Pinpoint: Electrophysiology Planning and Automation Tool

Our brains hide the mysteries of their inner workings in a black box. One effective method to pierce through and uncover the secrets to our cognition and its ailments is known as electrophysiology. Electrophysiology is the process of using electrodes placed inside the brain to record electrical activity. When cells in the brain communicate, they give off electrical signals which can be recorded by electrodes to provide insight into brain function. To precisely target brain regions, neuroscientists rely on anatomical atlases and experience. Yet, even with intense training and expertise, neuroscientists can often accidentally miss their target region[i]. This process is also hindered by inter-animal variability and obstacles such as blood vessels or other probes. Think of a time you reached into a bag to grab something. Sometimes, you could not see what you were doing and had to just feel around and guess. My project, Pinpoint, is a platform aimed at helping neuroscientists tackle these difficulties and speed up their electrophysiology experiments.

Currently, scientists rely on software such as the Paxinos Atlas for Mice[ii] and the Neuropixels Trajectory Planner[iii] for planning experiments, but these tools do not aid in conducting experiments. Pinpoint improves the experiment planning and execution experience by providing scientists with a 3D interactive model of the brain, real-time probe position visualization, and multi-probe insertion automation. These features enable scientists to view their targets in the brain and conduct simultaneous recordings across multiple regions, revealing hidden interactions missed by traditional single-region recordings.[iv] (see an example of a multiprobe insertion visualized in pinpoint in fig. 1). Over the Summer of 2022, I developed a system that enabled Pinpoint to interface with electrophysiology manipulators like the Sensapex uMp Micromanipulators. I designed a server application that utilizes standardized web technologies like WebSockets to allow the manipulator-controlling computer to connect directly to Pinpoint. This system enables scientists to view in real-time the positions of probes inside the brain while driving them in real life (see Pinpoint connected to a live manipulator in fig. 2). During the Fall of 2022, I added manipulator control and automation functionality to Pinpoint, enabling scientists to simply press a button and allow Pinpoint to automatically move probes to desired insertion points. Now with the tools to visualize and automate probes, the next step in the development of Pinpoint is to aid scientists in coordinating these probes to perform complex multi-probe electrophysiology experiments.

My goal for this quarter through the Summer of 2023 is to develop and refine a user experience in Pinpoint that can help scientists orchestrate complex multi-probe insertions for brain-wide recordings. On average, setting up an electrophysiology rig and positioning probes manually can take 30 minutes to an hour. While the features we have now already help make the experience smoother for one or two probe recordings, our goal is to cut that time in half or more once experiments start to scale up to three, four, or more probes in simultaneous brain-wide recordings. My work will focus on collaborating with other scientists to build the best experience for their experiments. This will involve building out user interfaces, testing them in live recording sessions, and getting feedback from scientists on how well they felt Pinpoint accelerated their experiments. For many scientists, Pinpoint will be the tool that makes multi-probe recordings possible for them. I will focus on sharing Pinpoint with other scientists outside of the Steinmetz Lab to gain their feedback on how Pinpoint can be used to accelerate their electrophysiology experiments. For instance, the Steinmetz Lab is a member of the International Brain Lab (IBL). Through the IBL I will connect with many more labs worldwide and enable them to conduct more advanced electrophysiology experiments. Gaining feedback from scientists on ways I can tailor Pinpoint to speed up their workflow is how I will be able to make Pinpoint a more effective tool for all neuroscientists.

Pinpoint is being developed as open-source technology with collaboration in mind. My project mentor Dr. Daniel Birman and I worked on software features both independently and together in pair programming sessions. As open-source software, the project is also designed to allow anyone else to contribute and expand upon Pinpoint for their needs. Many software tools in academia are one-off tools a single scientist developed for their project. Over time, these tools became obsolete, and no developers stayed to help maintain and support them for other labs. Pinpoint was designed to be an open and flexible platform capable of connecting with any lab's equipment and any electrophysiology workflow. Dr. Birman and I often accompany other scientists doing recordings in the Steinmetz Lab to get feedback on how useful the current iteration of Pinpoint is and if there are any features we should consider adding. We regularly advertise Pinpoint at conferences and workshops, and I was recently able to help run a demonstration of my automation tools during the Allen Institute Neuropixels Course in August of 2022. During the course, I showed about three dozen participants how Pinpoint can be used to automate their experiments. In November, I co-authored a poster on Pinpoint which was presented at the Society for Neuroscience (SfN) conference in San Diego. This event introduced Pinpoint to an even wider audience and gained us new users for the platform. Both events generated significant enthusiasm for the potential Pinpoint can bring to electrophysiology and neuroscience research.

My plan for funding received through this scholarship is to help provide financial security for my undergraduate education. This will allow me to focus more of my time and energy on research rather than seeking out other part-time jobs and internships. I consider research an important aspect of my college education and a source for me to learn about fields outside of pure computer science. From this research project, I hope to gain experience and practice in developing something that makes an innovative impact. I came to UW as a computer science student who wanted to get involved in research. In the world of computer science, developing something new is often driven by its revenue potential rather than its value to the community. My interest in computer science and technology stems from my drive to solve problems and inefficiencies in the world around me. I wanted to get myself involved in research because research is how real groundbreaking innovations happen. Working on Pinpoint has allowed me to contribute an innovative solution to the neuroscience community. I have also gained experience iterating a product with researchers, learning about what scientists need, and understanding the general workflow of the research world. These are valuable tools for me going forward in my education, computer science, and research career.

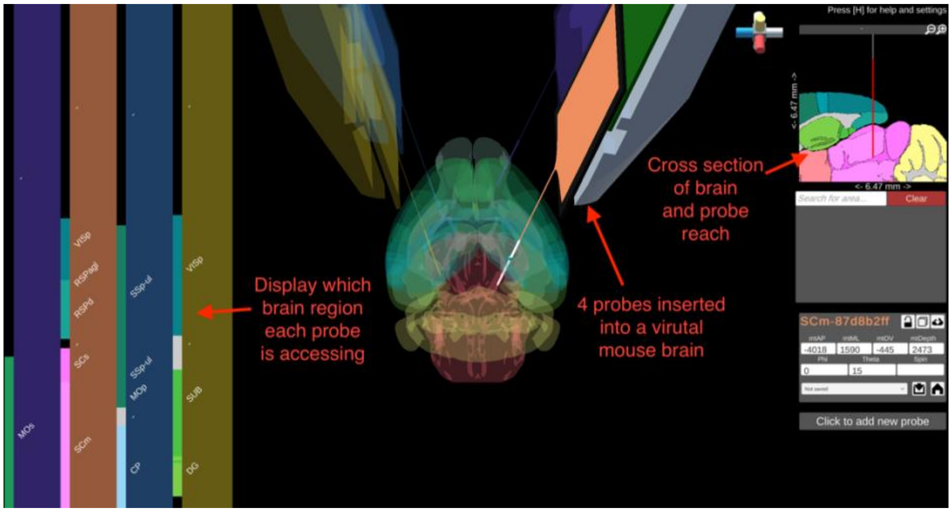

Figure 1 - Screenshot from Pinpoint demonstrating a four-probe multi-region recording setup. In the center is a virtual brain with four color-coded probes inserted at various locations. On the left is a panel displaying what brain regions each probe is accessing. On the right is a panel displaying information for the currently selected probe (in this image the orange probe is selected).

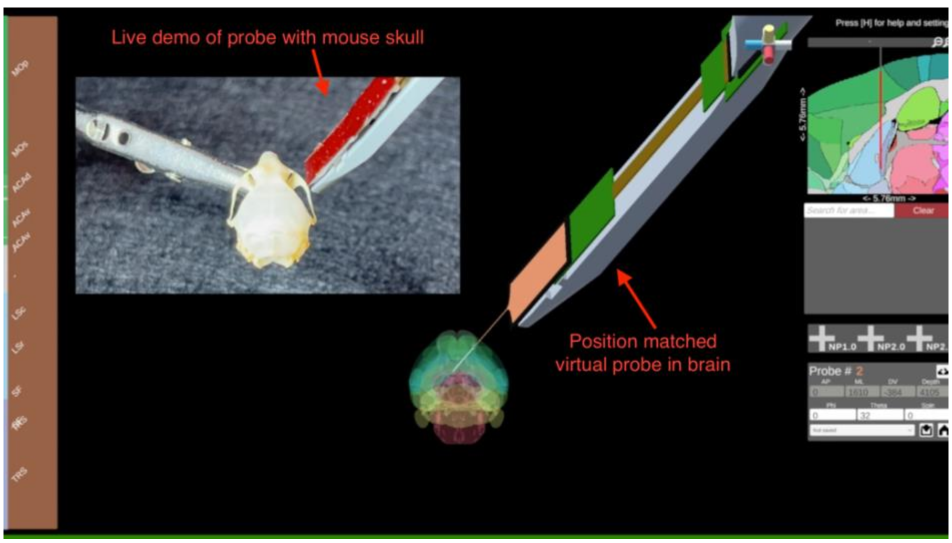

Figure 2 - Screenshot from a Pinpoint demo video. The orange probe is connected to a live manipulator which is being moved around to demonstrate an insertion into the brain. The movements in real life are being reflected by the virtual probe with details regarding which brain regions are accessible being displayed on the panel to the left. A cross-section of the brain is visible to the right. See the full demo here: https://www.youtube.com/watch?v=_dGe-PESiE0.

[i] International Brain Laboratory, Banga, K., Benson, J., Bonacchi, N., Bruijns, S. A., Campbell, R., Chapuis, G. A., Churchland, A. K., Davatolhagh, M. F., Lee, H. D., Faulkner, M., Hu, F., Hunterberg, J., Khanal, A., Krasniak, C., Meijer, G. T., Miska, N. J., Mohammadi, Z., Noel, J.-P., … Witten, I. B. (2022). *Reproducibility of in-vivo electrophysiological measurements in mice* [Preprint]. Neuroscience. https://doi.org/10.1101/2022.05.09.491042

[ii] Paxinos, G. F. K. T. M. B. S., & Franklin, K. B. (2004). The mouse brain in stereotaxic coordinates: compact. *Amsterdam, Boston: Elsevier Academic Press). Pazos, A., Cortes, R., and Palacios, JM (1985)*

[iii] Peters, AJ. (n.d.) Neuropixels Trajectory Explorer. https://github.com/petersaj/neuropixels_trajectory_explorer

[iv] Steinmetz, N. A., Zatka-Haas, P., Carandini, M., & Harris, K. D. (2019). Distributed coding of choice, action and engagement across the mouse brain. *Nature*, *576*(7786), 266–273. https://doi.org/10.1038/s41586-019-1787-x