USC Viterbi

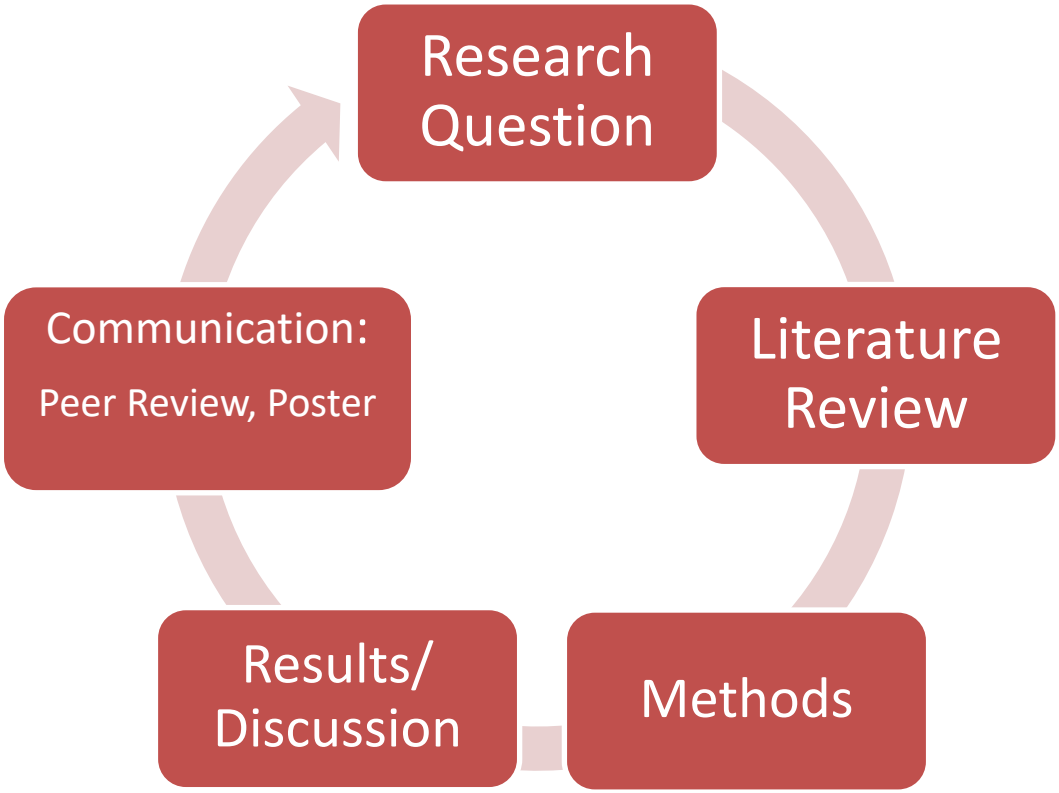
SHINE

Summer High School Intensive in Next-Generation Engineering

USC School of Engineering

University of Southern California

Connecting Scholarly Literature to Your SHINE Research



R1 University Labs

- 1 or 2 BIG research question(s)
- Several smaller research questions pursued by different lab members.

How to use this information:

- When thinking about your role in your lab this summer
- When reading scholarly literature

When thinking about your role in your SHINE lab:

- Remember IMRAD
- Identify your lab's big question. Ask yourself: "What problem is my SHINE lab trying to solve?" Why are they are they pursuing an answer to this question in their particular field? This helps you focus on why your lab's research is being done.
- Summarize your lab's background. Is there research question brand new, or does the lab have a history of working on this question? What are other labs working on related questions doing, and how does your lab differ? What questions does your lab hope to answer next? You need to be able to succinctly explain what research your lab has already done in order to understand the research the lab is currently doing.
- Identify the specific research question(s) you will be helping to answer this summer. What exactly is your lab trying to answer with your research? How is that related to your lab's BIG question?
- (adapted from Dr. Jennifer Raff's "How to read and understand a scientific article)

3 sentence challenge: Articulate the general research question your SHINE lab is asking. Then, articulate the specific research question your will contribute to answering.

Challenge Parameters:

- Use **ONLY 3** sentences
- Use language a layperson can understand

Ask yourself: What should I include? What can I leave out?
What's most important to convey for a lay reader?
Spend 10 minutes drafting response, then upload to Google Doc

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

Link shared via Slack

We will check back with these responses at a later date.

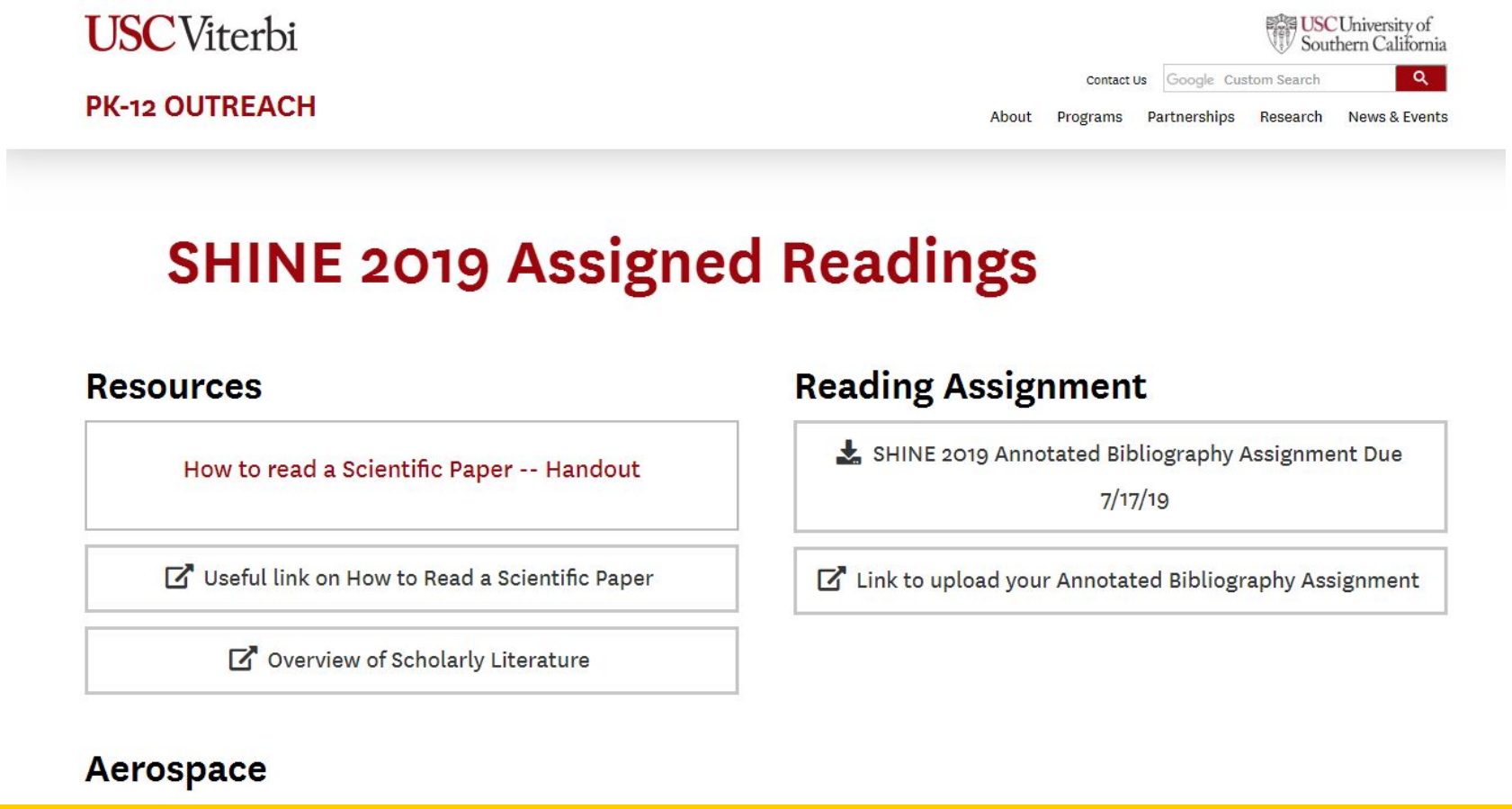
R1 University Labs

- 1 or 2 BIG research question(s)
- Several smaller research questions pursued by different lab members.

How to use this information:

- When reading scholarly literature
- When thinking about your role in your lab this summer

Scholarly Readings, cont'd:



Tips for reading scholarly literature:

- Remember IMRAD and read strategically.
- Identify the big question. Not "What is this paper about?" but "What problem is this entire field trying to solve?" This helps you focus on why this research is being done. Look closely for evidence of agenda-motivated research.
- Summarize the background in five sentences or less. What work has been done before in this field to answer the big question? What are the limitations of that work? What, according to the authors, needs to be done next? You need to be able to succinctly explain why this research has been done in order to understand it.
- Identify the specific question(s). What exactly are the authors trying to answer with their research? There may be multiple questions, or just one. Write them down. If it's the kind of research that tests one or more null hypotheses, identify it/them.
- Now, ask yourself why your SHINE lab assigned you this reading. How is it related to your SHINE research?
- (adapted from Dr. Jennifer Raff)

A canceled trial sought to determine whether a single drink a day could have heart benefits.

RESEARCH ETHICS

NIH kills alcohol trial, starts hunt for other suspect studies

Agency says research protocol was skewed to find benefits of moderate drinking

By **Meredith Wadman**

After an investigation found senior officials at the National Institutes of Health (NIH) in Bethesda, Maryland, secretly and improperly wooed the alcoholic beverage industry to fund a study of the potential heart benefits of moderate drinking, NIH Director Francis Collins last week shut down the $100 million industry—in all, beverage companies would contribute $68 million—and had seen to it that a principal investigator (PI) whom the officials favored ran the trial. Three days later, Collins announced that a working group of external advisers would review the trial. In May, NIH suspended enrollment after 105 participants had signed up.

The advisers' 165-page report concludes NIAAA staffers broke NIH rules by directly

The report says NIAAA staffers also manipulated the grant application process to ensure that a favored scientist—Kenneth Mukamal of Beth Israel Deaconess Medical Center and Harvard Medical School in Boston—won awards to plan and then run the trial. Mukamal, who had given presentations to industry groups stressing the "unique opportunity" such a trial presented, was the only applicant for both grants.

"Many of the [NIH staff] who have seen the working group report were frankly shocked to see that so many lines were crossed," Collins said. It was clear, he said, that backers of the study had shaped the trial protocol to ensure an outcome favorable to the sponsors. NIH epidemiologists who reviewed the study said it did not enroll enough people or follow them for long enough to determine whether moderate alcohol consumption increases cancer risks, potentially offsetting any heart benefits. They also faulted the protocol for not including heart failure—which can be caused by alcohol—as a primary endpoint. The MACH trial, they concluded, "could show benefits while missing the harms."

Mukamal responded with a vigorous defense of the trial's integrity. In a statement "on behalf of the [MACH] investigators," he wrote: "We stand fully and forcefully behind the scientific integrity of the [MACH] trial protocol and team. ... Every design consideration was carefully and deliberately vetted with no input or direction whatsoever from private sponsors." NIAAA has spent $4 million of the $20 million it had committed to the trial, and the foundation has disbursed $11.8 million in industry funds.

For more tips:

- Check out PDF created specifically for SHINE on Readings page: https://viterbipk12.usc.edu/shine/readings-2019/
- Drew Dennis's "How to Read Scientific Papers Quickly and Efficiently": https://medium.com/@drewdennis/how-to-read-scientific-papers-quickly-efficiently-e7030c4018fa
- Elysium Heath"The Non-Scientist's Guide to Reading and Understanding a Scientific Paper": https://endpoints.elysiumhealth.com/how-to-read-a-scientific-paper-695188037080
- Dr. Jennifer Raff's "How to read and understand a scientific article": https://violentmetaphors.files.wordpress.com/2018/01/how-to-read-and-understand-a-scientific-article.pdf
- Ashley Hamer's "How to Read a Scientific Paper in 5 Steps": https://curiosity.com/topics/how-to-read-a-scientific-paper-in-5-steps-curiosity/

USC Viterbi SHINE 2019

Prep for Library Day on 6/28/19

Searching as Strategic Exploration

Searching as Strategic Exploration

- Handout prepared by Cari Lyle and Dr. Shalini Ramachandran
- Assignment can be completed w/o library log-in credentials
- We hope to have log-in credentials for you by next week.
- But if this doesn't happen, please use the search function, select articles, and have your SHINE mentor track down the articles for you

Searching as Strategic Exploration:

Library Searching Assignment

Purpose

This assignment will introduce you to searching and refining your search for scholarly literature using a university catalog. The librarians will then build off this assignment during our in class session, which will prepare you for your annotated bibliography assignment.

What is Scholarly Literature?

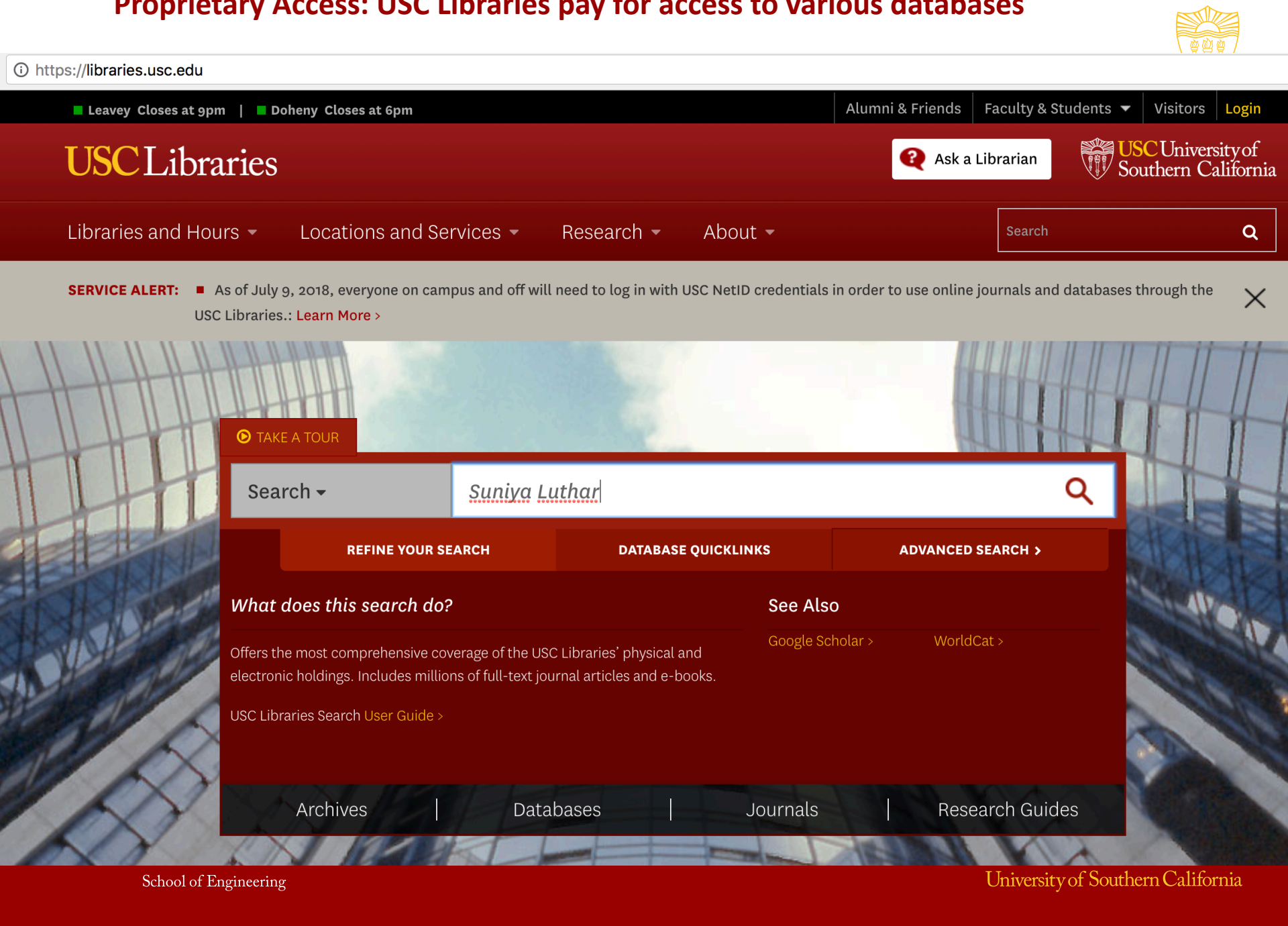
Scholarly literature is written by experts in the field. They usually publish their research in academic journals and are employed by universities and other educational or research institutions. They submit their articles to editors of academic journals, who decide on whether or not the article should be published. This peer review process means that before the article is accepted and published, it will be reviewed by several other experts in the field, who suggest changes and/or make the recommendation to publish the article.

Scholarly Journal vs. Popular Periodicals

Scholarly Journal Article	Popular Magazine Article
Published in an academic journal, described also as refereed or peer-reviewed.	Published in a popular, general interest, or news magazine.
Author is an expert on the topic or a scholar.	Author may be a lay reporter.
The piece is written to a specialized audience of peers or students.	The audience includes the general audience
Includes: in text citations of sources or footnotes, and bibliography	Sources may not be cited formally
Vocabulary is complex and technical	Vocabulary is familiar, non-technical
Graphics are used to illustrate a point	Graphics are used for visual impact
Titles may include the words *Journal, Review*, or *Annals*; and/or refer to a field of study. Examples: *Anthropology & Education Quarterly, Journal of Higher Education.*	Titles are often general, usually catchier. Examples: *People, Newsweek, GQ*
Published monthly, quarterly, semi-annually, or annually	Published weekly or monthly.

https://dornsife.usc.edu/writingcenter/handouts/

Proprietary Access: USC Libraries pay for access to various databases



Libraries.usc.edu

- Finish assignment for homework
- Bring it to cohort-wide meeting on Friday 6/28/19

Library Session Next Friday 6/28

With Cari Lyle and
Dr. Shalini Ramachandran

9:30am – 1:30pm in LVL 17
Basement of Leavey Library

MATLAB next week!

- Tuesday 6/25/19 – Part 1
- Wednesday 6/26/19 – Part 2

Welcome Prof. Zavaleta!

USC Viterbi School of Engineering

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Annotated Bibliography Assignment – Due 7/18

As you participate in the research process here in SHINE, you are refining important skills by researching scientific literature on a topic that interests you. Starting in Week 1, you have been reading peer-reviewed studies assigned to you by your professors. Next Friday (7/6) and Monday (7/9), we will meet with Science Librarians Shalini Ramachandran and Sheree Fu to learn how to use the USC library database plus some proprietary databases. Their aim is to prepare you to conduct your own literature searches and delve more deeply into your area of SHINE research or any research topic that interests you. The databases you will explore are convenient sources of published literature, but access to them also costs money, so you will need to have access to an institutional subscription, which USC provides. Your Ph.D. mentors can help you access these special databases—just ask for help. You can also ask mentors about how they themselves conduct a literature search, which databases they find useful, and how they use a literature search.

On Wednesday, July 18, 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. student mentor, or you can look up a reference 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. It doesn't matter what you select for your topic. Next, we want you to learn what an Annotated Bibliography is and practice writing one. This skill is widely applicable: you will use it when you create a poster for the final Poster Session and you'll use it in college and beyond. Here are some links that explain writing Annotated Bibliographies, their purpose, and their format. The format for citations we use in science is APA (American Psychological Association), and every single comma, period, capital or lower case letter is specific. But don't worry, because all the links below grant you access to sites that can help you format your references correctly using APA style.

By practicing creating an Annotated Bibliography and using APA format, you will be ahead of the curve even as a first year college student, which is when these skills are usually taught.

https://owl.english.purdue.edu/owl/resource/614/01/

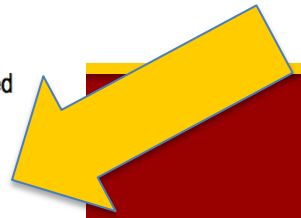
http://guides.library.cornell.edu/annotatedbibliography

Upload your Annotated Bibliography here by July 18, naming your file in this way: LAST NAME – Annotated Bibliography 2018: https://uscviterbi.qualtrics.com/jfe/form/SV_enCTa4CzLbMLTuJ

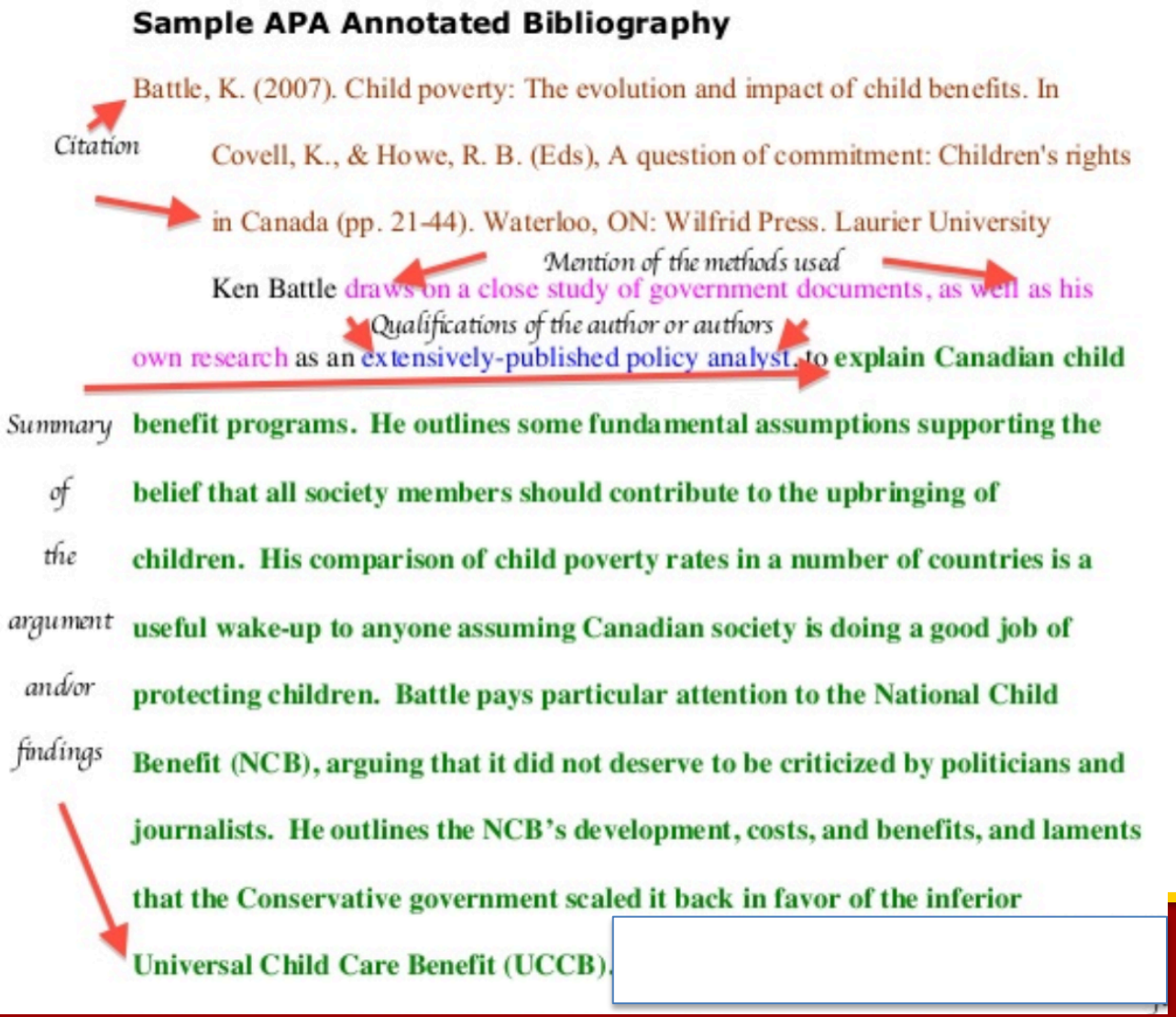
Open office hours with Dr. Herrold – Wednesday 7/11 from 10-11 and Thursday 7/12 10-11 at Tudor Hall Café (RTH). Stop by and say hi, let me know how the research is coming along, ask any questions, check in!

- Due Wed. 7/18
- 2-3 Sources
- Topic of your choice

Dr. Herrold office hours:
10-11 AM In RTH Café
Wed. 7/11 and Thurs. 7/12



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



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

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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*

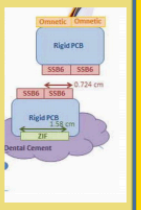

Figure 2: Electrical connection scheme from traces on probes to electrical recording system. *Photo credit: Ahuva Weltman.*

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.

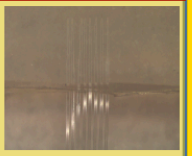

Figure 3: Released parylene C coated probes. The probes are flexible and prone to physical deformation. Acetone was applied for easier removal from wafer. *Photo credit: Leo Siow*

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.

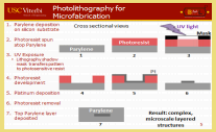

Figure 5: Step-by-step process of photolithography. The alignment step; was noted as the most difficult step. *Photo credit: Ahuva Weltman*

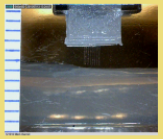

Figure 6: insertion of released probe coated with a PEG block into agarose gel. This is one of many trials. *Photo credit: Ahuva Weltman*

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.

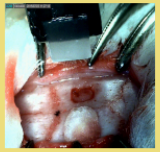

Figure 7: Insertion of our probe into a live rat. Probe was positioned carefully above insertion zones. We were careful to avoid contact between the insertion tool and cranium. PC: Ahuva Weltman, Leo Siow

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

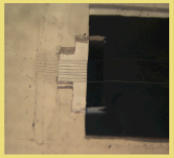

Figure 9: One of our PEG block models. We desired a slower melting rate for the PEG, thus we attempted to split the block into thirds. PC: Ahuva Weltman

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.

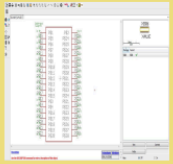

Figure 10: Schematic on Eagle software. Often the first step in fabricated a PCB. Thirty-four pins are visible in the diagram. which will eventually become a SSB6 plug. *Photo credit: Leo Siow*

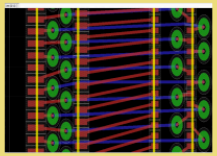

Figure 11: A broad view of a ZIF to SSB6 connector. Many traces are drawn. Interestingly, none of them are intersecting, due to the creative connection scheme in which both sides of the board is utilized. *Photo credit: Ahuva Weltman*

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