Carbon Fiber Microelectrode Array for Chronic Neural Recording in Mice

Progress Report

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Introduction

For our senior design project, team 12 is creating a manufacturing process for the carbon fiber neural recording array for Dr. Keith Hengen. The Hengen Lab's single-neuron chronic recording capabilities are currently limited by the low biostability of their nichrome microelectrodes, and they seek the development of a more biostable carbon fiber neural recording array that will enable long term (over 1 year) *in vivo* neural recordings. A previous BME senior design team designed a printed circuit board (PCB, Figure 1) for use with carbon fiber microelectrodes (CFMEs) in early 2019. However, this group was unable to design a process for manufacturing the CFMEs or attaching the CFMEs to their PCB. Many challenges are presented when working with CFMEs due to their small diameter of ~ 5 μm and lack of rigidity and structure. Our project focuses on the manufacturing of the CFMEs and the attachment of the CFMEs to the PCB. The outcome of our project will be a fully functioning CFME recording array that the Hengen lab can use for chronic neural recording of mice.

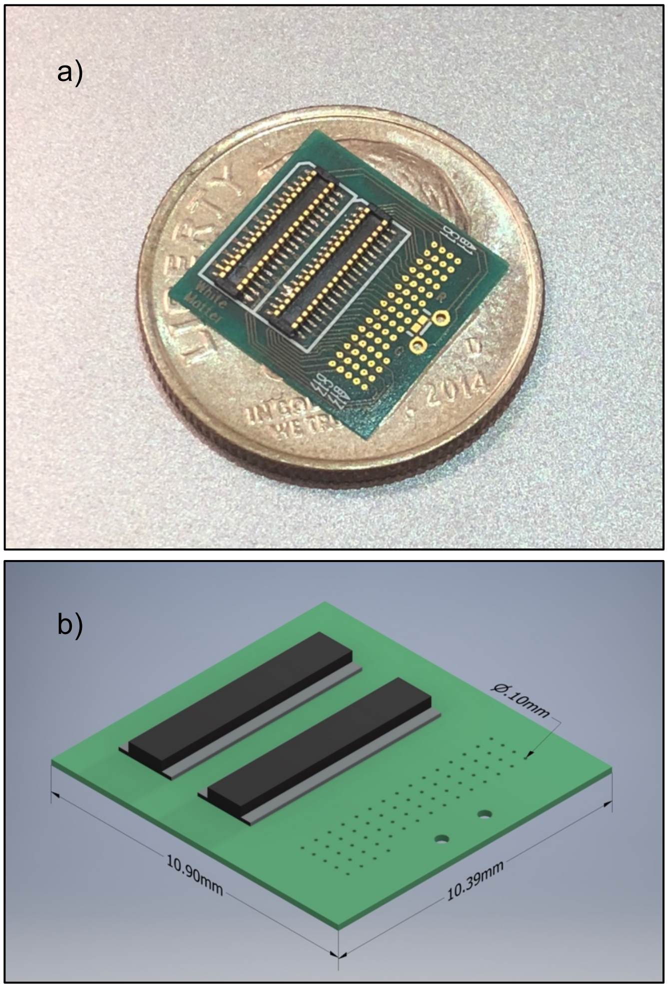

Figure 1: a) 64-channel PCB developed by last year's Senior Design Group. Shown on a Dime for reference. B) 3D CAD model of the PCB with exact dimension. Note the 64 "vias" on the right side of the board. These are where the 64 CFMEs are going to be connected. Also note the 2 larger vias on the right side – these are the "ground" and "reference" pins.

Updates from Preliminary Report

Since our preliminary report, we have not modified our Needs Statement or Project Scope. However, we have refined our design specifications and updated some of our group responsibilities and timelines.

As shown in the updated design specification table (appendix A), we refined the dimension specifications for the PCB. This change arose from more accurate specifications being discovered following detailed CAD modeling of the current PCB.

As shown in the updated team responsibility table (appendix B), we changed the general research lead from Luis to David. This change has given Luis more time to focus on CAD modeling, since the modeling has proven more challenging than expected.

Finally, we updated Gantt chart (appendix C) to more accurately reflect our work this semester and our expected timeline for the Spring 2020 semester. We added a time frame for working with the current CFME manufacturing process to get a better feel for working with the fibers and areas for improvement, specific tasks for testing coatings and 3D modeling, a time frame for communication with suppliers/manufacturers, and a more detailed overview of our goals in the spring semester to deliver our project on time.

Carbon Fiber Electrode Coatings

Coating Alternatives

Carbon microfibers are a very attractive alternative to traditional silicone or nichrome counterparts because their pliability and small diameter (~ 5 μm) leads to virtually no biological immune response when implanted in the mouse brain. However, this lack of structure and rigidity makes working with CFMEs very difficult. Thus, one design solution we pursued is a viable coating for the CFMEs to provide them with added rigidity during handling.

We investigated 8 alternative coating substrates and used a Pugh chart to compare our options (table 1).

Table 1: Pugh chart for various properties[1] of CFME coating substrates. Property weights were defined from a subjective point of view in creating the ideal coating to address our problem. Polyvinyl alcohol (PVA) scored the highest, followed closely by a sugar coating and agar coating.

Property	Weight	PEG 8000	Polyvinyl Alcohol	Calcium Alginate	Agar	PDMS	Collagen	Sugar
Cost	4	7	9	5	6	7	5	8
Curing Time	3	2	4	10	9	5	6	5
Health Risks/Safety	9	8	8	8	8	7	7	9
Biocompatibility	8	8	9	9	10	7	8	9
Mixing Time	4	6	5	9	9	5	5	8
Handling/Removability	8	5	10	9	8	1	2	9
Solvent	7	9	9	9	9	2	4	9
Thickness	5	1	9	7	6	4	5	9
Appearance	2	10	10	8	6	10	6	6
Stiffness/Rigidity	8	1	9	5	7	8	6	8
Heat Dependence	5	5	5	5	3	4	6	5
Availability	7	10	9	7	9	6	4	7
Density	4	10	10	8	10	5	5	9
Total Score	**N/A**	**465**	**620**	**562**	**582**	**390**	**392**	**598**

PVA and sugar coatings scored the highest in the Pugh chart analysis (table 1), and therefore we decided to do further research on these 2 coating substrates. PEG 8000 scored lower than other options, but the Hengen lab had it readily available so we decided to test PEG 8000 as well. Further research on PEG 8000, PVA, and Sugar coatings are summarized in table 2.

Table 2: Summary of polymer classification and properties.[2] These polymers describe the top 3 choices in producing a coating for CFMEs and some important metrics that dictate their use. Most important is the water solubility so that any coating can be removed before implantation.

Property	PEG	PVA	Sugar
Type of polymer	Polyether	Alcohol	Polysaccharide
Water Soluble	Yes	Yes	Yes
Cost	Low	Low	Low
Biocompatible	Yes	Yes	Yes
Rigidity	Low	High	Medium
Availability	High	High	Low

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[1] Sabu et al.

[2] IBID

Since Sugar didn’t seem to have any significant advantages over PVA, and because David, Brennan, Luis, nor anyone else in the Hengen lab had worked with it before, we decided not to continue testing sugar coatings. We decided to begin testing with both polyethylene glycol (PEG) and polyvinyl alcohol (PVA) for several reasons. PEG was trialed first because previous literature on CFMEs suggested it would serve as a viable solution and because the Hengen lab already stocked it. The Hengen lab stocks a high molecular weight PEG labelled as PEG 8000. PVA was also tested as an alternative because it has similar properties to PEG and has previously been used by Brennan in his work with the Huebsch lab, a biomaterials lab in the BME department at Washington University in St. Louis. PVA samples were provided by the Huebsch lab.

Another consideration with our CFME coatings was the application technique. One application alternative is dipping the fibers into a coating solution by creating a bath of the polymer solution and dipping fibers into the bath. Dipping the fiber allows for extended coating time, but it requires a large amount of solution and is often wasteful. A second coating application alternative is spraying the solution on the fibers. A significant advantage of spray coating is that the solution is broken into small droplets that can easily adhere to the carbon fiber. A disadvantage is that many coatings must be applied to build up a thick enough layer on the fibers.

Analysis of Coating Alternatives

We began by testing a PEG 8000 coating. First, a 10% PEG 8000 solution in dH2O was mixed and poured into a petri dish in order to qualitatively observe the dried gel. After multiple overnight drying steps, it was understood that the available molecular weight of the PEG does not gelate as expected. PEG 8000 instead forms a viscous fluid but is unable to crosslink to form a solid. Thus, PEG 8000 was treated as a failure until a lower MW could be attained and tested.

The next polymer we tested was polyvinyl alcohol (PVA). Nathaniel Huebsch in the BME department kindly lent us PVA to trial in coating the fibers. A concentration of 5% PVA was dissolved in deionized water for 3 hours at a temperature of 90º C to form a low viscosity, colorless liquid. The polymer gelates when given time to dry but can be stored in a sealed container indefinitely. We used syringes to submerge individual carbon fibers in the 5% PVA solution. However, the surface tension of the solution was too strong, and it flowed off of the CFMEs when we took them out of solution. Next, we attempted to atomize the polymer with a spray bottle. The 5% polymer solution was placed into a small spray bottle and sprayed onto individual carbon fibers. While there was improved droplet adhesion to the CFMEs through spraying vs dipping, the high viscosity 5% PVA solution didn't spray as smoothly as we had hoped, resulting in bubbles and inconsistent droplet size. To address this, we tried a 1% PVA solution with a lower viscosity. The 1% PVA solution sprays onto the fibers better but will produce a thinner coating and require more sprays than the 5% to achieve a full, functional coating.

Chosen Coating Solution

PVA will be used to coat CFMEs to increase their structure and rigidity and make them easier to work with. PVA's ease of use, biocompatibility, and water solubility make it the most attractive solution and contribute to its high score on the Pugh Chart (Table 1). Additionally, PVA is extremely cheap and available at many biomaterial labs. PVA coating will be done by spraying multiple coatings of a 1% PVA solution in dH2O with an atomizing spray bottle. Further testing is required to determine exactly how many spray coatings are needed to produce a full, functioning coating.

Jig to load CFMEs into a PCB

Loading Jig Alternatives:

It is crucial for us to create a device that assists with the alignment and insertion of the CFMEs into the PCB vias to speed up the CFME array manufacturing process. We have come up with multiple methods to assist with the insertion of CFMEs into the 64 PCB vias. Ranging from a simple funnel to a complex alignment jig, we brainstormed as many designs as we could, hoping that one will make loading CFMEs into the PCB easy and fast.

Our first alignment solution is a simple funnel to help align each CFME with its respective via. We would use a very thin plastic film to create the funnel. While we haven't identified an appropriate film yet, we will have to pay special attention to the interaction between the funnel and coated CFMEs. One pro to using a funnel design is the simplicity and ease of manufacturing the funnel. The big con of the funnel design, however, is that manufacturing is still done fiber by fiber for all 64 fibers on the PCB. This may result in long manufacturing times that might exceed the 1-hour specification.

Our second alignment solution is a grid that lays on top of the PCB to help align the fibers with their respective via (figure 2). The idea behind the grid is that the entry point for each

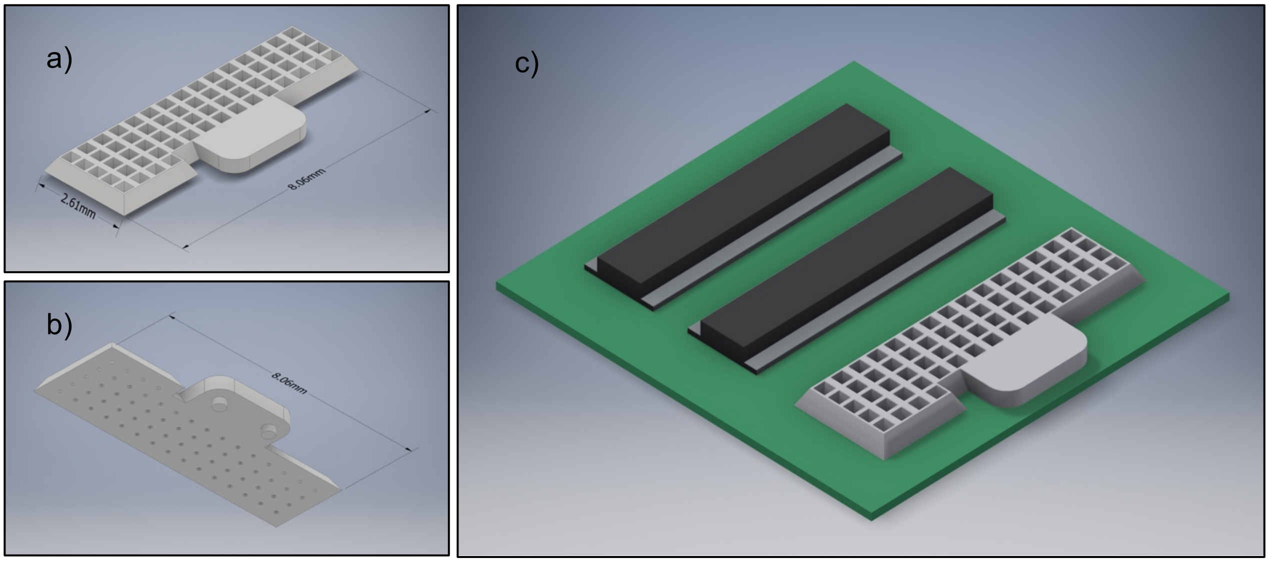


Figure 2: CFME alignment grid on a PCB. a) top view of the alignment grid. The larger openings that funnel down into the vias make inserting the CFMEs easier. b) bottom view of the alignment grid. Note the alignment pins used to correctly place the grid above the vias. b) alignment grid shown on model PCB.

CFME is much larger than the diameter of the via, which should make inserting the individual CFME much easier than inserting it directly into a via. Furthermore, the holes of the grid can potentially be used as a reservoir for holding solder paste or silver epoxy to help make the electrical connection between the CFMEs and PCB. Initial designs of the grid didn't have the alignment pins for the ground and reference vias. However, these alignment pins were added to help align the grid with the vias and to hold the grid in place while fibers are placed in the vias. In depth technical schematics and dimension for the grid design alternative can be found in appendix D. Manufacturing of the grid will be done by high resolution 3D printing or deep reactive-ion etching. Special attention will have to be paid to the material the grid is made of. The material must be strong enough to maintain its structure, but soft enough to be printed or ion etched. Furthermore, the material must interact favorably with the CFMEs with limited static interaction and no sticking.

Our third alignment solution is a 15-fiber alignment jig that will allow a full row of 15 fibers to be loaded at the same time (figure 3). The alignment jig consists of a flat board with 15 parallel grooves cut with the exact spacing as 1 row of vias on the PCB (figure 3a). 15 CFMEs will be placed in these grooves on the jig and fixed into place. The loaded alignment jig will be placed in the base (figure 3b), which aligns the jig perpendicularly with the PCB (also placed in the base, figure 3c). Perpendicular alignment between the jig and PCB is ideal to ease insertion of the fibers through the vias. With the PCB and alignment jig both in the base, the 15 fibers can be easily slid into their respective vias. Since the fibers are fixed to the alignment jig, it is easy to flip the whole assembly upside down and solder the CFMEs to the PCB. This loading and insertion process must be repeated three more times to load 60 CFMEs, then one final time with only the last 4 fibers. By loading full rows all at the same time, the manufacturing speed is increased compared to the funnel or grid solutions. Furthermore, you are only loading one row of fibers at a time which means you only have to worry about alignment in 1 dimension and the fibers won't be overcrowded. Lastly, the fibers are fully supported by the alignment jig at all

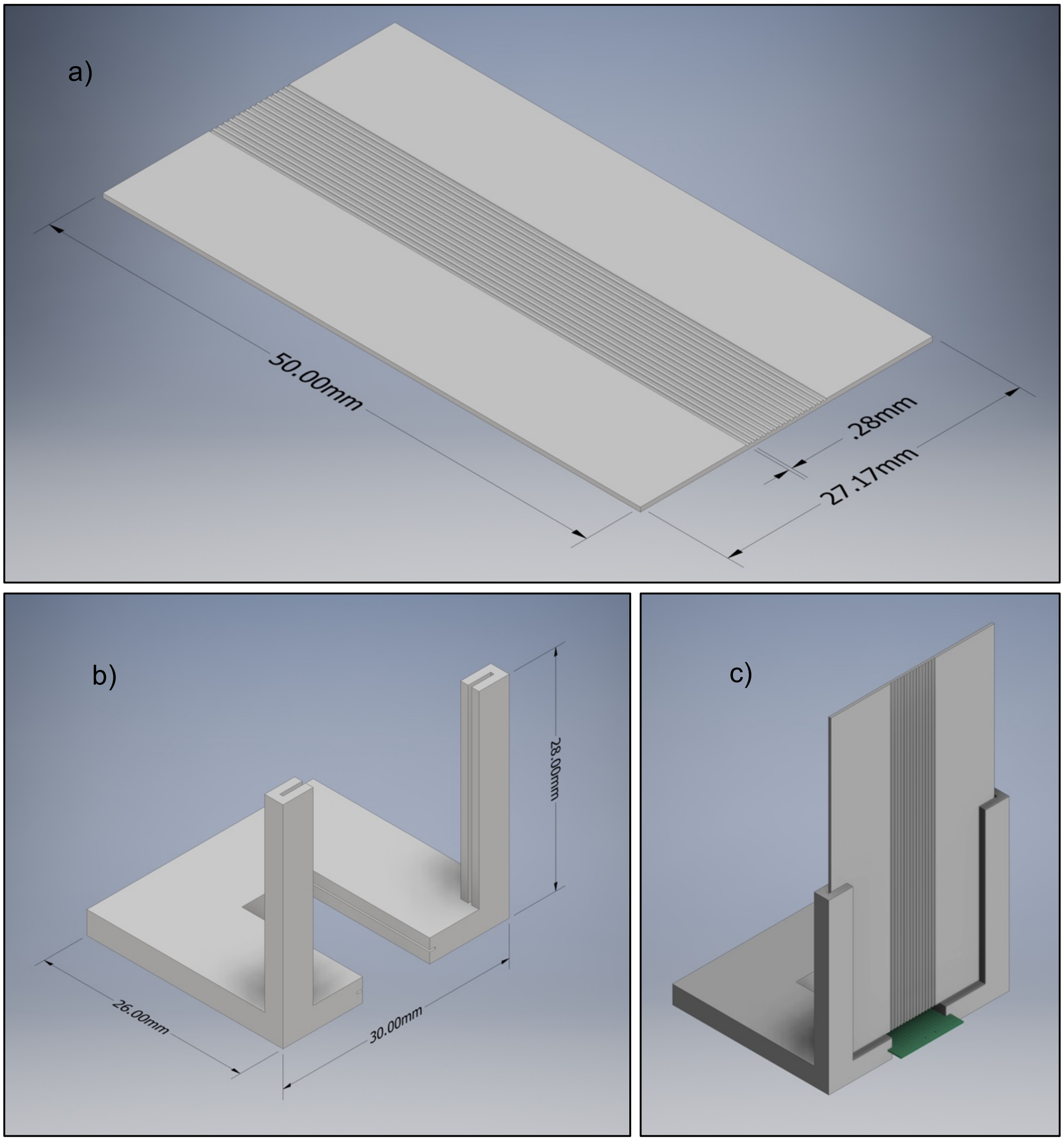


Figure 3: a) 15-fiber alignment jig. b) base. c) alignment jig and PCB in the base.

times, so you do not have to worry about the fiber flopping around while working with it. Manufacturing the 15-fiber alignment jig grooves will be done by deep reactive-ion etching. Manufacturing of the base will be done with high resolution 3D printing. Special attention will have to be given to the material that the 15-fiber alignment jig is made of so that it is able to be ion etched.

Analysis of Loading Jig Alternatives

We used a Pugh chart to analyze our 3 different loading jig alternatives (table 3). The most important factors in the Pugh analysis were the speed at which the jig would allow us to load the CFMEs into the PCB, the ease of loading the CFMEs into the PCB, and the feasibility of manufacturing such a device given the small tolerances needed. The 15-fiber jig scored the highest in all three of these categories, so it had the highest overall score in the Pugh analysis.

Table 3: Pugh Chart for the 3 loading jig alternatives we designed. The 15-fiber jig scored the highest, followed by the grid design.

Property	**Weight**	**Funnel**	**Grid**	**15-Fiber Jig**
Speed of Loading	4	2	4	8
Ease of Loading	4	2	4	7
Cost to manufacture	1	9	3	1
Feasibility to manufacture	5	9	3	7
Reusability	2	6	6	2
Total Score	**N/A**	**82**	**103**	**126**

The only way to fully test the functionality of these designs will be to make prototypes. We are planning to begin with a full prototype of the 15-fiber jig and move to the grid design if the 15-fiber jig fails. Unfortunately, our ability to test the 15-fiber jig in the Fall semester has been limited by the deep reactive-ion etching equipment in the WUSTL clean room being broken. Once the equipment is fixed, we will proceed with further testing to fully analyze the 15-fiber jig as an effective loading jig.

Chosen Loading Jig Solution

We have chosen to pursue the 15-fiber alignment jig as our loading solution. This is due to the high Pugh chart score and our overall optimism that this design is the best alternative we have at the moment.

Figure 4 shows more details of our CAD renderings of the 15-fiber jig, base, and loading process. As shown in figure 4b, the channels in the loading jig are much larger than the fibers. This is because the tolerance on the ion etching manufacturing process is much larger than the 5 μm diameter of the carbon fibers. To account for the fact that not every fiber will be aligned with the center of its channel, there is a small gap between the bottom of the loading jig and the PCB, which will allow space for manipulation to get each fiber into its respective via. Also, notice that the PCB can be slid deeper into the base to align the loading jig with each consecutive set of via rows. In depth technical schematics and dimension for the 15-fiber alignment jig and its base can be found in appendix E and F.

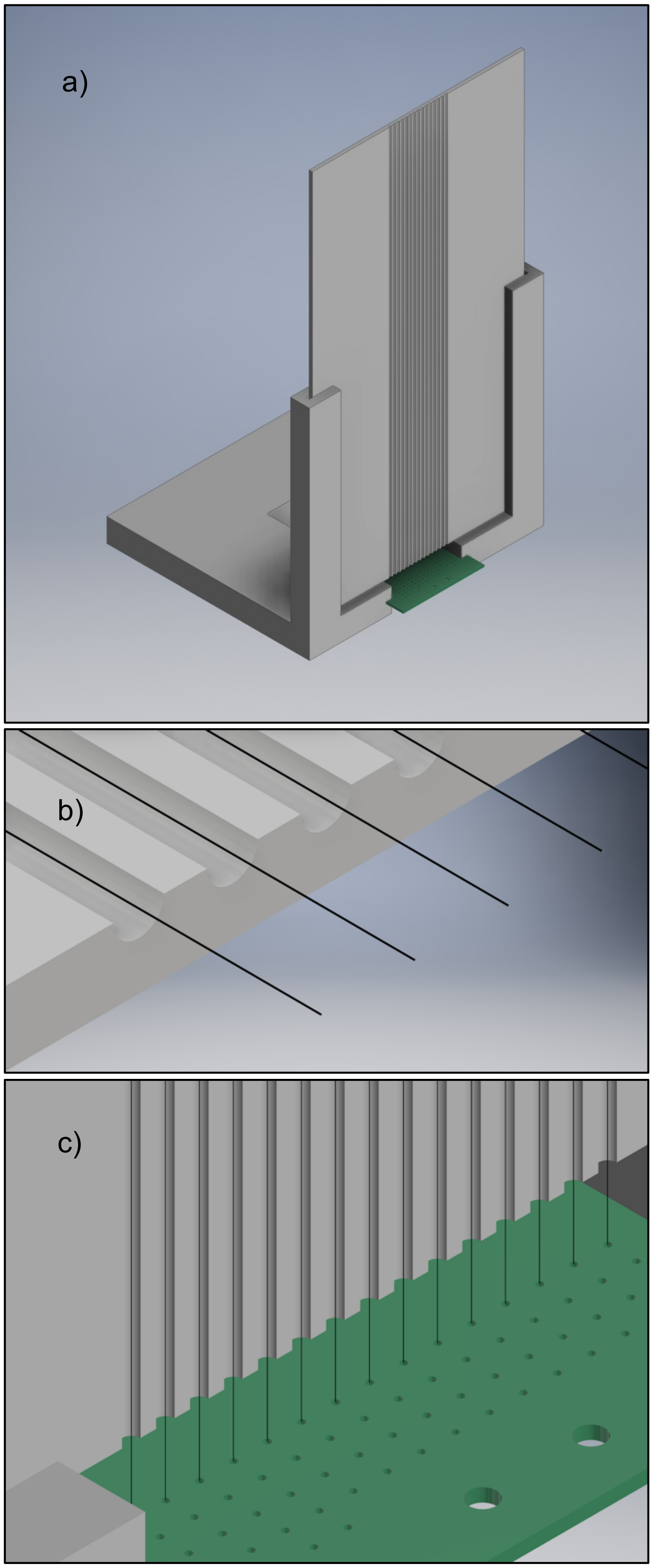


Figure 4: In depth look at the 15-fiber alignment jig solution. a) base with the 15-fiber jig and PCB in it. b) Detail of fiber in the loading jig. c) Detail of inserting fibers into the PCB.

Connecting the CFMEs to the PCB vias

Connection Alternatives

It is crucial for us to use a fast and effective method to electrically connect the CFMEs to the PCB vias. The Hengen lab has previously used silver epoxy to connect CFMEs to their old head stages. However, there are concerns of bridging across vias on the new 64-channel PCB with the current silver epoxy.

The first solution we have is to simply optimize the silver epoxy joining technique. Silver epoxy is a very attractive alternative to soldering for many reasons. First of all, silver epoxy can be administered through a very fine syringe which will provide much needed precision when working with the tiny vias. Second, no heating is needed so there will be minimal chance for damage to the PCB or CFMEs. Lastly, the setting process is quick (under 5 minutes) meaning that we can rapidly join CFMEs in a timely manner. Ways to optimize the current silver epoxy process is to use a more viscous epoxy to prevent bridging between vias.

Another solution is to use some type of reflow soldering to join the CFMEs to the PCB vias. One advantage of reflow soldering is that the solder paste can be applied and taken off before the connection becomes permanent. One big disadvantage is that the entire assembly will have to be heated and cooled every time we wish to form a connection, which may significantly increase manufacturing times.

Analysis of connection alternatives

We have not yet tested silver epoxy or reflow soldering since the electrical connection step comes after the insertion of the fibers into the vias, which we have not yet solved.

Chosen connection solution

We are hoping to optimize the use of silver epoxy as opposed reflow soldering for several reasons. The primary reason we chose silver epoxy is the speed at which we can make the connection (< 5 minutes hardening time) is much faster than that of reflow soldering. Second, we believe the precision that comes with using a syringe to apply the epoxy is high enough to avoid bridging between the vias. Lastly, silver epoxy does not require repeated heating and cooling to form a solid physical and electrical connection like reflow soldering, which we believe will minimize the chance of damage to the CFMEs and the PCB.

Budget Proposal

If successful, our project will bring many novel neural recording opportunities to the Hengen lab. Dr. Hengen has already invested significantly in the design and production of the 64-channel carbon fiber PCB, designed by last year's Senior design team. Dr. Hengen is willing to invest up to $10,000 in the development of our manufacturing process to make the 64-channel carbon fiber neural recording array a reality.

Although we have significant funding from Dr. Hengen, we believe our costs will be below his $10,000 budget. We have outlined an estimated budget for our project in table 4.

Table 4: Proposed Budget for our first prototype.

Item	**Description**	**Price Estimate**
PVA	PVA used for coating. A few hundred grams needed.	$20
Atomizer	Spray bottle for application of PVA solution. 20 mL	$10
Jig Base	3D printed Jig base, outsourced to https://realizeinc.com	$100
15-fiber Jig	Materials and Cleanroom time	$500
Silver Epoxy	Conductive epoxy to be used to make electrical connections	$50
Other Costs	Fiber manipulation tools needed or other costs	$50
Total	**Best guess estimate for total project budget**	**$730**

Two major costs will be the manufacturing of our 15-fiber alignment jig and base. The base will likely have to be outsourced to Realize Inc., a 3D printing company that the Hengen Lab has worked with in the past. Outsourcing will be necessary due to the high resolution needed for the part. Our estimate for the price of the 3D printed part comes from past small 3D printed parts the lab has ordered from Realize Inc. However, the actual price of these prints will not be known until we receive a quote from Realize Inc. for our specific part with the correct material, resolution, and fill density.

Another high cost will be the development of our 15-fiber alignment jig with deep reactive-ion etching. First, we will need to invest in the wafers that constitute the body of the alignment jig. Second, we will have to pay to use the WUSTL clean room and deep reactive-ion etching technology. We might have to produce a high quantity of these alignment jigs because we do not know if they will be reusable.

The next step for our team will be reaching out to manufacturers and the clean room to request quotes for the 2 parts described above (appendix C). Once we have these quotes, we will bring forward a more accurate budget proposal for Dr. Hengen before we proceed with ordering the parts to build and test our first prototype.

References

1. Thomas, Sabu, et al. Fundamental Biomaterials: Polymers. Woodhead Publishing, 2018.

Appendix

Appendix A:

Appendix A: Updated design specifications (changes highlighted in green). After creating detailed CAD models for the CFME PCB, we refined the dimension specifications for the PCB.

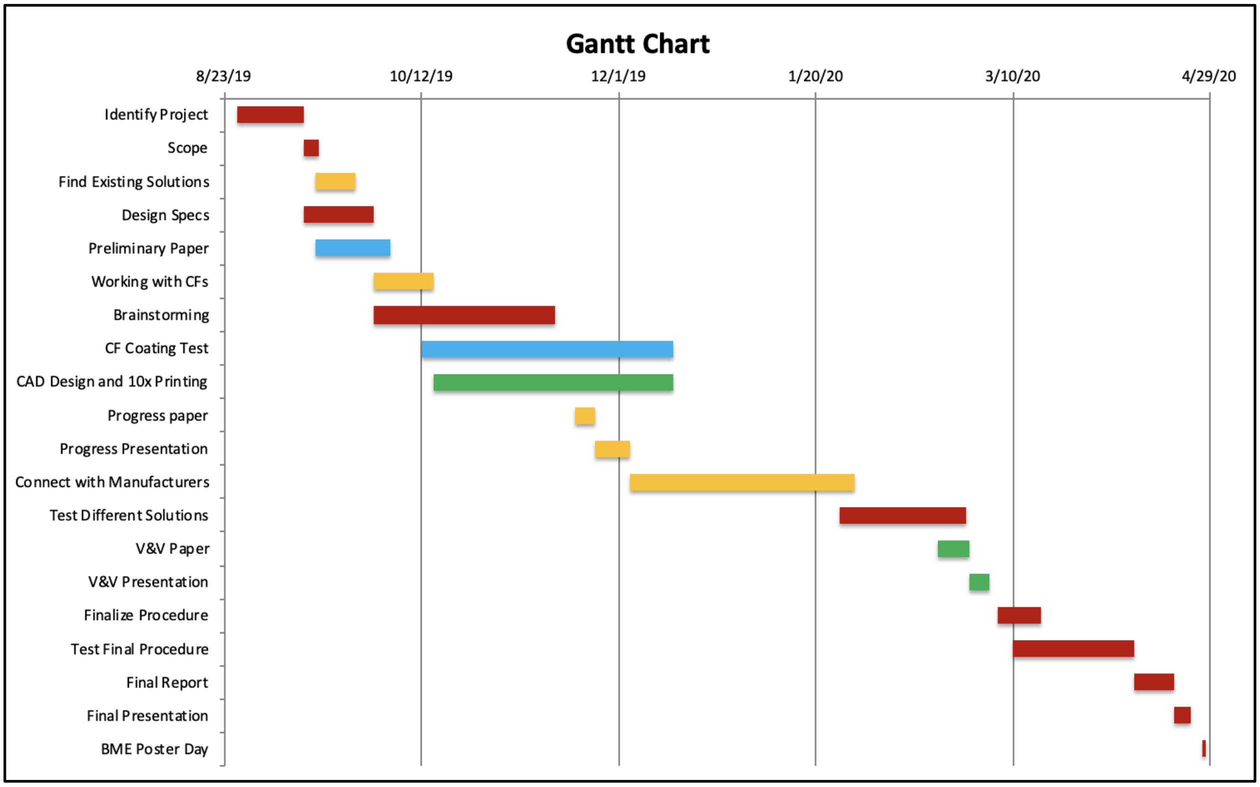
Specification	Metric
Cost of Development	< $10,000
Number of Available Recording Channels	64 channels per PCB - 512 for 8 stacked PCBs
Channel Functionality	64/64 channels function properly per PCB
# of PCBs that can be stacked	8 PCBs with one headstage (512 channels total)
Headstage compatibility	Any redesigned PCB must remain compatible with the current stackable HS-640 E-cube headstage system
Time to manufacture 1 functional PCB (64 channels)	< 1 hour
Single PCB mass	< 5 grams
Single PCB length	< 10.4 mm
Single PCB width	< 10.9 mm
Single PCB height	< .68 mm
Electrode Biological Response	No glial scarring around carbon electrodes
Electrode Functional Time Course	Electrodes must be able to record properly for longer than 1 year

Appendix B:

Appendix B: Updated team responsibilities (changes highlighted in green). After beginning the project, we changed the general research lead from Luis to David. This change has given Luis more time to focus on CAD modeling, since the modeling has proven more challenging than expected.

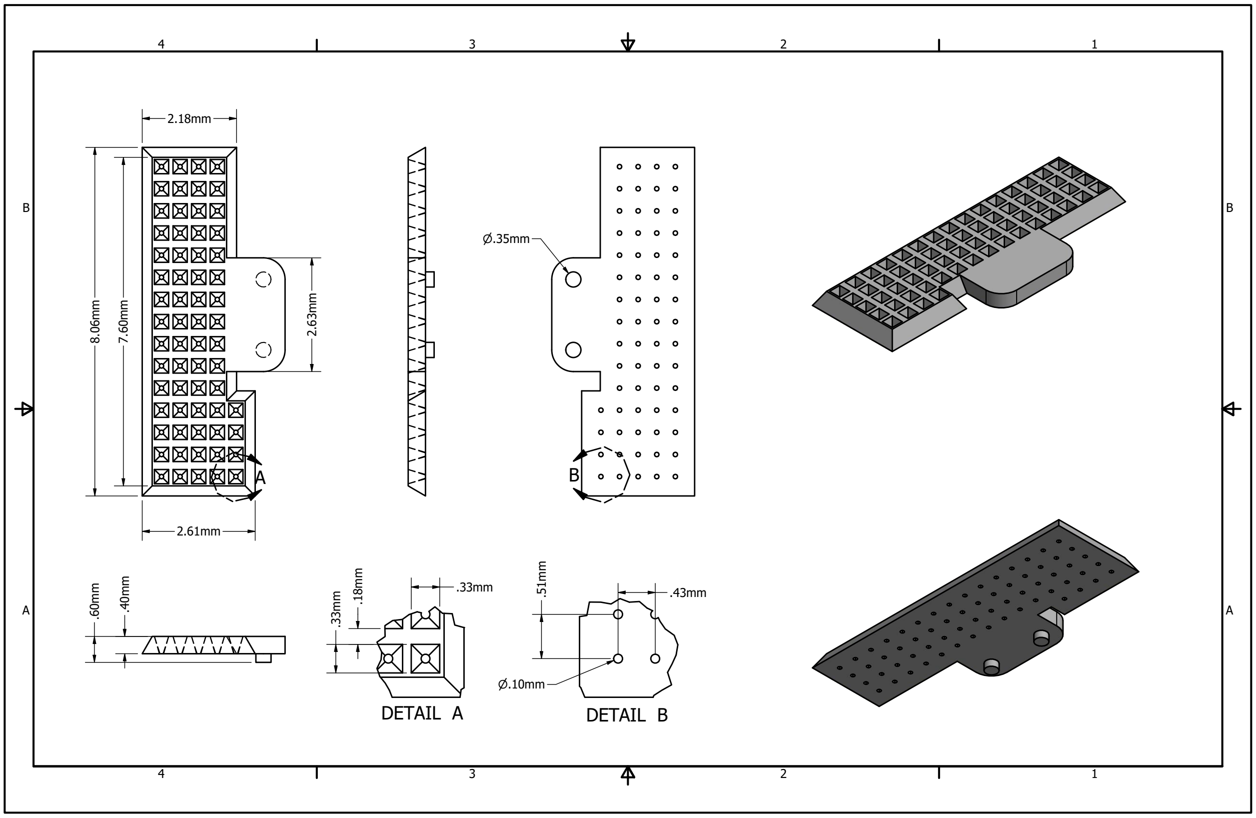
Category	Task	Team Member
Administrative, Note-keeping, Presentations	Scheduling	Brennan
	Communicating with Dr. Hengen	David
	Notebook Updating	Luis
	Weekly Reports	Brennan
	Prelim Report and Presentation	Brennan
	Progress Report and Presentation	David
	V&V Report and Presentation	Luis
R&D	General Research	David
	Materials Research and Testing	Brennan
	PCB Modifications	David
	3D Modeling	Luis
Manufacturing	Communication with Suppliers	David

Appendix C:



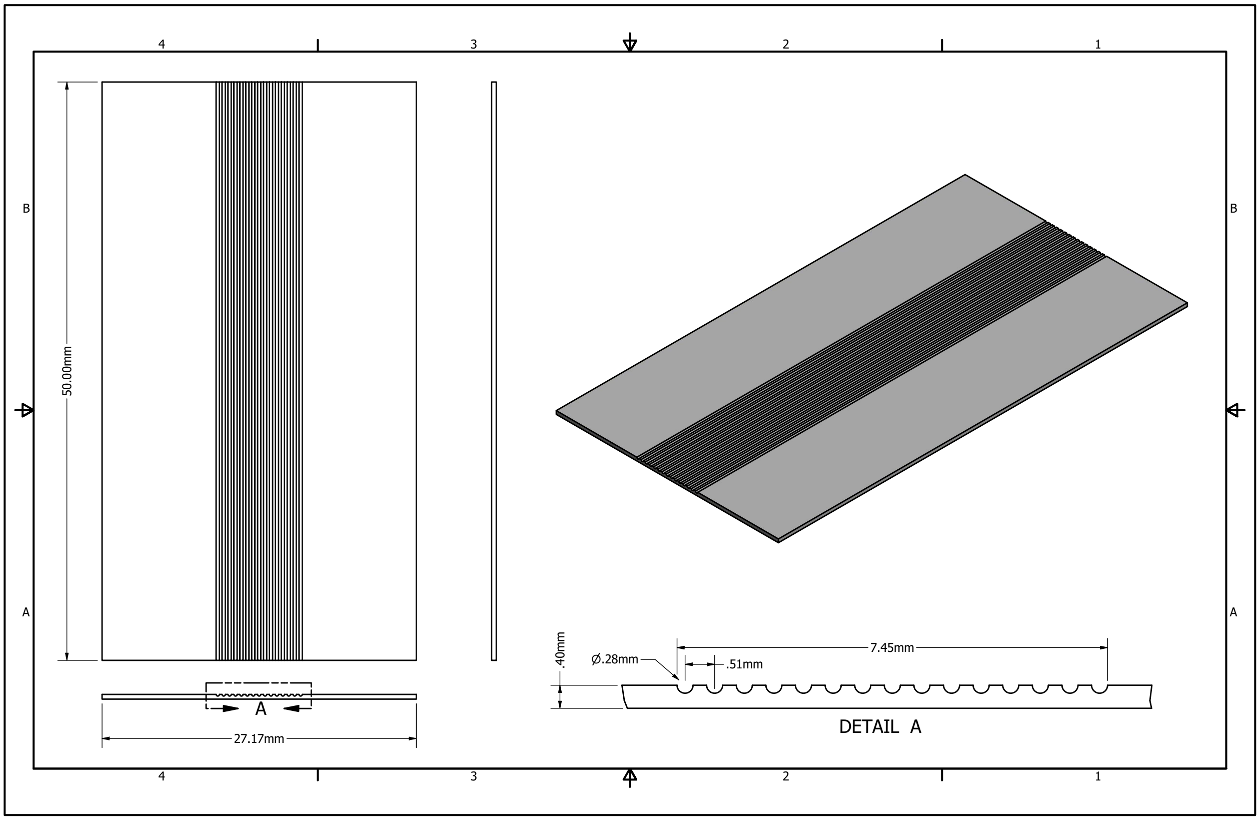
Appendix C: Updated Gantt Chart (Luis, David, Brennan, All). Changes to our Gantt chart include time for working with the current CFME manufacturing process to get a better feel for working with the fibers and areas for improvement, specific tasks for testing coatings and 3D modeling, a time frame for communication with suppliers/manufacturers, and a more detailed overview of our goals in the spring semester.

Appendix D:



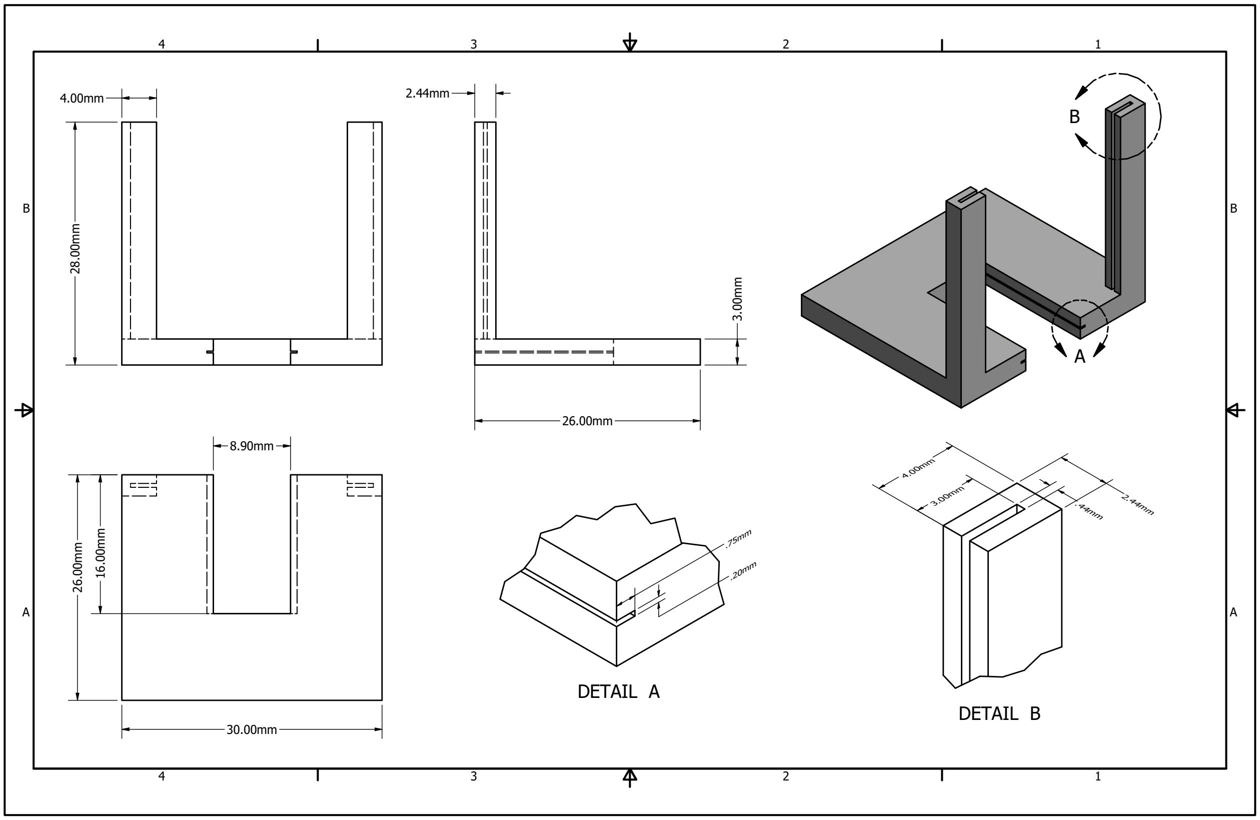
Appendix D: Technical schematics for the grid alignment solution.

Appendix E:



Appendix E: Technical schematics for the 15-fiber alignment jig.

Appendix F:



Appendix F: Technical schematics for the 15-fiber alignment jig base.