Harvard Medical School Research

On a superficial account, the brain contributes to the adaptive success of animals through the control and coordination of effector organs like muscles. Survival of an animal requires the timing of effector activation to bear some relation to purpose: “An animal must contract its jaw muscles when its jaw contains something worth biting and contract its leg muscles when there is something worth running to or away from.” <br>

However, as the environment that animals interact with becomes more complex, the decision for current action very often depends on past sensory information no longer present to the animal. Foraging rodents need to remember which patches were already searched to save energy, and humans need to remember where to reach their fingers each morning for their car keys. Both humans and animals demonstrate the ability to use past experiences to plan and simulate future actions, which are important characteristics for higher order brain function and complex decision making. <br>

My work at Lee Lab as a research assistant models these tasks to study memory recall and imagination in the rodent model system. We train mice and rats to perform spatial navigation tasks that require them to either actively recall past experiences or imagine possible future scenarios. During behavior, we record from them using multisite silicon probes and population calcium imaging. The data we collect is then interpreted with an array of methods simple and complex, including anything from firing rate analysis to RNN-based experiment variable decoders.

My current project uses a T-maze based DNMTS (delayed nonmatch-to-sample) task to study how working memory information is maintained through long delay period in rodents. The task requires the subject to remember a sample stimulus over a long delay and then choose a novel nonmatching option when presented with the sample and a new alternative. In the T-maze setting, both sample stimulus and the new alternative are navigation targets equipped with reward ports. We record from free moving animals during experiment to obtain large-scale electrophysiological data, and we look for reliable patterns that appear consistently during delay period that signals the sample stimulus. An interesting method that I’ve implemented for the analysis uses a LSTM-based decoder architecture and a special loss objective that classifies the animal’s location while differentiating the spatial geometries of different classification target. This makes the model aware of the consequences of different classification errors that reflect the spatial geometry of the maze’s layout. The model was able to improve by 2.4 times on evaluation metrics and converge faster in training, which is helping us to both detect representation of future navigation goals and past navigational experience in mice.

UCLA Summer Research

Knowing the structure of the brain is essential for understanding how neural circuits give rise to behavior. In recent years we saw many examples where connectomics datasets reveal previously unknown pathways and motifs of communication that helps to explain circuit computation and population activity in system neuroscience.

In the summer of 2023, I was awarded the UCLA Neuroscholar Scholarship for undergraduate summer research opportunity at the Dong Lab (Dr. Hongwei Dong). Dong Lab, or the UCLA Brain Research & Artificial Intelligence Nexus (B.R.A.I.N.), is dedicated to constructing a comprehensive, mesoscopic mouse connectome employing multidisciplinary approaches including genetics, 3D imaging, artificial intelligence, and advanced histological. Mentored by Dr. Nicholas Foster, my summer’s project used virial tracing methods to investigate the connectivity of the subthalamic nucleus (STN). The synaptic projection pattern in basal ganglia is especially interesting because, unlike other regions, it’s composed of recurrently connected nuclei with highly specialized input–output relationships. STN is the main modulator of basal ganglia output and an important deep brain stimulation (DBS) target. In our review of past literature, we found that previous studies of STN afferent projection using chemical tracers were prone to inconsistent results, where retrogradely labeled regions couldn’t trace back to STN when they were injected with anterograde chemical tracers. To address this non-specificity, we used a viral tracing construct known as TRIO, targeting STN and its main input source substantia nigra pars reticulata (SNr). This construct uses a clever combination of retrograde tracer with Cre expression system to restrict the expression of fluorescence reporter to a specific path of projection. It enables trans-synaptic input tracing from specific subsets of neurons based on their projection and cell type, which avoid false positive signal from injection leaks.

Our result from the summer contributed to addressing the inconsistency from previous publications, and additionally also identified new anatomical structures connected to STN. We also found initial evidence of internal organization in several structures including globus pallidus external segment (GPe) and caudoputamen, where neighboring regions in those structures demonstrated distinctive connectivity patterns. These findings were presented in an abstract at a conference event to the department at the conclusion of the event.

Cornell Undergraduate

During undergraduate, I’ve been working at the Bass Lab (Professor Andrew Bass) with a novel model organism for multiphoton imaging in system neuroscience : Danionella dracula. This miniature teleost fish species is a close relative of zebrafish that not only remains transparent throughout its lifetime but also lacks a skull roof, making them an attractive model for optical neuroimaging studies of brain function. The projects I was involved in addressed their social structure, brain development, and neural activity mapping.

The very first research project I contributed to in the lab was a neurobehavioral study to characterize social interactions in the species so that we could develop suitable behavior paradigms. We analyzed the interaction between Danionella adult males to see how often an individual directed or received aggression from another male. During aggressive interactions, males extend their hypertrophied lower jaw and make sounds as an integrated aggressive display. Our data demonstrated a sophisticated hierarchical social relationship with aggressive “higher-ranking” individuals gaining more frequent access to spawning sites in the tank than “lower-ranking”, less aggressive conspecifics. In 2022 summer, I stayed at Cornell during summer break to work on another project in the lab to investigate the development of different brain regions in Danionella dracula. Working with Dr. Rose Tatarsky, a graduate student at the time, we employed three-photon microscopy to image the entire CNS of intact Danionella. This method required no physical intervention other than simple mechanical stabilization. With anatomical landmarks, we can identify the boundary between different brain regions in 3P imaging data, which enable us to use contour tracing and volumetric estimations to quantify how different brain regions increase in size across time. A particularly interesting result was that we were able to demonstrate that the emergence of specific behavioral patterns (e.g., aggressive displays) correlates with the rapid growth of certain brain regions. My last research project before I graduated in 2024 investigated sensory responses in the Danionella dracula telencephalon to construct a sensory map for the Danionella brain, relying on the fact that sensory representation is often topographically organized in these species. I’ve initially been helping to conduct viral vector injections to establish a transgenic line expressing pan-neuronal GCaMP, but achieving homogeneous expression across the brain has proven challenging. To guarantee that the activity readout is not confounded by uneven GCaMP expression, I am instead employing an alternative endogenous activity marker known as phosphorylated extracellular signal-related kinase (pERK); pERK concentration has been shown to correlate strongly with GCaMP activity in larval zebrafish. Leveraging pERK immunostaining, I am identifying what regions are stimulated when we present light, acoustic, and lateral line stimuli.

High School Research

My early interest in biological science was more general, and I was involved in research projects of very different topics, including molecular genetics of neuronal regeneration, animal courtship behavior, and wildlife conservation & ecology.

At Sichuan University, I investigated how metformin, a type-2 diabetes medicine with a nuanced profile of therapeutic benefits, affects the neural system repair of a highly regenerative flatworm species called planaria. With a team of three highschool researchers, I treated groups of planaria to different concentrations of metformin and observed their neural system repair through immunostaining. To further explore metformin’s operating mechanism, we consulted publications and found GSK3β/Wnt, a possible biomolecular pathway through which metformin affects the regeneration process. To test this hypothesis, we blocked the pathway and discovered metformin could no longer affect neural system repair. This evidence suggests that GSK3β/Wnt is a major biological pathway for metformin.

In the Emei mountains, where the habitat of the Rana Daunchina frog lies, I assisted two graduate students with their behavior research. The study used sound playbacks to examine what pattern of mating call do female frogs prefer to explain why animals share a preferred sound pattern. To make sure the experiment would be conducted during their natural mating time, I adjusted my bio-clock to a more nocturnal awake cycle. I captured the frogs that we used in experiments each morning before I went to sleep, and I woke up in the late afternoon to prepare for the experiments at midnight. Our results showed that not only are the females highly selective in their mating call preference, the structure of male-built nests changes the male’s mating call acoustically to match the female’s preferred frequency profile.

Under the invitation of a professor from the National Department of Biology-Sichuan Division, I joined a sponsored research team to Tangjiahe National Reserve. The purpose of the trip was to analyze how local animal populations changed their navigation and spatial distribution in response to local tourist constructions. We used mapping software to survey how the population distribution of indicator species like reptiles and snakes has changed due to human construction. We also installed infrared cameras to trace the Takin population, a gentle animal that looks like a sheep with a buffalo head. With special government permission, we were able to enter restricted nature zones. Our report gave park officials information to build new fences and better protect local wildlife.

POMDP Research

Navigation-based delayed nonmatch-to-sample task (DNMTS) is the classical behavioral paradigm in rodent model systems to study working memory, decision-making, and cognitive flexibility. One approach to understanding how the brain solves such tasks is to employ reinforcement learning agents as mathematical proxies for neural computations, under the assumption that any agent—biological or artificial—must share core computational characteristics to successfully perform the same cognitive task.

To this end, I implemented and training agent on a custom OpenAI Gymnasium environment that simulates the T-maze–based DNMTS task that our animals run on real laboratory experiments. Consistent with the structure of the DNMTS paradigm, I formalize the task as a partially observable Markov decision process (POMDP), reflecting the fact that the agent has limited access to the full environment state and must rely on memory and inference to perform correctly. The agent receives observations about its spatial location, audio tone information, and taste information. The spatial information, which was initially designed as one-hot vector encoding in a grid world, is modified to simulated place cell (gaussian bump model) / grid cell (cosine interference model) population activation (after the realization that one-hot vector encoding can be simply regarded as place cell activity with extremely sharp place fields). The agent obtain reward from successfully completing the navigation tasks, explorative behavior, thigmotaxis, and gets penalty for timing-out and energy expenditure. The environment code handles time-out, which is when the animal has prolonged episodes of actions without achieving the criterion for phase transition, and wrong-choice, which is when the animal chooses the wrong arm at task phase. The environment can be executed in terminal rendering mode for training, and it is also rendered visually with PyGame graphics. This allows the behavior of the agent to be visualized on the maze and also allow human interaction with the environment.

Because the task is complex and the observation histories can span long sequences, I am employing the DQN algorithm with architectures such as LSTMs and transformer-based agents to capture temporal dependencies and support effective decision-making. The LSTM is explicitly designed with two “pathways”: the cell state (long-term memory), and hidden state (short-term memory). This architecture allows us to look for how activation in these two states progresses as the agent behave to understand how past observation is kept alive.

Undergraduate Projects

During my undergraduate period at Cornell, I was involved in a range of different programming projects that involves topics from simulating canonical spiking neural network circuits to designing RISC-V CPU circuits with logic gates. These projects allow me to think thoroughly about implementation details that in return allow me to grasp a better understanding of the inner workings of biological and artificial circuits. More importantly, I acquired the skills to do the analysis and simulation work that I now perform in my analysis of high-dimensional neural dynamics.

In the computational neuroscience domain, my simulation projects involved using standard SNN (spiking neural network) paradigms—such as leaky integrate-and-fire (LIF) and McCulloch–Pitts (MCP) neurons—to construct canonical network motifs such as oscillatory circuits and Hopfield networks. An example would be the Hopfield network, an auto-completion model of hippocampus that, which provides content-addressable memory to retrieve a pattern from noisy input. In the computer architecture domain, I’ve constructed a complete CPU logic circuit based on the 32 bit RISC-V instruction set architecture, an open-source CPU programmable interface. Shown on the right you can find the logic gate structure for the ripple-carry-ahead adder unit, which implements binary addition in the ALU (arithmetic logic unit). In NLP (natural language domain), my projects involved fine-tuning a text summarization model with a light-weight transformer (BERT-light). The model takes a full paragraph and performs extractive summarization by classifying the “sentence-essence” CLS tokens. In RL (reinforcement learning), my projects involved implementing algorithm to solve simple MDP (Markov Decision Process) environments like the Lunar Lander game from OpenAI gymnasium. This particular experience working with OpenAI Gymnasium environments and training RL agent particularly helps me in my current TMazing Project (The POMDP project mentioned above on this page). In ML theory, I’ve implemented a basic backpropagation engine that performs automatic gradient calculation on computational graphs. Backpropagation is the backbone (pun-intended) of deep learning architectures, and our backpropagation engine is using the same logic (reverse model automatic differentiation) as that used in popular libraries such as pytorch.