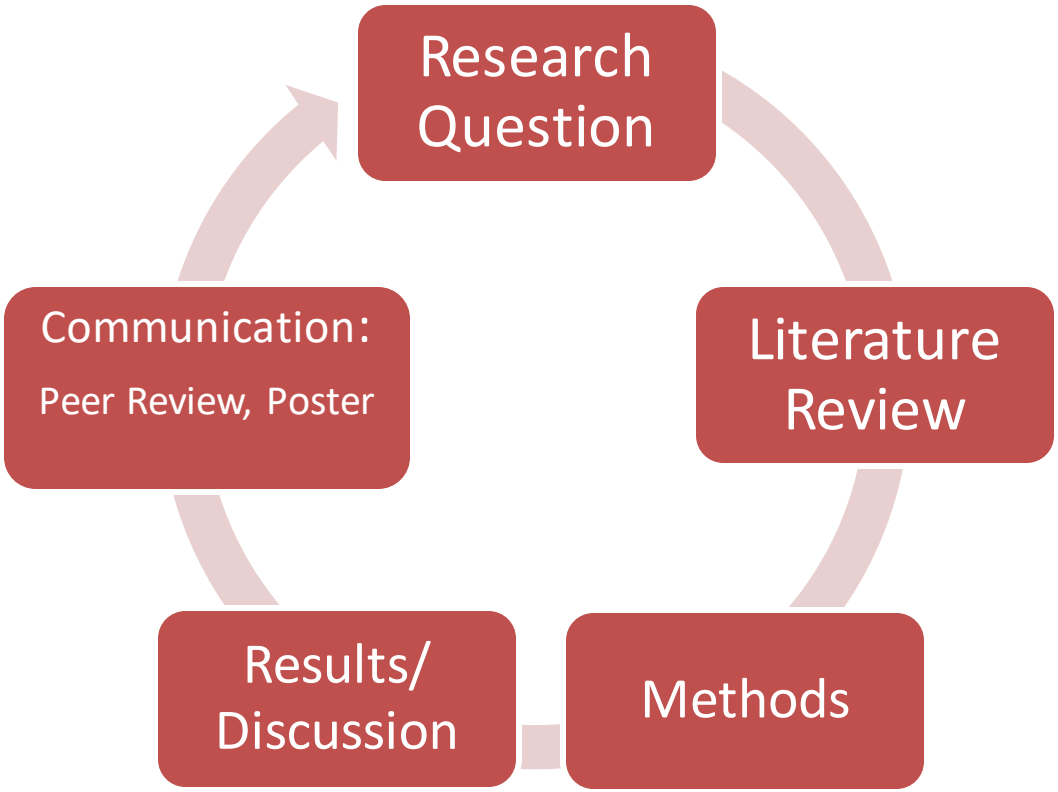
USC Viterbi

SHINE

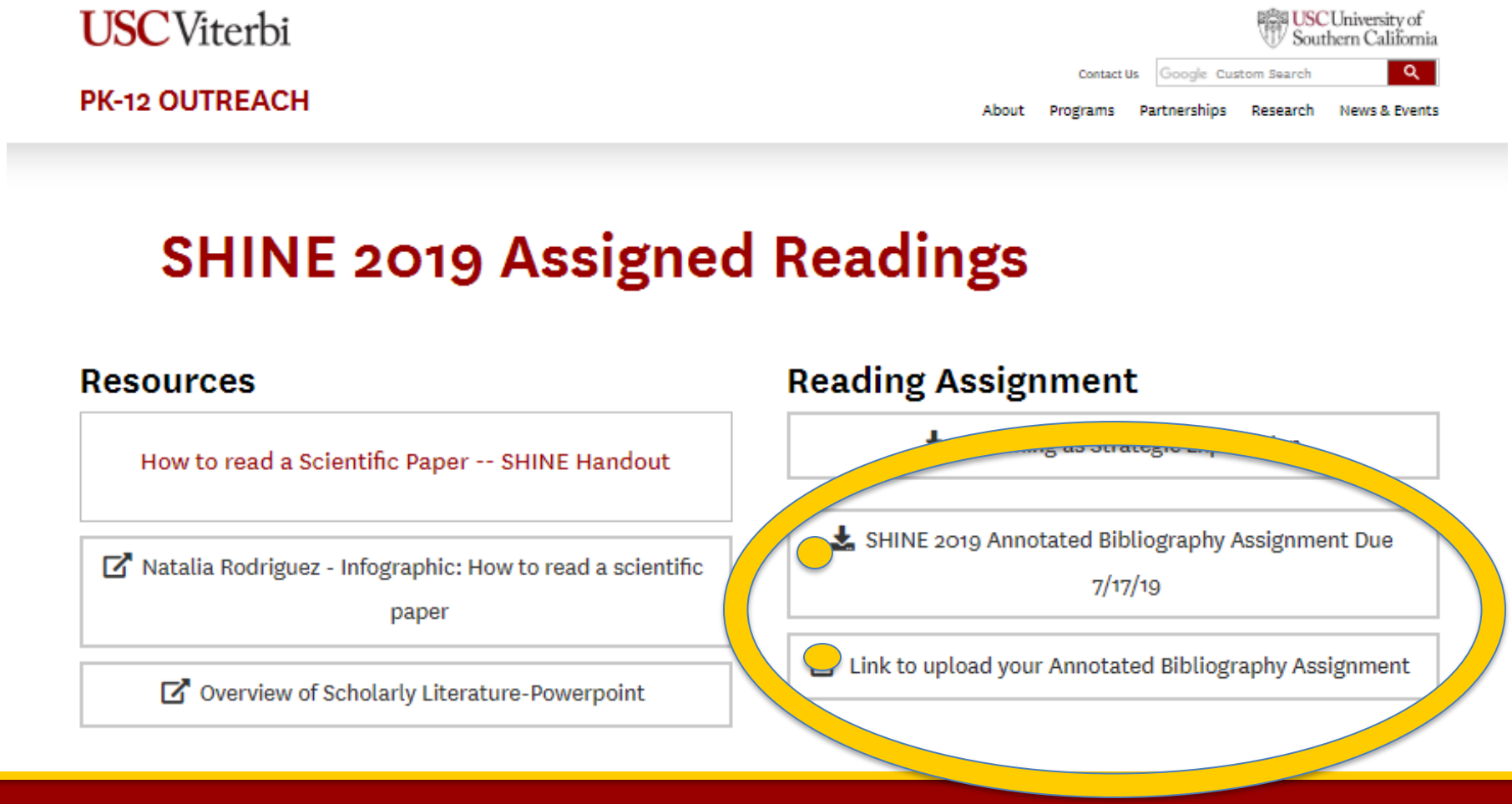
Summer High School Intensive in Next-Generation Engineering

USC Viterbi SHINE 2019
Annotated Bibliography Assignment

The Research Cycle



Annotated Bibliography Assignment: Extra copies & Where to Turn In



USC Viterbi School of Engineering

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Annotated Bibliography Assignment – Due 7/17/19

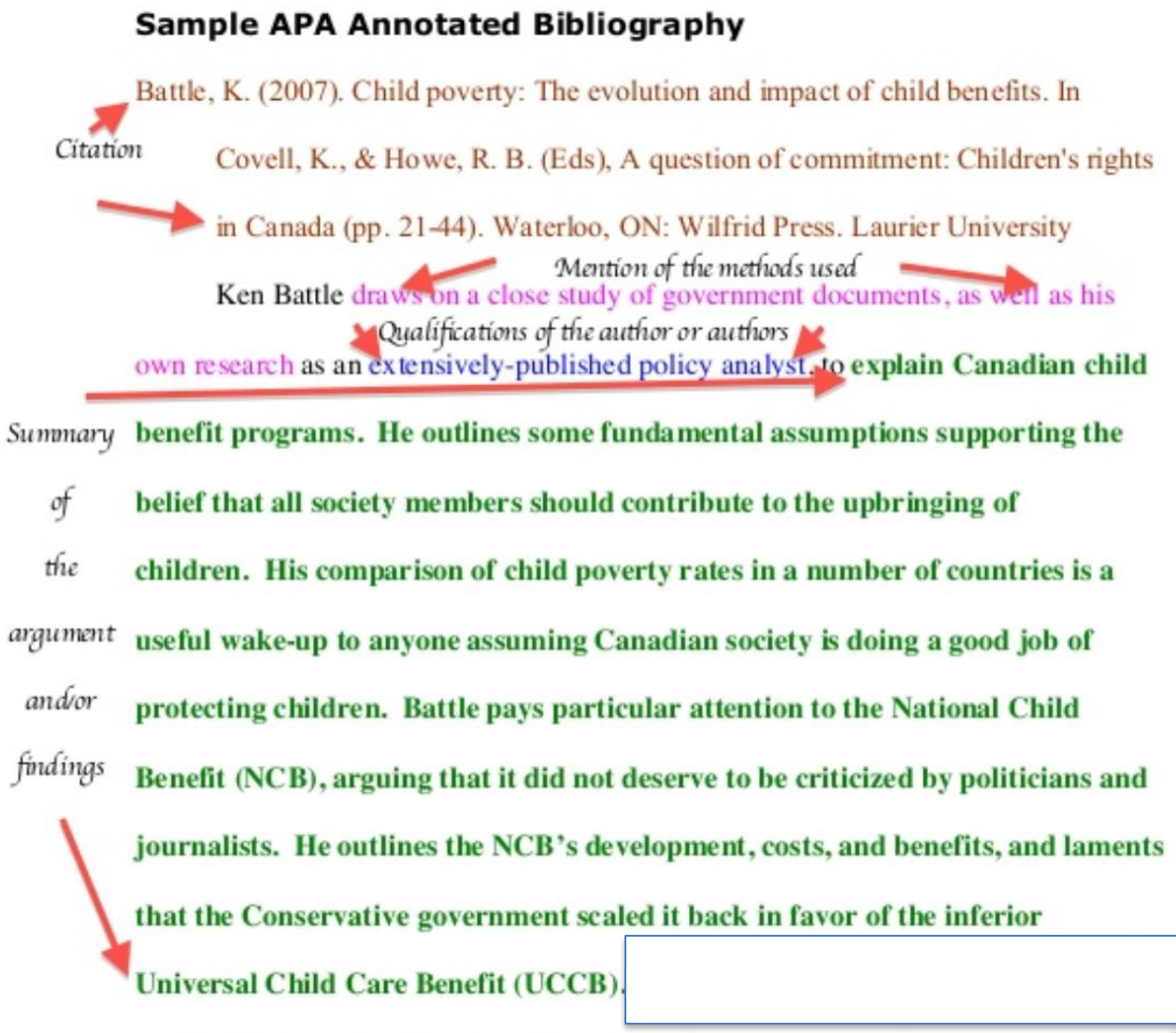
Introduction to Library Research: As you engage in laboratory research during SHINE, you are refining important skills and performing the scientific method in action. But the goal of lab research is to share it with other researchers and therefore build on the existing body of scholarly knowledge. Starting in Week 1, your professors and Ph.D./postdoctoral mentors have introduced you to peer-reviewed scientific studies pertinent to your SHINE lab. Today (6/28), we will meet with Science Librarians Dr. Shalini Ramachandran and Cari Lyle to learn how to access USC library databases to further refine your research on a topic of your choice. Their aim is to prepare you to conduct your own academic literature searches and delve more deeply into your area of SHINE research or any research topic that interests you. The databases you will explore provide convenient access to published scholarly literature, but this access also costs money, so you will need an institutional subscription to do so. During your time at SHINE, you have been granted institutional access, courtesy of USC's Associate Dean of Public Services, Ruth Wallach. But if you are having any trouble accessing material to help you complete your annotated bibliography assignment, please contact ITS about your NET ID error at 213-740-5555 and/or ask your Ph.D. mentors to help you access these files. You should also ask your mentors about how they themselves conduct a literature search, which databases they find useful, and how they use a literature search in their research.

Assignment details: On Wednesday, July 17, we ask you to please submit an Annotated Bibliography of 2 – 3 sources you found that interest you. If you'd like, you can search the databases for more studies by your professor or Ph.D. mentor, or you can look up a reference mentioned in any of the articles you have already read, or you can look up an entirely different field to satisfy your curiosity about other areas of research. For each entry, please include a citation in APA (American Psychological Association) style of your source and a paragraph summarizing the source in question, including reference to the study's IMRAD

- Due Wed. 7/17
- 2-3 Sources
- Topic of your choice

Dr. Herrold office hours:
10am-12pm In RTH Café
Wed. 7/10

Annotated Bibliography on topic of your choice: Due Wednesday 7/17



Former SHINE student sample Annotated Bibliography:

Chung, E. J., & Mlinar, L. B., & Sugimoto, M. J., & Nord, K., & Roman, B. B., & Tirrell, M. (2014). *In vivo* biodistribution and clearance of peptide amphiphile micelles. *Nanomedicine: Nanotechnology, Biology, and Medicine*, 11, 479-487.

To assess the toxicity and clearance of peptide amphiphiles, researchers at the University of Chicago and UC Berkeley intravenously administered two different types of peptide amphiphile micelles, CREKA (Cys-Arg-Glu-Lys-Ala) micelles (cy7-labeled micelles containing the peptide CREKA) and non-targeting micelles (NT), control micelles lacking a peptide, in ApoE knock-out mice to examine their biocompatibility, biodistribution, and clearance. Results revealed that the micelles were cleared through the renal system, that both types of micelles were mostly found to be in the liver and kidney, and that no tissue damage was observed via histology in the mice injected with either NT or CREKA micelles. This article is significant because according to the authors, it was the first study in which the *in vivo* biodistribution, clearance, and toxicity of peptide amphiphiles were analyzed.

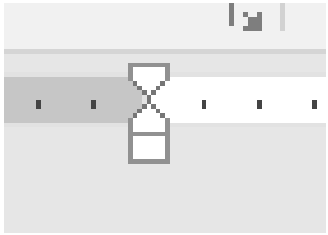
Citation help:

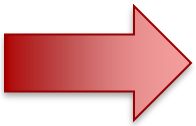
- Purdue Owl (Online Writing Lab) – a great site for guides to all of the citation styles
  - https://owl.purdue.edu/owl/research_and_citation/apa_style/apa_formatting_and_style_guide/reference_list_basic_rules.html
  - They have an automatic citation generator, but BEWARE of these – always double check them against the style guide.

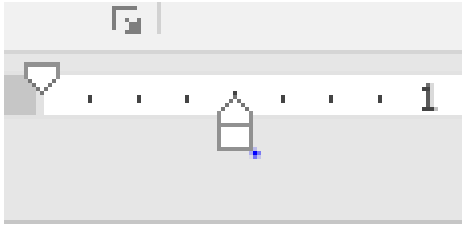
A word on citations:

The “hanging indent”: a common style convention for References pages

Author, A. A., Author, B. B., & Author, C. C. (Year). Title of article. *Title of Periodical, volume number* (issue number), pages. https://doi.org/xx.xxx/yyyy







Category	Excellent	Commendable	Satisfactory	Submitted
Summary	Annotations provide a thorough but concise summary of the topic and main arguments presented in each source.	Annotations provide a brief and/or basic summary of the topic and main arguments presented in each source.	Annotations provide some information concerning the topic and main arguments presented in each source.	Annotations provide little to no information concerning the topic and main arguments presented in each source.
Quality of Sources	Sources are professional and reliable (peer-reviewed or similar quality). They are acceptable for research purposes.	Sources are professional but not reliable. They would not necessarily be recommended for research purposes.	Sources are neither professional nor reliable. They would not be acceptable to use for research.	No sources are given.
Significance of Source	Annotations reference the greater significance of the source and/or its relationship to the chosen research topic.	Annotations present a brief and/or basic reference to the greater significance of the source and/or its relationship to the chosen topic.	Annotations present some reflection on the source's greater significance and/or its relationship to the chosen research topic.	Annotations present little to no reflection on the source's greater significance and/or its relationship to the chosen research topic.
Readability of Annotation	Annotation is very well written, concisely phrased and clear in its articulation of the topic explored and source summarized. Perfect or very few word choice issues. Very readable.	Annotation is well written and makes a good effort to be clear and concise in its phrasing. Despite some word choice issues, the entry is readable.	Annotation displays some issues with readability, clarity, and/or concision. More revision for logic and flow of sentences is recommended.	Annotation is difficult to understand due to word choice issues, problems with logical flow, and/or lack of clarity in phrasing. Extensive revision is recommended.
APA Citation Formatting	APA format contains no or very few errors. The reader would be able to find the article referenced.	APA format contains several errors. The reader would have to make several search attempts to find the article referenced.	Consistent errors in APA format. Reader would struggle to find the article referenced.	APA format is not attempted.

Annotated Bibliography "Grading" Rubric

!!!HAPPY BIRTHDAY!!!

!!!Justin Jang!!!

3 Sentence Challenge: ROUND 2

- Take out a blank document
- Spend no more than 7 minutes
- Write a 3-sentence description of your Professor's research and your role in it.
- On Google Drive, post your new description under your description from last week and date it to differentiate from last week. ☺

3-Sentence Challenge Google Doc Link:

https://docs.google.com/document/d/1yMQjb3NbzACjQhMzZYrnNj9os3EHQ8mv3hcngz1CLPM/edit?usp=sharing

Announcements for Next Weeks:

Thursday & Friday: Campus closed for 4th of July—no SHINE—have fun!!

Wed. 7/10/19: Dr. Herrold office hour, 10 – 11 AM RTH Café
-Office hours are chill—please utilize them now & @college

Fri. 7/12/19: Supercomputing & Chemical Engineering workshop with Professor Sharada MCB 102

Wed. 7/17/19: Annotated Bibliography Due! Cohort-wide meeting – Professor Nikolaidis Workshop on Robotic-Arm

Anyone having trouble obtaining their NET IDs?

- I want names
- Call ITS & lodge ticket:
  - 213-740-5555
- In meantime: ask your SHINE Mentor for help (they have login credentials)

Welcome Dr. Shalini Ramachandran and Ms. Cari Lyle!

Development of Multi-Electrode Neural Probes for Rat Hippocampal Recordings

Leo Siow, siowleo@yahoo.com
Glen A. Wilson Class of 2016
University of Southern California, Department of Biomedical Engineering

USC Viterbi School of Engineering

SHINE Summer High School Intensive in Next-Generation Engineering

Introduction

The primary purpose of MEMS is to engineer extremely miniscule technology, which can be implemented in the medical field. Our research objective strives to fabricate a neural probe designed to observe the neural networks responsible for the formation of memories in the hippocampus. The process to create a device capable of recording electrical signals within a rat's brain is a long and complex one. First, we created brain probes using the process of photolithography. We designed and fabricated flexible, multi-electrode Parylene probes to record spikes from the Cornu Ammonis (CA) areas CA1 and CA3 and the Dentate Gyrus (DG) regions of rat hippocampi. This array of eight, custom made, flexible neural probes with eight recording sites per probe, targets particular hippocampal cell layers. The array also enables long-term hippocampal recordings of rats as they interact with complex, environmental spatial cues. The flexibility of the probes enables better integration with surrounding brain tissue and less micro-damage to nearby neurons when compared to damage caused by metal microwires to neurons. Since the probes are flexible, they must be temporarily stiffened in order to insert into brain tissue. Our research utilizes a block of a biocompatible adhesive, Polyethylene Glycol (PEG), to temporarily decrease the effective length of the probes, enabling them to penetrate brain tissue. In parallel to helping to develop an effective insertion technique, I designed and fabricated a printed-circuit board to connect the electrical traces on our probe to the appropriate electrical recording system.

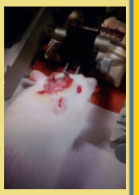


Figure 1: Probe insertion into live rat. *Photo credit: Jamie Chen*

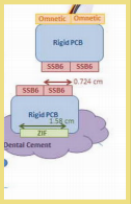


Figure 2: Electrical connection scheme from traces on probes to electrical recording system. *Photo credit: Ahuva Weltman.*

Objectives

1. Fabricate flexible neural probes:

- Inserting probes is a traumatic event for the brain, which causes a scar and dead zone to form around the recording sites and limits the probe's ability to obtain neural signals.
- Using a more flexible material, rather than the traditional metal substrates, attenuates this damage.
- We use Parylene, a USP Class VI material that is flexible and micromachinable to construct the devices.

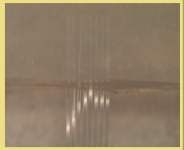


Figure 3: Released parylene C coated probes. The probes are flexible and prone to physical deformation. Acetone was applied for easier removal from wafer. *Photo credit: Leo Siow*

2. Test various techniques to provide temporary stiffness to neural probes:

- Flexible probes must be temporarily stiffened during insertion in order to penetrate brain tissue.

3. Design a printed-circuit board to connect probes to electrical recording system:

- We will be using software to design our printed-circuit boards, which will be part of our electrical connection scheme.

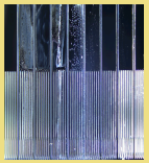


Figure 4: Unreleased sham probes on silicon wafer. The probes are flexible and made of Parylene. *Photo credit:: Leo Siow*

Research Process

Neural Probe Fabrication:

- Probes were microfabricated by using photolithographic techniques. (Fig. 5)
- Parylene served as the base substrate and insulation layer for our devices.
- Platinum electrode recording sites, traces, and contact pads will be lithographically patterned on top of the base layer using e-beam deposition at a thickness of 2,000 Å, followed by lift-off.
- Electrodes and contact pads will be subsequently exposed by DRIE and the probes will be cut out from the substrate.

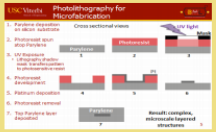


Figure 5: Step-by-step process of photolithography. The alignment step; was noted as the most difficult step. *Photo credit: Ahuva Weltman*

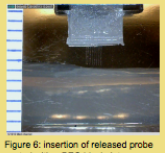


Figure 6: insertion of released probe coated with a PEG block into agarose gel. This is one of many trials. *Photo credit: Ahuva Weltman*

Optimizing Insertion of Probes into Brain

- Temporary stiffening techniques range from coating probes with a dissolvable, biocompatible stiffener to using microwire scaffolds to support the probes during insertion.
- We explored the use of Polyethylene Glycol (PEG) blocks to temporarily stiffen flexible probes during insertion into brain phantom gel (Fig. 9).
- The process of creating these PEG blocks involved the use of molds made from polydimethylsiloxane (PDMS) cut-outs. We used a three-layer mechanism, with the first layer as a base. The second layer served as a proprietor for our insertion tool (black rectangular object). The third layer contained an opening for the PEG to be poured into.
- In collaboration with the Berger lab, we inserted our sham probes into the rats. First, these rats were ensured to be sterile and clean. Next, we applied anesthesia to the rat with the correct quantity, to ensure the rat will have a painless experience.
- The sham probes were carefully positioned above the proper insertion zone.
- We used dental cement to secure the probe in place. When we retracted our insertion apparatus, the probe would remain robust and secure. The procedure was concluded to be successful, as the probes inserted properly without fail.
- A vivisection was performed to drain the blood by flushing formaldehyde through the rat's body, known as a perfusion.

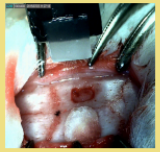


Figure 7: Insertion of our probe into a live rat. Probe was positioned carefully above insertion zones. We were careful to avoid contact between the insertion tool and cranium. PC: Ahuva Weltman, Leo Siow

Figure 8: Our insertion setup. Insertion apparatus and camera were positioned to record live insertions. PC:Leo Siow

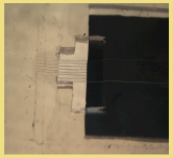


Figure 9: One of our PEG block models. We desired a slower melting rate for the PEG, thus we attempted to split the block into thirds. PC: Ahuva Weltman

Fabrication of PCB for Electrically Connecting Probes to Neural System:

- Eagle was used to develop printed-circuit boards and molds for our device. We used Eagle to create multiple parts for our device. This includes schematics, devices, symbols, and packages.
- After we complete all elements of our design, we will send the file to a fabrication house. The fabrication house uses our file to create a printed-circuit board, which will be used in our device to encode the memories from a rat into data readable by computers.

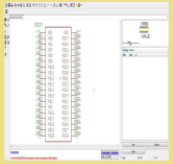


Figure 10: Schematic on Eagle software. Often the first step in fabricated a PCB. Thirty-four pins are visible in the diagram. which will eventually become a SSB6 plug. *Photo credit: Leo Siow*

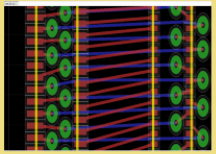


Figure 11: A broad view of a ZIF to SSB6 connector. Many traces are drawn. Interestingly, none of them are intersecting, due to the creative connection scheme in which both sides of the board is utilized. *Photo credit: Ahuva Weltman*

Relativity to My STEM Coursework

The research we did at the lab involves heavy use of theoretical knowledge to comprehend. For example, when we were exploring different options of inserting our probes into the brain phantom gel, we came up with the possibility of utilizing magnetism. Background knowledge from my Advanced Placement physics class provided valuable insight. Without this knowledge, I would not have been able to communicate with my fellow peers in the lab. In addition, our lab group wanted to find the force of insertion of the probe. Again, my experience from Advanced Placement physics provided me the ability to suggest mechanics-based solutions to the given problem. Such solutions included the use of the impulse-momentum formula, as well as Newton's second law. The scientific method was also presented to me at a higher level. Overall, my research abilities were greatly enhanced and also increased in formality. In high school, this will give my lab reports an edge compared to my other peers. The scientific integrity of my lab report will increase, due to the overlapping factors between high school and university science. Overall, my background knowledge from high school courses was beneficial in my participation.

Future of Project

The device will undergo many revisions, particularly to perfect the electrodes and traces. After the device is successfully fabricated, it will be tested on a live rat. The device is expected to analyze brain waves and neuron firing in the rat's hippocampus. This beneficial data will contribute to the study of the formation of memories in the brain. Eventually, if the project proves to be efficient, there is a possibility of commercialization. This may benefit millions of lives, including but not limited to, people who suffer from Alzheimer's disease. Other memory-related disorders may also be treated with this device.

Acknowledgements

Dr. Ellis Meng, Ahuva Weltman, David King, Huijing Xu, Craig Timms. Dr. Katie Mills, Luping Wang, Biomedical Microsystems Lab, Kenny Chan

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