faraguna, provided a specific set of requirements essential to the function of the system during experimentation. Most importantly, we must cool a region in the brain to approximately 20°C. This region is defined as a hemispherical portion of brain matter with a diameter of 3mm. As the device reaches the desired cooling temperature, it must minimize harm to the brain cells. The client believes it is impossible to completely avoid killing a few brain cells, but there still should be a temperature that will avoid extensive damage to the

tissue. The device should be able to cool down the area efficiently—meaning it should only take about 30 to 60 minutes to reach the ideal temperature. After the device has cooled the brain volume to the desired temperature, the client will run various tests. As such, the temperature should be held constant during these tests ($\pm 0.5^{\circ}\text{C}$) and should be sustained for three to six hours. As mentioned previously, it is important that the device does not cause any interference to the EEG signal. If the device does produce interference, it would defeat the purpose of the client's experiment which is predicated on the suppression of EEG signals. Additional criteria are the mobility and ease of use of the device. Ideally, the device should be able to fit on a cart so it may be taken from room to room if needed in more than one experiment. It should also be easy to use, so that the temperature can be controlled by the client in order to successfully carry out the desired experiments.

Project Aims

The main goal of the device is to cool down a 3mm hemispheric region in a mouse's brain. The area should be cooled to approximately 20°C , which is the first priority of the device. The second priority of the device is to make sure the device does not interfere with obtaining an EEG signal. This is critical because if there is noise in the EEG signal, it will appear as if there is activity in the brain. The third priority involves temperature measurement. Once the previous two aims are complete, a temperature display should be placed at the site of the cooling to allow the client to obtain the tissue temperature. Realistically, the first two aims should be accomplished this semester.

Similar Devices

Similar devices have been built in multiple research labs. The most similar apparatus was constructed at Yamaguchi University School of Medicine in Ube, Japan. The reason for the construction was quite different than in the case of our project, and focused on creating a device to treat patients with epilepsy. They hypothesized they could decrease the effects of seizures by cooling the brain with a Peltier chip. A Peltier cell is a circuit component that transfers heat in electron flow (a more detailed explanation can be found in the *Design Alternatives* section). This hypothesis was tested on the brains of rats. In this experiment, the Peltier cell was used to cool the brain tissue to between 14°C and 23°C. According to the article (Imoto 2006), the researchers were satisfied with the Peltier device's performance to provide cooling. A very important component in their construction was a heat sink because the hot side of the Peltier device reached temperatures over 60°C and was not able to function for a period of time due to damage to the component. A schematic of the device is shown below:

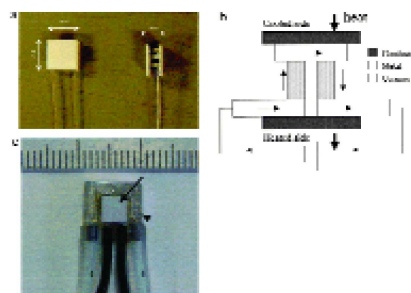


Figure 1 (Imoto 2006): Photograph of the thermoelectric device (Peltier chip). b: Diagram demonstrating the Peltier chip. Two conductors are connected in parallel. When the electrical current is passed between them, heat is transferred from one side, which then cools, to the other, which then heats (*bold arrows*). *Arrows* depict the flow of electrons c: Photograph of the newly devised cooling system. *Arrow* depicts the Peltier chip; *arrowhead* indicates the heat sink made of aluminum containing a fluid channel (*asterisk*).

Product Uniqueness

Our product will strive to create a more efficient cooling device by trying to obtain a more consistent temperature gradient. We plan on making it removable from the animal as well, so the same Peltier cell and heatsink combination can be used in multiple animals. We will also use the vortex tube with compressed nitrogen to provide airflow through the heatsink. In essence, however, the device is accomplishing the same task mentioned above.

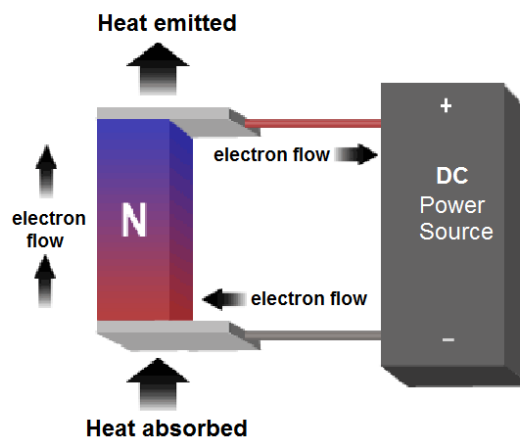
Design Alternatives

Peltier Cell

A Peltier cell is a circuit component that transfers heat in the direction of electron flow, as in Figure 2. The cell itself consists of two plates and a solid-state semiconducting compound between the plates that allows heat transfer against the thermal gradient—creating a “cold” side and a “hot” side. The energy transfer in this manner is changed by current—higher currents create a greater heat transfer. The “hot” side of the cell can overheat and cause damage to the circuit, however, so in order for the cell to properly function continuously, the heat needs to be dissipated in another fashion.

The Peltier cell has been used by the client before, without a heat sink on the hot side. The client said that the cell worked marvelously for a short while, until damage to the component occurred due to excessive heat concentration. This design, however, is advantageous due to its accuracy, adjustability, biocompatibility, and size. Accurate temperature measurements are obtainable by calculation based upon the cell's

specifications and the voltage that is passed through. Changing the temperature is likewise simple—current changes across the cell will produce a temperature change. Furthermore, it is highly biocompatible, since it makes no noise, and it can provide a cooling surface smaller than 3mm (including heatsink), making it the ideal size for this application.



Adapted from: http://www.marlow.com/TechnicalInfo/images/faq_fig1.gif

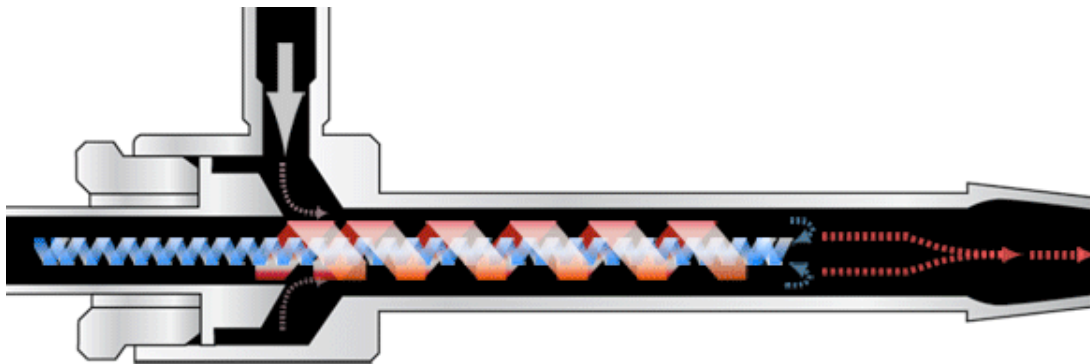
Figure 2. Diagram of Peltier Cell.

Vortex Tube

In this method, air is forced through a tube where it is rotated at nearly 1,000,000 rpm to separate air particles based on their kinetic energy. In this way, hotter air particles are forced toward the outside and cooler air particles are displaced to the inside of the tube. Once the particles reach the right side of the tube as seen in Figure 3, only the hot air is allowed to escape. The cold air is then further compressed within this outer warm air cycle, before being released through the left side of the tube in Figure 3. This results in even greater cooling based on the ideal gas law, since the air expands in volume upon

exit. This process can produce temperature differentials of up to 150°C: cold air at -40°C and hot air at 110°C.

The benefits of this method include its accuracy, adjustability, and its complete mechanical operation. The vortex tube requires no electrical components or movement of dense fluids, making it the most compatible with EEG measurements. Also, the device can be easily adjusted to emit the correct temperature air simply by changing the input pressure. However, the device can have loud airflow, which could prevent the mouse from being able to sleep.



Source: http://www.process-controls.com/techsales/Nex_Flow/vortex_tube.htm

Figure 3. The inner workings of a vortex tube during operation. The red lines represent warm air and the blue lines represent cold air.

Liquid Cooling

In this method, liquid is cooled to the correct temperature and moved through a heat exchanger over the mouse's brain. In the heat block, the liquid absorbs heat from the mouse, and the warmed liquid is then moved through another heat exchanger where it is cooled by forced convection. This cooled liquid is then cycled back through the heat block. This process would continue until the brain has reached the desired temperature.

One of the major benefits of this method would be its relatively low cost and simple construction. It is also relatively efficient at removing heat and easy to operate. However, some liquid coolants are highly toxic if absorbed into the body and it can be difficult to adjust the temperature of the liquid to an accurate value and hold it for up to 6 hours.

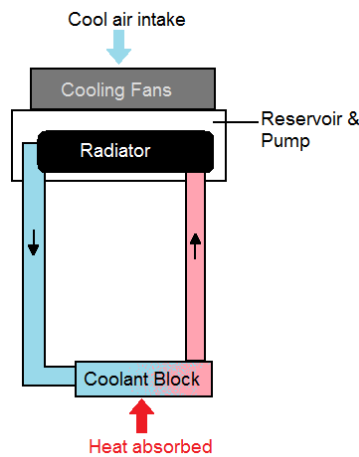


Figure 4. Liquid cooling method diagram.

Phase-Change Cooling

Similar to the liquid cooling method, phase-change cooling instead involves the conversion of a gas to a liquid instead of just using a liquid. Compressing a gas and moving it through a heat exchanger to remove heat energy creates this liquid. After this heat is removed the compound is depressurized, which causes sufficient decrease in temperature for condensation. The liquid is then cycled as described in the liquid cooling method to cool the mouse's brain tissue.

The major benefit of this method over the liquid cooling method is the ability to reach much lower temperatures, potentially even below -50°C . However, low temperatures such as this would create a greater temperature gradient between the heat

block and brain tissue, possible leading to damage of the upper layer of tissue and cell death.

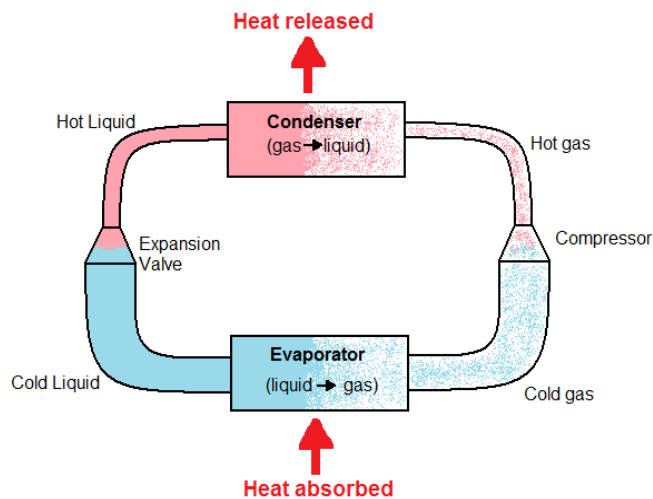


Figure 5. Phase-change cooling method.

Design Matrix

From the previous four design alternatives, the following design matrix was developed (Figure 6). The categories accounted for include accuracy of the cooling method; compatibility with EEG signals; compatibility with the mouse; size of the area that could be cooled; the temperature gradient between the device and the brain tissue; the adjustability of temperature; ease of operation; cost; durability; and efficiency. Cooling accuracy, EEG compatibility, and mouse compatibility were determined to have the greatest importance in design of the device. After evaluation, it was determined that the Peltier cell would be ideal followed by the vortex tube, liquid cooling, and phase-change cooling.

	Weight	Peltier Cell	Vortex Tube	Liquid Cooling	Phase-Change Cooling
Cooling Accuracy	15	13	10	7	7
EEG Compatibility	15	7	13	10	10
Mouse Compatibility	15	13	7	10	10
Cooling Area	10	9	7	5	5
Temperature Gradient	10	9	8	7	3
Temperature Adjustment	10	9	7	3	3
Ease of Operation	10	9	5	7	7
Cost	5	4	3	5	3
Durability	5	3	5	4	4
Efficiency	5	4	3	4	5
TOTAL	100	80	68	62	57

Figure 6: Design Matrix

Thermodynamics

Because the project has a large amount to do with heating and cooling, it is imperative to discuss thermodynamics. In order to understand how much energy is needed to cool the desired area in the brain, Newton's law of cooling must be used.

Newton's law of cooling is the following:

$$Q = mC_p\Delta T$$

Where Q is heat, m is mass, C_p is the specific heat capacity of the substance, and ΔT is the change in temperature. In order to find the energy needed to cool the 3mm space in the brain, the parameter values are necessary. The ambient internal body temperature of a mouse is 39°C (Imoto 2006). As previously stated, the goal of the project is to cool the hemisphere in the brain by approximately 20°C. Therefore, ΔT is the ambient body temperature of the mouse minus the intended temperature, which in this case is:

$$\Delta T = T_1 - T_2 = 39^\circ\text{C} - 20^\circ\text{C} = 19^\circ\text{C}$$

The mass was calculated via density. The volume of the target region is a hemisphere and was thus calculated using a 2 to 3 mm diameter. The density of brain tissue is 1.071 g/cm³. These measurements were used in the following equation to find the mass of the area being cooled.

$$\text{mass} = \text{volume} \times \text{density} = \frac{1}{2} \left(\frac{4}{3} \pi r^3 \right) \times \rho = \frac{1}{2} \left(\frac{4}{3} \pi (.15)^3 \right) \times (1.071)$$

Using these measurements the mass of the area to be cooled is 7.57 mg.

The specific heat of tissue is 3.6 J•g⁻¹•m⁻¹ (Elwassif 2006), so the energy to liberate is:

$$Q = (0.00757)(3.6)(19) = 0.518 \text{ J}$$

Using the parameters previously discussed with Newton's law of cooling, it was found that 0.518 J need to be liberated to cool the area of the brain to 20°C. These calculations, however, assume that the system involved is static. A dynamic system was also modeled to determine some of the thermodynamic properties involved.

The specific values used for the dynamic test are shown in the table below.

Healthy blood flow to brain	54ml per kg brain tissue per min (McCaffery)
Average mouse brain weight	2.0g (Chudler)
Healthy blood flow to mouse brain	$[54]/[1000]*2 = 108 \mu\text{L} / \text{min}$
Density of blood	1.05g/ml (Kenner 1977)
Total mass transfer of blood	$(0.108)(1.05) = 0.1134 \text{ g} / \text{min}$

Figure 7. Table showing calculations to determine mass transfer of blood.

Thus, we can use the equation for dynamic heat transfer, with the calculated mass transfer to determine the energy needed to be liberated per unit time.

$$dQ/dt = (dm/dt) c_p \Delta T$$

$$dQ/dt = (0.1134)(3.6)(39-20)$$

$$dQ/dt = 7.756 \text{ J/min}$$

The geometry necessary to determine the temperature of the Peltier cell needed to reach the desired internal temperature based on a real array of blood vessels is rather complex. Therefore, to determine temperature required to reach desired temperature, we will assume a model based on a single blood vessel flowing between the brain tissues as seen below.

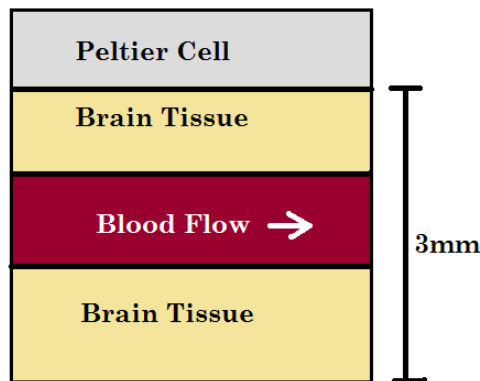


Figure 8. Diagram showing the model setup for a dynamic system.

Thus, to determine the temperature of the Peltier cell necessary to reach the desired temperature at a depth of 3mm we get:

$$dQ/dt = U * A * (T_{hot} - T_{cold})$$

From here, it is necessary to determine a proper heat transfer coefficient.

$$1/ U_{overall} = 1/U_1 + 1/U_2 + 1/U_3 + 1/U_4$$

Where U_1 is the heat transfer resistance in inner blood vessel, U_2 is the heat transfer resistance in blood vessel, U_3 is the heat transfer resistance in surrounding tissue, and U_4 is the heat transfer resistance in Peltier cell interface. Substituting these values into the original equation, we get:

$$1/U_{overall} = \{1/h_i (D_o/D_i) + x_{bv}/k_{bv}(D_o/D_{Li}) + x_{bt}/k_{bt}(D_o/D_{Li}) + 1/h_o\}^{-1}$$

Where D_o is the outer diameter, D_i is the inner diameter, D_L is the Log mean diameter (defined as $[D_o - D_i] / \ln(D_o/D_i)$), X_{bv} is the thickness of the blood vessel, K_{bv} is the thermal conductivity of blood vessel, X_{bt} is the thickness of brain tissue, K_{bv} is the thermal conductivity of blood vessel, H_i is the heat transfer coefficient at the inner surface, and H_o is the heat transfer coefficient at the Peltier cell. These values would normally have to be determined through experimentation. Assuming that the heat transfer coefficient for the tissue is approximately that of water, $U = 5000 \text{ W} / \text{m}^2 / \text{K}$.

Therefore, we can substitute into the original equation:

$$\begin{aligned} dQ/dt &= U \cdot A \cdot (T_{desired} - T_{cold}) \\ 7.756 \text{ (1/60sec)} &= 5000 \text{ (0.004)} \text{ (0.004)} (20 - T_{cold}) \\ T_{cold} &= 18.4^\circ \text{C} \end{aligned}$$

Therefore, the cold side of the Peltier cell must be able to reach 18.4°C to reach the desired temperature of 20°C accounting for blood flow (Thomas 2009).

Ergonomics

The main ergonomic considerations for our design on the technical side were that the device needs to fit onto a cart and be able to be moved from lab to lab inside of our client's building. Due to this we needed to consider what was available in all lab rooms, as well as the size and weight of our design. From this, we were able to determine that if we used a vortex tube, we had to consider the availability of compressed air in each room of the lab. Our client suggested using either a nitrogen or carbon dioxide canister to fuel the vortex tube, which are readily available throughout the building.

Another ergonomic factor in the design was the interaction with the actual mouse. The sound of the device needed to be considered since the mouse needs to sleep during monitoring of the brain activity. We have not yet been able to formally test the sound level of any of our devices so far, but initial informal tests have indicated that the vortex tube is rather noisy. Another constraint was the weight of the device. Part of the apparatus will be attached to the mouse's brain tissue using dental cement, and therefore it needs to be light weight so it will not hinder the mouse or cause discomfort.

The ergonomics of the design of our device needed to be considered right from the start of the project. These constraints were not explicitly given by the client, but we needed to formulate and consider them throughout the design process.

Final Design

The final prototype used a vortex tube and Peltier cell in conjunction. Although these two devices act as one whole machine, their functions within the final prototype are very different.

The vortex tube was used strictly as a heat sink for the Peltier device. A picture of the heat sink setup is shown in Figure 9.



Figure 9. Vortex tube. The vortex tube was used as the heat sink to keep the Peltier cell from overheating.

The device works by streaming compressed nitrogen to the vortex tube via ¼ in. polyethylene tubing at 20-30 psi to get the correct amount of cooling from the vortex tube. The cold air output of the vortex tube was about 20°C, following the mechanism discussed previously. The cooled nitrogen travels via ¼ in tubing from the vortex tube output into an aluminum pipe. The aluminum pipe was glued onto the Peltier cell using thermal adhesive, allowing for maximum heat transfer. This aluminum pipe, Figure 10, was used because of aluminum's superior thermal properties.



Figure 10. Aluminum tube. The aluminum tube used nitrogen cooled from the vortex tube to cool down and in turn, take heat away from the Peltier cell.

The cooled aluminum tube removes the heat from the Peltier cell allowing the cell to function for extended periods of time. As the cooled nitrogen leaves the other side of the aluminum tube, it travels through another ¼ tubing line so the escaping nitrogen does not interfere with the EEG signal or cause noise near the animal. The heat sink was critical in maintain the Peltier cell's function, but the Peltier cell is the device that accomplishes the actual cooling of the brain.

The Peltier cell was the most important part of the final design (a diagram and explanation of the Peltier cell's function can be found in the *Design Alternatives* section). After attaching the heat sink, the Peltier cell was connected to a voltage source. The voltage source was set at 0.9 V and cooled down to 12°C. The Peltier device reached this

temperature in approximately five minutes. The voltage was then set to 0.6 V to sustain this voltage indefinitely. It is important to note that during this time the heat sink was turned on to keep the Peltier cell from overheating.

The complicated element of the Peltier cell was creating the interface between the brain and the cell so that the Peltier cell was removable after surgery. To do this, a connection device was glued to the bottom of the Peltier cell using thermal adhesive. This device will act as a clamp of sorts that specifically clips into a diamond tipped drill bit that will be cemented into the mouse's head brain. This allows the user to cement only a needle into the brain. The Peltier cell is then easily removed, allowing the same device to be used on multiple mice. Unfortunately, this device was not able to be tested before this report was finished, but will be tested in the next week. Rough proof-of-concept tests were run, and the team believes this idea will be sufficient for the heat transfer necessary.

The final device showing both the heat sink and the Peltier cell are shown in Figure 11. The device will be implemented in a mouse's head similar to how it appears in Figure 12.

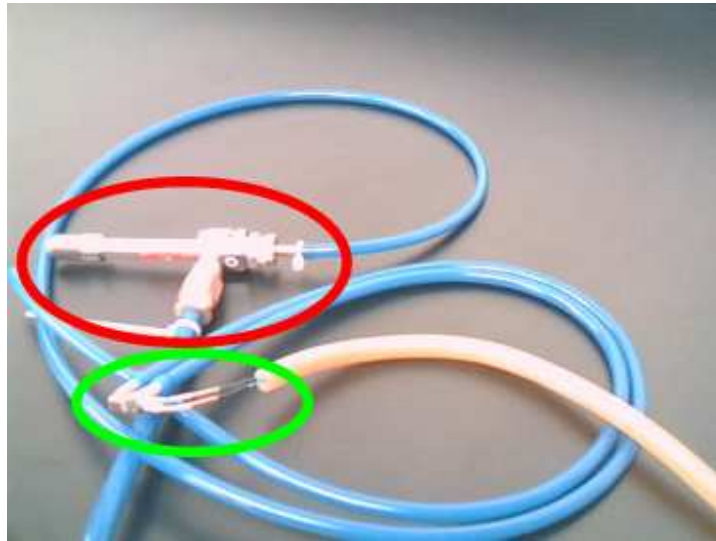


Figure 11. The final device. Circled in red is the vortex tube. Circled in green is the Peltier cell and aluminum rod used as the heat sink device.

s



Figure 12: Example of implant in mouse. Although this is a mock up using agar, the setup in the mouse itself will be very similar if not identical.

Testing

Final prototype testing was conducted to determine several aspects of the device, such as the voltage/temperature relationship, the effectiveness of the device with different tissue interfaces, and the thermal gradient generated by the device. In order to test the

varying aspects of the device, an apparatus was developed using agarose gel, which approximates the thermal conductivity of tissue. This gel was placed in a hot water bath to simulate the dynamic system of a living mouse, which would be able to re-heat a cooled part of the body.



Figure 13. Picture of the testing setup. The agarose is in the blue container in a hot water bath. The water bath has its temperature monitored by a thermometer; thermocouples were used to monitor the temperature of the agarose.

Test 1: Voltage/Temperature Relationship

The Peltier Cell is designed to take a variety of voltages and amperages, ranging up to 2.0V and 1.6A. In order to determine the output temperature of the Peltier cell, various voltages were used as inputs to determine the relationship with temperature. The temperature data was collected by thermocouples placed on the cold surface of the Peltier cell, in contact with the air. This test was run three times, starting from 0.0V and

increasing progressively to 1.6V, then decreasing back to 0.0V. The values were then averaged and plotted as shown below.

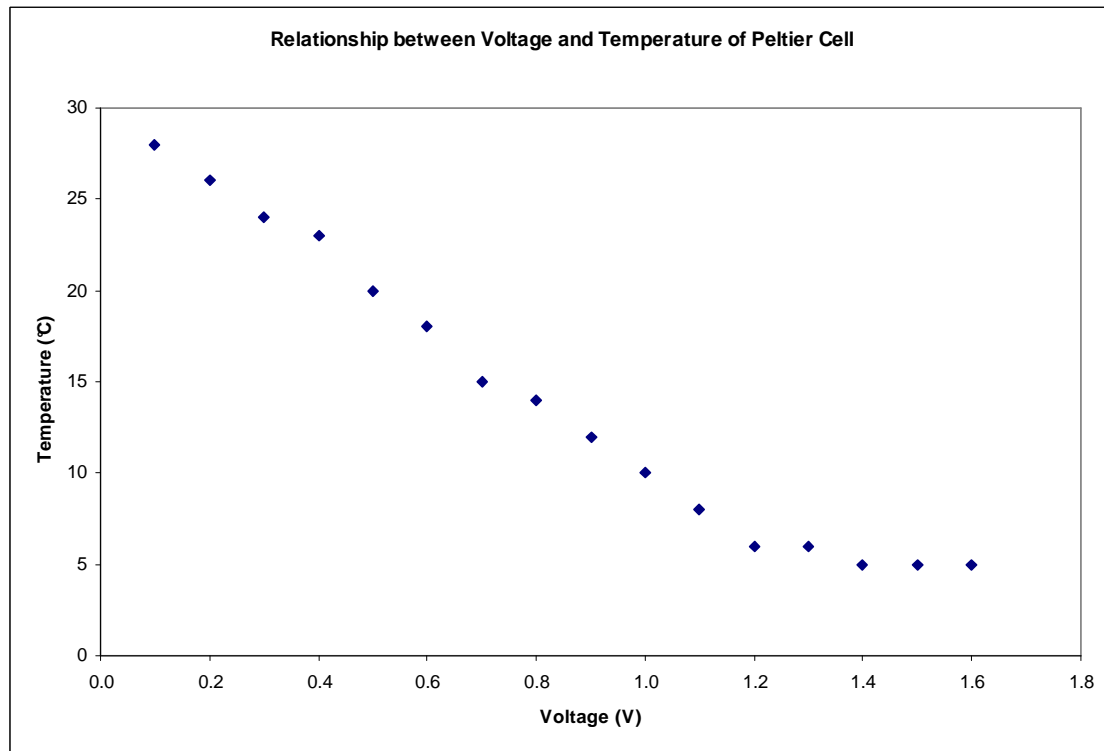


Figure 14. Graph showing the relationship between temperature and voltage of the Peltier Cell. Temperature data was collected from the surface of the cell.

From the data shown, we determined that a voltage between 0.6V and 0.8V would be ideal for the client's purposes.

Test 2: Using different interfaces to test for efficiency

The method of attaching the device to the tissue depends on the interface used between the cell and the tissue. The original design planned on the use of an aluminum plate in contact with the Peltier device that would then contact the tissue. However, we suspected that the thermal conductivity of aluminum would not be sufficient to cool the gel, so we carried out testing using the aluminum plate between the device and agar and subsequently using the device directly on the agar. In both cases, temperature was

collected from 1mm below the surface of contact with the device. The input voltage was 0.8V, and the agarose temperature was 42°C.

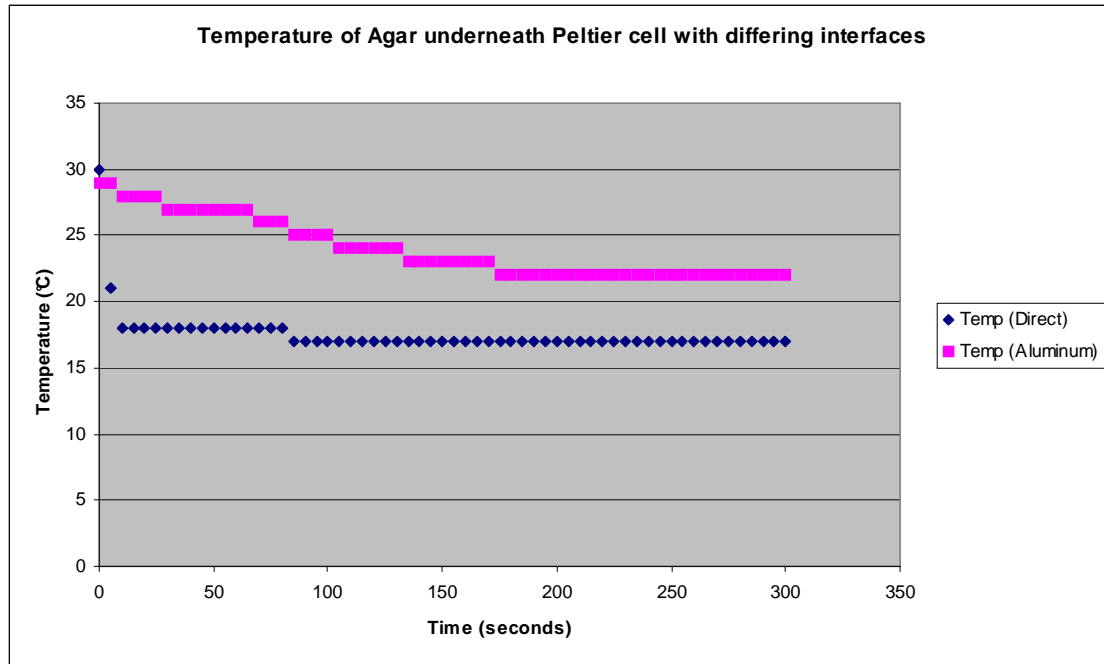


Figure 15. Temperature vs. Time using different interfaces. The Aluminum is given in pink; and the direct contact is given in blue.

As shown, the final temperature of the aluminum in contact with the agar was about 22°C, in comparison to the direct contact which could bring the agar down past the target temperature of 20°C. Therefore, we opted to use direct contact for generating the thermal gradient, since that provided the best results.

Test 3: Thermal Gradient of the device

The device is designed to have a local cooling effect, but it will still produce temperature changes in adjacent tissue. As a result, knowledge of the thermal gradient will allow the client to maintain specific control over his experiment. To carry out the test, thermocouples were placed at fixed intervals in the agarose gel from the contact point of the device. This test was carried out on horizontal planes, allowing for a three-

dimensional view of the effects of the cooling device. The input voltage was 0.775 V with an agarose temperature of 46°C. Data was collected 5 minutes after the device was attached and turned on.

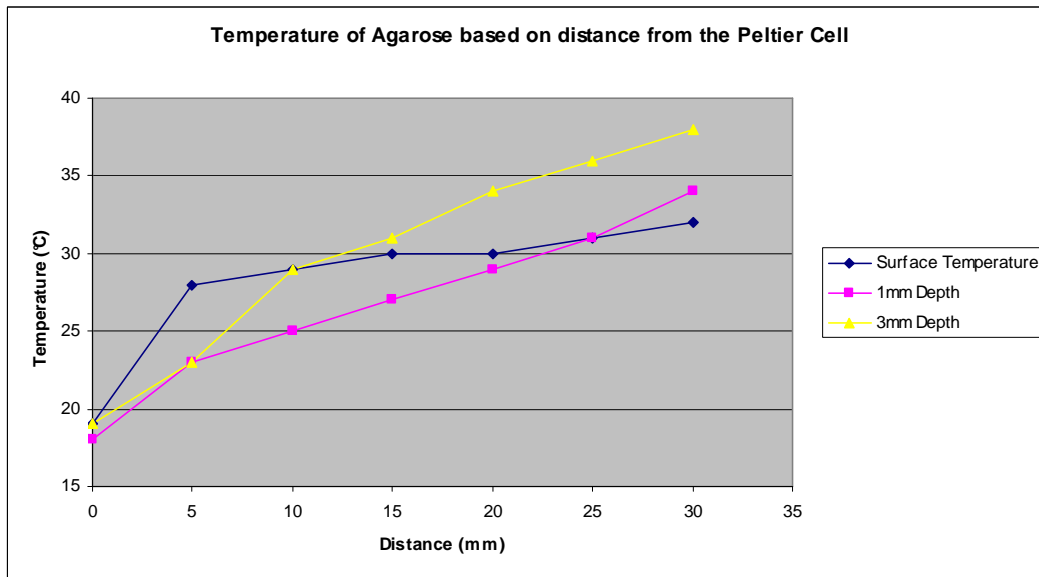


Figure 16. Graph showing the temperature of the agarose based upon distance away from the Peltier cell. Temperature was collected at each distance at three differing depths.

From this data, a linear gradient was assumed from data point to data point. This allowed us to generate a thermal gradient showing the effect of the device.

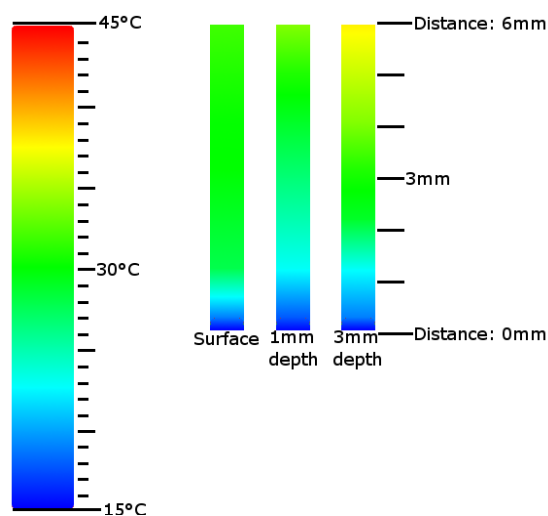


Figure 17. Diagram showing the temperature gradient of the agar with the Peltier cell applied. As shown, the temperature rapidly rises within 2mm of the cell, indicating the effectiveness of the cooling.

One problem with the data collection, however, is that the surface was in contact with the air, and as such, the temperature away from the Peltier cell may not accurately reflect that of tissue. However, the actual gradient will more likely approximate that at 3mm for the mouse.

Future Work

Future work on the project consists mostly of items that have either been unimplemented or untested. The method of attaching the device to the brain of the mouse is something that has not been completely implemented into our project. This interface between the Peltier cell and the brain would allow the Peltier cell to be able to be reused and place less weight on the top of the mouse's head when the device is not in use. Our proposed method of doing so includes a small needle that would localize cooling in a region of the brain selected by the client. The needle would either be a 300 μ m diameter gold needle or a 500 μ m diameter diamond-tipped drill bit. These ideas need to be tested to determine proper functionality and heat transfer with the Peltier cell. Additionally, the device has not been tested for EEG interference. Testing for EEG interference would involve placing the device onto the mouse's brain first, which requires a properly working interface. The client would also like to have an idea of the thermal gradient in an actual mouse's brain which has not yet been found, since the device has not yet been implanted. Finally, a non-electronic method of finding temperature during the use of the actual device needs to be obtained.

APPENDIX A

Project Design Specifications

PRODUCT DESIGN SPECIFICATIONS

Date: February 5th, 2009

Project Title: #28 Brain Cooling Device

Team Members:

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Function:

Sleep is homeostatically regulated; the more we are awake, the more intensely we need to sleep. However, while this is a common experience, the actual mechanism behind the regulation of sleep is poorly understood. In order to further our understanding of this phenomenon, *in vivo* imaging of genetically engineered YFP fluorescent mice will be performed on brain synapses. It is believed that comparing the activities of neurons while awake and asleep could conclude that sleep is regulated by these metabolic changes. In order to rule out other possibilities such as simply kinetic regulation, neurons in a specific area of the brain must be silenced for a span of time and its effect on sleep analyzed. In order to do this, a miniature device must be constructed to cool the temperature in an area of the brain of a mouse to a low enough temperature to silence neural activity while preventing necrosis.

Client Requirements:

- Create a device to silence neurons in an area of 1-3 mm in diameter by cooling.
- The device needs to have a way of recording the temperature gradient that is formed in the 1-3 mm area
- The device must not interfere with the EEG signals.
- The device must be able to cool a mouse's brain and thus must be very small.
- The device must cool a mouse's brain (38-39°C) to as low as 19-20°C
- The device must be able to cool the tissue to a selected temperature in the range of 19-25°C and be able to keep the tissue at the selected temperature for up to 6 hours. Thus it must have variable temperature controls.
- Materials used should be durable with little need for maintenance.
- The device must be completed and functional by the end of the semester
- The budget for the device and prototypes is \$1000.

Physical and Operational Characteristics

- *Performance requirements:* The device will be used in multiple studies and must be continuously operational for 1-6hrs.
- *Safety:* The device must be biocompatible, nontoxic, and easily cleaned to reduce the possibility of spreading infection amongst animals.
- *Accuracy and Reliability:* The device must be able to record, adjust, and maintain to temperatures within $\pm 0.5^{\circ}\text{C}$. The device will be used continuously for up to 6hrs.
- *Shelf Life:* The device will be stored at standard temperature and pressure in non-condensing humidity.
- *Operating Environment:* The device will be operated at standard temperature and pressure in non-condensing humidity, however temperatures as low as 19°C will be produced. The device will be in direct contact with brain fluids and tissue during operation.
- *Ergonomics:* The device will rest on the brain of a mouse and must not induce any pain or unnecessary stress.
- *Size:* The device must cool an area of 1-3mm, but other working components may be much larger. The device must be portable by one human with a cart.
- *Weight:* The device must weigh within the limits of a human's ability to move from room to room.
- *Materials:* Must be biocompatible and nontoxic with direct contact to brain tissue and bodily fluids. Materials that conduct electricity are discouraged.
- *Life in Service:* 1-2 years.

Production Characteristics

- *Quantity:* One unit
- *Time of Manufacture:* Within Semester
- *Target Product Cost:* <\$1000

Miscellaneous

- *Standards and Specifications:* Device will need to be approved by the IACUC (Institutional Animal Care and Use Committee)
- *Customer:* The customer has attempted using a small Peltier cooling device, but had difficulty with creating an adequate heat sink. Also, a rough liquid cooled device had been used, but it produced noise in the EEG signal.

APPENDIX B

Expenses

FINAL REPORT

May 8, 2009

Expense Sheet			
Product	Date	Where	Cost
Vortex Tube	2/12	Icoolsmart.com	\$200.00
Valves	2/19	Home Depot	\$45.00
Air Compressor	3/6	Home Depot	\$90.00
Peltier Cells	3/12, 4/12	Customthermoelectric.com	\$180.00
Polyethylene Tubing	4/12	USPlastics.com	\$40.00
Power Supply	4/12	Texsoinstruments.com	\$200.00
Artic Silver Thermal Adhesive	4/12	Newegg.com	\$10.00
		Total	\$765.00

References

- Bakken, H. E., et al. "A Device for Cooling Localized Regions of Human Cerebral Cortex. Technical Note." Journal of neurosurgery 99.3 (2003): 604-8.
- Battista, A. F. "Effect of Cold on Cortical Potentials in the Cat." Experimental neurology 19.2 (1967): 140-55.
- Benita, M., and H. Conde. "Effects of Local Cooling upon Conduction and Synaptic Transmission." Brain research 36.1 (1972): 133-51.
- Burton, J. M., et al. "Transcortical Cooling Inhibits Hippocampal-Kindled Seizures in the Rat." Epilepsia 46.12 (2005): 1881-7.
- Cespuglio, R., et al. "Alterations in the Sleep-Waking Cycle Induced by Cooling of the Locus Coeruleus Area." Electroencephalography and clinical neurophysiology 54.5 (1982): 570-8.
- Chafee, M. V., and P. S. Goldman-Rakic. "Inactivation of Parietal and Prefrontal Cortex Reveals Interdependence of Neural Activity during Memory-Guided Saccades." Journal of neurophysiology 83.3 (2000): 1550-66.
- Chudler, Eric. Brain Facts and Figures.
<http://faculty.washington.edu/chudler/facts.html>
- Clarey, J. C., R. Tweedale, and M. B. Calford. "Interhemispheric Modulation of Somatosensory Receptive Fields: Evidence for Plasticity in Primary Somatosensory Cortex." Cerebral cortex (New York, N.Y.: 1991) 6.2 (1996): 196-206.
- Clark, D. L., and F. Colbourne. "A Simple Method to Induce Focal Brain Hypothermia in Rats." Journal of cerebral blood flow and metabolism : official journal of the International Society of Cerebral Blood Flow and Metabolism 27.1 (2007): 115-22.
- Elwassif MM, Kong Q, Vasquez M and Bikson M. "Bio-heat transfer model of deep brain stimulation-induced temperature changes." Journal of neural engineering 3(4) (2006): 306-15.
- Everson, C. A. (1995). "Functional consequences of sustained sleep deprivation in the rat." *Behav Brain Res*, 69(1-2), 43-54.
- Fingas, M., D. L. Clark, and F. Colbourne. "The Effects of Selective Brain Hypothermia on Intracerebral Hemorrhage in Rats." Experimental neurology 208.2 (2007): 277-84.

- Imoto, H., et al. "Use of a Peltier Chip with a Newly Devised Local Brain-Cooling System for Neocortical Seizures in the Rat. Technical Note." Journal of neurosurgery 104.1 (2006): 150-6.
- Kenner, Thomas et. al. The continuous high-precision measurement of the density of flowing blood. *Pflügers Archiv European Journal of Physiology*: Vol 370, No. 1 / January, 1977.
- Long, M. A., and M. S. Fee. "Using Temperature to Analyse Temporal Dynamics in the Songbird Motor Pathway." Nature 456.7219 (2008): 189-94.
- McCaffrey, Patrick. Neuroanatomy of Speech, Swallowing and Language. <http://www.csuchico.edu/~pmccaffrey//syllabi/CMSD%20320/362unit11.html>
- McCulloch, J., et al. "Local Cerebral Glucose Utilization in Hypothermic and Hyperthermic Rats." Journal of neurochemistry 39.1 (1982): 255-8.
- Rothman, S., and X. F. Yang. "Local Cooling: A Therapy for Intractable Neocortical Epilepsy." Epilepsy currents / American Epilepsy Society 3.5 (2003): 153-6.
- Tanaka, N., et al. "Effective Suppression of Hippocampal Seizures in Rats by Direct Hippocampal Cooling with a Peltier Chip." Journal of neurosurgery 108.4 (2008): 791-7.
- Thomas, Joel. Personal Communication in Thermodynamics. May 5, 2009.
- Tononi, Giulio. (2005) "Research Overview—The Center for Sleep and Consciousness." http://tononi.psychiatry.wisc.edu/research_overview.html
- Turner, T. H., Drummond, S. P. A., Salamat, J. S., & Brown, G. G. (2007). "Effects of 42 hr sleep deprivation on component processes of verbal working memory." *Neuropsychology*, 21, 787-795
- Waleszczyk, W. J., M. Bekisz, and A. Wrobel. "Cortical Modulation of Neuronal Activity in the Cat's Lateral Geniculate and Perigeniculate Nuclei." Experimental neurology 196.1 (2005): 54-72.
- Yang, X. F., and S. M. Rothman. "Focal Cooling Rapidly Terminates Experimental Neocortical Seizures." Annals of Neurology 49.6 (2001): 721-6.
- Zager, A., Andersen, M. L., Ruiz, F. S., Antunes, I. B., & Tufik, S. (2007). "Effects of acute and chronic sleep loss on immune modulation of rats." *Regulatory, Integrative and Comparative Physiology*, 293, R504-R509